University of Michigan Journal of Law Reform

Volume 35

2002

Seeds of Distrust: Federal Regulation of Genetically Modified Foods

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SEEDS OF DISTRUST: FEDERAL REGULATION OF GENETICALLY MODIFIED FOODS

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This Article describes and evaluates the existing federal regulatory regime for protecting public health from risks posed by foods derived from GM plants. Part I briefly describes the technology involved in genetically modifying plants and relates the ongoing debates over the risks and benefits of GM food plants. Part II examines in detail the regulatory regime that has evolved in the United States to regulate the safety of GM foods, focusing in particular upon the pervasive role that the substantial equivalence doctrine has played in that regime. Finally, Part III suggests a more precautionary approach toward regulating GM foods that should command a higher level of public trust than the substantial equivalence approach.

With the aid of modern agricultural biotechnologies, scientists can cross biological boundaries that have heretofore limited plant breeders to relatively modest and incremental changes.[1] Scientists have already spliced genes from bacteria, viruses, chickens, and moths into the chromosomes of ordinary potatoes, and the technology is only in its infancy.[2] Spectacular changes in the human food supply may lie just around the corner.[3]

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1. *See Hearing Before the Senate Comm. on Agric., Nutrition and Forestry*, 106th Cong. (Oct. 7, 1999) (statement of James H. Maryanski, Biotechnology Coordinator, Ctr. for Food Safety & Applied Nutrition, Food & Drug Admin.) [hereinafter Maryanski Senate Testimony, Oct. 7, 1999]; ORGANISATION FOR ECON. COOPERATION & DEV., SAFETY EVALUATION OF FOODS DERIVED BY MODERN BIOTECHNOLOGY: CONCEPTS AND PRINCIPLES 7 (1992) [hereinafter OECD, SAFETY EVALUATION, 1992] (stating that biotechnology has "vastly increased the variety of new traits that can be introduced into plants"); Karl-Heinz Engel, Gary R. Takeoka & Roy Teranishi, *Foods and Food Ingredients Produced via Recombinant DNA Techniques, in* GENETICALLY MODIFIED FOODS: SAFETY ISSUES 1 (Karl-Heinz Engel et al. eds., 1995) [hereinafter Engel, Takeoka & Teranishi, *Foods and Food Ingredients*]; COMM. ON GENETICALLY MODIFIED PEST-PROTECTED PLANTS, NAT'L RESEARCH COUNCIL, GENETICALLY MODIFIED PEST-PROTECTED PLANTS: SCIENCE AND REGULATION 22 (2000) [hereinafter NRC GM PEST-PROTECTED PLANTS REPORT].

2. *See* NRC GM PEST-PROTECTED PLANTS REPORT, *supra* note 1, at 22.

3. Modern biotechnologies can also enhance both the range of food ingredients that fermentation technologies can produce and increase the efficiency of fermentation production of food ingredients that are currently produced through traditional means. *See* J.B. Hallagan & R.L. Hall, *Safety Assessment of Flavor Ingredients Produced by Genetically Modified Organisisms, in* GENETICALLY MODIFIED FOODS: SAFETY ISSUES 57, 60-61 (Karl-Heinz Engel et

Modern gene-splicing techniques were born in controversy, and the recent introduction of genetically modified (GM) foods into neighborhood grocery stores has stimulated renewed debates about their safety and propriety.[4] Since food matters a lot to most people, these debates have attained a high level of public visibility.[5] Given the enormous potential for profit in the budding agricultural biotechnology industry, consumer groups worry that companies unconstrained by appropriate governmental regulation will rush to the market with products that could pose serious risks to human health.[6] The companies maintain that existing federal statutes provide more than adequate protection from any health risks of genetically engineered foods and warn that "over-regulation" of agricultural biotechnologies may delay or forestall entirely the enormous benefits that they offer to farmers and consumers.[7]

Although the agricultural biotechnology industry has grown at an extraordinary pace during the past decade, recent controversies over StarLink® corn in the United States[8] and GM foods in

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al. eds., 1995). Because the legal aspects of food production through fermentation technologies have been widely discussed in the literature, this Article will not analyze that topic in detail. *See, e.g.*, Thomas O. McGarity, *Federal Regulation of Agricultural Biotechnologies*, 20 U. MICH. J.L. REFORM 1089 (1987) [hereinafter McGarity, *Agricultural Biotechnologies*]; Thomas O. McGarity & Karl O. Bayer, *Federal Regulation of Emerging Genetic Technologies*, 31 VAND. L. REV. 1 (1983).

4. *See* Organisation for Econ. Cooperation & Dev., *Proceedings of the Organisation for Economic Cooperation and Development Conference on the Scientific and Health Aspects of Genetically Modified Foods* (Edinburgh, Scotland, Feb. 28–Mar. 1, 2000), *available at* http://www.oecd.org/subject/biotech/ed_prog_sum.html [hereinafter *OECD Edinburgh Conference Proceedings*].

5. *See Public Meeting on Biotechnology in the Year 2000 and Beyond by the U.S. Food and Drug Administration* (Nov. 30, 1999) (remarks of Carol Tucker Foreman, Consumer Federation of America) [hereinafter Foreman Remarks, Nov. 30, 1999] ("Since food is so basic to us both physically and emotionally, it is really not surprising that consumers are extremely averse to any food-related risk, especially if that risk is perceived as imposed by someone else beyond our individual control and without any countervailing benefit."); Lars Noah & Richard A. Merrill, *Starting From Scratch?: Reinventing The Food Additive Approval Process*, 78 B.U. L. REV. 329, 330 (1998) [hereinafter Noah & Merrill, *Starting from Scratch*] (alluding to "the popular and journalistic salience of putative hazards created by modern food production methods").

6. *See* Anthony J. Cavalieri, *Paper Presented to the Industrial and Economic Perspectives Workshop*, *in* NAT'L AGRIC. BIOTECHNOLOGY COUNCIL REPORT 10, AGRICULTURAL BIOTECHNOLOGY AND ENVIRONMENTAL QUALITY: GENE ESCAPE AND PEST RESISTANCE 29, 30 (Ralph W.E. Hardy & Jane Baker Segelken eds., 1998) (describing how the vice-president of a major biotechnology company acknowledges that companies that are "technology generators" are "more likely to concentrate on their business and their technology, and not have the resources or time to devote to addressing larger societal issues").

7. *See* NRC GM PEST-PROTECTED PLANTS REPORT, *supra* note 1, at xii (noting the belief of many observers that "the risks are minimal, that benefits outweigh risks, and the current regulatory scheme is too onerous").

8. *See infra* Part VII.H.

Europe[9] suggest that a protective regulatory regime is a critical precondition to public acceptance of an industry about which most consumers currently have serious misgivings.[10] Yet, the adequacy of the existing U.S. regulatory regime has never been convincingly established.[11] In part, disagreement over the adequacy of existing regulatory oversight stems from the fact that the statutes that form the underlying regulatory framework were not enacted with biotechnology in mind and therefore leave several serious institutional and interpretational questions unresolved.[12] Much of the disagreement, however, concerns the way that the relevant federal agencies have gone about implementing existing regulatory requirements.

With strong encouragement from the White House, the two federal agencies with primary regulatory jurisdiction over GM foods—the Food and Drug Administration (FDA) and the Environmental Protection Agency (EPA)—have relied upon a controversial regulatory principle called "substantial equivalence" as the primary vehicle for assessing and managing the risks that GM foods pose to human health. As a result, GM crops have gained easy access to U.S. agricultural markets with very few regulatory constraints. The speed with which GM foods have entered the food supply has surprised many American consumers.

This Article describes and evaluates the existing federal regulatory regime for protecting public health from risks posed by foods derived from GM plants. Part I briefly describes the technology involved in genetically modifying plants and relates the ongoing

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9. *See* Susan Ladika, *Austria Approves One of the Toughest Laws in Europe on Genetically Modified Organisms*, 21 Int'l Envtl. Rep. (BNA) 409 (Apr. 29, 1998); *France Issues Labeling Rules to Implement EU's Directive on Genetically Modified Food*, 14 Int'l Trade Rep. (BNA) 304 (Feb. 19, 1997).

10. The recent report of an expert committee appointed by the National Research Council of the National Academy of Sciences concluded that "[w]ith careful planning and *appropriate regulatory oversight*, commercial cultivation of transgenic pest-protected plants is not generally expected to pose higher risks and may pose less risk than other commonly used chemical and biological pest-management techniques." NRC GM PEST-PROTECTED PLANTS REPORT, *supra* note 1, at 47 (emphasis added).

11. *See* Robert A. Bohrer, *Food Products Affected By Biotechnology*, 55 U. PITT. L. REV. 653 (1994) [hereinafter Bohrer, *Biotechnology*]; McGarity, *Agricultural Biotechnologies*, *supra* note 3; McGarity & Bayer, *supra* note 3.

12. According to one recent report, "[t]he varieties and uses of genetically altered (transgenic) crops have grown much more rapidly than our ability to understand or appropriately regulate them." WINROCK INTERNATIONAL, HENRY A. WALLACE CENTER FOR AGRICULTURE & ENVIRONMENTAL POLICY, TRANSGENIC CROPS: AN ENVIRONMENTAL ASSESSMENT 5 (2000) [hereinafter WINROCK REPORT ON TRANSGENIC CROPS].

debates over the risks and benefits of GM food plants.[13] Part II examines in detail the regulatory regime that has evolved in the United States to regulate the safety of GM foods, focusing in particular upon the pervasive role that the substantial equivalence doctrine has played in that regime. Finally, Part III suggests a more precautionary approach toward regulating GM foods that should command a higher level of public trust than the substantial equivalence approach.

I. THE DEBATES OVER THE RISKS AND BENEFITS OF GENETICALLY MODIFIED FOODS

Modern gene-splicing techniques allow scientists to introduce genes from a living organism (called the "donor") into a plant (called a "host") in several ways, including: (1) direct DNA uptake by the plant cells mediated by chemical or electrical treatments; (2) microinjection of DNA directly into plant cells; (3) biolistics, or firing tiny metal particles coated with the DNA of interest into plant cells; and (4) infecting the plant with a bacterium that scientists have modified to carry the DNA into plant cells.[14] In each of these techniques, scientists insert DNA segments from the "donor"

13. Until very recently, the primary focus of public interest in GM foods was on GM plants intended for human consumption or consumption by animals consumed by humans. The recent media attention given to a genetically modified "supersalmon" has raised the possibility that GM animals will soon enter the human food supply. *See* Frederic Golden, *Who's Afraid of Frankenfood?*, TIME, Nov. 29, 1999, at 49 [hereinafter Golden, *Frankenfood*]. Although the adequacy of the federal regulatory regime for regulating genetically engineered food animals is looming on the horizon, it is beyond the scope of this report. The relevant agencies will no doubt face even more controversial ethical, environmental and safety issues when the question of regulating farm animals is concerned.

14. Secondary Direct Food Additives Permitted in Food for Human Consumption; Food Additives Permitted in Feed and Drinking Water of Animals; Aminoglycoside 3 minutes—Phosphotransferase II, 59 Fed. Reg. 26,700 (May 23, 1994) (to be codified at 21 C.F.R. paras. 173 & 573) [hereinafter FDA, 1994 Kanamycin Resistance Gene Approval]; ROYAL SOCIETY OF CANADA, ELEMENTS OF PRECAUTION: RECOMMENDATIONS FOR THE REGULATION OF FOOD BIOTECHNOLOGY IN CANADA: EXPERT PANEL REPORT OF THE FUTURE OF FOOD BIOTECHNOLOGY 17 (2001) [hereinafter ROYAL SOCIETY OF CANADA REPORT, 2001]; *see also* Engel, Takeoka & Teranishi, *Foods and Food Ingredients*, *supra* note 1, at 2; NRC GM PEST-PROTECTED PLANTS REPORT, *supra* note 1, at 22 ("Genetic engineering is the transfer of a [gene] or a few genes into a cultivar with the use of *Agrobacterium tumefaciens*, microprojectile bombardment, electroporation, or microinjection."); MARC LAPPE & BRITT BAILEY, AGAINST THE GRAIN: BIOTECHNOLOGY AND THE CORPORATE TAKEOVER OF YOUR FOOD 29–32 (1998).

organism into the chromosome of the "host" plant cells in a semi-random fashion.[15]

A successful transformation occurs when one of the host cells "takes up" or incorporates a fragment of the donor DNA that contains the desired donor gene and "expresses" the new gene by producing the protein for which the new gene "codes." The presence of the protein (or a carbohydrate, fat or oil produced by the protein) changes the host organism, and the new characteristic (or "trait") of the host plant brought about by the change should be perpetuated in succeeding generations as the host plant reproduces. To distinguish those cells that have successfully taken up the donor gene from those that have not, scientists typically attach an additional DNA segment containing a gene that is capable of rendering the host cell resistant to a particular antibiotic, herbicide, or other toxic agent. The cells that do not contain the "marker" gene for antibiotic or herbicide resistance die in the presence of the toxic agent, and the researcher then tests the surviving cells to determine whether some or all of them express the desired trait as well as the resistance trait.[16]

Both the number of copies of the inserted gene and its location along the recipient chromosome can affect its level of expression (i.e., the amount of coded-for protein that the host cell produces).[17] The inserted gene can also affect the level of expression of other genes in the host organism.[18] In the case of genetically engineered plants, breeders frequently attempt to ensure greater genetic stability by using traditional breeding techniques to "back cross" the modified plant with unmodified plants to produce still a third plant line in which the new trait is expressed at only one location on the modified chromosome.[19] Similarly, since not all plant lines are equally amenable to genetic engineering techniques, scientists frequently accomplish the gene transfer in a less desirable

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15. A gene transfer typically involves more than the mere insertion of a single gene from one organism into another. For example, the transfer that inserted a gene coding for a *Bacillus thuringiensis* toxin into corn also included promoters (genetic material that initiates transcription of the gene) and terminators (genetic material which stops transcription of the gene) from a virus and another bacterium. *See* COUNCIL ON ENVIRONMENTAL QUALITY & OFFICE OF SCIENCE AND TECHNOLOGY POLICY; CEQ AND OSTP ASSESSMENT: CASE STUDIES OF ENVIRONMENTAL REGULATION FOR BIOTECHNOLOGY, BT MAIZE CASE STUDY 1 (2001) [hereinafter CEQ/OSTP CASE STUDIES, 2001].

16. *See* FDA, 1994 Kanamycin Resistance Gene Approval, *supra* note 14, at 26,702; ROYAL SOCIETY OF CANADA REPORT, 2001, *supra* note 14, at 18.

17. Statement of Policy: Foods Derived From New Plant Varieties, 57 Fed. Reg. 22,984, 22,986 (Food & Drug Admin., May 29, 1992) [hereinafter 1992 FDA Policy Statement].

18. *Id.*

19. *Id.*

line and then use traditional plant breeding techniques to cross the gene into more desirable lines.[20]

Thus genetic engineers can in a generation or two design plants to produce different types and quantities of proteins, carbohydrates, fats and oils, the primary building blocks of human food.[21] Perhaps more significantly, modern biotechnologies allow scientists to accomplish genetic exchanges that traditional breeding practices could never bring about.[22] The outcomes, however, are not always predictable. In the new genetic background of the host plant, the inserted gene may not behave in the same way that it did in the donor species, and the expression products may likewise react differently in the new host environment.[23] Consequently, gene-splicing experiments frequently yield unexpected results.[24] Most GM plants are therefore tested extensively in the field for unusual agronomic characteristics before the sponsoring companies move to the next stage of scaling up for commercial production.[25]

A. The Potential Benefits of Genetically Modified Foods

The agricultural biotechnology business has "come of age."[26] Since the first commercial planting of GM crops in 1995, more than 40 GM food plants (mostly corn and soy) have been introduced for general use in the United States.[27] According to one estimate, global sales of genetically modified crops rose from about $75 million in 1995 to $1.6 billion in 1998 and increased another

20. *Id.*

21. *Id.* at 22,984. Although genes are expressed only as proteins, many proteins are enzymes that in turn metabolize other substances to produce fats and oils. *See* Bohrer, *Biotechnology*, *supra* note 11, at 664.

22. *See* JANE RISSLER & MARGARET MELLON, THE ECOLOGICAL RISKS OF ENGINEERED CROPS 4-6 (2000).

23. 1992 FDA Policy Statement, *supra* note 17, at 22,986 (noting that the phenotypic effects of a new trait may not always be completely predictable in the new genetic background of the host).

24. MARTIN TEITEL & KIMBERLY A. WILSON, GENETICALLY ENGINEERED FOOD: CHANGING THE NATURE OF NATURE 11 (1999).

25. *House Comm. on Sci., 106th Cong., Seeds of Opportunity: An Assessment of the Benefits, Safety, and Oversight of Plant Genomics* 18 (Comm. Print Apr. 13, 2000) [hereinafter *U.S. House Seeds of Opportunity Report*] ("By the time a new variety of plant is ready for release or commercialization, it has undergone significant review and testing.").

26. *See id.*

27. NRC GM PEST-PROTECTED PLANTS REPORT, *supra* note 1, at ix–xi, 33.

50 percent in 1999 to almost $2.3 billion.[28] The size of the worldwide GM crop increased more than twenty-fold from 1996 to 1999, when farmers planted about 70 million acres in GM crops in the U.S. and about 98.6 acres worldwide.[29]

Proponents predict that the new agricultural biotechnologies will increase crop yields, reduce pesticide use and generally improve the efficiency of farming throughout the world.[30] Consumers will benefit from cheaper and more nutritious foods that will taste better and last longer. The most enthusiastic supporters believe that agricultural biotechnologies will someday feed starving populations of developing countries, reduce pressures on sensitive environmental resources, and provide economic security to U.S. farmers.[31] In their view, the vast potential that agricultural biotechnologies offer for improving human life is limited only by the political threat posed by "well-financed activist groups."[32]

The industry's performance to date has only partially borne out these optimistic predictions.[33] Public ambivalence about the benefits of GM foods is partially attributable to the industry's decision to focus first upon improving "input traits" of plants for the convenience of growers, processors and marketers, rather than modifying "output traits," such as enhanced nutritional characteristics and

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28. Elizabeth Parle, *GM Crops: More Food, or Thought?*, CHEMICAL MARKET REPORTER, Mar. 20, 2000, at FR10 [hereinafter Parle, *GM Crops*] (citing statistics compiled by the International Service for the Acquisition of Agri-biotech Applications).

29. *Hearing Before the House Comm. on Agric. Subcomm. On Risk Management, Research, and Specialty Crops*, 106th Cong. (Mar. 3, 1999) (testimony of L. Val Giddings, Vice-President of Food and Agriculture, Biotechnoogy Industry Organization) [hereinafter Giddings House Testimony, Mar. 3, 1999]; NRC GM PEST-PROTECTED PLANTS REPORT, *supra* note 1, at xi; Parle, *GM Crops*, *supra* note 25, at FR 10 (citing statistics compiled by the International Service for the Acquisition of Agri-biotech Applications).

30. *See* NRC GM PEST-PROTECTED PLANTS REPORT, *supra* note 1, at viii ("Genetic engineering of plants for resistance to pests and disease, creating transgenic pest-protected plants, is one of the many tools for increasing food security.").

31. *See Hearing Before the House Comm. on Agric. Subcomm. on Risk Management, Research, and Specialty Crops*, 106th Cong. (Mar. 3, 1999) (testimony of James M. Murphy, Jr., Assistant U.S. Trade Representative For Agricultural Affairs, Office Of The U.S. Trade Representative) [hereinafter Murphy House Testimony, Mar. 3, 1999] (arguing that "our ability to market goods developed with biotechnology is more than just an economic issue"); *U.S. House Seeds of Opportunity Report*, *supra* note 25, at 2 (arguing that "agricultural biotechnology has tremendous potential to reduce the environmental impact of farming, provide better nutrition, and help feed a rapidly growing world population").

32. *U.S. House Seeds of Opportunity Report*, *supra* note 25, at Letter of Transmittal.

33. *See* ORGANISATION FOR ECONOMIC COOPERATION AND DEVELOPMENT, RAPPORTEURS' SUMMARY, PRESENTED AT THE OECD EDINBURGH CONFERENCE ON THE SCIENTIFIC AND HEALTH ASPECTS OF GENETICALLY MODIFIED FOODS 3 (Feb. 28–Mar. 1, 2000) [hereinafter OECD EDINBURGH RAPPORTEURS' SUMMARY] (noting that the potential benefit of GM foods "has yet fully to be realized and will only be so if the technology is put to use under appropriate conditions").

improved food quality, that directly benefit consumers.[34] Of the thousands of field trials that biotechnology companies have completed to date, 83 percent have involved plants genetically engineered for pest resistance or herbicide tolerance and only 22 percent tested plants with improved product quality traits.[35] If GM foods were clearly distinguishable and priced lower than non-GM foods to reflect the enhanced efficiency of the GM technologies, the benefits might be more apparent at the grocery store.[36] So far, however, the agricultural and food processing industries have strongly resisted segregating GM foods from non-GM foods for any purpose, including pricing.[37]

1. Input Characteristics

a. Pest and Disease Resistance—Although human beings have used chemical pesticides to defend their crops from pests for thousands of years,[38] the "green revolution" of the 1950s gave rise to a chemical dependent agriculture that posed serious risks to human health and the environment.[39] Modern biotechnology offers the potential to avoid some of the adverse health and environmental consequences of chemical pesticides by allowing scientists to custom design plants to be resistant to insect and disease infestations.[40]

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34. *See* Bohrer, *Biotechnology*, *supra* note 11, at 679 (noting that "biotechnology applications that fill a strongly perceived public need are likely to win acceptance more easily than those which merely increase producer or farmer profits"); Ray A. Goldberg, *Transforming Life, Transforming Business: The Life-Science Revolution*, HARV. BUS. REV., Mar./Apr., 2000, 94, 103 [hereinafter Goldberg, *Transforming Life*] (arguing that GM foods "have not provided consumers with food that is significantly cheaper, safer, or tastier"); Margaret Kriz, *Global Food Fights*, NAT'L J., Mar. 4, 2000, at 688 [hereinafter Kriz, *Global Food Fights*] (noting that "[s]ome supporters of the new technology speculate that the public has been cool to genetically engineered foods because the products so far have been designed to benefit farmers, not consumers"); David Stipp, *The Voice of Reason in The Global Food Fights*, FORTUNE, Feb. 21, 2000, at 164 [hereinafter Stipp, *Voice of Reason*] (interview with Cordon Conway of the Rockefeller Foundation) (commenting that "[t]he companies' really big mistake, though, was to concentrate on things that had no benefit to the consumer").

35. Eric Lichtenberg, *Costs of Regulating Transgenic Pest-Protected Plants*, NRC GM PEST-PROTECTED PLANTS REPORT, *supra* note 1, at Appendix A, Table A.3. The totals exceed 100 percent, because some field trials were devoted to testing plants that had been modified for both product quality and one of the input characteristics.

36. *See* Jim Papanixalaw, *GMOs Feel Impact of Softer Ag Sales*, CHEMICAL MARKET REPORTER, Jan. 10, 2000, at 3 ("Crops containing output traits are expected to be less controversial than ones containing input traits, and they should help alleviate concerns about GMOs.").

37. *See infra* note 534.

38. *See* NRC GM PEST-PROTECTED PLANTS REPORT, *supra* note 1, at 21 (describing various chemical pesticides in use since 1000 B.C.).

39. *See, e.g.*, RACHEL CARSON, SILENT SPRING 16–17 (1962).

40. *See* NRC GM PEST-PROTECTED PLANTS REPORT, *supra* note 1, at 48–55; SHELDON KRIMSKY & ROGER WRUBEL, AGRICULTURAL BIOTECHNOLOGY AND THE ENVIRONMENT 61 (1996).

Naturally occurring microorganisms are capable of infecting and killing insects, and companies have commercially marketed them for many years. One of the most successful biological pesticide, the *Bacillus thuringiensis* (Bt) soil bacterium, produces more than 50 different proteins capable of killing several varieties of insects and nematodes by binding to receptors in the insect gut and disrupting digestion.[41] Because these Bt toxins have been in the human environment for as long as there have been humans, the levels ordinarily found in human foods, even foods intentionally treated with Bt, cause no observable adverse effects in people.[42] The fact that Bt loses its efficacy within a few days after application, however, makes it less attractive to many growers and limits it to a relatively small niche of the pesticide market.[43]

Using modern agricultural biotechnologies, scientists can now transfer the genes that code for Bt toxins from the bacterium into plants in such a way that susceptible insects are killed when they consume the GM plants.[44] In addition to ensuring that feeding insects are exposed to the Bt toxins even if they feed on parts of the plant that are hard to treat with chemical pesticides, this technique retains its efficacy for as long as the plant remains alive.[45] Genetic engineering techniques can also render plants resistant to plant viruses, thus effectively "vaccinating" them against certain plant diseases.[46] Since an estimated 20 percent of pest-related crop loss in

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41. *See* NRC GM PEST-PROTECTED PLANTS REPORT, *supra* note 1, at 28–29 (noting that during the last twenty years scientists have identified about sixty proteins from more than fifty subspecies of Bt); LAPPE & BAILEY, *supra* note 14, at 65 (explaining in lay language how Bt toxins disrupt the digestive processes of insect larvae); DANIEL JONES, *Paper Presented to the Research and Development Perspectives Workshop*, in NAT'L AGRIC. BIOTECHNOLOGY COUNCIL REPORT 10, AGRICULTURAL BIOTECHNOLOGY AND ENVIRONMENTAL QUALITY: GENE ESCAPE AND PEST RESISTANCE 11 (Ralph W.E. Hardy & Jane Baker Segelken eds., 1998) (explaining that "[t]here are more than 50 different Bt proteins with differing toxicities for caterpillars, beetles, flies, and nematodes"); TEITEL & WILSON, *supra* note 24, at 24–28.

42. *See* TEITEL & WILSON, *supra* note 24, at 25.

43. *See* NRC GM PEST-PROTECTED PLANTS REPORT, *supra* note 1, at 29.

44. TEITEL & WILSON, *supra* note 24, at 26. By 1998, farmers had planted about 25 percent of the total cotton acreage and 21 percent of the total corn acreage in Bt-modified pest-resistant crops. NRC GM PEST-PROTECTED PLANTS REPORT, *supra* note 1, at 33.

45. NRC GM PEST-PROTECTED PLANTS REPORT, *supra* note 1, at 29.

46. *See* Giddings House Testimony, Mar. 3, 1999, *supra* note 29 (arguing that "[b]iotechnology arms disease-protected varieties with the plant equivalent of a 'vaccine' "); NRC GM PEST-PROTECTED PLANTS REPORT, *supra* note 1, at 53; KRIMSKY & WRUBEL, *supra* note 40, at 82–87; Lynn E. Murry, *Use of Plant Virus Geners to Produce Disease-Resistant Crops*, in GENETICALLY MODIFIED FOODS: SAFETY ISSUES 113 (Karl-Heinz Engel et al. eds., 1995) [hereinafter Murry, *Disease Resistance*]. For example, the chromosomes of many plants contain "race-specific" genes ("R genes") that trigger an immune response within the plant to a specific pathogen that attacks the plant. Scientists have for many years employed traditional plant breeding technologies to transfer R genes from one variety of plant to closely related

the U.S. is attributable to plant viruses, agricultural biotechnologies may provide an important new weapon for farmers to use in protecting their crops.[47]

b. Herbicide Resistance—Cultivated agricultural plants compete with wild plants for access to the sun, available water and the nutrients that the soil provides. In the latter half of the twentieth century, scientists developed chemical herbicides that can kill many varieties of weeds while leaving crop plants comparatively unaffected.[48] Currently, more than 90 percent of the U.S. soybean, corn and cotton acreage receives at least one herbicide treatment per year.[49] Scientists can genetically engineer crops tolerant to herbicides by inserting into a host plant a single gene that codes for the production of an enzyme that neutralizes the herbicide's active ingredient.[50] Farmers can then kill the weeds in fields containing herbicide-tolerant crops without fear of reducing crop yields.[51]

c. Increased Yields—If fewer plants are lost to insects, weeds and diseases, farmers should be able to extract more end-use commodity from an acre of planted land. Thus, widespread cultivation of pest-resistant and herbicide-tolerant crops should result in increased yields of important food and feed crops.[52] If the benefits of high-yield agriculture are distributed in an equitable fashion, modern biotechnologies could contribute life-sustaining food to millions of impoverished human beings.[53] Thus far, however, hard evidence of increased yields is lacking. For example, a recent expert panel assessment concluded that "[t]he first generation of transgenic corn and soybeans, if these crops were to be adopted

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varieties. NRC GM PEST-PROTECTED PLANTS REPORT, *supra* note 1, at 50. In addition to speeding up this process, modern genetic engineering technologies allow scientists to transfer R genes to entirely unrelated plants. *Id.* at 50–51; *see also* KRIMSKY & WRUBEL, *supra* note 40, at 73–76.

47. Murry, *Disease Resistance*, *supra* note 46, at 117.

48. *See* KRIMSKY & WRUBEL, *supra* note 40, at 29–30, 33–34. The widespread availability of herbicides made possible "minimum till" agricultural practices that help protect valuable topsoil from erosion. *See id.* at 44.

49. *Id.* at 30.

50. *See id.* at 37–38.

51. *See id.* at 38–40. Not surprisingly, the companies that developed herbicide-resistant crops were frequently manufacturers of the relevant herbicides. *Id.* at 35.

52. *See* Giddings House Testimony, Mar. 3, 1999, *supra* note 29 (arguing that healthier pest-resistant plants should "result in higher yields and improved fertilizer efficiency"); Jack Doyle, *Biotechnology Research and Agricultural Stability*, 2 ISSUES IN SCI. & TECH. 111, 114 (1985); NRC GM PEST-PROTECTED PLANTS REPORT, *supra* note 1, at 48 ("Crop losses or damage can be eliminated or minimized resulting in improvement of both yield and quality.").

53. *See U.S. House Seeds of Opportunity Report*, *supra* note 25, at 2 ("Biotechnology will be a key element in the fight against malnutrition worldwide.").

globally, would increase production by only an estimated two percent or less," hardly enough to eliminate world hunger.[54]

d. Improving Crop Adaptability to a Wider Variety of Growing Conditions—Although conventional breeding techniques have achieved little success in expanding the range of conditions under which important crops can survive,[55] scientists employing modern gene splicing techniques may be able to design crops that can grow in temperatures, soils, weather and climatological conditions that prohibit cultivation of natural strains.[56] For example, scientists have identified "master switch" genes in some plants that control freezing tolerance, and they hope to use this knowledge to improve the temperature range of commercially important food and feed crops.[57] Scientists in Mexico discovered that inserting a gene coding for the production of citric acid into the DNA of papaya and rice plants allowed them to grow in aluminum-rich local soils that were otherwise inhospitable to those cultivars.[58] Modern genetic engineering techniques may also yield economically important plants with increased tolerance to drought.[59] However, such "supercrops" exist today primarily on the drawing board.

e. Improved Food Handling, Distribution and Processing Capabilities—The very first GM food submitted to FDA for approval was a tomato containing an "antisense" gene that inhibited the action of an enzyme that causes tomatoes to rot.[60] The presence of the new

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54. WINROCK REPORT ON TRANSGENIC CROPS, *supra* note 12, at 8.

55. *See Plant Genome Science: From the Lab to the Field to the Market: Hearing Before the House Comm. on Sci. Subcomm. on Basic Research*, 106th Cong (Oct. 5, 1999) (testimony of Michael F. Thomashow, Michigan State University) [hereinafter Thomashow Testimony, Oct. 5, 1999] (noting that the temperature range that wheat can survive has not varied greatly during the last century, despite efforts by scientists using traditional breeding techniques to increase that range).

56. *See U.S. House Seeds of Opportunity Report*, *supra* note 25, at 16; *Hearing Before the House Comm. on Agric. Subcomm. on Risk Management, Research, and Specialty Crops*, 106th Cong. (Mar. 3, 1999) (testimony of August Schumacher, Under Secretary for Farm and Foreign Agricultural Services) (stating that the benefits of biotechnology include "improving plant adaptability to harsh growing conditions, such as drought, salinity, and temperature extremes").

57. *See* Thomashow Testimony, Oct. 5, 1999, *supra* note 55. Another approach to increasing temperature range is to splice into crop plants genes from fish that code for freeze-resistant proteins. 1992 FDA Policy Statement, *supra* note 17, at 22,986.

58. *See* Dennis T. Avery, *Why Biotechnology May Not Represent the Future in World Agriculture, in* NAT'L AGRIC. BIOTECHNOLOGY COUNCIL REPORT 10, WORLD FOOD SECURITY AND SUSTAINABILITY: THE IMPACTS OF BIOTECHNOLOGY AND INDUSTRIAL CONSOLIDATION 97 (Donald P. Weeks et al. eds., 1999) [hereinafter Avery, *Biotechnology Future*].

59. Robert W. Herdt, *Agricultural Biotechnology in the 21st Century: Promises and Pitfalls, in* NAT'L AGRIC. BIOTECHNOLOGY COUNCIL REPORT 9, RESOURCE MANAGEMENT IN CHALLENGED ENVIRONMENTS 33 (Ralph W.E. Hardy et al. eds., 1998).

60. Bohrer, *Biotechnology*, *supra* note 11, at 671.

gene allowed ripe tomatoes to remain intact for a longer period of time, thus increasing their "shelf life" and allowing them to ripen on the vine before being harvested for market.[61] Although the plant was a failure with consumers,[62] companies continue to use modern agricultural biotechnologies to develop fruits and vegetables that have the capacity to stay fresh and firm for longer periods of time.[63]

2. Output Characteristics

a. Improved Nutritional Content—Modern agricultural biotechnologies are capable of adding nutritional value to commonly consumed foods by causing plants to produce more or less of a nutrient or anti-nutrient.[64] For example, scientists are developing a GM strain of rice that makes both Vitamin A and iron available to consumers with diets that might otherwise be deficient in those two important nutrients.[65] Other GM varieties of common staples that contain enhanced levels of nutrients are on the near-term horizon.[66] Some skeptics, however, caution against great expectations for nutritionally enhanced foods, noting that they may also result in human diets with less overall variety. One scientist, only half facetiously, warned that human diets may someday consist primarily of "Purina human chow."[67]

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61. Calgene, Inc. Request for Advisory Opinion, 57 Fed. Reg. 22,772 (1992).

62. LAPPE & BAILEY, *supra* note 14, at 21; Parle, *GM Crops*, *supra* note 28; *see also* TEITEL & WILSON, *supra* note 24, at 23 (concluding that the endless summer plant did not make it to the market because it failed its field trials).

63. Parle, *GM Crops*, *supra* note 25.

64. Thomashow Testimony, Oct. 5, 1999, *supra* note 55 (noting that "[g]enetic engineering offers a powerful tool to improve the nutritional content of plants through metabolic engineering and thereby improve the health of individuals throughout the world"); 1992 FDA Policy Statement, *supra* note 17, at 22,986 (noting that genetic engineering techniques can be used "to transfer genetic material for the production of seed storage protein conferring improvements in nutritional balance of important amino acids in the new plant varieties").

65. *See U.S. House Seeds of Opportunity Report*, *supra* note 25, at 3 ("Biotechnology has been used to produce a new strain of rice—Golden Rice—that contains both vitamin A (by providing its precursor, beta-carotene) and iron."); Gordon Conway, *Crop Biotechnology: Benefits, Risks and Ownership*, presented at the OECD EDINBURGH CONFERENCE ON THE SCIENTIFIC AND HEALTH ASPECTS OF GENETICALLY MODIFIED FOODS 8 (Feb. 28 – Mar. 1, 2000) [hereinafter Conway, *Crop Biotechnology*] (reporting the results of Rockefeller Foundation-funded research on Vitamin A-enhanced rice).

66. *See U.S. House Seeds of Opportunity Report*, *supra* note 25, at 3 (predicting near-term availability of nutritionally enhanced GM varieties of "food staples, such as cassava, corn, rice, and other cereal grains"); Marc E. Weksler, *GM Foods: Opportunities to Improve Human Health*, in *OECD Edinburgh Conference Proceedings*, *supra* note 4, at 5 (describing foods containing enhanced levels of Vitamin E and iron).

67. Lila Gutterman, *Scientists Leave the Lab to Defend Bioengineered Food*, J. HIGHER EDUC., Apr. 14, 2000, at A29, A30.

b. Improved Food Quality—Biotechnology proponents maintain, and most opponents acknowledge, that modern agricultural biotechnologies can improve food quality.[68] Pest-resistant GM crops will yield better-looking agricultural commodities with less damage from insects, fungi and viruses.[69] Scientists can manipulate the genes of plants to cause fruits, grains and vegetables to ripen more uniformly and retain freshness for longer periods of time.[70] Specialty crops with particular traits designed for particular consumer needs or desires are on the near-term horizon.[71]

c. Improved Food Safety—While scientists have raised a number of concerns about the risks that GM foods may present to human health, proponents note that genetic engineering techniques also allow scientists to remove from plants the genes that code for naturally occurring toxins.[72] In addition, scientists may soon be able to insert genes that code for proteins that reduce allergenic responses to GM foods in sensitive people.[73] Both improvements could render GM foods safer to eat than their natural counterparts.

B. The Risks Posed by Genetically Modified Foods

If agricultural biotechnologies have not yet produced the enormous benefits that some of their proponents envisioned, neither have they caused the pandemics that worried their detractors. Not a single confirmed case of disease or illness attributable to those

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68. *See Hearing Before the House Comm. on Agric. Subcomm. on Risk Mgmt., Research, and Specialty Crops*, 106th Cong. (Mar. 3, 1999) (testimony of Harry Collins, American Seed Trade Association) [hereinafter Collins Testimony, Mar. 3, 1999]; Donald P. Weeks, *Workshop A: Promises and Problems Associated with Agricultural Biotechnology*, in NAT'L AGRICULTURE BIOTECHNOLOGY COUNCIL REPORT 11, WORLD FOOD SECURITY AND SUSTAINABILITY: THE IMPACTS OF BIOTECHNOLOGY AND INDUSTRIAL CONSOLIDATION 16 (Donald P. Weeks et al. eds., 1999) [hereinafter Weeks, *Workshop A Report*] (reporting consensus of participants of a Workshop sponsored by the National Agricultural Biotechnology Council).

69. *See* NRC GM PEST-PROTECTED PLANTS REPORT, *supra* note 1, at 48 ("Crop losses or damage can be eliminated or minimized resulting in improvement of both yield and quality."); Weeks, Workshop A Report, *supra* note 68, at 17 (noting that genetic engineering can add nutritional and aesthetic value to plants).

70. *See* Parle, *GM Crops*, *supra* note 28 (noting that Zeneca Plant Sciences is developing a mold-resistant banana that will ripen at a time that is more propitious for marketing); Weeks, *Workshop A Report*, *supra* note 68, at 16–17.

71. Weeks, *Workshop A Report*, *supra* note 68, at 17.

72. Collins House Testimony, Mar. 3, 1999, *supra* note 68 ("Benefits that can be expected in the near future will include: a reduced level of natural toxins in plants. . . .").

73. *See* NRC GM PEST-PROTECTED PLANTS REPORT, *supra* note 1, at 36 (citing an experiment in which scientists reduced the major allergen in rice by about 80 percent).

foods has been reported in the published literature,[74] though two reports of severe allergenic reactions are under serious investigation.[75] Still, this powerful new technology undeniably has the potential to cause significant harm to human health. Although the genetic engineers usually detect these undesirable traits during initial trials and eliminate the plants that bear them before commercialization,[76] they can go undetected until the engineered plants have become part of the human diet.[77] Most scientists agree that much more research on the health effects of modern agricultural biotechnologies will be necessary before it is possible to perform reasonably accurate risk assessments for GM plants.[78]

A recent report of a panel assembled by the National Research Council of the National Academy of Sciences (NAS Panel) stated that the panel was "not aware of any evidence that foods on the market are unsafe to eat as a result of genetic modification."[79] Despite its generally sanguine conclusions, the NAS panel was clearly troubled by the sparseness of the existing health and safety testing database for GM foods, and it was especially concerned about the risks of allergenicity.[80] A very similar report issued by a panel convened by the Royal Society of Canada (Canadian Royal Society Panel) came to a similar conclusion.[81] The following discussion draws heavily upon the analysis in those reports.

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74. John Krebs, Chairman's Report, presented at the OECD EDINBURGH CONFERENCE ON THE SCIENTIFIC AND HEALTH ASPECTS OF GENETICALLY MODIFIED FOODS 3 (Feb. 28–Mar. 1, 2000) [hereinafter Krebs, Chairman's Report].

75. During the recent controversy over human consumption of StarLink® corn, *see* Section V.H., *infra*, there have been some reports of illnesses allegedly caused by consumption of that corn. *See Forty-Four Claim Biotech Corn Caused Illness*, WASHINGTON POST, Nov. 29, 2000, at A10; Marc Kaufman, *Biotech Corn is Test Case for industry; Engineered Food's Future hinges on Allergy Study*, WASHINGTON POST, Mar. 19, 2001, at A01.

76. *See Plant Genome Science: From the Lab to the Field to the Market: Hearing Before the House Comm. on Sci. Subcomm. on Basic Research*, 106th Cong. (Oct. 5, 1999) (testimony of R. James Cook, Washington State University) [hereinafter Cook Testimony, Oct. 5, 1999] (arguing that "it is hard to imagine what more can be done to assure the safety of genetically modifed crops to people and the environment"); 1992 FDA Policy Statement, *supra* note 17, at 22,987; *Public Meeting on Biotechnology in the Year 2000 and Beyond by the U.S. Food and Drug Administration* (Dec. 13, 1999) (remarks of John Fagan, Chairman and CEO, Genetic ID) [hereinafter Fagan Remarks, Dec. 13, 1999] (arguing that plant breeders have "developed extensive systems to evaluate these plants over time and to eliminate those that have traits, or metabolic changes, that are not beneficial").

77. *See* Fagan Remarks, Dec. 13, 1999, *supra* note 76, at 105 (questioning the assumption that industry will identify all harmful GM plants).

78. *See* Weeks, *Workshop A Report*, *supra* note 68, at 18 (reporting "consensus" that more research is necessary).

79. NRC GM PEST-PROTECTED PLANTS REPORT, *supra* note 1, at 9.

80. *Id.* at 7–8.

81. ROYAL SOCIETY OF CANADA REPORT, 2001, *supra* note 14, at 53.

1. Direct Risks to Human Health—The magnitude of the direct risks posed by a GM food item is a function of the likelihood that the inserted gene will code for a substance that is toxic to some or all human beings, the nature and potency of that substance's toxicity, and the extent of dietary exposure to that substance.[82] The biotechnology industry and the current leadership of the relevant U.S. regulatory agencies have gone to great lengths to persuade the public that modern GM foods pose minimal direct risks to human health.[83] Critics point out that these assurances are not based upon extensive testing of GM foods in laboratory animals as in the case of chemical additives and contaminants, but instead depend heavily upon assumptions derived from knowledge about the risks posed by non-GM plants.[84]

a. Pesticides in GM Foods—Since GM pest-resistant plants are designed to be toxic to the target organisms, their potential to affect human health adversely is of obvious concern. The toxic proteins produced by *Bacillus thuringiensis* (Bt toxins) are of the most immediate concern, because the vast majority of pest-resistant GM crops currently in commerce have been modified to produce those toxins in plant tissues. Unlike Bt microorganisms, which rapidly break down in the environment, human consumption of the Bt toxin in GM plants is virtually assured.[85] EPA has required fairly extensive short-term health and safety testing of the Bt microorganisms,[86] and most studies have reported no adverse effects.[87] Tests indicating that the toxins do not bind to cells in the human gut in the same way that they bind to cells in the midguts of

82. NRC GM PEST-PROTECTED PLANTS REPORT, *supra* note 1, at 55. Because the risk of allergenicity is fairly unique and because it is one of the more likely risks that consumers will encounter with respect to GM foods, this Article will address that risk separately. *See infra* part I.B.1.b.

83. *See* Maryanski Senate Testimony, Oct. 7, 1999, *supra* note 1 (reporting that substances added to food via biotechnology "are commonly and safely consumed in the diet and so will be presumptively generally recognized as safe").

84. *See* LAPPE & BAILEY, *supra* note 14, at 2 (observing that "no studies exist that measure the impact of chronic ingestion of finished products containing increased amounts of transgenic crops").

85. *See* TEITEL & WILSON, *supra* note 24, at 51.

86. *See* NRC GM PEST-PROTECTED PLANTS REPORT, *supra* note 1, at 65.

87. *See* P.B. Lavrik et al., *Safety Assessment of Potatoes Resistant to Colorado Potato Beetle, in* GENETICALLY MODIFIED FOODS: SAFETY ISSUES 134 (Karl-Heinz Engel et al eds., 1995); H.P.J.M. Noteborn et al., *Safety Assessment of the Bacillus thuringiensis insecticidal Crystal Protein CRYIA(b) Expressed in Transgenic Tomatoes, in* GENETICALLY MODIFIED FOODS: SAFETY ISSUES 134 (Karl-Heinz Engel, Gary R. Takeoka & Roy Teranishi eds., 1995).

insect larvae suggest that the mode of toxicity to insects may not be relevant to human exposures.[88]

Some scientists, however, have speculated that Bt toxins may be toxic to human beings at the high exposure levels associated with GM plants and to individuals with compromised immune systems at much lower levels.[89] Moreover, it is unclear whether the genes coding for Bt toxins in microorganisms express precisely the same proteins when inserted into plants, and very little testing has been performed on plant-expressed Bt toxins.[90] Finally, EPA has required very little in the way of *long-term* toxicity testing of Bt toxins, because human beings are not chronically exposed to Bt toxins from the microorganisms.[91] By contrast, chronic exposure is quite likely in the case of foods containing genes that code for Bt toxins.[92] In the words of the NAS Panel, EPA's current assumption that plant-expressed Bt toxins are no more toxic to humans than bacteria-expressed Bt toxins is unwarranted in the absence of "clear, scientifically justifiable criteria for establishing biochemical and functional equivalency" and such criteria are currently lacking.[93]

In addition to creating Bt pest-resistant plants, scientists can transfer into food plants resistance genes (R genes) to protect them from viruses. Although scientists have not thoroughly studied the health risks of such transfers, many believe that they are quite low because the proteins that the transferred R genes express are likely to be in the class of proteins that humans ordinarily encounter in foods.[94] Moreover, since the R genes are usually expressed only when the plant encounters a specific pathogen, humans will be exposed to any toxic proteins only when they consume diseased plants.[95] Modern genetic engineering techniques, however, allow scientists to cause R genes to express toxic proteins at higher levels than naturally occur in the host plant and to transfer genes (perhaps from nonfood plants) that code for proteins that the host

88. *See* Lavrik et al., *supra* note 87, at 152; Noteborn et al., *supra* note 87, at 136–37.

89. *See* TEITEL & WILSON, *supra* note 24, at 51.

90. NRC GM PEST-PROTECTED PLANTS REPORT, *supra* note 1, at 66. In part, this lack of testing is due to the difficulty scientists face in isolating a sufficient quantity of the proteins that the Bt genes express from plants to support extensive testing. *Id.*

91. *Id.* at 65.

92. *Id.* at 65; TEITEL & WILSON, *supra* note 24, at 51.

93. NRC GM PEST-PROTECTED PLANTS REPORT, *supra* note 1, at 66.

94. *Id.* at 56 ("Transfer of race-specific R-gene from a nonedible plant species to an edible species would result in new exposure of consumers and nontarget species to a specific R-gene product, although not to a new class of proteins.").

95. *Id.* at 56.

plant was otherwise incapable of producing.[96] In either case, food plants containing such genes could pose a risk to human health.[97]

b. Allergens in GM Foods—Some substances in the environment cause individuals with allergies to suffer abnormally adverse acute effects. A food allergy is "an aberrant or hyperimmune response to non-noxious proteins or glyco-proteins in foods or environment."[98] The response can be relatively innocuous (e.g., a runny nose) or quite severe (e.g., anaphylactic shock leading to coma or death).[99] Allergic reactions to foods occur most commonly in infants and pre-school children.[100] Foods that induce allergenic responses in children include cow's milk, soy, egg, wheat, and peanuts.[101] Although foods are not the primary source of allergies in adults,[102] they are relatively common.[103] Common adult allergens include fish, shellfish, tree nuts, corn and tomatoes.[104] The amount of an allergen in food capable of causing an allergic reaction in susceptible individuals "can be remarkably small."[105]

Although sensitive persons can usually minimize the risk of allergenic responses by avoiding particular foods, they may be caught unawares if GM food manufacturers transfer the genes that code for allergenic proteins from one food plant to another.[106] Since scientists do not necessarily know which genes code for allergenic proteins, they will not always know whether they have accomplished such a transfer.[107] While the history of the donor and

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96. *Id.* at 56–57.

97. *Id.*

98. Oscar L. Frick, *The Potential for Allergenicity in Transgenic Foods*, in GENETICALLY MODIFIED FOODS: SAFETY ISSUES 100, 102 (Karl-Heinz Engel et al. eds., 1995) [hereinafter Frick, *Allergenicity*]; *see also* ROYAL SOCIETY OF CANADA REPORT, 2001, *supra* note 14, at 54. All food allergens are proteins. 1992 FDA Policy Statement, *supra* note 17, at 22,987.

99. *See* ROYAL SOCIETY OF CANADA REPORT, 2001, *supra* note 14, at 53 (noting that "trace amounts of an allergenic food contaminant may cause a severe, potentially life-threatening allergic reaction").

100. Frick, *Allergenicity*, *supra* note 98, at 104; ROYAL SOCIETY OF CANADA REPORT, 2001, *supra* note 14, at 54.

101. Frick, *Allergenicity*, *supra* note 98, at 105; 1992 FDA Policy Statement, *supra* note 17, at 22,987.

102. Frick, *Allergenicity*, *supra* note 98, at 104.

103. NRC GM PEST-PROTECTED PLANTS REPORT, *supra* note 1, at 67.

104. Frick, *Allergenicity*, *supra* note 98, at 105.

105. ROYAL SOCIETY OF CANADA REPORT, 2001, *supra* note 14, at 57.

106. 1992 FDA Policy Statement, *supra* note 17, at 22,987; ROYAL SOCIETY OF CANADA REPORT, 2001, *supra* note 14, at 53.

107. 1992 FDA Policy Statement, *supra* note 17, at 22,987. For example, scientists working for Pioneer Hi-Bred transferred into soybeans a gene from Brazil nuts in the hope of creating a soybean with a higher nutritional value. The experiment produced a soybean that was allergenic to people who were allergic to Brazil nuts. NRC GM PEST-PROTECTED PLANTS REPORT, *supra* note 1, at 67; TEITEL & WILSON, *supra* note 24, at 35. The company then de-

host plants can serve as a rough guide to assessing allergenicity when both are used in food, the allergenicity of "a large number of non-food proteins that could be potentially used in genetic engineering is essentially unknown."[108] Unfortunately, the allergenic potential of any given protein is very difficult to detect and measure.[109] Indeed, there are no standardized scientific tests in laboratory animals for determining whether or not a particular protein will or will not be allergenic.[110] Thus, most allergenicity testing is undertaken in human volunteers and is therefore quite expensive.[111]

Some scientists believe that the likelihood that a gene transfer from an allergenic donor plant will result in an allergenic host plant is extremely small.[112] Since only a few hundred of the millions of proteins found in nature are allergens, it is highly unlikely that any given protein will be allergenic.[113] Thus, even when the donor is a nonfood plant with an unknown allergenic potential, biotechnology proponents believe that the risk of allergenicity host is quite small. In any event, they are confident that manufacturers will be able to assess the allergenic potential of transferred genes without extensive testing by searching for "valuable clues" that point toward potential allergenicity.[114]

c. Risks Due to Changes in Host Plant Metabolism—Modern genetic engineering techniques have the potential to change internal plant metabolic processes in several ways that make them riskier for consumers. First, the transfer of a gene coding for a toxic protein from a food that is typically cooked to remove that protein to one that is not generally cooked could pose health risks to unsuspecting con-

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cided voluntarily to stop most of its work on the product. NRC GM PEST-PROTECTED PLANTS REPORT, at 36; TEITEL & WILSON, *supra* note 24, at 36.

108. ROYAL SOCIETY OF CANADA REPORT, 2001, *supra* note 14, at 62.

109. *See* NRC GM PEST-PROTECTED PLANTS REPORT, *supra* note 1, at 67.

110. *See* 1992 FDA Policy Statement, *supra* note 17, at 22,987; ROYAL SOCIETY OF CANADA REPORT, 2001, *supra* note 81, at 60 (noting that "[t]here is currently no single assay or combination that will accurately predict the allergenic potential of proteins from food or non-food sources not previously identified as being allergenic in human subjects").

111. *See* NRC GM PEST-PROTECTED PLANTS REPORT, *supra* note 1, at 139 (recommending more research on "[m]ethods for more efficiently and accurately identifying potential food allergens in transgenic pest-protected plants").

112. *See* Frick, *Allergenicity*, *supra* note 98, at 105.

113. *See Public Meeting on Biotechnology in the Year 2000 and Beyond by the U.S. Food and Drug Administration* (Nov. 18, 1999) (remarks of Steven Taylor, University of Nebraska) (arguing that "the risk that novel proteins will become allergens is probabilistically very small, especially when the novel protein is expressed with foods at a very low level").

114. *U.S. House Seeds of Opportunity Report*, *supra* note 25, at 46.

sumers.[115] Second, a genetic modification could cause a plant to produce a toxic metabolite in much larger quantities than it normally produces.[116] Third, the higher levels of amino acids in GM herbicide-resistant crops could also cause changes in the plants' metabolisms that render them toxic to humans.[117] Fourth, gene transfers could cause a previously quiescent gene to become activated and express a toxic protein that the host plant would not otherwise contain.[118]

Manufacturers of GM plants can test for some of these possibilities prior to marketing to ensure that foods do not contain novel proteins in concentrations high enough to be toxic.[119] Because conventional breeding techniques can also inadvertently produce plants that contain human toxins, thorough probing of the makeup of hybrid plants is commonplace among producers of hybrid crops.[120] Biotechnology proponents argue that, as in the case of allergens, foods containing toxins are fairly well characterized, and companies can be trusted to approach "carefully and with thorough testing" gene transfers from potentially toxic donor plants.[121] It is not clear, however, that existing private testing regimes are up to the challenge of modern biotechnologies.[122]

d. New Chemicals Not Formerly Present—In many genetic engineering experiments, scientists attempt to introduce a protein into a food plant line that differs significantly in structure or function

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115. *See Id.* at 47–48; 1992 FDA Policy Statement, *supra* note 17, at 22,987; OECD, SAFETY EVALUATION, 1992, *supra* note 1, at 7–8.

116. *See* ROYAL SOCIETY OF CANADA REPORT, 2001, *supra* note 81, at 46; NRC GM PEST-PROTECTED PLANTS REPORT, *supra* note 1, at 71; 1992 FDA Policy Statement, *supra* note 17, at 22,987.

117. LAPPE & BAILEY, *supra* note 14, at 115. In the case of soybeans, for example, one of the primary metabolic products is a class of compounds called "isoflavonoids" that are, in the view of many scientists, very similar to human estrogens. If these "phytoestrogens" behave like human estrogens in the human body, consumption of GM soybeans could subtly affect "sexual differentiation, calcium metabolism, immune function, carcinogenesis, and blood clotting" in human beings. Since soy products now constitute a large proportion of the diet of many infants, these subtle changes could have large, but quite subtle long-term consequences. *Id.*

118. 1992 FDA Policy Statement, *supra* note 17, at 22,987; NRC GM PEST-PROTECTED PLANTS REPORT, *supra* note 1, at 62.

119. NRC GM PEST-PROTECTED PLANTS REPORT, *supra* note 1, at 63.

120. *Id.*

121. *U.S. House Seeds of Opportunity Report*, *supra* note 25, at 47.

122. For example, it remains to be seen whether manufacturers will know how to test for inadvertently enhanced levels of previously existing toxic metabolites in food plants. *Public Meeting on Biotechnology in the Year 2000 and Beyond by the U.S. Food and Drug Administration* (Dec. 13, 1999) (remarks of Philip Regal, University of Minnesota) [hereinafter Regal Remarks, Dec. 13, 1999].

from the proteins already present in the plant.[123] Although the new protein usually is genetically engineered into the plant for a predetermined purpose, the exercise can produce unexpected results.[124] Some scientists have suggested that the characteristics of the host plant may even change over time as the inserted gene moves to different positions on the host plant's DNA.[125] Since it is often impossible to tell at the outset whether the new proteins or the new composition of carbohydrates, fats and oils produced by those proteins could be harmful to consumers, further analysis of the plant's composition and perhaps toxicity testing (possibly for several generations) may be required for adequate safety assessment.[126]

A cautious manufacturer will attempt to assess the health risks posed by any new proteins, carbohydrates, fats or oils in GM foods before putting them on the market. Yet, in many cases, it is not clear how manufacturers should go about testing for the presence of unanticipated toxins.[127] Moreover, despite the possibility of latent manifestation of unanticipated traits, manufacturers seldom test GM plants for more than a single generation prior to putting seeds into full production.[128]

2. Indirect Risks to Human Health

a. Changes in Levels of Nutrients and Anti-Nutrients—Genetic engineers attempting to design a food plant with one characteristic in mind might inadvertently produce a plant in which the levels or bioavailability of important nutrients are altered in significant ways.[129] For example, in a 1999 paper, two scientists concluded that Monsanto's Roundup Ready® soybeans were twelve to fourteen percent lower in phytoestrogens, which are associated with protection against heart disease, osteoporosis and breast cancer.[130] It is

123. *See* 1992 FDA Policy Statement, *supra* note 17, at 22,987; NRC GM PEST-PROTECTED PLANTS REPORT, *supra* note 1, at 60.

124. NRC GM PEST-PROTECTED PLANTS REPORT, *supra* note 1, at 59 (noting that "breeding can lead to indirect effects, such as the effects of extraneous genes linked to the protective genes and pleiotropic effects caused by the protective genes"); LAPPE & BAILEY, *supra* note 14, at 14 (noting that "many plant genes produce a variety of effects (called 'pleiotropy'), where changes in form and function result from a single gene insertion").

125. LAPPE & BAILEY, *supra* note 14, at 30 (arguing that inserted DNA "may unbalance or disrupt the normal functioning of the resident genes" and that "it may be several generations before the resulting disruption is fully realized").

126. *See* 1992 FDA Policy Statement, *supra* note 17, at 22,987.

127. *See* OECD EDINBURGH RAPPORTEURS' SUMMARY, *supra* note 33, at 5 (alluding to unanswered questions regarding how safety of "neutraceuticals" should be assessed).

128. LAPPE & BAILEY, *supra* note 14, at 30–31.

129. 1992 FDA Policy Statement, *supra* note 17, at 22,987.

130. *See Hearing on Biotechnology Before the Senate Comm. on Agric., Nutrition & Forestry*, 106th Cong. (Oct. 6, 1999) (testimony of Mark Silbergeld, Co-Director, Consumers Union of the U.S., Inc.), *available at* http://www.agriculture.senate.gov/Hearings/Hearings_1999/

also possible that genetic modifications could inadvertently increase the levels of "antinutrients" in foods.[131]

b. Antibiotic Resistance—Scientists engaged in gene transfer experiments typically enhance their ability to isolate plant cells that have incorporated the desired gene by physically linking that gene to a "marker gene" that has the property of antibiotic resistance.[132] Once a plant variety with the desired genetic trait has been isolated and reproduced, the gene coding for antibiotic resistance no longer performs any useful function. The GM plants, however, continue to produce the antibiotic resistance enzyme, and anyone who eats the plants will consume the enzyme as well.[133] In theory, the enzyme could deactivate the same antibiotic in human beings, thus reducing the drug's therapeutic value to persons who consume the GM food.[134] In addition, foods containing marker genes could transfer those genes to naturally occurring pathogenic bacteria. The ultimate result could be a strain of pathogenic bacteria that is resistant to an important antibiotic or, worse, a whole family of antibiotics.[135]

Noting that the scenario outlined above requires a number of sequential steps, each of which has a low probability of occurrence,[136] biotechnology proponents argue that such risks are vanishingly small.[137] Furthermore, since a pool of antibiotic-resistant bacteria already exists in most human guts, any additional risk posed by GM foods is probably trivial by comparison.[138] Some biotechnology critics concede that the risk of antibiotic resistance arising out of human consumption of GM foods pales in

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sil199107.htm [hereinafter Silbergeld Testimony, Oct. 6, 1999]; TEITEL & WILSON, *supra* note 24, at 48. The American Soybean Association and Monsanto disputed the study. TEITEL & WILSON, *supra* note 24, at 48.

131. *See* ROYAL SOCIETY OF CANADA REPORT, 2001, *supra* note 14, at 82. Although the subject of some dispute, anti-nutrients are secondary plant metabolites that "appear to have deleterious effects over time on animal or human consumers." *Id.*

132. 1992 FDA Policy Statement, *supra* note 17, at 22,987.

133. *See Id.* at 22,988.

134. *Id.*

135. TEITEL & WILSON, *supra* note 24, at 38; *see also Plant Genome Science: From the Lab to the Field to the Market: Hearing Before the House Comm. on Sci. Subcomm. on Basic Research*, 106th Cong. (Oct. 5 1999) (testimony of Rebecca Goldburg, Environmental Defense Fund) [hereinafter Goldburg Testimony, Oct. 5, 1999], *available at* http://www.house.gov/science/goldburg_100599.htm (noting that antibiotic resistance genes can in theory "be transferred from genetically engineered food to bacteria that live in the GI tract").

136. *U.S. House Seeds of Opportunity Report, supra* note 25, at 50.

137. *Id.* at 49.

138. *Id.* at 51.

comparison to risks posed by the enormous overuse of important antibiotics to prevent diseases in cattle and poultry.[139]

Other skeptics insist, however, that the consequences of the emergence of virulent antibiotic-resistant pathogens are so high that even a small probability is too risky. The Canadian Royal Society Panel and the British Medical Association have both recommended that all use of antibiotic marker genes in GM foods be prohibited.[140] The OECD Edinburgh Conference on the Scientific and Health Aspects of Genetically Modified Foods concluded that it was no longer necessary to use antibiotic marker genes to achieve effective gene transfers in plants, and it recommended that biotechnology companies and other researchers phase out antibiotic resistance markers.[141]

3. The Search for Scientific Accuracy in the Midst of Large Uncertainties—The preceding analysis suggests that substantial uncertainties permeate the existing state of knowledge regarding the risks and benefits posed by GM foods. Agricultural biotechnology companies have undertaken very little testing of whole GM foods and of novel proteins and other products expressed in GM foods.[142] Indeed, it is not even clear that animal feeding studies can play a useful role in assessing the health risks posed by GM foods.[143] The existing knowledge base concerning reproductive and developmental effects is especially weak.[144] Huge uncertainties still plague assessments of allergenicity risks of gene transfers from donor organisms that are not known to be allergenic.[145] In the final analysis, a genetically engineered plant remains a "black box" containing

139. *See* Goldburg Testimony, Oct. 5, 1999, *supra* note 135 (arguing that "the current use in animal agriculture of 40 to 50% all antibiotics in the United States poses a far larger human health threat from antibiotic resistance than the use of antibiotic resistance genes as selective markers").

140. BRITISH MED. ASS'N, THE IMPACT OF GENETIC MODIFICATION ON AGRIC, FOOD AND HEALTH (1999), *available* at http://www.global-reality.com/biotech/articles/othernews012.htm; ROYAL SOCIETY OF CANADA REPORT, 2001, *supra* note 14, at 49.

141. OECD EDINBURGH RAPPORTEURS' SUMMARY, *supra* note 33, at 3.

142. *See Hearing Before the House Comm. on Sci. Subcomm. on Basic Research*, 106th Cong. (Oct. 19, 1999) (testimony of Stephen L. Taylor, University of Nebraska) [hereinafter Taylor Testimony, Oct. 19, 1999] (noting that "toxicologists rarely attempt to assess the safety of whole foods").

143. *Id.* at 4 (noting that it is unclear whether animal feeding studies will be useful for GM foods).

144. *See id.* (noting "uncertainty about the potential long-term effects of GM food on human health and on worker safety").

145. *See id.* (noting that current methods for testing toxicity and allergenicity "leave some uncertainties and need to be improved").

many unanswered questions, some of which may never be fully resolved.[146]

Biotechnology proponents frequently take the public position that regulatory decision-making regarding GM foods should be a matter of "sound science."[147] Critics complain that the "sound science" rhetoric ignores both the fact that considerations other than science have always played profound roles in determining the foods that people choose to eat and the fact that existing scientific studies cannot answer some basic questions that arise in assessing the health risks of GM crops.[148] Even when testing has been conducted and data are available, experts often disagree about how to interpret those data. In an era in which much of the attraction of agricultural biotechnology research is the prospect of reaping financial rewards, it is not always clear that the scientists in the companies and the universities can be trusted to interpret equivocal data in an unbiased way.[149] To the extent that science cannot definitively answer the critical questions that arise in assessing the health risks of GM foods, regulatory agencies must answer them on the basis of sound public policy.[150]

Lacking accurate information on the risks posed by GM plants, regulatory decision makers must employ fallback or "default"

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146. *See* LAPPE & BAILEY, *supra* note 14, at 14 (arguing that "genetically modified plants may be much more of a black box than the pseudoscientific terminology of 'transgenic' and implied genetic control connotes").

147. *See* 1992 FDA Policy Statement, *supra* note 17, at 22,987; *Public Meeting on Biotechnology in the Year 2000 and Beyond by the U.S. Food and Drug Administration* (Nov. 30, 1999) (remarks of Samuel B. Lehrer, Tulane University) (arguing that "we should base any decisions on sound scientific principles").

148. *See* Ralph Nader, *Foreword* to MARTIN TEITEL & KIMBERLY A. WILSON, GENETICALLY ENGINEERED FOOD: CHANGING THE NATURE OF NATURE at ix (1999) (arguing that "[g]enetic *engineering*—of food and other products—has far outrun the *science* that must be its first governing discipline").

149. *See* TEITEL & WILSON, *supra* note 24, at 7 (arguing that "[b]ecause so many experts seem to be tied to personal gain from their involvement in the new technologies, we have to be careful where to look to find objective and fair information"); EU-U.S. BIOTECHNOLOGY CONSULTATIVE FORUM, FINAL REPORT 6 (Dec. 2000) (noting that when technological developments "offer the possibility of considerable immediate benefits and revenues the tendency—or even temptation—to underestimate potential longer-term risks and dangers is there").

150. *See* ROYAL SOCIETY OF CANADA REPORT, 2001, *supra* note 14, at 8 (observing that "[i]t is now generally recognized in the scholarly literature on the nature of risk analysis that many aspects of the task of assessing the magnitude of technological risks and managing them within the limits of safety involve judgments and decisions that are not themselves strictly scientific"); EU-U.S. CONSULTATIVE FORUM, FINAL REPORT, *supra* note 149, at 5 ("judgments about risk cannot be reduced to scientific assessment alone").

assumptions in assessing those risks.[151] To some extent default assumptions depend upon general scientific understandings of how biological organisms interact with themselves and their environments. Given the novelty of modern biotechnology and the aforementioned difficulty in assessing the health risks of GM plants, however, these understandings may not offer a reliable basis for deciding how to manage those risks. The fallback assumptions must therefore depend to a very large degree upon the policies underlying the relevant regulatory programs.[152] If a program is designed primarily to foster new technologies, then the agency should employ "realistic" assumptions that do not overestimate the risks that the technologies pose to health and the environment. If the program is designed primarily to protect human health and the environment, then the agency should adopt "conservative" assumptions that avoid underestimating risks.

II. THE SCIENCE AND POLICY OF "SUBSTANTIAL EQUIVALENCE"

Almost any food can cause harmful effects in human beings if care is not taken in its preparation and consumption. Meat must be cooked to eliminate dangerous microorganisms, some vegetables must be cooked to neutralize natural toxins that they contain, and spoiled fruit can make anyone ill. Hence, safety evaluation of whole foods ordinarily draws on long-time experience with existing foods and begins with the not unreasonable assumption that foods prepared and used in traditional ways are generally safe for human consumption.[153] Thus, few traditionally eaten foods have undergone the sort of extensive safety testing that is required for registering new food additives or new pesticides for uses on food crops.

Proponents of modern agricultural biotechnologies have attempted to quell what they believe to be irrational public fears by stressing that genetic engineering is nothing new.[154] It is only the

151. *See* NAT'L ACAD. OF SCIENCES, NAT'L RESEARCH COUNCIL, RISK ASSESSMENT IN THE FED. GOV'T: MANAGING THE PROCESS (1983) [hereinafter NAS RED BOOK].

152. *See* ROYAL SOCIETY OF CANADA REPORT, 2001, *supra* note 14, at 8 (risk assessment involves "value judgments related to such issues as the appropriate way to handle uncertainties in scientific data and results, assignment of the burden of proof among stakeholders in risk issues, standards of proof, definition of the scope of the risk issue . . . and, of course, the central issue . . . of what levels of risk should be considered 'acceptable' ").

153. *See* OECD, SAFETY EVALUATION, 1992, *supra* note 1, at 10.

154. *See, e.g.*, Cook Testimony, Oct. 5, 1999, *supra* note 76 (noting that "genetic modification of plants for food, agriculture, and the environment is nothing new").

most recent tool made available through a constantly evolving process of using scientific knowledge to make safer and higher quality food available to more human beings.[155] A regulatory agency should therefore focus its attention on the *product* that a manufacturer is marketing and not upon the *process* used to make the product.[156] Furthermore, there is no particular reason to believe that the "offspring" of modern genetic engineering techniques will be any more dangerous that the foods that have resulted from traditional breeding technologies.[157] Thus, if the GM food product is "substantially equivalent" to a non-GM food that has a history of safe use, it should not be regulated any more stringently simply because it resulted from the novel process.[158]

Critics believe that modern gene splicing techniques are *sui generis* and therefore reject the major premise underlying the "substantial equivalence" doctrine.[159] Although traditional breeding techniques are not strictly "natural," they do "take advantage of nature's vast storehouse of information, accumulated over millions of years of experimentation, as to what works and what doesn't," thus greatly reducing the potential for catastrophic mistakes.[160] Modern gene splicing tools, by contrast, can accomplish in a single generation changes that could never occur in nature.[161] Because modern genetic engineering is a hit-or-miss process that "disrupt[s] the existing genome in a random way," it is more likely to

155. *See* Giddings House Testimony, Mar. 3, 1999, *supra* note 29 (arguing that "biotechnology represents another step along the continuum"); *U.S. House Seeds of Opportunity Report, supra* note 25, at Letter of Transmittal (stressing that "this technology represents the latest tool in the continuum of techniques that plant breeders have developed and adopted over centuries"); OECD EDINBURGH RAPPORTEURS' SUMMARY, *supra* note 33, at 3.

156. *See Public Meeting on Biotechnology in the Year 2000 and Beyond by the U.S. Food and Drug Administration* (Nov. 30, 1999) (remarks of Peter Day, Rutgers University) (agreeing with FDA focus on product, rather than process); NRC GM PEST-PROTECTED PLANTS REPORT, *supra* note 1, at 26 ("the products, not the process, would be regulated").

157. *See* Cook Testimony, Oct. 5, 1999, *supra* note 76 (finding "no scientifically-based reason to discriminate against food from genetically modified crops"); *U.S. House Seeds of Opportunity Report, supra* note 25, at 3 (finding "nothing to substantiate scientifically the view that the products of agricultural biotechnology are inherently different or more risky than similar products of conventional breeding").

158. *See* Engel, Takeoka & Teranishi, *Foods and Food Ingredients, supra* note 1, at 7; *see also U.S. House Seeds of Opportunity Report, supra* note 25, at 51.

159. *See* OECD EDINBURGH RAPPORTEURS' SUMMARY, *supra* note 33, at 3 (noting that some see genetic modification "as a fundamental change in the way new crops are produced").

160. TEITEL & WILSON, *supra* note 24, at 12.

161. *See* Goldburg Testimony, Oct. 5, 1999, *supra* note 135 (noting that traditional breeding techniques can import desirable traits from a wild variety of potato into potatoes used for crops, but they "cannot add viral, insect, moth or chicken genes to potatoes"); Engel, Takeoka & Teranishi, *Foods and Food Ingredients, supra* note 1, at 3–4.

create unexpected, unintended side effects than the conventional approaches.[162] Convinced that modern agricultural biotechnologies represent a "radical departure from traditional plant breeding," many critics argue that the regulatory agencies should focus especially carefully on the potential health risks of GM foods.[163]

Assuming that the substantial equivalence doctrine is correct in theory, its practical implementation raises a number of conceptual, policy and institutional questions. Since the purpose of the genetic engineering exercise is to change the engineered plant in some commercially useful way (and thereby render the changed plant not equivalent to the unchanged plant in at least that regard), the "substantial equivalence" determination requires some exercise of judgment as to the "substantiality" of the change. What criteria should guide that exercise of judgment? What evidence is necessary to support a substantial equivalence determination? Who is qualified to make a substantial equivalence determination? Can it be made generically for whole classes of GM foods or must each product be evaluated separately on a case-by-case basis? The legitimacy of substantial equivalence as a guiding regulatory principle depends importantly upon the answers to these questions as well as on the plausibility of the theory as a scientific matter.

The "substantial equivalence" concept as applied to GM foods was the brainchild of a 1992 Working Group established by the Organisation of Economic Co-Operation and Development (OECD) to study how countries should go about evaluating the safety of GM foods.[164] Drawing on material from several international conferences and intergovernmental consultations, the OECD Working Group decided that "substantial equivalence" was "the most practical way to address the issue of food safety at this time."[165] The Working Group suggested that the substantial equivalence determination should be based upon three primary factors:

> (1) knowledge of the composition and characteristics of the traditional or parental product or organism;

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162. Fagan Remarks, Dec. 13, 1999, *supra* note 76, at 90; *see also* Conway, *Crop Biotechnology*, *supra* note 65, at 3; TEITEL & WILSON, *supra* note 24, at 12.

163. TEITEL & WILSON, *supra* note 24, at 12.

164. OECD, SAFETY EVALUATION, 1992, *supra* note 1 at 11; *see also* ROYAL SOCIETY OF CANADA REPORT, 2001, *supra* note 14, at 179.

165. OECD, SAFETY EVALUATION, 1992, *supra* note 1, at 6. The idea of comparing a modified plant with the unmodified predecessor to assess the effects of the changes in the plant is the traditional way of assessing the novel traits of hybrid plants designed through conventional breeding technologies. ROYAL SOCIETY OF CANADA REPORT, 2001, *supra* note 14, at 178.

(2) knowledge of the characteristics of the new component(s) or trait(s) derived . . . ;

(3) knowledge of the new product/organism with the new components or trait(s) . . . .[166]

For GM foods and food components determined to be substantially equivalent to the parental products, the Working Group believed that further safety concerns were likely to be "insignificant" and the GM food could be treated for regulatory purposes just like the natural counterpart. For foods and food components determined not to be substantially equivalent, the Working Group recommended that the regulatory agency focus on the identified differences between the GM food and its natural counterpart. Only when there was no basis whatsoever for comparisons with unmodified foods should the GM food be evaluated on the basis of "its own composition and properties."[167]

Several aspects of the Working Group's list of decision-making criteria are noteworthy. First, the fact that the change was accomplished through genetic engineering, rather than traditional plant breeding, is noticeably absent from the list because the baseline assumption of the substantial equivalence doctrine is that there is nothing inherently novel about plant breeding through modern genetic engineering. Second, the fact that the decision maker must make the determination upon knowledge of a highly technical character strongly suggests that the decision maker must be an expert in understanding the composition and characteristics of plants and in comparing plant traits. Third, the determination apparently may be based upon existing knowledge, and additional scientific study of the characteristics of the modified plant is required only when comparisons are otherwise impossible. Finally, it is not clear on the face of the criteria whether generic, rather than individual, determinations are generally acceptable.

Proponents of agricultural biotechnologies are strong supporters of the "substantial equivalence" doctrine.[168] They caution that "[d]etermining conclusively that genetic modification—whether done through traditional breeding techniques or biotechnology—has not resulted in any unexpected events in the plant is extremely

166. OECD, SAFETY EVALUATION, 1992, *supra* note 1, at 11.

167. *Id.* at 11–12.

168. *U.S. House Seeds of Opportunity Report*, *supra* note 25, at 51; Engel, Takeoka & Teranishi, *Foods and Food Ingredients*, *supra* note 1, at 7.

difficult."[169] For starters, it could require testing of whole foods in laboratory animals, a practice that is very difficult to accomplish in the real world and may not in any event yield useful results.[170] The substantial equivalence doctrine represents a more "practical" (and, incidentally, less expensive) approach, because it does not require a great deal of testing and modeling.[171] It makes little sense, in their view, to go to the trouble of toxicity testing for GM foods that are substantially equivalent to unmodified foods when the GM foods are not likely to be any more dangerous that their unmodified counterparts.[172]

For someone less concerned about the cost of winning approval for new foods, however, "there would appear to be an intrinsic contradiction between the presence of 'novelty' in a new plant genotype and a designation of 'equivalence.'"[173] Critics of the substantial equivalence doctrine argue that a regulatory system based upon substantial equivalence is not "set up to identify unexpected changes in food."[174] They do not trust expert decision makers employing the substantial equivalence doctrine to take into account all of the subtle changes in delicately balanced biochemical pathways within genetically engineered plants that may affect the safety or environmental impact of those plants.[175] Since it is sufficient under the substantial equivalence doctrine to compare the modified organism with any varieties within the same species, the modified organism "could have the worst characteristics of all the varieties and still be considered substantially equivalent."[176]

The most disturbing aspect of the substantial equivalence doctrine to its critics is its subjectivity. No standardized objective tests for determining equivalence and measuring substantiality exist, and the OECD criteria are sufficiently vague and flexible to permit

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169. *U.S. House Seeds of Opportunity Report*, *supra* note 25, at 52.

170. Taylor Testimony, Oct. 19, 1999, *supra* note 142 (arguing that laboratory animal testing of whole GM foods "would be tremendously unfocused, wasteful of laboratory animal resources, and unlikely to detect any harmful substances, even if they were present").

171. OECD, SAFETY EVALUATION, 1992, *supra* note 1, at 11.

172. *See* Taylor Testimony, Oct. 19, 1999, *supra* note 142 (arguing that "testing would be tremendously unfocused, wasteful of laboratory animal resources, and unlikely to detect any harmful substances, even if they were present").

173. ROYAL SOCIETY OF CANADA REPORT, 2001, *supra* note 14, at 181.

174. Andy Coghlan, *Judging Gene Foods*, NEW SCIENTIST, Apr. 15, 2000, at 4 (quoting Sue Mayer of GeneWatch UK).

175. Regal Remarks, Dec. 13, 1999, *supra* note 122 (arguing that inserted genes may change "delicately balanced biochemical pathways").

176. Mae-Wan Ho, *Dangerous Liaison—Deadly Gamble*, *in* NAT'L AGRIC. BIOTECHNOLOGY COUNCIL REPORT 10, AGRICULTURAL BIOTECHNOLOGY AND ENVIRONMENTAL QUALITY: GENE ESCAPE AND PEST RESISTANCE 105, 107 (Ralph W.E. Hardy & Jane Baker Segelken eds., 1998) [hereinafter Ho, *Dangerous Liaison*].

a great deal of discretion.[177] To the extent that the expert decision makers work for the regulated industries, they cannot be trusted to exercise their discretion in the broader public interest. To the extent that they are relatively low-level agency employees, industry lobbyists can quietly but effectively influence discretionary decision-making. Because it is based in large part on a policy determination that agencies and companies should not have to waste resources on unnecessary testing and evaluation, the substantial equivalence doctrine is not so much a "scientific" risk assessment tool as it is an excuse for regulatory agencies to avoid their responsibilities.[178]

Despite these criticisms, the substantial equivalence doctrine is the bedrock principle underlying the current regulatory regime for biotechnology in the United States. The initial regulatory structure for biotechnology was erected in a 1986 "Coordinated Regulatory Framework" devised by an Administration that was very reluctant to impose regulatory restrictions on a rapidly developing new industry. The bedrock principles underlying that framework were that the "techniques of biotechnology are not inherently risky and that biotechnology should not be regulated as a process, but rather that the products of biotechnology should be regulated in the same way as products of other technologies."[179] Toward the end of the first Bush Administration, the White House Office of Science and Technology Policy published a "Statement of Scope" for regulating biotechnology that adopted a "risk-based approach" under which regulatory oversight would focus on the "characteristics and risks of the biotechnology product—not the process by which it was created."[180] In a private meeting, Vice President Dan Quayle ensured representatives of the biotechnology industry that the new policy was designed to provide "regulatory relief" for the

177. *See id.* at 107 (noting that "there are no defined tests that products have to go through to establish substantial equivalence").

178. *See id.* at 107 (substantial equivalence doctrine is "the stuff of farce"); TEITEL & WILSON, *supra* note 24, at 68 (an agency applying substantial equivalence doctrine "has decided in advance not to conduct the prudent steps toward protecting public health and safety that would in fact fulfill the agency's mandate"). The Royal Society of Canada expert report concluded that, in practice, the substantial equivalence doctrine "does not function as a scientific basis for the application of a safety standard, but rather as a decision procedure for facilitating the passage of new products, GM and non-GM, through the regulatory process." ROYAL SOCIETY OF CANADA REPORT, 2001, *supra* note 14, at 182.

179. NRC GM PEST-PROTECTED PLANTS REPORT, *supra* note 1, at 26.

180. Office of Science and Technology Policy, *Exercise of Federal Oversight Within Scope of Statutory Authority: Planned Introductions of Biotechnology Products Into the Environment*, 57 Fed. Reg. 6753 (1992).

fledgling industry so that it would remain a world leader.[181] The Clinton Administration did nothing to change that approach until its waning moments when FDA proposed regulations that implicitly rejected the major premise in requiring companies to provide notice to the agency of their plans to market new GM foods.[182] The current Bush Administration, however, has not finalized that proposal.

The following description of the programs established by FDA and EPA for regulating GM foods reveals an almost impenetrable complexity that is easily capable of discouraging all but the most determined efforts by the uninitiated observer to ascertain how the agencies are fulfilling their regulatory responsibilities. The observer's somewhat surprising reward for the effort is the discovery that for all its complexity, the regulatory regime requires remarkably little of the companies that develop and market GM foods. The sponsor of a GM food can at all critical junctures either substantially diminish regulatory oversight or avoid it altogether by successfully invoking the principle of substantial equivalence.

III. FDA REGULATION OF GM FOODS

FDA's authority to regulate GM foods ultimately flows from its authority to regulate "adulterated foods." Under Section 402(a)(1) of the Food, Drug and Cosmetics Act (FDCA), a food is deemed adulterated if it "bears or contains any poisonous or deleterious substance which may render it injurious to health."[183] Foods that are adulterated are subject to the full range of enforcement measures under the act, including seizure, injunction, and criminal prosecution.[184] Interestingly, the statute does not define "poisonous or deleterious," and the FDA has consistently declined to provide a definition for those terms in its implementing regulations.[185]

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181. Warren E. Leary, *Cornucopia of New Foods Is Seen as Policy on Engineering Is Eased*, N.Y. TIMES, May 27, 1992, at A16.

182. *See* discussion *infra* Part III.C.

183. 21 U.S.C. § 342(a)(1)(1994). According to the statute and FDA regulations, the word "food" means "(1) articles used for food or drink for man or other animals, (2) chewing gum, and (3) articles used for components of any such article." 21 U.S.C. § 321(f)(1994). The term includes human food, substances migrating to food from food-contact articles, pet food, and animal feed. 21 C.F.R. § 170.3(m).

184. *See* 21 U.S.C. § 333 (1994) (penalties); 21 U.S.C. § 334 (1994) (seizure).

185. *See* Poisonous or Deleterious Substances, 42 Fed. Reg. 52,814, 52,816 (Sept. 30, 1977); Noah & Merrill, *Starting from Scratch*, *supra* note 5, at 335 n.17.

Although a GM pest-resistant plant might otherwise fall within FDA's authority to regulate adulterated foods, the agency in 1992 announced that it had ceded to EPA all regulatory authority over plants genetically modified to express pesticidal substances so long as they have not also been modified to express nonpesticidal substances.[186] FDA and EPA agree that such plants are in fact pesticides and thus subject to EPA's exclusive jurisdiction.[187] Questions over whether a particular genetically engineered plant species is or is not subject to EPA's exclusive jurisdiction are to be raised with EPA, not FDA.[188] Plants genetically engineered to enhance plant resistance to chemical herbicides, on the other hand, are generally not pesticides and are therefore subject to FDA's exclusive jurisdiction.[189]

A substance in food that is not an added substance (a "naturally occurring substance" in FDA parlance)[190] does not render the food adulterated if the quantity of that substance in the food does not ordinarily render the food "injurious to health."[191] FDA reads the statute to impose a legal duty on those who introduce food into the market place, including food derived from new crop varieties, to ensure that the introduced food satisfies the "injurious to health" standard.[192] The agency has relied almost exclusively upon this

186. 1992 FDA Policy Statement, *supra* note 17, at 23,005.

187. *Id.*

188. *Id.*

189. *Id.*

190. *Id.* at 22,988.

191. 21 U.S.C. § 342(a)(1) (1994). A food is also deemed adulterated if it "bears or contains any *added* poisonous or *added* deleterious substance (other than a pesticide, a food additive, a color additive, or a new animal drug) that is unsafe within the meaning of section 406." 21 U.S.C. § 342(a)(2)(A) (1994) (emphasis added). Section 406 in turn provides that any "poisonous or deleterious substance" deliberately added to any food must be deemed unsafe under section 402(a)(2)(A), unless it is "required in the production" of the food or "cannot be avoided by good manufacturing practice," in which case FDA must promulgate regulations limiting the quantity of the added substance to the extent "necessary for the protection of public health," after which any quantity exceeding those limits must also be deemed to be unsafe. 21 U.S.C. § 346 (1994). In setting "tolerances" limiting the quantity of added substances in food, FDA must "take into account the extent to which the use of such substance is required or cannot be avoided in the production of each such article, and the other ways in which the consumer may be affected by the same or other poisonous or deleterious substances." 21 U.S.C. § 346 (1994). This provision will probably not be applicable to GM foods in the near term, because any added substances resulting from genetic modification are probably not required in the production of most foods and can be avoided merely by allowing the food to go unmodified. It could become relevant in the future as manufacturers use modern genetic engineering techniques to design new foods that did not exist prior to the genetic modification. It is, for example, conceivable that some substance resulting from the genetic modification might be required in the production of the GM food or otherwise unavoidable.

192. 1992 FDA Policy Statement, *supra* note 17, at 22,988.

legal obligation "to ensure the safety of whole foods."[193] FDA has rarely taken regulatory action with respect to naturally occurring substances in whole foods because, in FDA's experience, "such cases are typically well known and carefully avoided by food producers."[194]

Under Section 402(b)(1) of the FDCA, a food is deemed adulterated if "any valuable constituent has been in whole or in part omitted or abstracted therefrom. . . ."[195] Perhaps of greater relevance to genetically modified foods, section 402(b)(2) provides that a food is deemed adulterated if "any substance has been substituted wholly or in part therefor. . . ."[196] A food is also deemed adulterated if "damage or inferiority has been concealed," or if "any substance has been added" to it "to increase its bulk or weight, or reduce its quality or strength, or make it appear better or of greater value than it is."[197] Although some genetic modifications of foods have achieved the desired results by omitting constituents from the plant, and at least some genetic modifications of plants might arguably substitute a new substance for an existing substance, the agency has not invoked its authority under Section 402(b) to regulate GM foods.

A. Food Additives

In addressing GM foods, FDA has thus far relied almost exclusively on its power to regulate food additives. Section 402(a)(2)(C)

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193. *Id.*

194. *Id.* FDA's general reluctance to regulate naturally occurring substances in food is understandable for two reasons. First, since manufacturers of foods not containing added substances have no statutory obligation to test such foods or to notify FDA of the results of any testing, FDA is likely to become aware of any adverse effects attributable to such non-added substances only after illnesses or deaths have occurred and epidemiological investigations have identified the culprit. Second, as Professor Merrill has noted, in order to meet its statutory burden of proving that a non-added substance in food would "ordinarily render it injurious to health," FDA "would have to demonstrate a probability of harm to some significant number of consumers." Richard A. Merrill, *Regulating Carcinogens in Food: A Legislator's Guide to the Food Safety Provisions of the Federal Food, Drug, and Cosmetic Act*, 77 MICH. L. REV. 171, 189 (1978); *see also* Noah & Merrill, *Starting from Scratch*, *supra* note 5, at 334 n. 15. Meeting this burden might well require the agency to conduct extensive animal tests, exposure analyses, and pharmacokinetic studies. As a result, FDA has tended to search for some way to regard suspect substances in food as "added" so as to reduce the threshold for regulatory action. *Id.*; Richard A. Merrill & Michael Schewell, *FDA Regulation of Environmental Contaminants of Food*, 66 VA. L. REV. 1357 (1980).

195. 21 U.S.C. § 342(b)(1) (1994).

196. 21 U.S.C. § 342(b)(2) (1994).

197. 21 U.S.C. § 342(b)(3)–(4) (1994).

of the FDCA provides that a food shall be deemed adulterated if it contains "any food additive that is unsafe within the meaning of section 409," and that section provides that a "food additive" is deemed unsafe for purposes of section 402(a)(2)(C) unless the additive and its use or intended use conform to the terms of a regulation promulgated by FDA allowing that additive in food.[198] This broad grant of authority also allows FDA to regulate additives to the feed and water of animals from which meat, milk and eggs are derived for human consumption.[199]

Ordinarily, FDA issues a food additive regulation in response to a petition filed by the manufacturer of the additive or food under section 409(b). Among other things, the food additive petition must contain "full reports of investigations made with respect to the safety for use of such additive. . . ."[200] The regulation granting a food additive petition must specify "the conditions under which such additive may be safely used," including "labeling or packaging requirements for such additive deemed necessary . . . to assure the safety of such use."[201] The agency may not grant the petition if the information available to the agency "fails to establish that the proposed use of the food additive, under the conditions of use to be specified in the regulation, will be safe. . . ."[202] As FDA interprets section 409, the "safety" finding requires the proponent of a food additive "to demonstrate to a reasonable certainty that no harm will result from the intended use of the additive."[203]

The agency must publish notice of its receipt of a food additive petition in the Federal Register within thirty days of receiving it.[204]

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198. 21 U.S.C. § 348(a)(2) (1994). In addition to a regulation allowing the additive in food, FDA may grant an "investigational use" exemption provided for under section 409(j). For a good description of the food additive petition process, see generally Noah & Merrill, *Starting from Scratch*, *supra* note 5, at pt. III.

199. *See* 21 C.F.R. § 573 (2001) (listing approved food additives permitted in feed and water of animals).

200. 21 U.S.C. § 348(b) (1994); *see also* Noah & Merrill, *Starting from Scratch*, *supra* note 5, at 369.

201. 21 U.S.C. § 348(c)(1) (1994).

202. 21 U.S.C. § 348(c)(3)(A) (1994). In making the "safety determination," the agency must consider "the probable consumption" of the additive and related substances, the cumulative dietary effect of the additive and chemically similar substances, and (most importantly) "safety factors which in the opinion of experts qualified by scientific training and experience to evaluate the safety of food additives are generally recognized as appropriate for the use of animal experimentation data." 21 U.S.C. § 348(c)(5) (1994).

203. *See* 21 C.F.R. § 170.3(i) (2001). In addition, the agency may not issue a regulation if the data show that "the proposed use of the additive would promote deception of the consumer in violation of this [Act] or would otherwise result in adulteration or in misbranding of food within the meaning of this [Act]." 21 U.S.C. § 348(c)(3)(B) (1994).

204. 21 U.S.C. § 348(b)(5)(1994).

Although the statute does not provide explicitly for a period of public comment on the petition,[205] FDA allows interested members of the public to review the scientific information underlying the petition at any time, and the preamble to its rules of practice and procedure suggests a general willingness to consider any public comments that it receives during the time that it is conducting its review.[206] Any person aggrieved by an order approving or disapproving a petition may demand a formal rulemaking hearing,[207] but such hearings are extremely rare.[208]

B. The GRAS Concept

The term "food additive" is defined in the statute to mean any substance that is intended for use in or which may reasonably be expected to become a component of or otherwise affect the characteristics of any food, but only if the substance "is not generally recognized, among experts qualified by scientific training and experience to evaluate its safety, as having been adequately shown through scientific procedures (or, in the case of a substance used in food prior to January 1, 1958, through either scientific procedures or experience based on common use in food) to be safe under the conditions of its intended use. . . ."[209] Thus, ingredients derived from natural sources (e.g., salt, pepper, vinegar, and spices) and a large number of chemical additives (e.g., artificial flavoring agents) have escaped formal food additive review because they are "generally recognized as safe" (GRAS).[210] Since additives to animal feed can become a component of or otherwise affect the characteristics of food, they too are subject to FDA regulation to the extent that meat, milk and eggs derived from such animals are used for human consumption.[211]

FDA's regulations define "common use in food" for purposes establishing a substance's GRAS status as "a substantial history of

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205. *See* Noah & Merrill, *Starting from Scratch*, *supra* note 5, at 370.

206. Administrative Practices and Procedures; Notice of Proposed Rule Making, 40 Fed. Reg. 40,682, 40,699 (Food & Drug Admin., Sept. 3, 1975).

207. 21 U.S.C. 348(f)(1) (1994).

208. *See* Noah & Merrill, *Starting from Scratch*, *supra* note 5, at 374.

209. 21 U.S.C. § 321(s) (1994).

210. 1992 FDA Policy Statement, *supra* note 17, at 22,989.

211. *See* 21 C.F.R. § 570.3(g) (2001) (defining "substance" in the definition of "food additive" to include "a food or feed or a component of a food or feed consisting of one or more ingredients"); 21 C.F.R. pt. 573 (2001) (listing approved food additives permitted in feed and water of animals).

consumption of a substance for food use by a significant number of consumers."[212] While the prior use route to GRAS status does not require "the quantity or quality of scientific procedures required for approval of a food additive regulation," it must "ordinarily be based upon generally available data and information."[213] The alternative "scientific procedures" route to GRAS status must be based upon scientific studies of the "same quantity and quality" as the studies generally required to obtain approval of a food additive petition.[214]

The primary distinction between the requirements necessary for GRAS status and those necessary for food additive status is the element of "common knowledge" that must characterize conclusions about the former.[215] The manufacturer must be prepared to "show that there is a consensus of expert opinion regarding the safety of the use of the substance."[216] Although unanimity is not required,[217] "the existence of a severe conflict among experts regarding the safety of the use of a substance precludes a finding of general recognition."[218] A 1997 proposed clarification to the GRAS regulations observed that "[t]he usual mechanism to establish that scientific information is generally available is to show that the information is published in a peer-reviewed scientific journal."[219] The agency recognized, however, that common knowledge in the scientific community could also be based upon "(1) [p]ublication of data and information in the secondary scientific literature, such as scientific review articles, textbooks, and compendia; (2) documentation of the opinion of an 'expert panel' that is specifically convened for this purpose; or (3) the opinion or recommendation of an authoritative body."[220]

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212. 21 C.F.R. § 170.3(f) (2001).

213. 21 C.F.R. § 170.30(c)(i) (2001).

214. 21 C.F.R. § 170.30(b) (2001).

215. 21 C.F.R. § 170.30(a) (2001) (GRAS determination must be based upon "common knowledge about the substance throughout the scientific community knowledgeable about the safety of substances directly or indirectly added to food"); Substances Generally Recognized as Safe, Notice of Proposed Rulemaking, 62 Fed. Reg. 18,938, 18,940 (proposed Apr. 17, 1997) [hereinafter FDA, 1997 GRAS NPRM].

216. FDA, 1997 GRAS NPRM, *supra* note 215, at 18,939; *see also* Noah & Merrill, *Starting from Scratch*, *supra* note 5, at 352 (GRAS determination requires a "fairly high level of scientific consensus").

217. *See* United States v. Articles of Food & Drug, 518 F.2d 743, 746 (5th Cir. 1975) ("What is required is not unanimous recognition but general recognition."); *see also* FDA, 1997 GRAS NPRM, *supra* note 215, at 18,939 ("Unanimity among experts regarding safety of a substance is not required.").

218. FDA, 1997 GRAS NPRM, *supra* note 208, at 18,939.

219. *Id.* at 18,940.

220. *Id.* at 18,941.

Ultimately, the agency leaves it up to the manufacturer to determine whether an added substance is GRAS.[221] Manufacturers frequently contract with private standard-setting agencies or panels assembled by trade associations to make GRAS determinations for particular substances.[222] A manufacturer may even establish the GRAS status of a substance based upon "scientific procedures" when the substance has never been used in food at all.[223] Thus, it is conceivable that a manufacturer could design a brand new food additive (e.g., through genetic modification techniques), conduct its own scientific studies, publish the results of those studies in the scientific literature or circulate them widely (e.g., on the internet), monitor comments from interested scientists, and allow a favorably disposed panel assembled by a trade association to conclude on the basis of the resulting "common knowledge" that the substance is GRAS.

The manufacturer does not even need to tell the agency that it has made a GRAS determination with respect to a substance that it has added to food.[224] FDA has, however, established an "affirmation" process under which a manufacturer may petition for and receive an agency affirmation that a particular substance is GRAS, thereby shielding the product from enforcement actions.[225] Although the affirmation process is time-consuming,[226] the agency refrains from taking enforcement during the time that it considers the affirmation petition.[227] If the manufacturer declines to consult with FDA, the agency may exercise its powers to seize foods con-

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221. 1992 FDA Policy Statement, *supra* note 17, at 22,989 ("[C]ompanies developing new ingredients, new versions of established ingredients, or new processes for producing a food or food ingredient must make a judgment about whether the resulting food substance is a food additive requiring pre-market approval by FDA."); Bohrer, *Biotechnology*, *supra* note 11, at 659; Noah & Merrill, *Starting from Scratch*, *supra* note 5, at 359 (noting that "FDA has acknowledged, albeit with some reluctance, that the maker or user of a substance may reach its own conclusion that a particular food use is GRAS").

222. Noah & Merrill, *Starting from Scratch*, *supra* note 5, at 359–62.

223. *See* General Recognition of Safety and Prior Sanctions for Food Ingredients, 39 Fed. Reg. 34,194 (Food & Drug Admin., Sep. 23, 1974) ("GRAS status may be achieved for post-1958 food ingredients on the basis of scientific procedures even prior to any significant history of marketing and use.").

224. FDA, 1997 GRAS NPRM, *supra* note 215, at 18,941 (FDA concludes that "a manufacturer may market a substance that the manufacturer determines is GRAS without informing the agency").

225. 40 C.F.R. § 170.35 (2001); *see* Noah & Merrill, *Starting from Scratch*, *supra* note 5, at 364.

226. The GRAS affirmation process itself averages seven years to completion. Noah & Merrill, *Starting from Scratch*, *supra* note 5, at 379; *see also* FDA, 1997 GRAS NPRM, *supra* note 208, at 18,941 (observing that "GRAS affirmation involves the resource-intensive rulemaking process").

227. *See* Noah & Merrill, *Starting from Scratch*, *supra* note 5, at 364.

taining the additive as adulterated.[228] Although FDA takes the position that a manufacturer claiming GRAS status for a substance has the burden of proving that it meets the GRAS criteria in an enforcement action,[229] the agency may as a practical matter have the burden of demonstrating to a court in an enforcement action that the substance is in fact not GRAS and that the food is therefore adulterated before a court will be willing to order food containing that substance seized and held or destroyed.[230]

C. FDA Implementation Activities

On May 29, 1992, FDA issued a "Policy Statement" on "Foods Derived from New Plant Varieties" providing detailed guidance for voluntary compliance with the agency's regulatory requirements for GM foods.[231] The policy statement defined "genetic modification" broadly to mean "the alteration of the genotype of a plant using any technique, new or traditional."[232] Under this definition, "most, if not all, cultivated food crops have been genetically modified."[233] FDA thus specifically declined to allow the process used to manufacture the food determine (or even significantly affect) the regulatory approach that the agency applied.[234] Acknowledging that "[a]ny genetic modification technique has the potential to alter the composition of food in a manner relevant to food safety," FDA was convinced that "based on experience, the likelihood of a

228. FDA, 1997 GRAS NPRM, *supra* note 208, at 18,939; 1992 FDA Policy Statement, *supra* note 17, at 22,989; *see also* Noah & Merrill, *Starting from Scratch*, *supra* note 5, at 377 (warning that "[a] manufacturer that markets a food containing a novel and poorly studied ingredient faces a significant risk that the FDA will challenge the product on the ground that it contains an unapproved additive").

229. *See* FDA, 1997 GRAS NPRM, *supra* note 215, at 18,939. At least one court of appeals has agreed with FDA's position. United States v. An Article of Food, 752 F.2d 11, 15 (1st Cir. 1985) (stating that "[t]he burden of proving general recognition of safe use is placed on the proponent of the food substance in question").

230. *See* PETER BARTON HUTT & RICHARD A. MERRILL, FOOD AND DRUG LAW 333 (2d ed. 1991).

231. 1992 FDA Policy Statement, *supra* note 17. On September 29, 2000, the District Court for the District of Columbia dismissed a consumer group challenge to the 1992 policy statement. Alliance for Bio-Integrity v. Shalala, 116 F. Supp. 2d 166 (D.D.C. 2000). Two important aspects of that opinion will be discussed below. *See infra* Parts III.C., III.D.4.

232. 1992 FDA Policy Statement, *supra* note 17, at 22,984.

233. *Id.* at 22,984 n.3.

234. *Id.* at 22,988 (taking the position that "[t]he regulatory status of a food, irrespective of the method by which it is developed, is dependent upon objective characteristics of the food and the intended use of the food (or its components)").

safety hazard is typically very low."[235] The policy statement noted that "[p]lant breeders using well established practices have successfully identified and eliminated plants that exhibit unexpected, adverse traits prior to commercial use,"[236] and it anticipated that they would take the same precautions with GM plants.

The court in *Alliance For Bio-Integrity v. Shalala*, in a brief three-paragraph analysis, held that FDA had not been arbitrary and capricious in affording a presumption of GRAS status to GM foods.[237] The court noted that, under the 1992 Policy Statement, a manufacturer asserting GRAS status for a GM plant was required to meet two criteria: "it must have technical evidence of safety, usually in published scientific studies, and . . . this technical evidence must be generally known and accepted in the scientific community."[238] Because the agency had not made them part of the official record, the court ignored numerous internal agency documents produced during discovery that strongly suggested that there was "significant disagreement" among the agency's own scientists as to the safety of GM foods.[239]

FDA decided in late 1999 to hold a series of public hearings to revisit the 1992 Policy Statement. The agency's apparent willingness to consider a new approach inspired the same groups that challenged the 1992 Policy Statement in court to file a petition on March 21, 2000 demanding that FDA repeal that policy and promulgate rules requiring GM foods to be evaluated as food additives and to be appropriately labeled.[240] The petition made liberal use of internal FDA documents indicating that the agency staff did not agree with many of the scientific assessments underlying the 1992 Policy Statement. In particular, it quoted from numerous internal documents in which FDA scientists challenged the notion that modern genetic engineering techniques were merely extensions of traditional breeding techniques.[241]

On May 3, 2000, FDA announced that it would propose new regulations governing genetically modified foods, in light of the

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235. *Id.* at 22,986.

236. *Id.* at 22,987.

237. *Alliance for Bio-Integrity*, 116 F. Supp. 2d at 179.

238. *Id.* at 177.

239. *Id.*

240. Center for Food Safety, Petition Seeking the Establishment of Mandatory Pre-Market Safety Testing, Pre-Market Environmental Review & Labeling for All Genetically Engineered Foods (Mar. 21, 2000) [hereinafter Center for Food Safety, FDA Petition, 3/21/2000].

241. Center for Food Safety, FDA Petition, 3/21/2000, *supra* note 240, at § II.B. The documents also revealed staff concerns for the toxic and allergenic potential of GM plants and the possibility of stimulating antibiotic resistant pathogens. *Id.* at § II *passim.*

public hearings.[242] The proposed regulations, along with guidelines for labeling genetically modified foods, were published in the *Federal Register* on January 18, 2001.[243] The proposed regulations would require manufacturers and importers to provide FDA with pre-market notification of their intent to market GM foods that have not been subject to a previous pre-market notification. The labeling guidelines do not require that GM foods be labeled, but instead offer suggestions for statements that would be appropriate on labels of foods consisting of or containing materials from GM plants.[244]

Immediately following the 2001 inauguration of President George W. Bush, Chief of Staff Andrew H. Card wrote a memorandum to the heads and acting heads of all executive agencies asking them to withdraw from the Office of the Federal Register (OFR) all proposed and final regulations that the departments and agencies had submitted to the OFR but which hand not yet been published in the *Federal Register*.[245] The FDA proposed regulations had already been published, however, and they will presumably be reviewed by the new Administration during the time allowed for the public to comment on their contents. In the meantime, the agency apparently continues to adhere to the 1992 Policy Statement.

D. The Role of Substantial Equivalence in FDA's Regulation of GM Foods

FDA's May, 1992 Policy Statement recognizes that "the transferred genetic material and the intended expression product or products" in GM foods would ordinarily be "food additives" if those materials were not GRAS.[246] Although the agency may invoke the FDCA's formal food additive procedures "in cases where safety questions exist sufficient to warrant formal premarket review by

242. Press Release, Food & Drug Administration, FDA to Strengthen Pre-Market Review of Bioengineered Foods (May 3, 2000), *available* at www.fea.gov/bbs/topics/NEWS/NEW00726.html.

243. Premarket Notice Concerning Bioengineered Foods, 66 Fed. Reg. 4706 (Food & Drug Administration, proposed Sept. 22, 2000) [hereinafter FDA Proposed Bioengineered Food Regulations, 2000].

244. Draft Guidance for Industry: Voluntary Labeling Indicating Whether Foods Have or Have Not Been Developed Using Bioengineering, 66 Fed. Reg. 4839 (Food & Drug Administration, Nov. 15, 2000).

245. Memorandum for the Heads and Acting Heads of Executive Departments and Agencies from Andrew H. Card, Jr., 66 Fed. Reg. 7702 (Jan. 20, 2001) [hereinafter Card Memorandum, Jan. 20, 2001].

246. 1992 FDA Policy Statement, *supra* note 17, at 22,990.

FDA to ensure public health protection,"[247] it anticipates that "[i]n most cases, the substances expected to become components of food as a result of genetic modification of a plant will be the same as or *substantially similar* to substances commonly found in food, such as proteins, fats and oils, and carbohydrates" and would therefore pass the GRAS test.[248] The primary exceptions to the agency's willingness to presume that added substances are GRAS involve transfers of genes coding for proteins, carbohydrates, fats or oils that: (1) can cause allergenic responses in some consumers, (2) are known to be toxic, or (3) are likely to become a "macro-constituent in the human or animal diet" and thereby affect the nutritional value of the genetically modified food.[249]

The guidance document that accompanied the policy statement (the 1992 Guidelines) provides an "assessment scheme" that focuses on the "characteristics of the new plant variety, based on characteristics of the host and donor species, the nature of the genetic change, the identity and function of newly introduced substances, and unexpected or unintended effects that accompany the genetic change."[250] The heart of the assessment scheme is a group of flow charts that pose a series of relevant questions about the host plants, donor species, and the introduced substances. The flow charts lead to three possible endpoints—"(1) [n]o concerns, (2) new variety not acceptable, and (3) consult FDA."[251] The "scientific concepts" underlying the guidance document are "consistent with the concepts of *substantial equivalence* of new foods discussed in [the OECD document]."[252] Thus, the "substantial equivalence" doctrine sets the tone for the agency's general approach to evaluating the food additive status of GM foods. The following analysis of the agency's reasoning process suggests that the agency may have allowed substantial equivalence to serve as a convenient vehicle for avoiding its statutory responsibilities under the FDCA.

1. The Status of Proteins Produced by the Host Plant—The purpose of a gene splicing exercise is usually to cause a plant to increase or decrease the level of a protein that the plant previously produced or to produce a protein that the plant had not previously produced. When a genetic modification causes the plant to produce more or less of a protein that the plant previously produced, the

247. *Id.*
248. *Id.* at 22,985 (emphasis added).
249. *Id.* at 22,993 fig. 1.
250. *Id.* at 22,992.
251. *Id.*
252. *Id.* (emphasis added).

genetic modification might change the amount of the protein in the plant or change the amount of substances (carbohydrates, fats and oils) produced by the action of protein enzymes.[253] The host species itself is the primary focus of the safety inquiry in such cases, and the 1992 Guidelines suggest that the manufacturers first examine whether the host species has a history of safe use.[254]

a. Host Species With a History of Safe Use—The 1992 Guidelines reflect a "basic" premise, flowing from the substantial equivalence principle, "that a long history of safe use of the host species in food provides much information regarding the potential" of GM varieties "to produce toxicants and antinutrients (substances that adversely affect the nutritional quality of food)."[255] If the host plant has a history of safe use and additional testing does not appear "warranted," then the inquiry shifts to whether the concentration and bioavailability of important nutrients in the food produced by the modified plant are within the range ordinarily seen in the host species.[256] If so, "no concerns" are raised regarding the GRAS status of the GM food.[257] If not, appropriate labeling might be required under the FDCA's labeling authorities.[258]

The Guidelines offer only the vaguest suggestions for determining whether testing is "warranted" for host species with a history of safe use. Noting that it is "not possible to establish a complete list of all toxicants that should be considered for each plant species," the Guidelines suggest that the naturally occurring toxicants in the host species of highest concern are those that have been "documented to cause harm in normal or animal diets" or that have been "found at unsafe levels in some lines or varieties of that species or related species."[259] In many cases, "characteristic properties (such as a bitter taste associated with alkaloids)" provide telltale signs of the presence of specific natural toxicants.[260] When such characteristics provide "an assurance" that such toxicants are not present in unsafe levels, analytical or toxicological tests might not be necessary.[261]

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253. Bohrer, *Biotechnology*, *supra* note 11, at 657.

254. 1992 FDA Policy Statement, *supra* note 17, at 22,995 fig. 2. The Policy Statement suggests that testing may be required if the host species is an "exotic species" that does not have a history of safe use. *Id.* at 22,996.

255. *Id.* at 22,994.

256. *Id.* at 22,995 fig. 2.

257. *Id.*

258. *Id.* at 22,996.

259. 1992 FDA Policy Statement, *supra* note 17, at 22,996.

260. *Id.*

261. *Id.*

This wholesale delegation to the manufacturer of the safety assessment process seems inconsistent with the regulatory regime established by Congress for food additives. The Guidelines appear to erect an extra-statutory generic presumption that any change that results in an increase or decrease in the levels of a protein that already exists in a food plant, whether or not it is known to be toxic, is safe unless the manufacturer, in the exercise of its scientific judgment, concludes that further testing is necessary. If the legality of this subtle shift in the burden of proof from the manufacturer to the agency is questionable, its wisdom as a matter of public policy is even less clear.

Modifying a food plant with a history of safe use to *decrease* the level of a previously produced expression product might not at first glance appear to raise a "food additive" question at all, because the result of the modification is to take away, rather than add a substance to the food. A closer inspection, however, reveals that the food additive provisions of section 409 are implicated. The modification constitutes the addition of a substance (the gene) that "otherwise affects the characteristics" of the food.[262] The statutory definition of "food additive" does not require that the change affect the characteristics of the food in an adverse way. Thus, even changes that decrease the level of an expression product raise the GRAS question.

When the expression product being reduced is a substance that is "already present at generally comparable or greater levels in currently consumed foods," the Guidelines apply the substantial equivalence doctrine to conclude that there is "unlikely to be a safety question sufficient to call into question the presumed GRAS status of such naturally occurring substances."[263] The Guidelines further apply the substantial equivalence doctrine to conclude that "minor variations in molecular structure" in the expressed products that do not affect safety will not ordinarily affect the GRAS

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262. 21 U.S.C. § 321(s) (1994).

263. 1992 FDA Policy Statement, *supra* note 17, at 22,990. FDA's very first request for an informal food additive consultation regarding a GM food—a request from Calgene Corp. regarding the status of its new FLAVR SAVR® genetically modified tomato—involved a genetic engineering exercise that reduced the level of a previously expressed protein. Calgene, 1992 Advisory Opinion Request. Calgene had inserted into its tomato an "antisense" gene that inhibited the action of an enzyme that causes tomatoes to rot. As a result, ripe FLAVR SAVR® tomatoes remained intact for a longer period of time, thus increasing their "shelf life" and allowing them to ripen on the vine before being harvested for market. On May 17, 1994, FDA sent a letter to Calgene advising it of the agency's conclusion that "FLAVR SAVR® tomatoes have not been significantly altered when compared to varieties of tomatoes with a history of safe use" and were therefore GRAS. Availability of Letter Concluding Consultation, 59 Fed. Reg. 26,647 (Food & Drug Admin., May 23, 1994).

status of those substances.[264] This broad reliance on substantial equivalence may prove unduly optimistic. Some enzymes in plants digest toxins otherwise present in those plants. Reducing the levels of such enzymes could result in a corresponding increase in the level of the toxin, which could in turn result in adverse health effects in consumers.[265]

Adding a gene that *increases* the level of a previously produced expression product in a food plant with a history of safe use clearly raises the food additive question, because the modification constitutes the addition of a substance (the gene) that "otherwise affect[s] the characteristics" of the food.[266] The agency apparently assumes (no doubt accurately) that a manufacturer would not intentionally attempt to make a food plant more toxic by increasing the levels of previously produced toxic proteins, and the 1992 Guidelines do not address that scenario.[267] They only briefly allude to the possibility that gene splicing might inadvertently activate a quiescent metabolic pathway to cause a plant to produce more of a previously produced toxin, but they find the likelihood of such an unexpected event to be "extremely low."[268] Invoking the substantial equivalence concept, the Guidelines conclude that "the use of host plants with a history of safe use, coupled with a continuation of sound agricultural practice, will minimize the potential for adverse public health consequences that may arise from increased levels of unknown or unexpected toxicants."[269]

The Guidelines adopt essentially the same posture with respect to genetic modifications that result in increased levels of proteins not known to be toxic. The Guidelines note that "characteristic properties" of the host plant can provide telltale signs of the presence of specific natural toxicants and suggest that when such characteristic properties provide "an assurance" that such toxicants

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264. 1992 FDA Policy Statement, *supra* note 17, at 22,990.

265. *See* Bohrer, *Biotechnology*, *supra* note 11, at 672 (recognizing that reducing the level of a protein could cause adverse health effects if "*reduction* [sic] in the target protein level [resulted in the] diminution of an enzyme responsible for the breakdown of a natural plant toxicant").

266. 21 U.S.C. § 321(s) (1994).

267. Professor Bohrer likewise concludes that it is "unlikely that any producer of genetically engineered food plants would choose to introduce a protein known to be toxic or allergenic, or even one similar to known toxic or allergenic proteins." Bohrer, *Biotechnology*, *supra* note 11, at 663.

268. 1992 FDA Policy Statement, *supra* note 17, at 22,987. The Guidelines note that, in theory, "genetic modifications have the potential to activate cryptic pathways synthesizing unknown or unexpected toxicants, or to increase expression from active pathways that ordinarily produce low or undetectable levels of toxicants." *Id.* at 22,991-92.

269. *Id.* at 22,992.

are not present in unsafe levels, analytical or toxicological tests might not be warranted.[270] Otherwise, the Guidelines concede that it is "not possible to establish a complete list of all toxicants that should be considered for each plant species."[271] Apparently, the manufacturer is free to conclude without any testing whatsoever that a plant with a previous history of safe use containing increased levels of a previously produced protein not "known" to be toxic is substantially equivalent to the unmodified plant and is therefore GRAS. So long as qualified experts agree with the manufacturer's conclusion, it need not subject the GM plant to the food additive approval process.

b. Host Species Without a History of Safe Use—If the host plant does not have a history of safe use, the substantial equivalence doctrine is largely inapplicable. Even if the modified plant is substantially equivalent to the host plant, there is no basis for concluding that the GM plant is safe, because there is no history of safe use of the host plant. The Guidelines suggest that manufacturers conduct testing to "provide evidence that toxicant levels" in the genetically modified plant do not "present a safety concern."[272] The Guidelines offer some broad suggestions for determining what kind of tests could adequately "establish that the toxicant levels are in a safe range."[273] This approach appears consistent with the statutory definition of GRAS, which in the case of substances not recognized by experts to be safe because of experience based on common use in food still allows a GRAS determination to be based upon "scientific procedures."[274] It may nevertheless be disturbing to a public that is not inclined to trust manufacturers to make good decisions about whether to test and about how to interpret the test results.

First, the 1992 Guidelines allow the manufacturer to decide whether a food has a history of safe use. In some contexts, this decision can depend upon the resolution of technically complex and policy-rich questions. The manufacturer's decision may, however, be fairly transparent. A company attempting to market a genetically engineered plant without a significant history of use as a food (e.g., an edible pinecone) would probably attract the attention of the government and consumer activists. If, however, the manufac-

270. *Id.* at 22,996.

271. *Id.*

272. *Id.* 22,995 fig. 2. The Guidelines advise, for example, that "[i]f exotic species are used as hosts, testing may be needed to assure the safety and wholesomeness of the food." *Id.* at 22,996.

273. *Id.* at 22,996.

274. 21 U.S.C. § 321(s) (1994).

turer incorporated the GM plant into processed food (e.g., GM seaweed used as a stabilizer in ice cream), the decision might not be so transparent. Thus, to the extent that the decision raises close technical and policy questions, FDA has placed the burden of proof on itself to detect and prove that foods made from plants without a history of safe use are not GRAS.

Second, the 1992 Guidelines allow the manufacturer to decide what tests of the GM plant are appropriate for assessing a GM food's safety and how to interpret the test results. If the manufacturer does not select appropriate tests for supporting that determination or if the manufacturer is overly generous in interpreting the results of such tests, the government may still seize the resulting GM food if it can prove to a court that the food is not GRAS. While this should not be an especially difficult task in the case of host plants that are not foods, the agency's approach still leaves the product on the market during the time that it takes the government to act, and it requires the government to put together a convincing case.[275]

2. The Status of Expression Products Not Produced by the Host Plant—If the inserted gene results in an expression product that the host plant did not previously produce, the 1992 Guidelines draw an important distinction between a protein that is a constituent of some other food and all other proteins.[276] Underlying this distinction is the tacit conclusion, reflecting still another application of the substantial equivalence doctrine, that a protein that is a constituent of a plant that has traditionally been consumed as food is presumptively GRAS when it becomes a constituent of another food plant.[277]

a. Genes from Organisms Used in Foods—If the expression product of a transferred gene was a constituent of some other food in existence prior to 1958, then the GRAS provision of section 409 is applicable if experts qualified by scientific training and experience agree that "scientific procedures or experience based on common use in food" adequately demonstrate that the protein is "safe under

275. *See supra* Section III.B.

276. 1992 FDA Policy Statement, *supra* note 17, at 22,990. Before initiating that inquiry, however, the manufacturer may avoid food additive status by concluding that the newly produced protein did not wind up in any food derived from the plant. *Id.* at 23,000. Once again, it is apparently up to the manufacturer to make the critical determination whether or not the new expression product is in fact not present in food derived from the GM plant.

277. The 1992 Guidelines take the position that the transferred genetic material itself is normally GRAS, because "[n]ucleic acids are present in the cells of every living organism, including every plant and animal used for food by humans or animals, and do not raise a safety concern as a component of food." *Id.* at 22,990.

the conditions of its intended use."[278] According to the 1992 FDA Policy Statement, when the expression product is a substance that was "already present at generally comparable or greater levels in currently consumed foods," there is "unlikely to be a safety question sufficient to call into question the presumed GRAS status of such naturally occurring substances. . . ."[279] The agency also posits that "minor variations in molecular structure" in the expressed products that do not affect safety should not ordinarily affect the GRAS status of the protein.[280] The Guidelines urge the manufacturer to pay attention to (1) the characteristics of the plant or other organism from which the transferred genes originated (donor species), and (2) the proteins and any associated carbohydrates or fats and oils expressed by the transferred genes in the host plant (expression products).[281]

Donor Species. The 1992 Guidelines suggest that the manufacturer make two safety-related inquiries about the donor species. First, the manufacturer should ask whether "food from the donor [is] commonly allergenic," and, if so, whether it can "be demonstrated that the allergenic determinant has not been transferred to the new variety of host plant."[282] Since the 1992 Guidelines do not suggest any particular tests that might be useful in answering this question, the manufacturer may apparently base its conclusion upon "available" information and/or the manufacturer's general knowledge. If food from the donor species *is* commonly allergenic, the Guidelines imply that the manufacturer must be prepared to demonstrate that the allergenic determinant was not transferred to the host plant. Again, the manufacturer may rely upon its "knowledge," rather than "scientific procedures," to support its conclusion.[283]

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278. 21 U.S.C. § 321(s) (1994).

279. 1992 FDA Policy Statement, *supra* note 17, at 22,990; *see* Bohrer, *Biotechnology*, *supra* note 11, at 657–58.

280. 1992 FDA Policy Statement, *supra* note 17, at 22,990. This appears to conflict with the conclusion of Noah and Merrill that "general recognition of the safety of a substance in a different product, or at a different level, [will] not suffice." Noah & Merrill, *Starting from Scratch*, *supra* note 5, at 353.

281. 1992 FDA Policy Statement, *supra* note 17, at 22,997 fig. 3; 22,999 fig. 4; 23,001 fig. 5; 23,003 fig. 6. Interestingly, the Policy Statement applies the substantial equivalence approach to expression products derived from all "currently consumed" foods, and not merely to foods in existence prior to January 1, 1958. There is, of course, some possibility that plants that are "currently consumed" in the year 2000 were not commonly used in food prior to January 1, 1958. *Id.* at 22,996. The Policy Statement apparently does not view this as a troubling possibility.

282. *Id.* at 22,998.

283. *Id.* (concluding that "[k]nowledge of the identity of the allergenic determinant of the donor, coupled with appropriate knowledge of the genetic fragment that has been trans-

It is certainly conceivable that a manufacturer's "knowledge" of the donor plant and the transferred gene could meet the "experience based on common use in food" half of the GRAS test for substances commonly used in foods prior to January 1, 1958. Rather than trusting the manufacturers to make this determination accurately, however, consumers who are subject to food allergies may prefer to be apprised of the fact that an item of food came from a plant containing transferred genes from an allergenic donor plant so that they can apply their own "knowledge" in deciding whether to take the risk that the allergenic determinant has been transferred to the food.

The second inquiry with respect to the donor species is whether the "characteristics of the donor species, related species, or progenitor lines warrant analytical or toxicological tests."[284] The 1992 Guidelines offer very little guidance on how a manufacturer transferring genes from donor species commonly used in foods to other food plants would determine whether the characteristics of the donor plant or related or progenitor lines would "warrant" analytical or toxicological tests. In discussing the potential health effects of GM foods generally, the agency concedes that "genetic modifications have the potential to activate cryptic pathways synthesizing unknown or unexpected toxicants,"[285] but it finds the likelihood of such an untoward result of a genetic exchange to be "extremely low."[286] Thus, a manufacturer may generally rely upon the substantial equivalence concept to conclude that gene transfers from food-use species that do not contain known toxins will result in GM plants that are as safe to consume as the unmodified plants.

If the donor species does contains a gene coding for a known toxin, the manufacturer must be sure that the transfer does not bring the "toxic" gene across in a way that allows it to be expressed in a toxic protein, fat or carbohydrate. The Guidelines suggest that manufacturers approach this situation in the same way that they approach intraspecies transfers from food plants that contained genes coding for toxins.[287] Absent "sufficient evidence that the toxicant has not been transferred to the new variety of host plant, such transfer should be assumed, and analytical and/or toxicological tests

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ferred from the donor to the new plant variety, may provide sufficient evidence that the allergenic determinant has not been transferred to the new variety of the host plant").

284. *Id.*

285. *Id.* at 22,991–92.

286. *Id.* at 22,987.

287. *Id.* at 22,998.

may be warranted."[288] Thus the Guidelines apparently take the position that in cases where the donor species contains a gene that codes for a known toxin, the GRAS determination may not rely upon "experience based on common use in food," but must instead rely upon "scientific procedures."[289] In cases involving such "donor-associated toxicants," the Guidelines suggest that "analytical or toxicological studies" designed by the manufacturer may "provide assurance that the new variety is safe," and FDA encourages manufacturers "to consult with the agency on testing protocols."[290] This broad grant of discretion to manufacturers to come up with protocols for providing that an added substance is safe stands in stark contrast to the FDA's food additive regulations, which specify in some detail the kinds of tests that proponents of food additives must supply to the agency in order to obtain FDA approval of a food additive.[291]

Expression Products. Having examined the characteristics of the donor species, the manufacturer must next focus its attention on the expression products of the transferred genes in the host plant. If the introduced protein is derived from a food source that is not known to be allergenic,[292] the manufacturer must determine whether any expressed protein is "reported to be toxic."[293] The Guidelines do not suggest any sources for the manufacturer to consult in conducting this inquiry. Apparently, anything from a textbook example to a single citation in the worldwide literature will suffice. The Guidelines do provide an example of certain lectins in kidney beans that are known to be toxic but are inactivated by cooking. Transfers of genes coding for such lectins from kidney beans to foods, like tomatoes, that may be eaten raw would raise safety concerns.[294] The Guidelines suggest that manufacturers "[c]onsult FDA" in such situations.[295] The 1992 Guidelines suggest

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288. *Id.*

289. 21 U.S.C. § 321(s) (1994).

290. 1992 FDA Policy Statement, *supra* note 17, at 22,998.

291. 21 C.F.R. § 171.1 (2002); *see also* Food & Drug Admin., Office of Premarket Approval, Guidance for Submitting Petitions and Notifications, *available at* http://www.cfsan.fda.gov/~dms/opa-toc.html.

292. The 1992 Guidelines do not suggest that the manufacturer determine whether expression products from nonallergenic food sources are purported to be allergenic. The agency may have assumed that proteins expressed by genes transferred from nonallergenic foods are not likely to be allergenic, or it may have decided that it would be too difficult for manufacturers to determine the allergenicity of individual proteins, given the current absence of generally accepted allergenicity testing models. *See supra* Part I.B.1.b.

293. 1992 FDA Policy Statement, *supra* note 17, at 22,994.

294. *Id.* at 22,994.

295. *Id.* at 29,999 fig. 4 at 17c. The next inquiry is whether the intake of the introduced protein is "generally comparable to the intake of the same or similar protein in the donor or

similar toxicity-related inquiries for carbohydrates, fats and oils that are expression products of introduced genes.[296]

FDA has apparently made a generic determination that any introductions of new proteins into the host species and any alterations in the identity, structure, or composition of carbohydrates, fats and oils in the host plant due to gene transfers from donor species that are used in foods are presumptively GRAS in the host food based upon their common use in the donor food. Such food-species-to-food-plant transfers raise "safety concerns" that call for FDA consultation only if the new expression products are known to be toxic or otherwise raise vaguely specified red flags. Other than a general reliance upon the doctrine of substantial equivalence, the Guidelines make no attempt to support a generic conclusion that the addition of genes that affect the characteristics of food by adding a new protein, altering the host plant's carbohydrate profile or changing the identity, structure, or composition of host plant fats and oils are generally recognized by qualified experts to be safe. However reasonable this generic determination may be from the prospective of the agency's scientists, it does not comport with the statute under which the agency operates, because it effectively relieves the manufacturer of the burden of demonstrating that the food is GRAS.

b. Genes from Organisms Not Used in Foods—If the protein expressed by a transferred gene was not a constituent of some other food in existence prior to 1958, there would presumably be no "experience based on common use in food," and the GRAS provision of section 409 would apply only if the manufacturer demonstrated through "scientific procedures" that experts qualified by scientific training and experience have concluded that the protein or other expression product was "safe under the conditions of its intended use."[297] One might imagine that this would be an exceedingly difficult showing and that such transfers would ordinarily require the manufacturer to file a food additive petition in accordance with the regulations promulgated under section 409.[298]

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other food." *Id.* at 23,000. Again, the Guidelines do not suggest any scientific procedures or protocols for comparing intake routes of proteins for purposes of this inquiry. If the human intake of the introduced protein is not comparable, the Guidelines recommend that the manufacturer assess the biological function of the introduced protein in the same manner (discussed below) as if the protein had not been derived from a food source. *Id.* at 29,999 fig. 4 at 13.

296. *Id.* at 23,002.

297. 21 U.S.C. § 321(s) (1994).

298. One substance that meets this description and is of obvious interest is the antibiotic-resistance enzyme that gene-splicers use as a "marker" to identify plants for which the

The 1992 Policy Statement, however, applies the substantial equivalence doctrine to support a much more optimistic view of the possibility of GRAS status for transfers of genes from nonfood species into plants used for food. Once again, the 1992 Guidelines focus first on the donor species generally and then on the expression products of the transferred gene in the host food plant.[299]

Donor Species. If the manufacturer has "knowledge" of a toxic property of the donor species, a related species, or progenitor line, it must determine whether further testing is needed, preferably in consultation with FDA. Although it is certainly possible that a gene transferred from a toxic donor plant would code for a toxic protein in the host plant,[300] the 1992 Guidelines recognize that it is also possible safely to transfer genes that do not code for toxic expression products.[301] The Guidelines caution that "[u]nless there is sufficient evidence that the toxicant has not been transferred to the new variety of host plant, such transfer should be assumed, and analytical and/or toxicological tests may be warranted."[302] The Guidelines suggest that "analytical or toxicological studies" designed by the manufacturer could "provide assurance that the new variety is safe," and the agency encourages manufacturers "to consult with the agency on testing protocols."[303] The voluntary aspect of these testing suggestions, however, differs dramatically from the FDA's detailed testing requirements for food additives.

When the manufacturer does not have "knowledge" of any toxic properties of the donor species or related species, the 1992 Guidelines suggest that "[t]he potential of the donor(s) to contribute undesirable characteristics to the new plant variety should be assessed"[304] to the extent that information on attributes of the donor

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gene-splicing operation has been successful. The gene coding from this enzyme does not come from a species consumed as food, and some scientists have concerns about its allergenicity, its potential to reduce the therapeutic effect of the antibiotic in humans, and its potential to hasten the development of antibiotic-resistant pathogens. *See infra* Part I.B.2.b. In the case of the most prominently used antibiotic marker gene, a gene coding for an enzyme causing resistance to the antibiotic kanamycin, the manufacturer decided to file a full-fledged food additive petition. FDA approved the petition almost four years later after an extensive but controversial investigation. 1994 Kanamycin Resistance Gene Approval, *supra* note 14, at 26,700-01.

299. *See supra* text accompanying notes 276–90.

300. The Guidelines offer the example of a transfer of a gene coding for a toxicant during hybridization of a cultivated variety with a wild, poisonous relative. 1992 FDA Policy Statement, *supra* note 17, at 22,998.

301. *Id.*

302. *Id.*

303. *Id.*

304. *Id.* at 22,996.

plant is "available."[305] They do not, however, suggest how the manufacturer might determine the modified plant's potential for allergenicity or other toxicity when there is no relevant experience with human consumption of the donor species. They do not advise any particular testing of the donor organisms to determine their toxicological profiles. Indeed, they explicitly recognize that "routine procedures for testing foods derived from new plant varieties for the presence of unknown allergens are not currently available," and they frankly acknowledge in a footnote that "[i]f the donor has no history of use in food, the issue of allergenicity cannot be addressed at this time."[306]

If no "scientific procedures" capable of assessing the allergenicity of a genetically modified food exist and the donor has no history of use in food at all, then the statute rather plainly precludes a GRAS finding for the genetically engineered food. The failure of the 1992 Guidelines to require manufacturers of such foods to file food additive petitions suggests that manufacturers are free to ignore the potential for allergenicity and find that such foods are GRAS based upon such testing as the manufacturers deem appropriate.[307] Similarly, manufacturers are apparently free to employ the substantial equivalence doctrine and such information as the manufacturer cares to gather on donor plant toxicity to support a GRAS conclusion on the toxicity question. Although the Guidelines do not erect a presumption in favor of the GRAS status of foods containing genes from nonfood species, they give manufacturers a great deal of discretion to base GRAS determinations on "scientific procedures."

Expression Products. The substantial equivalence doctrine plays a surprisingly prominent role with respect to the expression products of genes transferred from nonfood species. The 1992 Guidelines suggest that manufacturers should ask whether a novel protein introduced by the gene transfer is "substantially similar to an edible protein."[308] Since the Guidelines do not suggest that any scientific testing or other procedures should precede this determination, a manufacturer may apparently conclude that an added protein is GRAS on the basis of "experience based on common use

305. *Id.*

306. *Id.* at 23,000 n.6. The Guidelines offered that "[c]omparison of gene sequences to data banks of known allergens may become increasingly useful as the information on such proteins expands." *Id.*

307. *See* Bohrer, *Biotechnology*, *supra* note 11, at 664 n.56 (noting that under the 1992 Policy Statement "the potential for rare allergenicity is simply ignored").

308. 1992 FDA Policy Statement, *supra* note 17, at 22,999 fig. 4.

in food" of a "substantially similar" protein that the manufacturer determines to be "edible."[309] The Guidelines do not limit the term "edible protein" to substances that have been commonly used in food or even to substances that have commonly been eaten.

The legality of this aggressive use of the substantial equivalence doctrine depends upon whether Congress meant for the term "common use in food" in the GRAS exception to encompass not only substances commonly used in foods, but also substances that have never been used in foods but that are "substantially similar" to substances that have been commonly used in foods. Arguably, the statute does not preclude that interpretation, because it does not say "experience based on *the additive's* common use in food." On the other hand, one could persuasively argue that Congress intended for the GRAS exemption to be a narrow one applicable only to substances for which experience with the substances themselves justified a finding of safety.

If the introduced protein is neither derived from a food source nor substantially similar to an edible protein, the Guidelines recommend that the manufacturer assess the "biological function" of the introduced protein to determine whether it is "reported to be toxic" or otherwise raises a "safety concern."[310] Although they surmise that proteins functioning as enzymes usually do not raise safety concerns, they recognize that enzymes capable of producing substances that are not ordinarily digested by vertebrates or that are otherwise toxic (e.g., snake venom and the diphtheria toxin) do raise safety concerns.[311] As previously noted, the Guidelines do not specify how broadly the manufacturer must inquire in its search for "reports" of toxicity or if the manufacturer must consult the published literature at all. Similarly, the Guidelines provide very little insight into how the manufacturer might go about determining whether the introduced protein raises a "safety concern."

The 1992 Policy Statement ultimately leaves the relevant toxicity inquiries to the manufacturer's discretion, and they permit manufacturers to ignore the potential for allergenicity in gene transfers from nonfood species not known to be allergenic. While consumers can probably rest assured that reputable companies will not insert genes coding for diphtheria toxin or rattlesnake venom into

309. *See* Bohrer, *Biotechnology*, *supra* note 11, at 662 (concluding that "FDA will not require a premarket review of all inter-generic genetically-engineered food plants, even those containing proteins not previously found in foods (in statutory terms, without a 'history of safe use in food')").

310. 1992 FDA Policy Statement, *supra* note 17, at 22,999 fig. 4, 23,000.

311. *Id.* at 23,000 & n.7.

food intended for human consumption, the Guidelines give manufacturers considerable leeway to rely upon their "knowledge" and the substantial equivalence principle. Consumers could be forgiven for worrying that at the margins, a manufacturer might expand or contract the universe of "known" toxic activities of transferred proteins to conclude that commercially valuable GM plants do not raise "safety concerns." They cannot rest assured that such proteins are subject to the full panoply of tests otherwise required of food additives.

3. Notice of GRAS Determinations—Although manufacturers and importers must provide notice to FDA of any change in GM food that results in the addition of a "food additive" within the meaning of section 409,[312] the statute does not require manufacturers and importers to inform FDA of any additions of substances that they determine to be GRAS. The 1992 Policy Statement leaves the GRAS determination up to the manufacturer or the importer and merely offers guidance on situations for which a "consultation" with the agency might be appropriate. As of late 2000, companies had invoked the consultative process about 50 times, but only six of those consultations occurred during 1999 and 2000.[313] It is not unlawful for a manufacturer or an importer to fail to "consult" with the agency or to fail to seek an "affirmation" of the GRAS status of a genetic modification.

On January 18, 2001, FDA issued proposed regulations that would require a manufacturer or importer to provide FDA with a pre-market biotechnology notice (PBN) of its intent to market any "bioengineered food" unless the food was derived from a previously addressed plant line for which FDA expressed no concerns.[314] After receiving the PBN, FDA would have 15 days to determine whether the submission contained all of the required information and 120 days to send the submitter FDA's evaluation of the submitter's conclusion that the GM food was as safe as comparable food.[315] A conclusion that a GM food is as safe as comparable food is, under the agency's application of the substantial equivalence doctrine, equivalent to a GRAS finding.[316] Expressing confidence

312. 21 U.S.C. 348(b)(5) (1994).

313. *See* Food & Drug Admin., Foods Derived from New Plant Varieties Derived through Recombinant DNA Technology: Final Consultations under FDA's 1992 Policy (Nov. 2000).

314. FDA Proposed Bioengineered Food Regulations, 2001, *supra* note 243, at 4732–33.

315. *Id.* at 4733.

316. The proposal recommends that the manufacturer consult with FDA prior to submitting the PBN "to identify and discuss relevant safety, nutritional, or other issues." FDA Proposed Bioengineered Food Regulations, 2001, *supra* note 243, at 4730. It also provides

that the food industry had already been consulting with FDA with respect to all GM foods,[317] the agency believed that compliance with regulations would not substantially burden manufacturers in the future.

In explaining why pre-market notification was needed, the agency appeared to depart somewhat from its prior embrace of the substantial equivalence doctrine. Because of the "greater range of sources of substances" that modern biotechnology could introduce into plants, FDA found "a greater likelihood" that some introduced substances "will be significantly different from substances that have a history of safe use in food or may otherwise not satisfy the GRAS standard."[318] Moreover, the agency acknowledged the greater potential of genetic engineering techniques "for introducing unintended effects through mutations."[319] FDA justified limiting the pre-market notification process to GM foods on the ground that the agency's fifty to sixty years' worth of experience with conventional breeding techniques had not produced any foods with unexpected adverse traits.[320] Since a greater potential existed for GM foods to "present legal status issues and thus require greater FDA scrutiny" than for foods developed using traditional breeding techniques, FDA decided to require manufacturers to notify the agency prior to marketing GM products.[321]

FDA cited as legal authority for the premarketing notification requirement its power under Section 701(a) of the FDCA to issue regulations for the efficient enforcement of the Act.[322] The agency concluded that this authority "extend[ed] to both regulations that supplement a specific statutory mandate as well as regulations that are justified by the statutory scheme as a whole."[323] Citing the 1978 D.C. Circuit opinion in *National Confectioner's Association v. Califano*,[324] the agency argued that it was "important to consider both the statutory purpose as well as the practical aspects of the situation, including the possible enforcement problems that may be

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procedures for maintaining the confidentiality of trade secret information during the consultation and evaluation process. *Id.* at 4733–34.

317. *Id.* at 4707.

318. *Id.* at 4709. The agency further believed that pre-market notification was important to give it an opportunity to ensure that GM foods are properly labeled under section 403 of the FDCA. *Id.* at 4709–10.

319. *Id.* at 4710.

320. *Id.* at 4711.

321. *Id.* at 4711.

322. 21 U.S.C. § 371(a) (1994).

323. FDA Proposed Bioengineered Food Regulations, 2001, *supra* note 243, at 4712.

324. 569 F.2d 690, 693 (D.C. Cir. 1978).

encountered by FDA."[325] Pre-market notification would, in the agency's view, ensure that it was aware of all GM foods entering commercial distribution that were subject to FDA's jurisdiction and would "help to ensure that all market entry decisions by the industry are made consistently and in full compliance with the law."[326]

While the agency's very brief legal analysis of its authority to require pre-market notification of all GM foods is plausible, it is by no means compelling. Section 701(a) grants FDA general authority "to promulgate regulations for the efficient enforcement of this [Act]."[327] Arguably, a broad pre-market notification requirement is necessary for the efficient enforcement of the Act's food additive provisions in the context of GM foods. Without premarketing notification, the agency cannot, as a practical matter, evaluate the manufacturer's determination that a GM food is substantially equivalent to a non-GM food and therefore GRAS, because the agency lacks the resources to conduct the vast food monitoring and testing program necessary to detect every possible GM food that some manufacturer has determined to be GRAS.

In *National Confectioners*, a trade association challenged an FDA regulation requiring candymakers to mark each shipping container with a code identifying the plant where the candy was packed and its production or packaging lot and to keep records of the initial distribution of the candy for a two-year period.[328] Although the FDCA did not explicitly authorize such regulations, the agency reasoned that it would advance the "efficient enforcement" of the Act by expediting recalls of dangerous or potentially dangerous products.[329] The court upheld the regulations. Like the regulations at issue in *National Confectioners*, the pre-market notification regulations for GM foods imposed somewhat burdensome requirements on all products to enhance effective enforcement against the presumably small minority of products that might violate the law.

Manufacturers might plausibly argue, however, that a general requirement for pre-market notification of all GM foods is so broad and burdensome that it cannot be justified as an exercise of FDA's general enforcement powers. A substance added to food is entirely outside of FDA's regulatory ambit so long as it is GRAS, because the term "food additive" is defined to exclude substances

325. FDA Proposed Bioengineered Food Regulations, 2001, *supra* note 243, at 4712.
326. *Id.*
327. 21 U.S.C. § 371(a)(1994).
328. 569 F.2d 690 (D.C. Cir. 1978).
329. *Id.* at 693.

that are GRAS. Arguably, FDA should not be allowed to leverage its authority to enforce controls that the statute empowers it to impose to support an assertion of authority over activities that are wholly outside its statutory reach. Noting that since 1992 FDA has consistently taken the position that the vast majority of all GM foods are likely to be GRAS, manufacturers could argue that it is arbitrary and capricious for FDA to cast so broad a net to capture so few fish.

At this point, the premarketing notification proposal is just that. The agency has given interested parties an opportunity to comment on the proposal, and it is subject to change or withdrawal. Should the Bush Administration allow this Clinton Administration proposal to go forward to final form, it would still be subject to judicial review for consistency with the FDCA and for arbitrariness and capriciousness. As things currently stand, the state of law is that manufacturers are free to market GM foods that they determine to be GRAS without consulting FDA.

4. Labeling GM Foods—Under section 403(a)(1) of the FDCA, a food is misbranded if its labeling is "false or misleading in any particular"[330] or if its labeling does not prominently feature "any word, statement, or other information" that FDA lawfully requires with "such conspicuousness (as compared with other words, statements, designs, or devices, in the labeling) and in such terms as to render it likely to be read and understood by the ordinary individual under customary conditions of purchase and use."[331] A food is also misbranded if its label does not bear "(1) the common or usual name of the food, if any there be, and (2) in case it is fabricated from two or more ingredients, the common or usual name of each such ingredient. . . ."[332] Under section 201(n), labeling is misleading if it fails to reveal all facts that are "material in the light of . . . representations or material with respect to consequences which may result from the use of the article to which the labeling . . . relates under the conditions of use prescribed in the labeling . . . or under such conditions of use as are customary or usual."[333]

The statute appears to grant FDA ample authority to require manufacturers and importers to label GM foods. The agency could, for example, conclude that the fact that a food derives from

330. 21 U.S.C. § 343(a)(1) (1994).

331. 21 U.S.C. § 343(f) (1994). The four main components of a food label as defined by the FDCA are: the common name or identity of the item, the quantity, name, and location of manufacturer, and ingredient and nutrition information. § 343.

332. § 343(i).

333. 21 U.S.C. § 321(n) (1994).

GM plants is "material" in light of implicit representations that it is what it appears to be (i.e., food derived from nonengineered plants). In addition, sufficient uncertainties surround the health "consequences" of GM plants that the agency could reasonably conclude that the fact that a food derives from GM plants is material in light of those consequences. The agency has, however, invoked the substantial equivalence doctrine to limit mandatory labeling primarily to GM foods that differ significantly from unmodified foods in ways that are nutritionally important.

In its 1992 Policy Statement, FDA specifically declined to require labels for all foods containing GM constituents.[334] The Policy Statement explains that modern genetic engineering techniques are merely "extensions at the molecular level of traditional methods,"[335] and it notes that the agency has not generally considered the methods used in the development of a new plant variety "to be material information within the meaning of section 201(n)."[336] FDA is "not aware of any information showing that foods derived by these new methods differ from other foods in any meaningful or uniform way, or that, as a class, foods developed by the new techniques present any different or greater safety concern than foods developed by traditional plant breeding."[337]

Public comments on the Policy Statement noted that in the context of irradiated foods the agency had concluded that "[w]hether information is material under section 201(n) . . . depends not on the abstract worth of the information but on whether consumers view such information as important and whether the omission of label information may mislead a consumer."[338] The Policy Statement explains that FDA had concluded that radiation could cause changes in the organoleptic properties of the finished food that, absent labeling, might mislead consumers into assuming that such foods were unprocessed.[339] It does not, however, explain how this distinguishes GM foods, at least some of which also experience organoleptic changes as a result of the genetic engineering

334. 1992 FDA Policy Statement, *supra* note 17, at 22,991.

335. *Id.*

336. *Id.*

337. *Id.*

338. FDA, Irradiation Regulations, 51 Fed. Reg. 13,376, 13,388 (Apr. 18, 1986); *see also* Silbergeld Testimony, Oct. 6, 1999, *supra* note 130.

339. Food Labeling; Foods Derived From New Plant Varieties, 58 Fed. Reg. 25,837, 25,837-41 (Food & Drug Admin., Apr. 28, 1993) [hereinafter 1993 FDA Labeling Policy Statement Request for Information].

technology.[340] Although the genetic engineering exercise unquestionably causes the engineered plant to be changed, the agency believes that the changes are generally not so substantial as to be "material" for purposes of the statutory labeling requirement.[341]

The 1992 Policy Statement does acknowledge a limited role for labeling in the context of GM foods. The agency reads section 403 to require manufacturers to inform consumers "by appropriate labeling, if a food derived from a new plant variety differs from its traditional counterpart such that the common or usual name no longer applies to the new food, or if a safety or usage issue exists to which consumers must be alerted."[342] In particular, the agency might require labeling to put sensitive subpopulations on notice of the possibility that a transfer from an allergenic donor plant to a previously nonallergenic food plant might have transferred a gene coding for an allergenic protein.[343] For example, labeling might be required for a tomato genetically engineered to produce a peanut protein absent sufficient information to demonstrate that the introduced protein could not cause an allergic "response in the potentially sensitive population."[344]

On the other hand, the 1992 Policy Statement does not propose to require labeling for gene transfers from species not known to be allergenic. Since the agency is "unaware of any practical method [to] predict or assess the potential for new proteins in food to induce allergenicity,"[345] it is apparently willing to assume either that such changes could never occur or that they would not be "material" if they did. This very aggressive reliance on the substantial equivalence principle effectively deprives consumers, who are likewise unaware of practical methods to assess the allergenic potential of such foods, of the option of playing it safe by avoiding such foods.

The 1992 Policy Statement also envisions a role for labeling when the "concentration and bioavailability of important nutrients in the new variety" are no longer within the "range ordinarily seen

340. The report of an expert panel convened by the Royal Society of Canada noted that "it could be argued that the case for labeling of GM food products is stronger than for irradiated ones, because genetic engineering may produce 'material changes' in the product itself." ROYAL SOCIETY OF CANADA REPORT, 2001, *supra* note 14, at 223.

341. 1993 FDA Labeling Policy Statement Request for Information, *supra* note 339, at 25,839.

342. 1992 FDA Policy Statement, *supra* note 17, at 22,991.

343. *Id.* at 22,987.

344. *Id.* at 22,991. The presence of the peanut protein gene "would be a material fact whose omission may make the label of the tomato misleading under section 403(a)...." *Id.*

345. *Id.* at 22,987.

in the host species."[346] Changes in bioavailability of a nutrient "due to changes in form of the nutrient or the presence of increased levels of other constituents that affect absorption or metabolism of nutrients" could have "potential nutritional impact" and thereby warrant changes in nutritional labeling.[347] For example, genetic modification of a fruit or vegetable that "produce[s] high levels of an indigestible carbohydrate that normally occurs at very low levels, or . . . convert[s] a normally digestible carbohydrate to an indigestible form" could raise nutritional concerns.[348] The Guidelines urge manufacturers to consult with FDA when genetic modifications result in any alterations that could affect the nutritional qualities in a carbohydrate "or the composition of fats or oils that are likely to be a macroconstituent in the diet."[349]

The court in *Alliance For Bio-Integrity v. Shalala*[350] upheld the agency's position on labeling GM foods. Rejecting the plaintiffs' arguments that FDA should have considered widespread consumer interest and the special concerns of religious groups and persons with allergies, the court held that the agency's conclusion that none of those concerns were "material" was not unreasonable.[351] In particular, the agency could reasonably interpret the word "material" to demand "unique risks to consumer health or uniform changes to food derived through rDNA technology."[352] The court

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346. *Id.* at 22,996.

347. *Id.*

348. *Id.* at 23,002.

349. *Id.* at 23,004. For example, "an alteration in the ratio of saturated to unsaturated fatty acids" could "have significant nutritional consequences, or result in marked changes in digestibility." *Id.* Surprisingly, the Policy Statement makes no attempt to define the critical term "macroconstituent," even by providing broad ranges of acceptable percentages in food. *See* Noah & Merrill, *Starting from Scratch*, *supra* note 5, at 410 n.353.

350. 116 F. Supp. 2d 166 (D.D.C. 2000).

351. 116 F. Supp. 2d at 181. The court applied the traditional *Chevron* two-step analysis. The Court in *Chevron* held that courts should be deferential to the agencies' interpretations of their own statutes:

> [I]f the statute is silent or ambiguous with respect to the specific issue, the question for the court is whether the agency's answer is based on a permissible construction of the statute. . . . If Congress has explicitly left a gap for the agency to fill, there is an express delegation of authority to the agency to elucidate a specific provision of the statute by regulation. Such legislative regulations are given controlling weight unless they are arbitrary, capricious, or manifestly contrary to the statute. Sometimes the legislative delegation to an agency on a particular question is implicit rather than explicit. In such a case, a court may not substitute its own construction of a statutory provision for a reasonable interpretation made by the administrator of an agency.

Chevron, U.S.A., Inc. v. Natural Resources Def. Council, Inc., 467 U.S. 837, 843–44 (1984).

352. 116 F. Supp. 2d at 178–79.

questioned whether FDA had the power under the FDCA to require labeling "in a situation where the sole justification for such a requirement is consumer demand."[353] In rejecting the plaintiffs' contention that the *process* of genetic modification was a "material" fact, the court relied upon FDA's application of the substantial equivalence principle to conclude that "foods produced through rDNA techniques do not 'present any different or greater safety concern than foods developed by traditional plant breeding.' "[354]

After *Alliance For Bio-Integrity*, FDA apparently has the authority to require labeling of GM foods that pose "unique risks to consumer health" or result in "uniform changes" to food. It is not at all clear, however, what either of these two findings requires by way of data and analysis. Surely, if some future GM food becomes ubiquitous in the food pipeline and subsequent studies reveal serious risks to the health of some human subpopulation (e.g., persons allergic to a protein uniquely present in the GM food) that were not anticipated by the manufacturer or importer, FDA would have the authority to require that products containing that food be labeled. The agency may have been unwise to impose upon itself the task of identifying and justifying "unique risks" attributable to a GM food. The "uniform" changes standard, however, might be easier to meet because a particular GM plant line will uniformly reflect changes induced by the genetic engineering process. Since most GM plants are changed in some major or minor way by the genetic engineering process, this avenue should allow FDA to justify labeling requirements for virtually any GM food. at the same time, the *Alliance For Bio-Integrity* opinion gives the agency considerable discretion not to require labeling of GM foods.[355]

As previously noted, FDA issued draft guidelines for labeling genetically modified foods on January 18, 2001.[356] The agency noted that during the eight intervening years since it had issued the 1992

353. *Id.* at 179.

354. *Id.*

355. The Policy Statement did not directly address the requirement in § 403(i) of the FDCA that if a food product is fabricated from two or more ingredients, the label must contain the "common or usual name of each such ingredient." 21 U.S.C. § 343(i) (1994). For example, a tomato that has been genetically engineered to contain a gene from a peanut plant seems to fit rather comfortably within the ambit of § 403(i). The agency's initial response to comments on the policy statement, however, noted that FDA has historically considered "ingredients" to be "substances from which a food is fabricated," and not "new constituents of plants introduced via breeding." 1993 FDA Labeling Policy Statement Request for Information, *supra* note 339, at 25,840. The agency solicited comments on whether there was a scientific basis for distinguishing between modern biotechnologies and traditional breeding technologies in defining the word "ingredient," but it has taken no further action in light of those comments. *Id.* at 25,840.

356. *See* FDA Draft GM Food Labeling Guidance, 2001, *supra* note 244.

Policy Statement, it had not become "aware of any data or other information that would form a basis for concluding that the fact that a food or its ingredients was produced using bioengineering is a material fact that must be disclosed under sections 403(a) and 201(n) of the act."[357] The agency therefore reaffirmed its 1992 decision not to require special labeling of all bioengineered foods.

Nevertheless, since it was clear to FDA that many consumers strongly believed that information about the GM status of food was "material," it decided to provide "guidance to assist manufacturers who wish to label their foods voluntarily as being made with or without the use of bioengineered ingredients."[358] The agency's goal was to "help manufacturers ensure that their labeling is truthful and not misleading."[359] For that reason, FDA cautioned manufacturers against using the word "free," as in "biotech free," because that term might imply that the food was superior to non-GM food, an implication that FDA has consistently rejected. In addition, the agency was not at all confident that manufacturers could deliver on the implicit promise that not a single molecule of GM material was present in food so labeled.[360] Thus, in FDA's view, "GM-free" labeling would be misleading to consumers and, hence, unlawful.

The guidance also warned that a manufacturer claiming that its food was not developed using GM material would have to substantiate that claim. It suggested that absent validated testing to ensure that specific food was free of bioengineered material, manufacturers would have to document handling practices in order to substantiate such claims.[361] Ultimately, however, the agency left it "to each firm's discretion to maintain appropriate documentation to demonstrate that the food was produced using traditional methods."[362]

Instead of requiring manufacturers of products containing GM foods to label those products, the labeling guidelines appear to employ the substantial equivalence doctrine to discourage companies who market products not containing GM foods from informing their consumers of that fact. Food suppliers are free to market most GM foods at will, but food suppliers attempting to appeal to consumers who are wary of GM foods must take great care in processing and labeling their products not to mislead

357. *Id.* at 4840.
358. *Id.*
359. *Id.*
360. *Id.*
361. *Id.* at 4841.
362. *Id.*

consumers into believing that non-GM foods are any better than GM foods. The document may have satisfied the demands of the biotechnology and food manufacturing trade groups for guidance. It did not respond to public interest group demands that consumers be told which products on the grocery shelves contain GM materials.

IV. EPA REGULATION OF GM FOODS

The Environmental Protection Agency exercises the primary authority for regulating pesticides under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA)[363] and the Food Drug and Cosmetic Act (FDCA).[364] Under FIFRA, no person may sell, distribute, or receive a pesticide unless it has been "registered" with EPA or has been exempted from the registration requirements.[365] The Act defines the term "pesticide" very broadly to include any substance "intended for preventing, destroying, repelling, or mitigating any pest" or "intended for use as a plant regulator, defoliant, or desiccant."[366] To obtain a registration for a pesticide, the registrant must demonstrate that when used in accordance with widespread and commonly recognized practice, it will not generally cause "unreasonable adverse effects on the environment."[367] This ordinarily requires the registrant to submit to EPA extensive information on the pesticide's identity, its environmental fate, its potential toxicity to humans and other animals, and its potential for ecological disruption.[368]

EPA does, however, have the authority to exempt whole classes of pesticides that the agency determines "to be of a character which is unnecessary to be subject to this [Act] in order to carry out the purposes of this [Act]."[369] The agency interprets this authority to allow it to exempt a pesticide or category of pesticides

363. 7 U.S.C. §§ 136–136y (1982 & Supp. IV 1986).

364. 21 U.S.C. § 346a (1994). EPA also has authority to regulate chemical substances under the Toxic Substances Control Act. 15 U.S.C. § 2601-2629 (1994). The agency has, however, apparently recognized that it would have to stretch the words "chemical substance" beyond recognition to apply the TSCA to genetically engineered plants. Environmental Protection Agency, Statement of Policy; Microbial Products Subject to the Federal Insecticide, Fungicide, and Rodenticide Act and the Toxic Substances Control Act, 51 Fed. Reg. 23,313, 23,324 (1986).

365. 7 U.S.C. § 136a(a) (1994).

366. *Id.* § 136(u).

367. 7 U.S.C. § 136c (1994).

368. 40 C.F.R. §§ 158.165, 158.170, 162.153 (2001).

369. 7 U.S.C. § 136w(b) (1994).

that possesses "a low probability of risk to the environment, and that is not likely to cause unreasonable adverse effects to the environment even in the absence of regulatory oversight under FIFRA."[370]

Under the FDCA as amended by the 1996 Food Quality Protection Act, a food is adulterated if it contains a pesticide residue, unless EPA has established a "tolerance" for the pesticide residue on that food or has exempted the food from the tolerance requirement.[371] The tolerance must be set at a "safe" level, and safety is defined to mean that "there is a reasonable certainty that no harm will result from aggregate exposure to the pesticide chemical residue, including all anticipated dietary exposures and all other exposures for which there is reliable information."[372] EPA may exempt a pesticide residue from the tolerance requirement only if the agency finds that the residue will remain "safe" in the absence of a tolerance in accordance with the same "reasonable certainty of no harm" standard.[373]

A. EPA Implementation Activities

As previously mentioned, FDA announced in its 1992 Policy Statement that it deferred to EPA all regulatory authority over plants that were genetically modified to express pesticidal substances, so long as they were not also modified to express nonpesticidal substances.[374] In November 1994, EPA issued a Proposed Policy Statement on GM pest-resistant plants (the 1994 Proposed Policy) that, *inter alia*, proposed comprehensive regulations aimed at clarifying the agency's role in the 1986 Coordinated Framework.[375] Although the agency took many years to finalize the

370. Regulations Under the Federal Insecticide, Fungicide, and Rodenticide Act for Plant-Incorporated Protectants (Formerly Plant-Pesticides), Final Rule 4, 66 Fed. Reg. 37,772, 37,773 (Envtl. Prot. Agency, July 19, 2001) [hereinafter EPA, FIFRA Plant-Incorporated Protectants Regulations, 2001].

371. 21 U.S.C. § 346a (1994).

372. 21 U.S.C. § 346a(c)(2)(A)(ii) (1994).

373. 21 U.S.C. § 346a(c)(2)(A)(i) (1994).

374. 1992 FDA Policy Statement, *supra* note 17, at 23,011.

375. Plant Pesticides Subject to the Federal Insecticide, Fungicide and Rodenticide Act and the Federal Food, Drug, and Cosmetic Act; Proposed Rule, 59 Fed. Reg. 60,496 (Envtl. Prot. Agency, proposed Nov. 23, 1994) (to be codified at 40 C.F.R. pts. 152, 174, and 180) [hereinafter EPA 1994 Proposed Policy]. In May 1997, the agency published a supplemental Notice of Proposed Rulemaking to elicit additional public comments on its evaluation of the requirements imposed by the recently enacted Food Quality Protection Act. Plant Pesticides;

proposal, the 1994 Proposed Policy in fact guided the agency's day-to-day decision-making process with respect to pest-resistant GM plants.[376]

On January 16, 2001, EPA submitted three sets of final regulations, promulgated under both the FIFRA and the FDCA, regarding pest-resistant plants to the Office of the Federal Register (OFR) and made them generally available to the public.[377] at the same time, the agency re-proposed for further comment regulations relating to several exemptions from the FIFRA's registration and the FDCA's pesticide tolerance requirements.[378] Immediately following the 2001 inauguration, however, White House Chief of Staff Andrew H. Card wrote a memorandum to the heads and acting heads of all executive departments and agencies asking them to withdraw from the OFR all submissions that had not yet been published in the *Federal Register* pending further review by newly appointed agency heads.[379] All of EPA's submissions were withdrawn pursuant to the Card Memo, and their current status remains unclear.

B. The Role of Substantial Equivalence in EPA's Regulation of GM Foods

The broad definition of "pesticide" in FIFRA easily includes all changes in a plant's genetic material that are "intended" to kill or even "mitigate" pests. Thus, EPA's overall authority to regulate GM

Supplemental Notice of Proposed Rulemaking, 62 Fed. Reg. 27132 (Envtl. Prot. Agency, proposed May 16, 1997) (to be codified at 40 C.F.R. pt. 180).

376. *See* NRC GM PEST-PROTECTED PLANTS REPORT, *supra* note 1, at 30 (noting that "[a]lthough the proposal has not been finalized, the agency has been implementing its essential elements in registering or exempting plant-pesticides since 1995"). As discussed below, the re-proposal of aspects of the 1994 proposal (along with the proposal of options for replacing aspects of the 1994 proposal) raises the question whether EPA may legitimately continue following the 1994 proposal in its day-to-day decisions.

377. EPA, FIFRA Plant-Incorporated Protectants Regulations, 2001 *supra* note 370; Exemption from the Requirement for a Tolerance Under the Federal Food, Drug, and Cosmetic Act for Residues of Nucleic Acids that are Part of Plant-Incorporated Protectants (Formerly Plant-Pesticides), 66 Fed. Reg. 37,817 (July 19, 2001) [hereinafter EPA, FDCA GM Plant Tolerance Exemptions, 2001]; Exemption from the Requirement of a Tolerance Under the Federal Food, Drug, and Cosmetic Act for Residues Derived Through Conventional Breeding from Sexually Compatible Plants of Plant-Incorporated Protectants (Formerly Plant-Pesticides), Proposed Rule, 66 Fed. Reg. 37,830 (July 19, 2001).

378. Environmental Protection Agency, Plant-Incorporated Protectants (Formerly Plant-Pesticides), Supplemental Proposal, 66 Fed. Reg. 37,855 (July 19, 2001) [hereinafter EPA, Supplemental Proposal for FIFRA and FDCA GM Plant Exemptions, 2001].

379. Card Memorandum, Jan. 20, 2001, *supra* note 245.

pest-resistant plants is not open to serious doubt.[380] Similarly, a gene inserted into a plant to express a pesticidal protein and the protein itself are rather clearly residues of a pesticide in the genetically engineered plant for purposes of the FDCA tolerance requirement.[381] To the extent that harvested plants containing residues of genetic material and pesticidal expression products are used in food or feed, they are also subject to the tolerance requirements of the FDCA.[382] EPA has in the past, however, invoked the substantial equivalence doctrine to grant broad categorical exemptions to some GM pest-resistant crops from both the FIFRA registration and the FDCA tolerance requirements.[383]

1. GM Plants as Pesticides—The November 1994 Proposed Policy Statement acknowledged that most plants have some natural ability to resist pests and disease, and it noted that companies had for many years extracted substances with pesticidal properties from plants to sell as pesticides.[384] Although the agency had always regulated such extracted substances as pesticides, it had not in the past directly addressed the use of traditional breeding techniques to enhance a plant's pre-existing ability to produce pesticidal substances.[385] In addition to facilitating the manipulation of crops to produce pre-existing pesticides, the agency recognized that modern genetic engineering techniques made it "possible to introduce into plants mechanisms of pest and disease resistance that are not found in the plant kingdom."[386]

The 1994 Proposed Policy Statement coined the term "plant-pesticide" to refer to "a pesticidal substance that is produced in a living plant and the genetic material necessary for the production of the [pesticidal] substance where the [pesticidal] substance is intended for use in the living plant."[387] The January, 2001 Final Rule replaced "plant-pesticide" with a new term, "plant incorpo-

380. EPA 1994 Proposed Policy, *supra* note 375, at 60,499 ("[A]ll plant-pesticides are potentially subject to EPA's regulatory authority under FIFRA."); *see* Bohrer, *Biotechnology*, *supra* note 11, at 666–67.

381. EPA 1994 Proposed Policy, *supra* note 375, at 60,499 ("Since FDCA defines pesticides in terms of the definition in FIFRA section 2, EPA also has the authority to regulate residues of plant-pesticides under FDCA sections 408 and 409. . . ."); *see also* Bohrer, *Biotechnology*, *supra* note 11, at 668.

382. EPA, FIFRA Plant-Incorporated Protectants Regulations, 2001, *supra* note 370, at 37,785.

383. EPA 1994 Proposed Policy, *supra* note 375, at 60,496.

384. For example, pyrethrums extracted from chrysanthemums had for many years been used as pesticides. *Id.* at 60,497.

385. *Id.* at 60,497.

386. *Id.* at 60,496.

387. *Id.* at 60,534.

rated protectant," which referred to a "pesticidal substance, along with the genetic material necessary to produce it, produced and used in living plants."[388] The critical factor distinguishing plant-incorporated protectants from chemical and other pesticides under the new rule is the fact that they are "intended to be produced and used in the living plant."[389]

EPA's determination to regulate pest-resistant plants under FIFRA and FDCA is clearly appropriate, given the broad definition of "pesticide" in that statute.[390] The agency's decision in the January 2001 final rule to include both the genetic material inserted into a plant and its pesticidal expression products is also fully authorized by the statute. While some commentators have insisted that manipulating a plant's natural defense mechanisms through either traditional or modern means should not subject the plant to regulation under FIFRA,[391] the agency quite properly concluded that since the intent of the human being causing the manipulation is to kill or mitigate a pest, both the genetic material used in the manipulation and the substances resulting from the manipulation are "pesticides" under section 2(u) of FIFRA.[392] The agency decided to

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388. EPA, FIFRA Plant-Incorporated Protectants Regulations, 2001, *supra* note 370, at 37,774. The name change was motivated by two factors. First, the term "plant-pesticide" in standard English means "plant killer," a term that strictly only applies to herbicides. Second, many commenters from the biotechnology industry were concerned that applying the term "pesticide" to the entire plant would attach a negative connotation to the plant in the minds of the public, "and the public perception of a promising branch of science could be tarnished." *See id.* at 37,780. No doubt for similar reasons, the agency rejected suggestions that the name be changed to "Franken-plants," "Pandora pesticides," "products-of-sexual-abuse," and "alien pesticides." *Id.* at 37,781.

389. *Id.* at 37,774. EPA meant for the term "plant incorporated protectant" to include plants engineered through traditional breeding technologies to contain higher levels of substances intended to kill pests. It then exempted all plant-incorporated protectants derived through conventional breeding from sexually compatible plants from all FIFRA requirements except the requirement that registrants report any observed adverse health or environmental effects. *Id.* at 37,786. The agency reasoned that conventional breeding using sexually compatible plants was unlikely to bring about quantitative changes in the levels of pesticidal substances in the resulting plants. *Id.* at 37,801. Recognizing that this exemption was based upon a process-oriented distinction between GM plants and non-GM plants, EPA explained that modern genetic engineering techniques made it possible to make "novel genetic modifications never before possible" and that it might "give the public more confidence that risk potential is being evaluated." *Id.* at 37,794.

390. A gene transfer typically involves more than the mere insertion of a single gene from one organism into another. For example, the transfer that inserted the gene coding for Bt toxin into corn also included promoters (genetic material that initiates transcription of the gene) and terminators (genetic material which stops transcription of the gene) from a virus and another bacterium. *See* CEQ/OSTP CASE STUDIES, 2001, *supra* note 15, at 1.

391. *See* EPA, FIFRA Plant-Incorporated Protectants Regulations, 2001, *supra* note 370, at 37,773.

392. 7 U.S.C. § 136(u) (1994 & Supp. IV 1986). EPA further decided to regulate as "inert ingredients" selectable marker genes inserted into GM plants to facilitate identification

cast its net broadly and use the exemptions process to address GM pest-resistant plants that posed insignificant risks to health or the environment.

2. *EPA-Created Exemptions*—Relying heavily upon the substantial equivalence doctrine, the 1994 Policy Statement proposed to exempt "certain categories" of pest-resistant plants that posed "low probability of risk" and would therefore not cause unreasonable adverse effects on the environment.[393] In particular, EPA proposed to exempt from the FDCA tolerance requirements "nucleic acids produced in plants as part of a plant-pesticide" and "categories of [plant-pesticides that would] not result in new dietary exposures."[394] The first exemption for nucleic acids was uncontroversial, and EPA retained it in the January 2001 final regulations.[395] The second exemption applied to the expression products of the transferred genes, and it contained two primary subcategories: (1) plant-pesticides from closely related (i.e., sexually compatible) plants; and (2) plant-pesticides derived from food plants that are not closely related to the recipient plant that do not involve "significantly different dietary exposures."[396] The agency's rationale for these much more controversial exemptions relied heavily upon the substantial equivalence doctrine.

With respect to the proposed exemption for closely related plants, the agency reasoned that "most plant varieties developed by plant breeders using genetic material from plants that meet the sexually compatible standard produce food that is safe for human consumption and/or that appropriate processing procedures are widely known and routinely used by consumers in preparation of food from such sources."[397] The agency speculated that transfers between closely related species would not result in levels of toxic proteins that greatly exceeded the normal range of levels exhibited in individual plants. It further noted that there were limits to which

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of plants with desired traits. EPA, FIFRA Plant-Incorporated Protectants Regulations, 2001, *supra* note 370, at 37,791.

393. EPA 1994 Proposed Policy, *supra* note 375, at 60,499.

394. *Id.* at 60,504. The agency also proposed to exempt coat proteins from plant viruses "based on virus-infected plants having always been a part of the human and domestic animal food supply without detectable adverse human health effects." *Id.* at 60,506.

395. EPA, FDCA GM Plant Tolerance Exemptions, 2001, *supra* note 377, at 37,820 (noting that "nucleic acids are ubiquitous in all forms of life, including food plants"); *see also* EPA, FIFRA Plant-Incorporated Protectants Regulations, 2001, *supra* note 370, at 37,797.

396. EPA 1994 Proposed Policy, *supra* note 375, at 60,505.

397. *Id.* at 60,505. For similar reasons, the 1994 Proposed Policy similarly exempted from FIFRA's registrations requirements all "plant-pesticides derived from closely related plants." *Id.* at 60,501.

registrants could increase the levels of pre-existing toxic proteins in food plants "without unwanted effects on other, desirable characteristics of the plant (e.g., yield or palatability of fruit)."[398] It therefore anticipated that "the majority of plants with modified levels of plant-pesticides will fall within existing ranges of pesticide levels," and it did not anticipate that "increasing the level of a plant-pesticide that is normally a component of a plant would lead to significantly different spectrum of exposure to the plant-pesticide."[399]

Most of the comments on the proposal were quite negative.[400] It is possible, for example, for a closely related donor plant to contain a gene coding for much higher levels of a pesticidal protein that is toxic or allergenic to some human beings at levels higher than those encountered in the diets of persons consuming the unmodified food plant. The increased levels of the protein induced by the transfer of that gene to the food plant could cross some threshold of allergenicity or toxicity. Reacting to the negative comments, the January 2001 publication declined to finalize that tolerance exemption. Instead, the agency re-proposed for further comment the sexually compatible donor plant exemption along with an alternative approach under which the agency would make "case-by-case" exemption determinations based upon individual demonstrations of "substantial equivalence."[401]

The second proposed exemption for expression products employed the substantial equivalence doctrine to exempt plant-pesticides derived from unrelated food plants that did not involve "significantly different dietary exposures." The agency reasoned that "there is experience with exposure [to such expression products] because both plants have contributed to the food supply."[402] So long as the gene transfer did not result in significantly different dietary exposures to the pesticidal expression product, the agency believed that the resulting plants should be safe to eat.[403] The Janu-

398. *Id.* at 60,503.

399. *Id.* at 60,503. The agency's implicit assumption that consumers will continue to use appropriate processing and preparation procedures with pest-resistant GM plants that result from transfers between closely related species is probably a reasonable one. Since the transferred gene will come from a closely related species, the potential for "surprise" insertions into unprocessed or unprepared foods of toxic proteins that are normally destroyed by processing or preparation should be very low.

400. EPA, Supplemental Proposal for FIFRA and FDCA GM Plant Exemptions, 2001, *supra* note 378, at 37,858.

401. *Id.* at 13–14.

402. EPA 1994 Proposed Policy, *supra* note 375, at 60,505.

403. *Id.* As an example of "significantly different dietary exposures," the agency suggested the transfer of a gene that codes for a pesticidal protein that exists only in an inedible portion of the donor plant. *Id.*

ary 2001 final regulation did not adopt this proposed exemption, either. Moreover, the supplemental proposal accompanying the January 2001 regulation did not even make reference to the second proposed exemption. It would therefore appear that the agency in January 2001 abandoned altogether the 1994 proposed exemption for expression products from food plants that do not involve significant dietary exposures.

EPA promised to complete the rulemaking with respect to its January 2001 supplemental proposal within nine to twelve months after the mid-March close of the comment period.[404] That promise, however, was made by the Clinton Administration EPA, and the status of the proposed rules in the Bush Administration is unclear. None of the documents that the agency made public in January 2001 alluded to the fact that the agency had been adhering to the 1994 Policy Statement for the previous six years. More importantly, none of the documents mentioned whether EPA would continue to apply the exemptions proposed in 1994 and re-proposed but not adopted in 2001 in the future. Given the agency's explicit determination that the available information did not warrant promulgating the proposed exemptions as final rules, the re-proposal could hardly be considered an affirmation of the exemptions. at the very least, the agency's complete silence in 2001 with respect to the proposed exemption for gene transfers that do not involve significantly different dietary exposures cannot legitimately be read as a continued recognition of such an exemption.

The January 2001 documents made it very clear that EPA regarded pest-resistant plants (now called "plant-incorporated protectants") to be pesticides. The FDCA tolerance requirements are therefore applicable to all such plant-incorporated protectants absent a determination by the Administrator that particular residues are exempt. Since a proposed exemption that the agency has explicitly refused to adopt can hardly be characterized as a genuine exemption, it would appear that all plant-incorporated protectants that do not come within the final exemptions promulgated in January 2001 must have a tolerance. It remains to be seen whether the agency adopts this view of the status of genetically modified food plants. If it does, then all GM pest-resistant plants that EPA previously exempted from its tolerance requirements must now have a tolerance, and the agency's previous heavy reliance on the substantial equivalence doctrine will have ended. The

404. EPA, Supplemental Proposal for FIFRA and FDCA GM Plant Exemptions, 2001, *supra* note 378, at 37,857.

new Administration, however, may take an entirely different approach to the proposed exemptions.

V. THE FAILURE OF THE EXISTING REGULATORY REGIME

A. Introduction

The substantial equivalence principle has played a dominant role in agency attempts to address the health risks of GM foods within the contours of the existing statutory framework. The extensive reliance of both FDA and EPA on that doctrine has had important consequences for the overall legitimacy of the regulatory program for GM foods. In the case of FDA, the agency's adherence to the substantial equivalence doctrine has combined with a statutorily mandated GRAS option to produce a system in which FDA has no way of knowing whether companies are distributing or importing new GM foods and therefore no way of managing the risks posed by those foods. Between 1994 and January 2001, EPA administered a similar program for pesticides through an administratively created exemptions process in which substantial equivalence played a prominent role.

The tentativeness with which the implementing agencies have fulfilled their regulatory responsibilities contributed to a crisis of public confidence in GM foods.[405] As a result, both agencies published documents in January 2001 designed to "reinvent" the federal approach to regulating GM foods and to restore public trust in the regulatory process. Substantial equivalence plays a less prominent, but still important role in FDA's proposed notification regulations. It plays a greatly reduced role in EPA's final regulations for plant-incorporated protectants, but those regulations may never go into effect, and serious questions remain about the status of the previously allowed exemptions that have either been reproposed or abandoned altogether. This section of the Article will analyze the weaknesses in the current regulatory regime and attempt to explain why public trust in the existing regulatory regime

405. *See* NRC GM PEST-PROTECTED PLANTS REPORT, *supra* note 1, at 38 (noting that "[m]any believe that transgenic crops present substantial human health and ecological risks, and that these are not properly assessed by the regulatory framework"); *Hearing Before the S. Gov't Affairs Subcomm. On Oversight of Gov't Mgmt. Restructuring and the Dist. of Columbia*, 106th Cong. (Aug. 4, 1999) (testimony of Carol Tucker Foreman, Consumer Federation of America) (arguing that "[t]he regulatory structure for reviewing and approving genetically engineered foods contributes to the confusion and fear").

is flagging. The following section will offer some solutions for repairing the existing regime.

B. The Crisis of Public Confidence

The agricultural biotechnology industry will succeed only if the public is convinced that the industry and the regulatory agencies that legislatures have created to protect consumers are trustworthy.[406] According to informed industry analysts, public distrust poses the single most important threat to the new industry.[407] No matter how strong the scientific evidence appears to the proponents of the technology, the ultimate test for the success GM foods in the marketplace is whether the public trusts the decision makers who interpret that scientific information and use it to assess and manage risks.

The U.S. biotechnology industry entered the GM foods debates with an arrogance reminiscent of the nuclear power industry in the 1950s.[408] Early in the highly contentious controversy in Europe over GM foods, a public relations specialist hired by an American biotechnology company told critics that "'people will have Roundup Ready soya, whether they like it or not.'"[409] An executive for another American company told the technical manager of a British supermarket chain that he was a "backward European" who should "just accept this is right for your customers."[410] This arrogance backfired in Europe (the supermarket chain made arrangements with Brazilian suppliers of non-GM foods, as did many of its competitors), and by the late 1990s, it was beginning to have a negative effect in the United States as well.[411]

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406. *See* ROYAL SOCIETY OF CANADA REPORT, 2001, *supra* note 14, at 211 (observing that "[s]tudies of risk perception are uniform in the finding that even the most minimal risks may be unacceptable if levels of trust in those who manage those risks are low or eroding"); EU-U.S. CONSULTATIVE FORUM, FINAL REPORT, *supra* note 149, at 10 (observing that the "regulatory processes must be sufficiently strong to ensure public confidence").

407. Goldberg, *Transforming Life*, *supra* note 34, at 104 ("Escalating public opposition poses the greatest single threat to the successful growth of the life-science business.").

408. *See generally*, ELIZABETH ROLPH, NUCLEAR POWER AND THE PUBLIC SAFETY (1979); KRISTIN SHRADER-FRECHETTE, NUCLEAR POWER AND PUBLIC POLICY (1980).

409. Maria Margaronis, *As Biotech "Frankenfoods" Are Stuffed Down Their Throats, Consumers Rebel*, THE NATION, Dec. 27, 1999, at 11 (quoting Ann Foster).

410. *Id.*

411. *See* Avery, *Biotechnology Future*, *supra* note 58, at 98 (complaining of "the shortsightedness—or arrogance—of modern agriculture and agribusiness"); Goldberg, *Transforming Life*, *supra* note 34, at 104 (biotech companies "have either ignored or derided their critics,

Well-publicized protests in Europe and (more recently) in the United States have focused public attention on the ease with which genetically modified foods found their way into the U.S. food supply, and many consumers are not pleased. In recent months, several large food processors, including Frito-Lay, Seagram, Gerber, and Heinz, have promised not to use GM foods in their products.[412] Whole Foods Markets, Wild Oats Markets, and the Iceland Supermarket Group have announced their refusal to market any GM foods.[413] In perhaps the most significant blow to GM foods in the United States, one of the two dominant grain distribution companies, Archer Daniels Midland, advised farmers in the Fall of 1999 to segregate GM grain from non-GM grain.[414] Reacting to the uncertainties in the market for GM crops, farmers reduced the percentage of genetically modified corn from thirty-three percent in 1999 to twenty-five percent in 2000.[415]

The condescending attitude of many federal officials has done little to inspire consumer confidence in the GM food economy.[416] The critics of agricultural biotechnologies can easily appeal to a general public distrust in large corporations, big science, and pliant public officials.[417] One of the dominant themes at the World Trade Organization protests in Seattle and the Bio2000 protests in Boston was that the federal government cannot be trusted to make

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insisting that the technologies they are pioneering are perfectly safe and that concerns about them are baseless").

412. Laura Tangley, *Of Genes, Grain, and Grocers: The Risks and Realities of Engineered Crops*, U.S. NEWS & WORLD REP., Apr. 10, 2000, at 49; David Stipp, *Is Monsanto's Biotech Worth Less than a Hill of Beans?*, FORTUNE, Feb. 21, 2000, at 157 [hereinafter Stipp, *Hill of Beans*]. Not all companies have abandoned GM crops. Despite parodies of Kelloggs' Tony-the-Tiger (a tiger called FrankenTony) and attempts to pass anti-GM resolutions at Kellogg shareholder meetings, the company continues to purchase GM corn. *See* Kevin McCauley, *Big Food Companies Face Anti-Biotech PR Assault*, O'DWYER'S PR SERVICES REP., Mar. 2000, at 1 [hereinafter McCauley, *Big Food Companies*]; *see also* Golden, *Frankenfood*, *supra* note 13.

413. Kriz, *Global Food Fights*, *supra* note 34, at 688; *Iceland Leads Non-Gm Drive*, FARMING NEWS, Feb. 25, 2000, at 1; Stipp, *Hill of Beans*, *supra* note 412, at 157. The Gerber action must have been particularly unnerving for its parent company, Novartis International, one of the world's largest agricultural biotechnology companies. *See* Goldberg, *Transforming Life*, *supra* note 34, at 94.

414. Stipp, *Hill of Beans*, *supra* note 412, at 158.

415. Paul Raeburn, *Biotech Foods Aren't Out of the Woods Yet*, BUS. WK., Apr. 17, 2000, at 56 [hereinafter Raeburn, *Out of the Woods*]. Similarly, the percentage of soybeans planted with genetically modified plants shrank from fifty-seven percent to fifty-two. *Id.*

416. *See* Foreman Remarks, Nov. 30, 1999, *supra* note 5 (arguing that "[i]t doesn't work to sit there and say, 'Jane, you ignorant slut, if you don't believe this is safe it's because you're stupid' ").

417. *See, e.g.*, Ho, *Dangerous Liaison*, *supra* note 176, at 105 (arguing that "bad science and big business, both out of control, have formed a dangerous liaison that is gambling with our food security, biodiversity, and health, and at the same time tearing at the fabric of civilized society").

protective decisions about genetically modified foods.[418] Unfortunately, the existing U.S. regulatory agencies, with their heavy reliance on the highly malleable substantial equivalence principle, provided little to undermine activist contentions beyond an unconvincing appeal to "trust us because the experts know better than you what is best for you."

Recent polls suggest that the American public is divided on the question of the safety of GM foods, but a slight majority is favorably disposed. A December, 1999 Gallup Poll found that fifty-three percent of more than 1000 participants thought that GM foods were not dangerous, twenty-five percent believed that they posed a serious health hazard, and twenty percent were uncertain.[419] A poll conducted by Roper Starch Worldwide in July and August 1999, found that seventy-three percent of the 1,002 adult consumers surveyed said that they would eat GM foods if it meant that farmers would use fewer chemical pesticides.[420] In a multi-year poll of American consumers conducted by North Carolina State Sociologist Thomas Hoban, seventy percent of the respondents supported agricultural biotechnology in 1992 and seventy-two percent supported it in 1994 and 1998.[421] at the same time, the fact that eighty-one percent of the respondents in a January 1999 *Time Magazine* poll and 70-90 percent of the respondents in other polls thought that GM foods should be labeled may suggest that the public does not have a great deal of faith in the federal regulatory agencies to protect individuals from the health risks posed by GM foods.[422]

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418. Kriz, *Global Food Fights*, *supra* note 34. The message has been especially well received in Europe where recent food-related safety incidents (e.g., mad cow disease, contaminated Coca-Cola, etc.) have undermined public trust in the regulatory authorities. *See* Goldberg, *Transforming Life*, *supra* note 34, at 94. Environmental activists have also aimed public education campaigns at companies like the Kellogg Corporation, Frito-Lay, and McDonalds that purchase large quantities of agricultural commodities and that are especially sensitive to adverse publicity because they are in highly competitive markets. *See* McCauley, *Big Food Companies*, *supra* note 412.

419. Deborah Silver, *Biotech Food Safety Doesn't Worry Consumers*, RESTAURANTS & INSTS., Dec. 15, 1999, at 66.

420. Robert Vosburgh, *Consumers Prefer Biotechnology to Pesticides: Poll*, SUPERMARKET NEWS, Jan. 24, 2000, at 43. The survey indicated that consumers also preferred other options to chemical pesticides, including paying higher prices (57%), smaller selection (68%), and seasonal availability (72%). *Id.*

421. Thomas J. Hoban, *International Acceptance of Agricultural Biotechnology*, *in* NAT'L AGRIC. BIOTECHNOLOGY COUNCIL REP. 10, AGRICULTURAL BIOTECHNOLOGY AND ENVIRONMENTAL QUALITY: GENE ESCAPE AND PEST RESISTANCE 59, 60 (Ralph W.E. Hardy & Jane Baker Segelken eds., 1998) [hereinafter Hoban, *International Acceptance*].

422. *See The Future of Food: Biotechnology and Consumer Confidence: Hearing Before the S. Comm. on Health, Educ., Labor and Pensions*, 106th Cong (2000) (testimony of Michael K. Hansen, Ph.D., Research Associate, Consumer Policy Institute, Consumers Union); Silbergeld Testimony, Oct. 6, 1999, *supra* note 130 (quoting *Time Magazine* poll).

The biotechnology industry and its allies in the Administration and Congress are beginning to recognize that its future depends upon public acceptance of the technologies and public trust in the processes through which the health and environmental risks they pose are managed.[423] In a widely publicized speech in July 1999, Agriculture Secretary Dan Glickman stressed that:

> With all that biotechnology has to offer, it is nothing if it is not accepted. That boils down to a matter of trust—trust in the science behind the process, but particularly trust in the regulatory process that ensures a thorough review, including complete and open public involvement.[424]

The head of the NAS Committee on Genetically Modified Pest-Protected Plants concluded that "[p]ublic acceptance of these foods ultimately depends on the credibility of the testing and regulatory process."[425] It remains to be seen whether the current regulatory regime can earn that trust.

C. Notice

One rudimentary element of any program for regulating health and environmental risks is a requirement that entities proposing to engage in new risk-creating activities provide notice of that fact to a governmental agency. Pre-release notification helps protect public health and the environment and ensure public trust by giving the appropriate agency an opportunity to decide whether to exercise its regulatory powers. Without pre-release notification, the agency can only assume a reactive mode, attempting to stem any damage that has already occurred and to prevent it from occurring in the future. Indeed, absent such notice, the damage caused by the introduction of a new technology may not even be detectable for

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423. *See* Collins Testimony, Mar. 3, 1999, *supra* note 68 ("Another key aspect of acceptance must include nurturing a higher level of comfort that includes consumer groups, environmental advocates and the scientific community in general."); Goldberg, *Transforming Life*, *supra* note 34, at 94 (noting that "life-science companies are beginning to engage in public dialogue").

424. Dan Glickman, Remarks at the National Press Club Newsmaker Luncheon with Agriculture Secretary Dan Glickman (July 13, 1999).

425. Adriel Bettelheim, *Reluctant Congress Drafted into Bioengineering Battle*, CQ WKLY, Apr. 22, 2000, at 938, 939 [hereinafter Bettelheim, *Reluctant Congress*] (quoting Perry Adkisson, Chancellor Emeritus of Texas A&M University, chairman of the panel that wrote the report).

many years (if at all), because the appropriate monitoring entities will not know to be looking for evidence of harm.

The regulatory regime prior to January 2001 gave manufacturers and importers broad discretion in deciding whether to notify regulatory agencies of their plans to introduce GM foods into commerce. Although a company that desired to "play it safe" would notify EPA and FDA in close cases, no serious consequences were likely to befall a company that declined to provide notice to those agencies if it could plausibly argue that its GM food was GRAS in the case of FDA or exempt in the case of EPA. Consumers were therefore at the mercy of the proponents of the technologies to exercise their judgment wisely in deciding whether to inform regulatory agencies of their plans to introduce GM foods into commerce.

Recognizing the weakness of the existing notice requirements, both EPA and FDA took steps at the very end of the Clinton Administration to ensure that they receive pre-market notification of most GM foods. EPA accomplished this result in a straightforward way by failing to finalize proposed exemptions from the FDCA tolerance requirements for GM pest-resistant plants involving gene transfers from closely related plants and from edible portions of unrelated food plants.[426] The legal status of this action, however, remains unclear, because the document supporting the action was never published in the *Federal Register*.[427] FDA proposed regulations requiring all manufacturers of GM foods to provide pre-market notification to that agency. The agency has not yet finalized those regulations, however, and its legal authority to promulgate them remains in some doubt.[428] At this point, it is not clear that either of the recent reforms will actually go into effect.

D. Transparency

Most observers would agree with the conclusion of the 1999 Edinburgh Conference that "risk analysis systems are only likely to generate public trust if based on transparency, provision of information (on monitoring, research results, etc.), and on greater inclusiveness of the various stakeholders."[429] To an informed

426. *See supra* Part IV.B.2.
427. *See supra* Part IV.A.
428. *See supra* Part III.D.4.
429. OECD EDINBURGH RAPPORTEURS' SUMMARY, *supra* note 33, at 8.

citizenry that has grown quite skeptical of well-orchestrated public relations campaigns and condescending assurances from professional risk assessors, the most effective way to restore public trust in regulatory agency decision-making is to make the regulatory process as transparent as possible and to give representatives of public interest groups a direct role in any decisions to regulate particular GM commodities.[430]

As currently administered, the regulatory process at the federal level is not very transparent. FDA does not automatically invite the general public to informal consultations between its staff and the manufacturers of GM foods, and the recently proposed notification process allows a company to prevent notice to the public by claiming the fact of notice to be confidential business information.[431] EPA publishes notice of pesticide registration and tolerance actions in the *Federal Register*,[432] and the public ordinarily has an opportunity to request a public hearing to challenge those actions.[433] EPA's past practice, pursuant to its 1994 Policy Statement, of exempting most GM pest-protected plants, however, has to some extent nullified these avenues to public participation. As discussed above, the status of EPA's recently promulgated regulations, which decline to finalize either of the exemptions, remains to be seen.

E. Data Collection, Data Evaluation, and Risk Assessment

Testing novel products in laboratory animals and/or other surrogate systems before allowing them onto the marketplace is usually necessary to protect human health. Careful testing also ad-

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430. *See* Professor John Durant, Widening the Circle: Engaging the Public in Policymaking for GM Food 11, presented at the OECD Edinburgh Conference on the Scientific and Health Aspects of Genetically Modified Foods (Feb. 28–Mar. 1, 2000) (factors promoting credibility include: openness to public scrutiny, procedural transparency, [and] inclusivity to ensure mindfulness of public concerns); EU-U.S. CONSULTATIVE FORUM, FINAL REPORT, *supra* note 149, at 6 (noting that "the transparency of decision-making processes and meaningful participation—involving all stakeholders—are matters of rapidly increasing importance").

431. *See Public Meeting on Biotechnology in the Year 2000 and Beyond by the U.S. Food and Drug Administration* (Nov. 30, 1999) (remarks of Rebecca Goldburg, Senior Scientist, Environmental Defense Fund) [hereinafter Goldburg Remarks, Nov. 30, 1999] (arguing that "because these consultations are outside the regulatory system, they are not subject to public scrutiny and are not a satisfactory substitute for a regulatory program").

432. 7 U.S.C. § 136a(c)(4)(1994); 21 U.S.C. § 346a(d)(3)(1994); *see also* CEQ/OSTP CASE STUDIES, 2001, *supra* note 15, at 42.

433. 21 U.S.C. § 346a(g)(2)(1994). In the case of initial pesticide registrations, the public hearing will be in court by way of a judicial challenge to EPA's action, and the pesticide may remain on the market pending judicial action. 7 U.S.C. § 136n(a)

vances the goal of scientific accuracy in consumer and regulatory decision-making. A regulatory agency must be capable of assessing the quality of testing data, analyzing the scientific studies, interpreting the results, and drawing scientifically valid conclusions. Finally, assessing the risks posed by novel products requires both scientific judgment and, when uncertainties cloud the science, policy judgment.[434] In the context of GM foods, risk assessment involves an assessment of probability and consequences of an adverse health effect resulting from the introduction of a GM plant into the food supply.

EPA and FDA have required very little long-term pre-market testing of whole GM foods or of the expression products of the inserted genes. In the vast majority of cases, the agencies have allowed manufacturers to forego all testing except that which is necessary to meet the threshold substantial equivalence showing required for GRAS status or pesticide exemptions. Although the industry and the agencies confidently assert that the risks posed by GM foods are very slight, these assurances are not based upon quantitative risk assessments of the sort that characterize federal regulation of chemical contaminants in food. For the most part, the agencies have based their safety determinations upon the assumption that GM foods that are substantially equivalent to existing foods probably pose no greater risks. Full-fledged scientific assessments of risks posed by particular GM plants based upon real scientific data are surprisingly rare.[435]

EPA has required no testing whatsoever for pesticides that come within its broad exemptions for gene transfers between sexually compatible plants and gene transfers between unrelated food plants.[436] For other GM pest-resistant plants, a category that includes all Bt pest-resistant plants, EPA has determined testing requirements on a "case-by-case" basis.[437] The agency has not

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434. *See* NAS RED BOOK, *supra* note 151, at 3 (stating that risk assessment is "the use of the [existing] factual base to define the health effects of exposure of individuals or populations to hazardous materials and situations"); *see also* Mark E. Shere, *The Myth of Meaningful Environmental Risk Assessment*, 19 HARV. ENVTL. L. REV. 409, 430–68 (1995) (providing a comprehensive explanation of four steps involved in risk assessment).

435. *See* Bettelheim, *Reluctant Congress*, *supra* note 425, at 942 (noting that "[t]he body of scientific work on potential problems is growing, but there is still very little risk assessment" (quoting Jane Rissler of the Union of Concerned Scientists)).

436. The 1994 Proposed Policy Statement provided no substantive criteria for determining what kinds of testing should be undertaken. *See* EPA 1994 Proposed Policy, *supra* note 375, at 60,508.

437. *Hearing Before the House Comm. on Sci. Subcomm. on Basic Research*, 106th Cong. (Oct. 19, 1999) (testimony of Janet L. Andersen, Director, Biopesticides and Pollution Prevention Division, Office of Pesticide Programs, EPA) [hereinafter Andersen Testimony, Oct. 19,

prescribed even rudimentary protocols for testing such plants for adverse health consequences, and it has made liberal use of the substantial equivalence doctrine to waive testing requirements that would otherwise be applicable to chemical pesticides.[438] Although the agency has promised to write testing regulations sometime in the future,[439] its current posture stands in stark contrast to the extensive testing regime that the agency has established for chemical pesticides.[440]

FDA may receive a limited amount of data from manufacturers in voluntary "consultations" with them over the GRAS status of particular GM foods. These data, however, need not reflect any particular testing protocols. Manufacturers are free to rely upon published reports and the conclusions of panels of experts based upon published reports or other information. When a manufacturer concludes that a GM plant contains a food additive that is not GRAS, it must comply with the food additive testing requirements, and they typically demand a great deal of testing.[441] So far, however,

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1999] (EPA "has worked with each company or individual developing plant-pesticide products to determine the appropriate data requirements for the particular product."). EPA has required some acute oral testing of GM plants in laboratory rodents. *See* CEQ/OSTP CASE STUDIES, 2001, *supra* note 15, at 16. It has also ordered testing in laboratory animals of the pesticidal proteins that the inserted genes express. *Id.* EPA may also order studies of digestion of the protein in simulated gastric assays to determine its stability after ingestion on the theory that proteins that resist digestion have a higher allergenic potential than those that are easily digested. *Id.* at 17.

438. *See* Sharlene R. Matten, *EPA Regulation of Plant-Pesticides and Bt Plant-Pesticide Resistance Management*, *in* NAT'L AGRIC. BIOTECHNOLOGY COUNCIL REP. 10, AGRICULTURAL BIOTECHNOLOGY AND ENVIRONMENTAL QUALITY: GENE ESCAPE AND PEST RESISTANCE 105–123 (Ralph W.E. Hardy & Jane Baker Segelken eds., 1998) [hereinafter Matten, *EPA Regulation*]. The 1994 Policy Statement provided "general guidance" for data gathering on product analysis, environmental fate, ecological effects, and human health effects, while "maintaining an appropriate flexibility to data needs for individual cases." EPA 1994 Proposed Policy, *supra* note 375, at 60,511. The agency staff typically demands that registrants submit data on five general topics: product characterization, toxicology, non-target organisms effects, exposure, and environmental fate. Andersen Testimony, Oct. 19, 1999, *supra* note 437.

439. *See* Andersen Testimony, Oct. 19, 1999, *supra* note 437; Matten, *EPA Regulation*, *supra* note 438, at 123. The January, 2001 final rule promised to establish "data requirements specific to plant-incorporated protectants through a public notice and comment process" sometime in the future. EPA, FIFRA Plant-Incorporated Protectants Regulations, 2001, *supra* note 370, at 37,783.

440. EPA, Data Requirements For Registration of Pesticides, 40 C.F.R. § 158 (2001). EPA has promulgated requirements for testing microbial pesticides, and these are constantly being reexamined to meet changing needs. *See* 40 C.F.R. §§ 158.65, 158.170, 158.162 (2002).

441. 21 U.S.C. § 348(b) (1994). The reports and investigations frequently include toxicological tests conducted in accordance with the principles outlined in the agency's "Toxicological Principles for the Safety Assessment of Direct Food Additives and Color Additives Used in Food," generally referred to as the FDA "Redbook." *See* FDA Proposed Bioengineered Food Regulations, 2000, *supra* note 243, at 4708. By some estimates, manufacturers of novel food additives spend about $20 million to conduct the studies necessary to obtain FDA approval, and the approval process can take five to seven years to complete. *See*

FDA has received one food additive petition, and that was limited to the kanamycin-resistance marker gene and its expression products. All other non-pest-resistant GM plants that are currently in GM foods are apparently GRAS.[442] Thus, manufacturers have conducted very little testing and FDA has undertaken very little risk assessment of GM plants.

The failure of the federal government to require manufacturers of GM foods to conduct the kind of testing, evaluation and risk assessment necessary for adequate safety regulation is perhaps the most frequently articulated criticism of the existing regulatory regime.[443] The contrast between the EPA and FDA approach to GM foods and the approach of the same agencies to chemical pesticides and additives is striking. In both agencies, the substantial equivalence doctrine provides the primary justification for the radical differences in testing, evaluation, and risk assessment requirements. If the substantial equivalence doctrine is not appropriate in the context of some plants to which it is currently applied, or if it has been misapplied by food manufacturers and/or the agencies to waive otherwise applicable testing, evaluation, and risk assessment requirements, then the existing regulatory regime is, on its own terms, inadequate.

F. Consumer Choice

In a mass market economy, accurate information about consumer products is critical to ensuring public trust in the marketplace, and modern democracies have generally substituted for the strict laissez-faire model a regulatory approach in which government agencies play a prominent role in protecting consumers

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Noah & Merrill, *Starting from Scratch*, *supra* note 5, at 375 (citing testimony of Rhona S. Applebaum, Exec. Vice President, Nat'l Food Processors Ass'n).

442. After conducting more than forty-five consultations with respect to GM plants since promulgating the 1992 policy, the agency has not required a single expression product of a genetic modification to be reviewed as a food additive. *See* NRC GM PEST-PROTECTED PLANTS REPORT, *supra* note 1, at 30 (observing that "FDA has not required that any of the proteins added to transgenic plants be reviewed as food additives").

443. *See* Bettelheim, *Reluctant Congress*, *supra* note 425, at 942 (quoting Jane Rissler of the Union of Concerned Scientists) (noting that "if you don't look for problems, you won't find them"); Silbergeld Testimony, Oct. 6, 1999, *supra* note 130 (criticizing FDA for letting "companies themselves answer [the relevant] questions and decide whether to talk to FDA about the product").

from fraud and misleading advertising.[444] Informational requirements can be burdensome and, in the extreme, can discourage technological advance. Product label requirements can also be both economically and administratively inefficient if the value of the information to consumers does not exceed the cost of the label and the opportunity cost of the information that otherwise might be conveyed in the limited space available on the label. Thus, legitimate disputes frequently arise over the extent to which government should force manufacturers to provide all consumers with information that some consumers might deem relevant to their purchase decisions, but is not needed to prevent deception and is not directly related to latent dangers.[445]

EPA and FDA have applied the substantial equivalence doctrine to relieve manufacturers of any obligation to label GM foods. EPA's regulatory authority over pesticides is largely irrelevant to consumer choice, because it focuses almost exclusively upon the information that seed manufacturers must convey to growers, and does not clearly empower EPA to require either seed manufacturers or growers to inform consumers of the fact that raw agricultural commodities or processed foods are composed of GM plants.[446] Only FDA has clear authority to require marketers and importers of GM foods to inform consumers directly of the fact that such foods have been genetically altered. However, FDA has very narrowly interpreted its labeling authority to require labeling only when GM food differs so greatly from its traditional counterpart that "the common or usual name no longer applies to the new food" and when "a safety or usage issue exists to which consumers

444. Kirsten S. Beaudoin, Comment, *On Tonight's Menu: Toasted Cornbread with Firefly Genes?* 83 MARQ. L. REV. 237, 239–40 (1999) (arguing that "[a] regulatory structure that monitors and labels GM foods will . . . ease the current consumer hostility to genetic engineering that threatens to obscure its potential benefits"); WINROCK REPORT ON TRANSGENIC CROPS, *supra* note 12, at 8 (concluding that "[m]ost people agree that consumers should have the right to know and choose products based on their personal values").

445. For example, FDA did not require manufacturers of food to provide nutritional information on the labels of mass-produced foods until the 1970s. *See* Advance Notice of Proposed Rulemaking and Request for Public Comment, 54 Fed. Reg. 32,610 (Food and Drug Admin., Aug. 8, 1989) (setting out history of FDA nutrition labeling requirements). Congress later enacted the Nutrition Labeling and Education Act of 1990, Pub. L. No. 101-535 (1990), to require additional nutrition labeling.

446. EPA manages pesticide risks primarily through its initial registration decisions (and some fairly rare pesticide cancellation actions) and through conditions that are specified on the pesticide label. EPA 1994 Proposed Policy, *supra* note 375, at 60,510. EPA may also require informational labeling to inform farmers about the risks posed by the labeled pesticides. *Id.* at 60,511.

must be alerted."[447] Consequently, FDA has not required labeling for a single GM food.

G. Risk Management

"Risk management" is "the process of weighing policy alternatives and selecting the most appropriate regulatory action, integrating the results of risk assessment with engineering data and with social, economic, and political concerns to reach a decision."[448] When a risk assessment suggests that particular agricultural biotechnologies pose unacceptable risks if left unregulated, the regulatory regime must be capable of reducing or eliminating those risks.[449] A wide variety of regulatory approaches exists to address the risks posed by dangerous technologies, ranging from outright bans to positive economic incentives.[450] Although this is not the proper place for an extended discussion of policy tools for risk management, one frequently employed risk management technique for new product risks is a licensing (or permitting) regime in which the proponent of the technology must demonstrate that it meets a prescribed test safety threshold.

Both EPA and FDA administer laws that could require manufacturers of GM foods to obtain permits prior to marketing them. As is generally the case with permit regimes, both of the relevant statutes place the burden of demonstrating that the GM food meets the regulatory criteria on the permit applicant. Manufacturers of pesticides must demonstrate that they will not have "unreasonable adverse effects" under FIFRA and will provide a reasonable certainty of no harm under FDCA.[451] The FDCA places the burden on the manufacturer to demonstrate that a food additive passes the reasonable certainty of no harm test.[452] Yet both agencies have

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447. 1992 FDA Policy Statement, *supra* note 17, at 22,991.

448. NAS RED BOOK, *supra* note 151, at 3.

449. *See* OECD EDINBURGH RAPPORTEURS' SUMMARY, *supra* note 33, at 6 (noting that "we need systems in place, trusted by citizens, for managing risks that encompass those measures that become effective after decisions on acceptability have been taken").

450. *See generally* OFFICE OF TECHNOLOGY ASSESSMENT, ENVIRONMENTAL POLICY TOOLS: A USER'S GUIDE ch. 3 (1995).

451. EPA has granted "conditional registrations" for all of the currently registered GM plant pesticides, and it will review those registrations under the evolving standards for evaluating the environmental risks and benefits of genetically modified organisms sometime in 2001. *See* Kriz, *Global Food Fights*, *supra* note 34, at 688.

452. FDA has approved one food additive petition for the kanamycin resistance gene and its expression products. *See supra* note 298.

relied upon the substantial equivalence principle to craft such broad exemptions for GM foods that the permit requirements are not a significant obstacle to marketing new GM foods. EPA has freely granted exemptions from the registration and tolerance requirements for gene transfers to food plants from sexually compatible plants and from unrelated food plants.[453] A food additive for which FDA has not granted a food additive petition is subject to seizure, but FDA's 1992 Policy Statement encourages manufacturers to conclude that changes brought about through genetic engineering are GRAS and therefore not subject to FDA approval. As previously discussed, the broad applicability of the substantial equivalence doctrine in FDA's 1992 Policy Statement has effectively shifted the burden of proof back to the government for the vast majority of GM foods.

Consumer groups are strongly of the opinion that FDA approval should be mandatory for all GM foods.[454] In their view, FDA's "voluntary and secret process leaves the industry on the honor system."[455] Biotechnology proponents argue that while the system is essentially voluntary, companies have a strong incentive to consult with FDA to avoid civil penalties and damaging accusations that

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453. Matten, *EPA Regulation*, *supra* note 438, at 129. In 1999, EPA published a *Federal Register* notice in connection with its review of a proposed expansion of a tolerance for a variety of GM-corn (called StarLink® corn) soliciting public input on the potential for allergenicity of non-digestible proteins (Cry9C) expressed as plant-pesticides. Allergenicity Assessment of Cry9C BT Corn Plant Pesticide, 64 Fed. Reg. 71,452 (Envtl. Prot. Agency, December 21, 1999). The staff determined that, unlike other Bt proteins, the protein Cry9C was stable to heat and gastric digestion and therefore could pose an allergenic risk to humans consuming Cry9C GM foods if the protein was in fact allergenic. *Id.* In the meantime, however, EPA registered StarLink® corn for use only as animal feed on the optimistic assumption that farmers would sell GM corn that appeared identical to non-GM corn at lower prices on the animal feed markets. The unfortunate consequences of this decision are detailed below. *See infra* Part V.H.

454. *See* Goldburg Remarks, Nov. 30, 1999, *supra* note 431 (urging FDA to subject GM foods "to the same regulatory requirements as substances added to foods via more traditional means"); *Public Meeting on Biotechnology in the Year 2000 and Beyond by the U.S. Food and Drug Administration* (Nov. 18, 1999) (remarks of Michael Jacobson, Executive Director, Center for Science in the Public Interest) [hereinafter Jacobson Remarks, Nov. 18, 1999] (arguing that there should be a formal approval process). In late March, 2000, more than fifty consumer and environmental groups petitioned FDA to regulate genetically modified foods as food additives under section 409 of the FDCA. Neil Franz, *Green Groups Want GM Testing Mandates; Transgenic Crops*, CHEMICAL WEEK, March 29, 2000, at 21.

455. *Public Meeting on Biotechnology in the Year 2000 and Beyond by the U.S. Food and Drug Administration* (Nov. 18, 1999) (remarks of Charles Margulis, Greenpeace Genetic Engineering Campaign); *see also* Jacobson Remarks, Nov. 18, 1999, *supra* note 454 (arguing that "the quasi-voluntary nature" of the FDA process "leaves questions in people's minds[:] are some of these big companies telling the FDA to stuff it?"); Kristi Coale, *Don't Look, Don't Find; Genetically-Modified Agriculture*, THE NATION, Dec. 27, 1999, at 19.

they are marketing unsafe products.[456] The critics respond that the threat of civil penalties and bad publicity has not prevented manufacturers from marketing dangerous products in the past,[457] and it is not adequate to inspire public trust in the federal regulatory regime in the future.

H. Monitoring and Enforcement

A regulatory regime should also be capable of monitoring regulated activities to detect violations of existing requirements.[458] Although monitoring can be burdensome, it is absolutely essential if the relevant agencies are to have any hope of detecting violations of food-related regulatory requirements. Hence, agencies concerned with effective enforcement must think about monitoring and enforceability when they promulgate regulations. Agency attention to monitoring can be especially useful in the context of GM foods, because it may be possible to use the tools of genetic engineering to design into GM plants characteristics that enhance that accuracy of monitoring for the presence of the plant or its offspring in the environment.

Neither EPA nor FDA has implemented an effective enforcement program to back up its relaxed regulatory approach toward the new agricultural biotechnology industry. For example, FDA has no systematic monitoring program in place to determine whether or not manufacturers and importers have been abusing the GRAS process and marketing GM foods that are legally subject to the food additive requirements.[459] Although both FDA and EPA

456. Kriz, *Global Food Fights*, *supra* note 34, at 688 (quoting Eric Flamm, a molecular biologist and policy analyst at FDA). One company representative has observed that although "[t]here is no requirement to get an FDA blessing for these products, . . . if you're wrong, there is a pretty heavy hammer at the other end." *Id.*

457. Critics point out that FDA paid little attention to sulfite preservatives, finding them to be GRAS on the basis of historical use in wine and other foods. Yet, when the agency examined the issue closely in response to public criticism, it discovered that many people were suffering severe allergenic reactions to sulfite preservatives that had previously gone unnoticed. *See* Jacobson Remarks, Nov. 18, 1999, *supra* note 454.

458. Although an adequate regulatory regime must also be backed up by sufficient civil and/or criminal penalties to deter unlawful conduct, this Article does not focus upon the penalty aspect of enforcement.

459. FDA has an inspectorate in place that monitors for violations of the food additive requirements. *See* Food and Drug Administration, Center for Food Safety Applied Nutrition, Food Compliance Program, Domestic Food Safety Program, Feb. 2, 2000, *available* at http://vm.cfsan.fda.gov/~comm/cp03803.html. The three categories for which the agency's Domestic Food Safety Compliance Program establishes separate compliance monitoring

conduct fairly extensive monitoring for and enforcement of violations of EPA tolerance requirements for chemical pesticides,[460] neither agency has established a program for testing crops and imports for pesticidal proteins produced through genetic modifications.

In late September, 2000, Kraft Foods announced that it had initiated a nationwide recall of taco shells to interdict those that had become contaminated with a Bt pest-resistant corn that EPA had registered for animal feed, but not for human food use.[461] The recall was precipitated by an environmental group's discovery of StarLink® corn in the taco shells.[462] EPA had registered StarLink® in 1998 for use in animal feeds and industrial processes, but it had declined to register the plant pesticide for human use because of concerns that the protein (Cry9C) that the inserted Bt gene coded for was nondigestable and therefore might be allergenic in humans. As StarLink® was detected in additional taco shells around the country and in exports to Japan, the registrant, Aventis CropScience, petitioned EPA for permission to allow it in food for a four-year period to prevent alleged widespread disruptions in the food and grain industries.[463] In the meantime, Aventis agreed to stop selling StarLink® corn and to attempt to remove all such corn produced during the year 2000 from the food supply.[464]

Further investigation revealed that millions of bushels of StarLink® corn had been commingled with food corn in at least 450 grain elevators.[465] As food companies began to test individual shipments for the presence of StarLink®, it became apparent that the contamination was widespread throughout the food supply.[466] Some farmers maintained that the companies that sold StarLink® to them did not inform them of the use restrictions, and others said that they were told not to worry about segregation because EPA

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regimes—food borne biological hazards, chemical contaminants, and food additives and color additives—do not appear to encompass GM foods that are not pesticides.

460. *See* ENVIRONMENTAL PROTECTION AGENCY, AVAILABLE INFORMATION ON ASSESSING EXPOSURE FROM PESTICIDES IN FOOD: A USER'S GUIDE II.A.3. (2000).

461. *See* Andrew Pollack, *Kraft Recalls Taco Shells with Bioengineered Corn*, N.Y. TIMES, Sept. 23, 2000, at B1.

462. *Id.*; Andrew Pollack, *Corn Developer Appeals to EPA*, N.Y. TIMES, Oct. 20, 2000, at C4 [hereinafter Pollack, Oct. 20, 2000].

463. Kurt Eichenwald, *New Concerns Rise on Keeping Track of Modified Corn*, N.Y. TIMES, Oct. 14, 2000, at A1 [hereinafter Eichenwald, Oct. 14, 2000]; Pollack, Oct. 20, 2000, *supra* note 462; Stephanie Strom, *Bioengineered Corn Reportedly Detected in Japan*, N.Y. TIMES, Oct. 26, 2000, at C1.

464. Pollack, Oct. 20, 2000, *supra* note 462.

465. Eichenwald, Oct. 14, 2000, *supra* note 463; *Kellogg Shuts Memphis Plant Over Genetically Altered Corn*, N.Y. TIMES, Oct. 22, 2000, at 24.

466. Eichenwald, Oct. 14, 2000, *supra* note 463.

approval was expected shortly.[467] Still others claimed that they had innocently sold elevators StarLink®-contaminated corn when the corn they planted became cross-fertilized by StarLink® corn from neighboring fields.[468] The press has reported at least two cases of severe allergenic reactions associated with consumption of StarLink® contaminated corn products.[469]

The StarLink® episode reveals in stark terms the size of the hole in the regulatory regime that can result from general noncompliance with registration requirements that are not clearly communicated to the farmers who are actually planting, harvesting, and selling GM plants. EPA's tiny pesticides inspectorate is wholly incapable of monitoring the thousands of grain elevators and the tens of thousands of cornfields for compliance with requirements that are either written in tiny type or merely incorporated by reference on the labels of bags of seed. As one food industry executive observed: "This whole system has been self-policing by the seed industry ... [a]nd obviously it hasn't worked."[470]

VI. RETROSPECTIVE EVALUATION

Any good regulatory program should periodically evaluate whether past decisions to regulate particular activities (or to exclude particular activities from regulation) have achieved the desired regulatory goals.[471] Frequent monitoring can reveal

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467. Barnaby J. Feder, *Farmers Cite Scarce Data in Corn Mixing*, N.Y. TIMES, Oct. 17, 2000, at C1.

468. David Barboza, *Gene-Altered Corn Changes Dynamics of Grain Industry*, N.Y. TIMES, Dec. 11, 2000, at A1. EPA later asked a scientific advisory committee to look into whether the agency could allow the sale and use of the StarLink® corn that was already in the food supply. The panel concluded that there was a "medium likelihood" that StarLink® was in fact allergenic to humans, but that there was a low probability that the U.S. population as a whole would suffer significant allergy problems. Andrew Pollack, *Federal Panel is Wary on Gene-Altered Corn*, N.Y. TIMES, Dec. 6, 2000, at C8. Citing many uncertainties in the existing information on the allergenicity of Cry9C, the panel called for further study of that protein's allergenic properties. *Id.*

469. Kaufman, *supra* note 75.

470. Eichenwald, Oct. 14, 2000, *supra* note 463.

471. *See* Bernard Chevassus-au-Louis, *Prevention, Precaution, Consumer Involvement: Which Model for Food Safety in the Future?*, presented at the OECD Edinburgh Conference on the Scientific and Health Aspects of Genetically Modified Foods 11 (Feb. 28–Mar. 1, 2000) [hereinafter Chevassus-au-Louis, Prevention] (arguing that "an effective monitoring system (traceability, biological monitoring) must be devised that provides for strong interaction between risk assessment and management").

whether regulated activities continue to pose unacceptable risks despite past regulatory efforts and can identify activities that should be subject to new regulatory requirements. at the same time, retrospective evaluations can identify situations in which past regulations have been too burdensome and can safely be modified or waived. Monitoring the results of past regulatory decisions can also increase the scientific accuracy of future decisions. Monitoring and evaluation may be especially important for GM foods, because the current regulatory regime was pieced together out of many different regulatory programs none of which envisioned the radical changes that modern biotechnology was capable of bringing about.

Both the EPA and the FDA have in the past supported extensive pesticide monitoring efforts for *chemical* pesticides in food beyond those undertaken in support of their enforcement responsibilities.[472] The agencies have thus far not expanded those programs to encompass GM pest-resistant crops.[473] EPA's decision to register GM plant-pesticides only "conditionally" until 2001 may yield retrospective data as the registrants attempt to support their applications for full registrations and EPA conducts a "comprehensive reassessment" of those registrations.[474] EPA also ensures a limited degree of retrospective evaluation through the general requirement that registrants report any observed adverse health or environmental effects of pesticides to EPA. To ensure that at least this degree of monitoring occurs, EPA's January, 2001 regulations leave the adverse effects requirement in place even for plant-incorporated protectants that are otherwise exempted from FIFRA's registration requirements.[475] Given the current lack of any FDA labeling requirements for GM foods, it is difficult to see how any monitoring and retrospective health and safety evaluations could be undertaken by the manufacturers, the agency, or anyone else.

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472. Envtl. Prot. Agency, Office of Pesticide Programs, Guidance for Performing Aggregate Exposure and Risk Assessments 10 (Draft, Feb. 1, 1999).

473. It does not appear that the current registrations for GM pest-resistant crops require anything in the way of monitoring beyond the general requirement that registrants report to EPA any evidence that they receive that their pesticides pose unreasonable adverse effects on the environment. Envtl. Prot. Agency, Response of the Environmental Protection Agency to Petition for Rulemaking and Collateral Relief Concerning the Registration and Use of Genetically Engineered Plants Expressing Bacillus Thuringiensis Endotoxins, Submitted by Petitioners Greenpeace International, International Federation of Organic Agriculture Movements, International Center for Technology Assessment, at 2 (Apr. 19, 2000) [hereinafter EPA Greenpeace Response, Apr. 19, 2000].

474. EPA Greenpeace Response, Apr. 19, 2000, *supra* note 473, at 2.

475. EPA, FIFRA Plant-Incorporated Protectants Regulations, 2001, *supra* note 370, at 37,805.

VII. TOWARD A MORE PRECAUTIONARY REGULATORY APPROACH

In the preamble to its January, 2001 rules, EPA noted that "consumer acceptance is key to the success of agricultural products, and . . . consumer acceptance is strongly influenced by confidence that regulatory agencies have ensured the public safety."[476] The foregoing analysis suggests that EPA and FDA may not have achieved the degree of consumer acceptance necessary to ensure the continued viability of the industry. at the very least, it suggests that a fresh look at the current regulatory approach and the policies underlying it may be in order. This section of the Article will suggest some changes that may impede the progress of new biotechnologies more than its proponents desire but should result in greater public trust in the ultimate regulatory output.

A. Beyond Substantial Equivalence

The foundation upon which the U.S. agencies have erected the current relaxed regulatory approach to GM foods is the "substantial equivalence" doctrine. While its viability as a "scientific" principle is debatable, as a risk management policy, substantial equivalence is extremely vague. It thus presents a troubling underpinning for a regulatory regime that, as a practical matter, has not successfully regulated. Put simply, expert-assessed similarities between a GM food and its natural counterpart do not provide an especially convincing assurance for ordinary consumers that the GM food is safe.

Although the substantial equivalence doctrine was adopted with little fanfare in the United States, Japan, and Canada soon after it was adopted by the OECD,[477] many are having second thoughts about its appropriateness as a regulatory tool. The NAS Plant Pest Report noted that "the use of 'familiarity' as a guideline to minimize testing can sometimes be inappropriate and warrants

476. *Id.* at 37,804.

477. *See* Anne Mackenzie, GM Food Safety: Facts, Uncertainties, and Assessment, presented at the OECD Edinburgh Conference on the Scientific and Health Aspects of Genetically Modified Foods (Feb. 28–Mar. 1, 2000); Ryoji Takahara, *Administrative Oversight to Ensure Safety of Biotechnologically Produced Foods in Japan, in* GENETICALLY MODIFIED FOODS: SAFETY ISSUES 33, 42 (Karl-Heinz Engel et al. eds., 1995).

caution."[478] The March 2000 OECD-sponsored Edinburgh Conference concluded that it was "timely now, after six years of using the tool, to undertake a more detailed review."[479] The Conference appeared to reject the doctrine in at least one regulatory context when it reached a consensus that all genetically modified foods should be labeled, even if they appeared identical to unmodified food.[480] The U.S.-EU Consultative Forum that arose out of one of the Edinburgh Conference's recommendations concluded that "[t]he fact that a biotechnology food is held to be substantially equivalent to a conventional food should not be taken automatically to mean that it needs less testing or less regulatory oversight than 'non-substantially' equivalent biotechnology foods."[481]

In perhaps the most thoroughgoing rejection of the substantial equivalence doctrine to date, the January, 2001 report of an expert committee convened by the Royal Society of Canada recommended that "[a]pproval of new transgenic organisms for environmental release, and for use as food or feed, should be based on rigorous scientific assessment of their potential for causing harm to the environment or to human health," and "[s]uch testing should replace the current regulatory reliance on 'substantial equivalence' as a decision threshold."[482] With the impending demise of the substantial equivalence doctrine as a credible theoretical underpinning, the fragile veneer that has protected the regulatory process in the United States from overwhelming criticism is cracking.

The documents published by EPA and FDA in January 2001 represented the Clinton Administration's attempt to address the rapidly eroding level of public confidence in federal regulation of agricultural biotechnology. If successfully implemented, FDA's hastily crafted proposal will ensure that it receives pre-market notification of plans to introduce new GM foods into commerce, but it will not adjust the agency's strong reliance on the substantial equivalence doctrine in any substantial way. EPA's final rule appears to abandon the substantial equivalence principle for purposes of granting across-the-board exemptions from its testing

478. NRC GM PEST-PROTECTED PLANTS REPORT, *supra* note 1, at 73. The report defined "familiarity" as "indirect knowledge or experience obtained from similar gene products, plant varieties, or progenitor varieties grown under similar conditions and used for the same purposes in the same way," a definition that fits the "substantial equivalence" concept to a tee. *Id.*

479. Krebs, Chairman's Report, *supra* note 74, at 3.

480. OECD EDINBURGH RAPPORTEURS' SUMMARY, *supra* note 33, at 3 (noting that "[a]lmost all participants recognized the value of labeling in enabling consumer choice").

481. EU-U.S. CONSULTATIVE FORUM, FINAL REPORT, *supra* note 149, at 13.

482. ROYAL SOCIETY OF CANADA REPORT, 2001, *supra* note 14, at 191.

and risk management requirements, but the doctrine may still affect case-by-case decision-making at the staff level. The agency's curious re-proposal of one exemption that depends heavily upon substantial equivalence, combined with its historical adherence to proposed regulations in day-to-day decision-making, suggests caution in concluding that it has abandoned that principle altogether.

The Bush Administration has attempted to withdraw both actions and has signaled its intention to undertake its own re-evaluation of the regulatory process for agricultural biotechnology. Whether or not it allows the last-minute piecemeal efforts of the preceding administration to go into effect, the new administration should discard the poorly aging 1986 Coordinated Framework altogether and abandon the heavy role that the substantial equivalence doctrine has played in the United States regulatory regime. If the executive branch agencies are unwilling to replace the existing administratively crafted regulatory regime with one that will command the public's trust, then Congress should consider whether the time has come to implement a new statutory regime for GM foods. The recommendations below presume that Congress and the relevant regulatory agencies will be willing to examine seriously regulatory options that do not rely upon substantial equivalence, despite the predictable opposition of the regulated industries.

B. The Precautionary Principle and the Risk of Over-Regulation

Despite the efforts of some biotechnology proponents to characterize the critics as Luddites, most consumer and environmental groups are not inalterably opposed to GM foods.[483] Instead, they offer the "precautionary principle" as an alternative to the subjectivity of substantial equivalence for managing the health risks of GM foods.[484] The precautionary principle generally permits government to impose restrictions on activities that pose risks to

483. *See* LAPPE & BAILEY, *supra* note 14, at 17 (authors "do not reject all manipulations as being intrinsically wrong because they alter nature"). The Center for Science in the Public Interest, for example, has recognized the benefits of agricultural biotechnology, has not identified any serious safety concerns with current GM food products, and has endorsed labeling on the condition that it does not lead people to conclude that GM products are inferior to non-GM products. *News from CPSI: Biotech Foods: Friends or Foes?*, Nutrition Action Health Letter (Ctr. For Sci. in the Pub. Interest, Washington, D.C.), June 2000, at 2.

484. *See* Goldburg Testimony, Oct. 5, 1999, *supra* note 135 (genetic engineering "should proceed with appropriate precautions"); Chevassus-au-Louis, Prevention, *supra* note 471, at 1.

health and environment in the absence of "scientific" proof concerning the nature and severity of those risks. When substantial uncertainties prevent accurate risk assessments, the precautionary principle suggests a protective policy of erring on the side of safety.[485]

The Chairman of the Board of Trustees of the French Health and Food Safety Agency recently offered a sophisticated articulation of the precautionary principle that provides for regulatory decision-making based upon four broad precautionary criteria: proportionality, consistency, reversibility, and comparative analysis.[486] The *proportionality* criterion suggests that the decision maker take action that is proportionate to the nature of the potential risk.[487] In applying the *consistency* criterion, the government should not discriminate unfairly against one regulated entity or unfairly advantage another, and it should take consistent positions with respect to risks of similar magnitude.[488] The *reversibility* criterion demands greater precautions for irreversible risks and suggests that the agency carefully monitor to detect reversible adverse effects of past decisions.[489] The *comparative analysis* criterion obliges the decision maker to compare the extent to which alternative precautionary requirements advance or detract from the relevant societal goals.[490]

In applying these criteria, the decision maker should carefully analyze all of the available information and pay attention to the opinions of all of the relevant experts, even those whose opinions are in the minority.[491] The agency should employ a multidisciplinary approach to eliciting expert opinion to ensure against decisions driven by a consensus of expert opinion in one narrow discipline that is not shared by experts in other disciplines.[492] Most importantly, the decision-making process must be broadly inclusive so as to bring before the decision maker the legitimate ethical and

485. *See* ROYAL SOCIETY OF CANADA REPORT, 2001, *supra* note 14, at 194 (precautionary principle "advises that, in the face of scientific uncertainty or lack of knowledge, it is better to err on the side of protecting human and environmental safety than to err on the side of the risks").

486. Chevassus-au-Louis, Prevention, *supra* note 471, at 6.

487. *Id.* at 7.

488. *Id.*

489. *Id.* at 7–8.

490. *Id.* at 8.

491. *Id.* at 9 (arguing that decision makers "must take into account all minority or non-conventional opinions, so as to ensure that it is as extensive as possible prior to undergoing a critical analysis").

492. *Id.*

public policy concerns of nonexperts who are affected by the decisions.[493]

The precautionary principle finds few champions among the proponents of agricultural biotechnology. Positing that sufficient "scientific" evidence is available to resolve most disputes over the health risks posed by GM foods, they argue that the regulators should focus upon "probable, not hypothetical, risks."[494] The principle is, in their view, too vague and arbitrary to provide a basis for case-by-case regulatory decision-making.[495] They warn that stringent regulation under the precautionary principle will stifle research and thereby reduce the potential of agricultural biotechnology to improve human existence.[496]

Proponents respond that the precautionary principle by no means disavows the scientific method when data exist and scientists agree on how to interpret those data.[497] They do not, however, share the industry's faith in the powers of risk assessment, given the current incomplete state of information on the risks posed by agricultural biotechnologies.[498] The precautionary principle simply implements a cautious public policy of looking before we leap when the scientific studies that would allow for accurate assessment of the particular risks posed by particular products have not yet been undertaken.[499] In their view, biotechnology industry's

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493. *Id.*

494. *U.S. House Seeds of Opportunity Report*, *supra* note 25, at 69; *see also Public Meeting on Biotechnology in the Year 2000 and Beyond by the U.S. Food and Drug Administration* (Nov. 18, 1999) (remarks of Ralph Hardy) (arguing that policymakers should focus "on what is rather than the nebulous and never-ending what if").

495. *See U.S. House Seeds of Opportunity Report*, *supra* note 25, at 69; ROYAL SOCIETY OF CANADA REPORT, 2001, *supra* note 14, at 195 (critics of precautionary principle believe that it "lacks a uniform interpretation. . . .").

496. *See* Per Pinstrup-Andersen & Rajul Pandya-Lorch, *Securing and Sustaining Adequate World Food Production for the Third Millennium*, *in* NAT'L AGRIC. BIOTECHNOLOGY COUNCIL REPORT 11, WORLD FOOD SECURITY AND SUSTAINABILITY: THE IMPACTS OF BIOTECHNOLOGY AND INDUSTRIAL CONSOLIDATION 45 (Donald P. Weeks et al. eds., 1999) (arguing that "[t]he attitude toward risk among the non-poor in both industrialized and developing countries is a constraint to the use of agricultural biotechnology in and for developing countries"); Stipp, *Voice of Reason*, *supra* note 34, at 166 (interview with Gordon Conway of the Rockefeller Foundation) (suggesting that "[i]f the GM controversy caused a real curtailment of private investment in biotech, a lot of the potential for using it in the developing world would be lost").

497. *See* Chevassus-au-Louis, Prevention, *supra* note 471, at 6.

498. *Id.* at 4–5. The unfortunate proliferation of StarLink® corn in the human food supply, despite the fact that EPA has registered that product only for use as animal feed, is a dramatic demonstration of the risk of the kind of human error that human risk assessors frequently ignore. *See supra* Part V.H.

499. *See* ROYAL SOCIETY OF CANADA REPORT, 2001, *supra* note 81, at 198 (noting that the precautionary principle "counsels restraint in proceeding with the deployment of a

rejection of the precautionary principle is not really a demand for the application of sound science; rather, it is a call for the application of a less protective regulatory policy.

C. Notice

It is hard to instill public trust in a regulatory regime that articulates a vague and highly manipulable test for entry and then leaves it to the discretion of the regulatees to decide whether their products meet that test. Although many biotechnology companies continue to question the advisability of pre-market notification,[500] some companies and trade associations have expressed support for making the governmental notice and consultation process mandatory.[501] Perhaps more than any other action, FDA could enhance public trust in its ability to protect consumers from the risks of GM foods by finalizing as rapidly as possible its proposed pre-market notification requirements. Failing that, Congress should consider "rifle shot" legislation clarifying that GM foods are not generally recognized as safe. That change would ensure not only that FDA received notice of all GM foods, but it would also place on FDA the responsibility for promulgating testing requirements for GM foods. In a similar vein, EPA should issue a guidance document clarifying that it no longer recognizes its previously proposed exemptions for gene transfers from sexually compatible donor plants and from unrelated food plants and therefore expects to receive full-fledged registration and tolerance applications for all GM pest-resistant plants.

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technology in the 'absence of evidence,' and requires that the greater the potential risks, the stronger and more reliable be the 'evidence of their absence' ").

500. *See Public Meeting on Biotechnology in the Year 2000 and Beyond by the U.S. Food and Drug Administration* (Nov. 18, 1999) (remarks of Dr. Val Giddings) (finding "no evidence based on science, no evidence based on experience for any requirement to change" the FDA procedures).

501. *See Public Meeting on Biotechnology in the Year 2000 and Beyond by the U.S. Food and Drug Administration* (Nov. 18, 1999) (remarks of Don Fitz, National Food Processors Association) (American Soybean Association states that if "replacing this voluntary process with a mandatory approval would strengthen FDA's ability to reassure consumers regarding the safety of these products we would endorse such a change").

D. Transparency and Public Participation

Consumer groups complain that the industry in the mid-1990s quietly introduced genetically engineered crops into the food supply without a full public debate.[502] As one observer noted, "[m]any people might be perfectly happy to eat genetically modified foods, but nobody likes to be fooled."[503] A similar attempt to move genetically modified crops quietly into the European food supply ran into sharp protests by environmental groups who successfully tapped a general distrust of American multinational corporations to produce a strong political reaction against GM foods.[504] Following this rough public reception in Europe, a consensus appears to be emerging that "[t]he general public—consumers and citizens—not only have the right to know, but they also have valid points of view, which need to be effectively voiced, understood, and given their due weight in the decision-making and policy process."[505] There is little agreement, however, on the details of how to increase the transparency and inclusiveness of the existing decision-making process.

Some biotechnology proponents apparently believe that sufficient transparency can be achieved through broad-based industry-sponsored efforts to educate the public about the large benefits and comparatively small risks associated with GM foods.[506] Consumer and public interest groups worry that industry- and

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502. *See* Kriz, *Global Food Fights*, *supra* note 34, at 688 (quoting Charles Margulis of Greenpeace, International) (contending that "[i]t's obvious that the food industry wanted to keep this a secret from the consumers"); LAPPE & BAILEY, *supra* note 14, at 1 (arguing that "[m]any of the key innovations have occurred behind academic and corporate doors with little public input."); Raeburn, *Out of the Woods*, *supra* note 415, at 56 (noting that most consumers did not find out that they were eating genetically modified foods until 1999, long after GM foods had become ubiquitous in the food supply).

503. Paul Raeburn, *Where Do We Go from Here? The View from Times Square*, *in* NAT'L AGRIC. BIOTECHNOLOGY COUNCIL REPORT 11, WORLD FOOD SECURITY AND SUSTAINABILITY: THE IMPACTS OF BIOTECHNOLOGY AND INDUSTRIAL CONSOLIDATION 151 (Donald P. Weeks et al. eds., 1999).

504. *See* Kriz, *Global Food Fights*, *supra* note 34, at 688.

505. OECD EDINBURGH RAPPORTEURS' SUMMARY, *supra* note 33, at 2.

506. *See U.S. House Seeds of Opportunity Report*, *supra* note 25, at 4 (arguing that "the Administration, industry, and scientific community have a responsibility to educate the public and improve the availability of information on the long record of safe use of agricultural biotechnology products"). In April 1999, a coalition of food producers and marketers called the Alliance for Better Foods hired the public relations/lobbying firm of BSMG to conduct a $50 million per year campaign to convince the public and lawmakers that GM foods were no different from foods derived through traditional breeding techniques. Bettelheim, *Reluctant Congress*, *supra* note 425, at 938; McCauley, *Big Food Companies*, *supra* note 412.

government-sponsored public information campaigns can easily degenerate into boosterish propaganda that hype unproven biotechnologies and belittle legitimate concerns about health and environmental risks.[507] In their view, "public education" is too often a top-down process in which supposedly objective experts convey their conclusions about the nature and magnitude of health and environmental risks to a supposedly confused and ignorant public.[508]

Communication about matters of great concern to consumers cannot be a one-way street. As defined by the Codex Committee on General Principles, "risk communication" is "the interactive exchange of information and opinions concerning risk among risk assessors, risk managers, consumers, and other interested parties."[509] Consumers may not be educated on the fine points of the biology of GM foods, but they are capable of understanding information about risks, and they resent being treated in a condescending fashion. If manufacturers of GM foods and the government expect consumers to trust governmental decisions about those foods, they will have to treat consumer representatives as equals in the debates about the nature and magnitude of the risks they pose.[510]

In the age of the Internet, there is simply no excuse for the opacity of the existing process. FDA should publish notice of informal GRAS consultations on its website, make the relevant information available to the public via the website, and elicit public

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507. *See Public Meeting on Biotechnology in the Year 2000 and Beyond by the U.S. Food and Drug Administration* (Nov. 18, 1999) (remarks of Edward Groth, Consumers Union) [hereinafter Groth Remarks, Nov. 18, 1999] (arguing that public educational efforts by federal agencies and the biotechnology industry are "designed essentially to make the public think the way the FDA and the industry think about the issues"); *Public Meeting on Biotechnology in the Year 2000 and Beyond by the U.S. Food and Drug Administration* (Nov. 18, 1999) (remarks of Marion Nestle, New York University) (complaining that "the industry is treating consumer perceptions as a public relations problem, one that can be fixed by an advertising or education campaign").

508. *See* Cornelia Butler Flora, *Agriculture Biotechnology: Social Implications and Integration of Landscape and Lifescape, in* NAT'L AGRIC. BIOTECHNOLOGY COUNCIL REPORT 11, WORLD FOOD SECURITY AND SUSTAINABILITY: THE IMPACTS OF BIOTECHNOLOGY AND INDUSTRIAL CONSOLIDATION 62 (Donald P. Weeks et al. eds., 1999) (industry response to consumer concerns about risk "was to state that they did not understand the science involved, thereby heightening opposition"); Groth Remarks, Nov. 18, 1999, *supra* note 507 (arguing that much public cynicism about GM foods is the result of "top down arrogant . . . communication that says, consumers, you don't understand this problem").

509. Chevassus-au-Louis, Prevention, *supra* note 471, at 12.

510. *See* Daniel E. Wueste et al., *Workshop Report: Regulatory and Public Policy Perspectives, in* NAT'L AGRIC. BIOTECHNOLOGY COUNCIL REPORT 10, AGRICULTURAL BIOTECHNOLOGY AND ENVIRONMENTAL QUALITY: GENE ESCAPE AND PEST RESISTANCE 23, 28 (Ralph W.E. Hardy & Jane Baker Segelken eds., 1998) (noting that "effective communication" must "be in the form of dialogues among concerned and impacted parties").

comments via snail or e-mail. EPA's pesticide registration procedures seem reasonably well tailored toward eliciting public participation in registration decisions to the extent that plant-pesticides are not exempt. Both agencies should continue to make liberal use of advisory committees, but they should recognize that advisory committees are not an adequate substitute for full public participation. The agencies should also err on the side of making health and safety testing data public despite industry trade secrecy claims.[511]

E. Data Collection, Data Evaluation, and Risk Assessment

The contrast between the substantial equivalence doctrine and the precautionary principle is readily apparent on the question whether the government should require manufacturers of GM foods to engage in health and safety testing prior to marketing them to consumers. Scientists can attempt to assess the direct risks that GM foods pose to human health with standard bioassays in laboratory animals,[512] but it is often difficult or even impossible to feed the animals sufficient quantities of whole foods to achieve a desirable margin of safety for human beings.[513] One solution is to switch from mice and rats to animals that consume large quantities of feed like cows and hogs, but it is not clear whether the results may be extrapolated to humans.[514] Biotechnology proponents therefore argue that testing of whole GM foods in laboratory animals "is not feasible, and would be wasteful in terms of laboratory animal resources."[515]

Normally, the toxicological concern with respect to GM foods is for the toxicity of the proteins or other expression products of the transferred genes. Toxicity testing of such expression products is

511. *See* ROYAL SOCIETY OF CANADA REPORT, 2001, *supra* note 14, at 214 (observing that "the more regulatory agencies limit free access to the data upon which their decisions are based, the more compromised becomes the claim that the regulatory process is 'science based'").

512. NRC GM PEST-PROTECTED PLANTS REPORT, *supra* note 1, at 69.

513. *See id.* at 69; ROYAL SOCIETY OF CANADA REPORT, 2001, *supra* note 14, at 48.

514. NRC GM PEST-PROTECTED PLANTS REPORT, *supra* note 1, at 70. Cows, for example, have a four-chambered stomach that can "serve as a buffer from the effects of some proteins." *Id.*

515. *U.S. House Seeds of Opportunity Report, supra* note 25, at 38; *Public Meeting on Biotechnology in the Year 2000 and Beyond by the U.S. Food and Drug Administration* (Dec. 13, 1999) (remarks of Susan L. Hefle, University of Nebraska) [hereinafter Hefle Remarks, Dec. 13, 1999.

possible in theory,[516] but sometimes problematic in practice, because it is difficult and expensive to isolate sufficient quantities of expressed proteins, fats, and oils for effective toxicity testing.[517] In addition, no universally applicable laboratory animal tests exist for assessing the allergenic potential of foods.[518] Although a number of standardized tests exist for testing in human volunteers, such testing is also quite expensive, and it will not necessarily identify substances that are allergenic in small subpopulations.[519] Thus biotechnology proponents argue that the substantial equivalence approach is a sensible way to ensure that GM foods are reasonably safe without going to a lot of expense on potentially useless testing.

Advocates of the precautionary principle, by contrast, believe that the scientific uncertainties surrounding GM foods are sufficiently large to warrant full-scale testing, not approval by analogy. While it may be expensive in the short run, testing is the only way to know whether the foods are not likely to be harmful when consumed by human beings.[520] If adequate animal models do not exist for allergenicity testing, the food industry and government scientific agencies should expend some of their considerable resources developing such tests.[521] To allow manufacturers to market untested GM foods to unsuspecting consumers because the tests are expensive or unavailable is to use human beings as involuntary guinea pigs.

It is unlikely that the present testing regime, in which a manufacturer can avoid virtually all testing by simply concluding that its product is substantially equivalent to existing food, is sufficient to command public trust in the efficacy of the regulatory process. In the future, GM foods should be tested comprehensively in accordance with prescribed testing protocols designed to detect risks of unintended and unanticipated adverse health effects.[522] Although

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516. *See* Hefle Remarks, Dec. 13, 1999, *supra* note 515 (noting that "[t]oxicological tests targeted to the novel protein are most appropriate").

517. *See supra* Part I.B.1.d.

518. *See* Goldburg Remarks, Nov. 30, 1999, *supra* note 431 (observing that "for most proteins, including those from foods that are not commonly allergenic and those from non-food sources such as bacteria, no such testing is possible").

519. NRC GM PEST-PROTECTED PLANTS REPORT, *supra* note 1, at 67.

520. *See Public Meeting on Biotechnology in the Year 2000 and Beyond by the in U.S. Food and Drug Administration* (Nov. 30, 1999) (remarks of Steve M. Druker, Alliance for Bio-Integrity) (asserting that rigorous long-term animal feeding studies are the only viable approach to determining whether GM foods meet the reasonable certainty of no harm test).

521. *See* Goldburg Remarks, Nov. 30, 1999, *supra* note 431 (complaining that FDA "has not used its scientific resources to develop and publish guidance to industry on how to assess the allergenic potential of proteins").

522. *See* ROYAL SOCIETY OF CANADA REPORT, 2001, *supra* note 14, at 189–90 (recommending that newly developed GM plants be "subjected to intense scrutiny at six relevant

allergenicity testing is in its infancy, some form of allergenicity assessment should be required for *all* GM foods.[523] The testing guidelines should be flexible enough to allow for changes as scientists learn more about allergenicity. at the very least, such a requirement could stimulate further industry-funded research aimed at developing dependable allergenicity testing in animal or other models.[524]

F. Consumer Choice

Perhaps the most contentious of the public policy debates over GM foods is the debate over whether GM food products should contain labels. Biotechnology proponents argue that since GM foods are substantially equivalent to unmodified foods, there is no legitimate reason to require special labeling for those products.[525] They maintain that labeling will "mislead" or "confuse" consumers[526] by sending

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levels (genomic, transcript, protein, metabolic, health impacts, environmental impacts) before they [are] approved for commercial production").

523. *See* ROYAL SOCIETY OF CANADA REPORT, 2001, *supra* note 14, at 73 (recommending "a specific, scientifically based, comprehensive approach for ensuring that adequate allergenicity assessment will be performed on a GM food. . . ."); NRC GM PEST-PROTECTED PLANTS REPORT, *supra* note 1, at 66 (noting that "[t]he strong likelihood that gene products currently found in commercial transgenic pest-protected plants are not allergens does not remove the need for a minimum of properly planned and executed tests").

524. Codex Alimentarius has established an Ad Hoc Task Force on Foods Derived from Biotechnology that is drafting guidelines for the conduct of safety assessment of GM foods. *See* Peter Menyasz, *Ottawa Meeting Produces Little Progress on Labels for Genetically Modified Foods*, 25 Chem. Reg. Rep. (BNA) 836 (May 15, 2001). These guidelines, once completed, will not be binding on manufacturers and importers. EPA and FDA could, however, use the guidelines as a model for promulgating specific protocols for safety assessment of GM foods.

525. *Public Meeting on Biotechnology in the Year 2000 and Beyond by the U.S. Food and Drug Administration* (Nov. 18, 1999) (remarks of Rhona Applebaum, National Food Processors Association) (Association supports FDA's labeling policy); *Public Meeting on Biotechnology in the Year 2000 and Beyond by the U.S. Food and Drug Administration* (Nov. 18, 1999) (remarks of Lisa Katic, Grocery Manufacturers of America) [hereinafter Katic Remarks, Nov. 18, 1999] (reporting support of Grocery Manufacturers of America for FDA labeling policy); *Public Meeting on Biotechnology in the Year 2000 and Beyond by the U.S. Food and Drug Administration* (Nov. 18, 1999) (remarks of Carl Loop, Vice President, American Farm Bureau Federation) (reporting views of American Farm Bureau Federation); *Industry Opposes Biotech Labeling*, CHEM. MKT. RPTR., Feb. 28, 2000, at 5 (quoting Michael Phillips of the Biotechnology Industry Association).

526. *U.S. House Seeds of Opportunity Report*, *supra* note 25, at 53 (arguing that "labeling of agricultural biotechnology products would confuse, not inform, consumers"); Katic Remarks, Nov. 18, 1999, *supra* note 525 (arguing that "[s]pecial mandatory labeling could mislead consumers into believing that foods produced through this technology are either different from conventional foods or that they present a risk").

an implicit message that consumers should be worried about genetically modified foods.[527]

Biotechnology skeptics argue that accurate labeling is essential to informed consumer choices about the quality, safety, and other important aspects of the food they eat. Even if GM foods pose only tiny health risks, many consumers see no reason why they should be subjected to those risks without their consent.[528] Unwilling to trust paternalistic companies and agencies to decide for them, consumers may want to await further testing of or broader experience with GM foods before consuming them.[529] Consumers with severe allergies or special dietary limitations may want to avoid foods that are not "tried and true."[530] Some consumers may want to discourage the trend toward environmentally damaging monocultures by refusing to purchase GM foods.[531] Others may have moral or religious reasons for avoiding GM foods containing genes from particular species of host organisms.[532] Finally, if GM foods are not identified by labels, it may be impossible for future epidemiologists

527. *See* William P. Barrett, *Food-Label Follies*, FORBES, Dec. 27, 1999, at 30 [hereinafter Barrett, *Food-Label Follies*] (labels "would . . . imply incorrectly that the buyer needs to be warned of unspecified dangers"); Kriz, *Global Food Fights*, *supra* note 34, at 688 (quoting Gene Grabowski of the Grocery Manufacturers Association) (a labeling requirement would be "telling consumers that there is something wrong with this product").

528. Stipp, *Voice of Reason*, *supra* note 34, at 172 (interview with Gordon Conway of the Rockefeller Foundation) ("What people really object to is being exposed to risks without their choice.").

529. Silbergeld Testimony, Oct. 6, 1999, *supra* note 130 (alluding to consumers who "want to wait until there is greater experience demonstrating long-term food and environmental safety before they try genetically engineered varieties").

530. *See* Goldburg Remarks, Nov. 30, 1999, *supra* note 431 (arguing that "should an allergen added to a genetically engineered food not be detected by industry's current screening procedures, allergic consumers will likely not be able to avoid foods containing the allergen"); Jacobson Remarks, Nov. 18, 1999, *supra* note 454 (arguing that without labeling "[p]eople with multiple or severe allergies, or with general safety concerns, fear that foods they were always able to safely consume might harbor new, unsafe substances").

531. *See* ROYAL SOCIETY OF CANADA REPORT, 2001, *supra* note 14, at 220 (referring to the "alleged right of consumers to participate intelligently in the marketplace and to exercise the 'power of the pocketbook' in support of the technologies and industries they prefer").

532. *See id.* at 7 (noting that "[r]eligious and ethnic groups that observe religious dietary rules prohibiting the eating of certain animals have obvious problems with the consumption of vegetable or other animal foods that may carry genes taken from the prohibited animal"); Jacobson Remarks, Nov. 18, 1999, *supra* note 454 (noting that "[v]egetarians and people with certain religious beliefs may not want to eat foods containing gene products derived from animals"); LAPPE & BAILEY, *supra* note 14, at 125 (noting that "many religious persons for whom diet is a significant part of their practice want assurances that the food they eat is not adulterated").

to design adequate studies to compare populations of exposed individuals with populations of unexposed persons.[533]

Noting that labeling necessarily requires segregation, the industry points to practical difficulties in keeping GM grain separate as it moves from field to elevator to processor to grocery stores.[534] Although few, if any, studies of the cost of segregation have been undertaken, labeling opponents argue that segregation is likely to be so expensive that processors and distributors will discourage farmers from growing GM crops.[535] Labeling advocates, however, point out that the $4 billion per year organic foods industry segregates and labels organically grown crops at every stage of production and still manages to make a profit.[536]

Supporters of agricultural biotechnology are confident that the market will provide non-GM foods that are labeled for people who are willing to pay for labeling in the same way that it has created niches for kosher and organic foods.[537] They would, however, demand that any explicit claims that a food is GM-free and any implicit claims that GM-free foods are superior to GM foods be substantiated to protect consumers from fraud.[538] Consumer advocates maintain that uniform federal labeling requirements would

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533. *See* KRIMSKY & WRUBEL, *supra* note 40, at 109 (food labels "make possible post hoc epidemiological studies"); LAPPE & BAILEY, *supra* note 14, at 2 (noting that in the absence of labeling, "epidemiologists are hamstrung").

534. Giddings House Testimony, Mar. 3, 1999, *supra* note 29 (arguing that "[f]or most food products, segregation from farm to grocery store would be impracticable and expensive"); Barrett, *Food-Label Follies*, *supra* note 527 (arguing that "[t]he need to segregate gene-spliced foods, especially the thousands of processed foods that contain small amounts of derivatives of corn or soybeans, would raise production costs in a low-profit-margin sector").

535. Giddings House Testimony, Mar. 3, 1999, *supra* note 29 (noting that "segregation would be a major disincentive for farmers, shippers, grain processors and food processors to grow or utilize the newer variety").

536. TEITEL & WILSON, *supra* note 24, at 67; Raphael Thierrin, *Placing Several Eggs in Our Basket: Keeping Diversity in Agriculture*, *in* NAT'L AGRIC. BIOTECHNOLOGY COUNCIL REP. 9, RESOURCE MANAGEMENT IN CHALLENGED ENVIRONMENTS 71, 77 (Ralph W.E. Hardy et al. eds., 1998) (noting that "[t]he organic industry is able to move a great diversity of certified organic products in a labeled, segregated environment, and it believes that distributors of bioengineered products can do the same").

537. Barrett, *Food-Label Follies*, *supra* note 527, at 30 (arguing that "[i]f large numbers of people really want to avoid gene-spliced food, niche markets will arise . . . as they do for kosher, halal and organic products"); Hoban, *International Acceptance*, *supra* note 421, at 71.

538. *Public Meeting on Biotechnology in the Year 2000 and Beyond by the U.S. Food and Drug Administration* (Nov. 30, 1999) (remarks of Richard Frank, attorney for Food Distributors International) (arguing that "[i]f the context implies that a food labeled biotech-free is safer or higher in quality, then that claim is misleading unless it can be substantiated"); *Public Meeting on Biotechnology in the Year 2000 and Beyond by the U.S. Food and Drug Administration* (Nov. 30, 1999) (remarks of Kendal Keith, President, National Grain and Feed Association) (arguing that "voluntary labeling means that FDA will be called upon to develop guidelines to ensure that such labeling is not false or misleading").

be far preferable to sporadic and most likely inconsistent market-driven efforts by some companies to label products as GM-free.[539]

Despite the concerns of the biotechnology industry, there appears to be an emerging worldwide consensus that GM foods should be labeled to allow consumers to choose whether or not to purchase such foods. at the OECD Edinburgh Conference "[a]lmost all participants recognized the value of labelling in enabling consumer choice."[540] The resulting U.S.-EU Consultative Forum concluded that "at the very least, the EU and U.S. should establish content-based mandatory labelling requirements for finished products containing novel genetic material."[541] Even many observers who generally support greater availability of GM foods believe that the industry could eliminate a great deal of needless controversy if it would simply place a discrete label on GM foods.[542]

The decision to require labeling, however, is not the end of the matter. Difficult questions remain concerning the content of the label and the kinds of GM foods to which the labeling requirement should apply. Given the fact that GM crops are already quite prevalent in some markets, it may be impossible to guarantee that a processed food contains not a single molecule of a GM constituent.[543] The European Union, for example, exempts from its labeling requirements foods containing no more than one percent material from GM plants.[544] Another possible approach would be a

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539. Groth Remarks, Nov. 18, 1999, *supra* note 507 (arguing that mandatory standards for labeling would be far more uniform and fairer to producers and consumers than relying on a voluntary system to grow up with market forces driving it).

540. OECD EDINBURGH RAPPORTEURS' SUMMARY, *supra* note 33, at 3.

541. EU-U.S. CONSULTATIVE FORUM, FINAL REPORT, *supra* note 149, at 19.

542. *See* Paul Raeburn, *Warning: Biotech Is Hurting Itself,* BUSINESS WEEK, Dec. 20, 1999, at 78 (suggesting that "putting a discreet label on GM foods somewhere near the ingredients list might be the smartest thing the industry could do").

543. *See Public Meeting on Biotechnology in the Year 2000 and Beyond by the U.S. Food and Drug Administration* (Nov. 18, 1999) (remarks of Robert Lake, U.S. Food and Drug Admin) ("[H]ow small does it have to be before one calls it free?"); Keith Remarks, Nov. 30, 1999, *supra* note 538 (arguing that "there has to be some reasonable tolerance established if we are going to go to . . . [a GM food labeling] standard").

544. European Commission, Commission Regulation 1139/98 of 26 May 1998, 1998 O.J. (L 159) 4, amended by Commission Regulation No. 49/2000 of 10 Jan. 2000 Amending Council Regulation (EC) No. 1139/98 Concerning the Compulsory Indication on the Labeling of Certain Foodstuffs Produced from Genetically Modified Organisms of Particulars Other Than Those Provided for in Directive 79/112/EEC, 2000 O.J. (L 6) 13–14 , art. 1.2(b); European Commission, Commission Regulation No. 50/2000 of 10 Jan. 2000 on the Labeling of Foodstuffs and Food Ingredients Containing Additives and Flavourings That Have Been Genetically Modified or Have Been Produced From GMOS, 2000 O.J. (L 6) 15–17.

The Australia New Zealand Food Authority (ANZFA) recently adopted a similar provision requiring mandatory labeling in food that is produced with, or contains an ingredient derived or developed from, a GMO. *See* Australia New Zealand Food Standards Code, Standard 1.5.2(2001), *available* at http://www.anzfa.gov.au/foodstandardscodecontents/standard15/

technology-based requirement that unlabeled foods be as free of GM-products as is technologically feasible. A regulatory regime that requires labeling will have to grapple with these questions, and the answers that it provides will no doubt fail to satisfy individuals on both sides of the labeling debate. The answer, however, should not be a generic label, inspired by the difficulties of segregation, that says that the labeled food "may or may not contain" GM ingredients. Such a label would not only be uninformative, it would provide food manufacturers and importers an excuse to ignore consumer demands for GM-free food.

Since FDA is the only agency with relevant labeling authority, it should require manufacturers and importers of all foods containing more than a prescribed percentage of material from GM plants to place appropriate labels on or near such foods.[545] FDA could attempt to accomplish this result by expanding its interpretation of the "materiality" concept in Section 201(n) to include changes that are in fact material to most consumers and especially to those with food allergies. This strategy, however, risks reversal in court at the behest of manufacturers of GM foods who read the materiality requirement very narrowly.[546] Failing that, FDA should explore its authority under Section 403(i) to require labeling for GM foods on the ground that they are fabricated from two or more ingredients.[547]

If FDA does not quickly initiate a rulemaking to require labeling of GM foods, Congress should enact a separate labeling

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standard152.cfm. *See generally* ANZFA, LABELING GENETICALLY MODIFIED FOODS, ANZFA FACT SHEET (Aug. 2000). Flavors that are present in a concentration of no more than 0.1% are exempted from the labeling requirement, as are foods, ingredients, and processing aids in which genetically modified food is "unintentionally present in a quantity no more than 10g/kg per ingredient." *See* ANZFA Standard 1.5.2, § 4(1)(f).

545. At the very least, FDA should require labeling for GM foods if they derive from GM plants containing genes transferred from plants that are known to be allergenic. Under the current regulatory regime, manufacturers may apply their "knowledge" to conclude that such gene transfers does not increase the allergenic potential of the host plant. *See supra* Part III.D.2.a. Consumers should at least be put on notice that manufacturers have drawn this conclusion, so that they may avoid such products if they disagree with the manufacturers' application of their own knowledge.

546. The court in *Alliance For Bio-Integrity v. Shalala* questioned in dicta FDA's authority to rely upon consumer demand to require labeling of GM foods. 116 F. Supp. 2d 166, 179 (D.D.C. 2000).

547. 21 U.S.C. § 343(i) (1994). A labeling strategy that focuses exclusively upon FDA must recognize that FDA does not attempt to regulate plants that have been genetically engineered to be plant-pesticides because FDA defers to EPA in that regard. Therefore, if FDA does decide to require labeling, it must expand its labeling regime to include plant-incorporated protectants. This should not be difficult as a legal matter, because FDA's authority under sections 403(a)(1), 201(n), and 403(i) clearly encompasses such foods.

requirement. In 1999, Rep. Dennis Kucinich introduced a bill that would have required labeling of all foods containing genetically modified substances.[548] In introducing a companion bill in the Senate,[549] Sen. Barbara Boxer stressed that in the absence of any FDA decisions to require pre-market testing of GM foods, "the least we can do is label the products."[550] Although more than a dozen public interest groups supported the bill,[551] the Clinton Administration joined the industry and farm state representatives in opposing it,[552] and it was not enacted. If GM foods are to be become a part of the national diet, the 107th Congress should enact labeling legislation as quickly as possible.[553]

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548. H.R. 3377, 106th Cong., 2d Sess. (1999).

549. S. 2080, 106th Cong., 2d Sess. (2000); *see* Bettelheim, *Reluctant Congress*, *supra* note 425, at 939.

550. Bettelheim, *Reluctant Congress*, *supra* note 425, at 939 (quoting Sen. Barbara Boxer).

551. Amy Borrus, *The "Frankenfood" Monster Stalks Capitol Hill*, BUS. WK., Dec. 13, 1999, at 55 [hereinafter Borrus, *Frankenfood Monster*].

552. *Id.* at 55; Kriz, *Global Food Fights*, *supra* note 34, at 688. An intense industry lobbying effort paid off when twenty-seven House members who originally signed a letter requesting FDA to require labeling for GM foods declined to sponsor the Kucinich bill after being contacted by industry lobbyists. Borrus, *Frankenfood Monster*, *supra* note 551, at 55.

553. A company that does not want to label GM foods may claim that the labeling requirement is inconsistent with its First Amendment right "not to speak." In *International Dairy Foods v. Amestoy*, several dairy companies and industry associations challenged a Vermont statute requiring dairy manufacturers to identify products that were, or might have been, derived from dairy cows treated with rBST. 92 F.3d 67 (2d Cir. 1996). The court held that the statute "contravene[d] core First Amendment values," because it "indisputably" required dairy producers "to speak when they would rather not." The state had not claimed that the labeling statute was intended to protect public health and safety; the governmental interest underlying the statute was only the public's "right to know." *Id.* at 73. The court found that consumer curiosity was "insufficient to justify compromising protected constitutional rights." *Id.* at 73. Absent "some indication that . . . information bears on a reasonable concern for human health or safety or some other sufficiently substantial governmental concern, the manufacturers cannot be compelled to disclose it." *Id.* at 74.

There are good reasons to believe that *Amestoy* was wrongly decided. The Supreme Court has explicitly stated that the Constitution "accords a lesser protection to commercial speech than to other constitutionally guaranteed expression," Cent. Hudson Gas & Elec. Corp. v. Pub. Serv. Comm'n, 447 U.S. 557, 562–63 (1980), and state and federal governments have considerable leeway in requiring corporations engaged in commerce to make information available to consumers to ensure that consumer decisions are "intelligent and well-informed." Va. Bd. of Pharmacy v. Va. Consumers Council, 425 U.S. 748, 765 (1976). The Federal Trade Commission has promulgated rules requiring labeling aimed an informing consumers without any serious constitutional objection. *See, e.g.*, FTC Care Labeling of Textile Wearing Apparel Rule, 16 C.F.R. § 423 (1991). The Court has also recognized a distinction between mandatory disclosure requirements on foods and products and regulations preventing companies from communicating with consumers. *See* Zauderer v. Office of Disciplinary Counsel, 471 U.S. 626, 650 (1985). The *Amestoy* court afforded very little deference to the state legislature's determination that the informational interests of its consumers were substantial and warranted protection.

In any event, Congress or the FDA could legitimately conclude that the health consequences of human exposure to GM foods are not sufficiently well-understood to support a

G. Risk Management

Risk management is largely a matter of public policy, and suggestions for changes in risk management aspects of the current regulatory regime will necessarily reflect some underlying view of proper regulatory policy. The following analysis assumes that recent indications of public distrust in the regulatory system will move policy in the direction of a more precautionary approach.

1. Product Bans and Moratoria—Some critics of GM foods are opposed to them for moral, religious, or other reasons or have so little trust in the regulatory process that they would ban all sale and distribution of GM seeds and GM crops. A ban would unquestionably protect consumers from any risks posed by GM foods, but it would also deprive growers and consumers of the potential benefits of GM crops. In the long run, it might prove self-defeating as other countries employed agricultural biotechnologies and exported GM foods to the United States. Rather than exploring whether a ban on GM foods is warranted, it is probably more useful (and more realistic) to explore how the regulatory regimes that are in place can better manage the health and environmental risks of GM foods.[554]

The conclusion that a universal ban is unwarranted does not, however, imply that the ban is an inappropriate regulatory tool in all cases. Product bans can play a very useful role in protecting consumers from some especially dangerous aspects of some GM plants and in stimulating alternative ways to produce and grow GM crops.[555] For example, there are very few reasons, beyond familiarity and cost, to continue using antibiotic resistance marker genes in GM plants when alternative marker technologies are available. The British Medical Association, an expert panel appointed by the Royal Society of Canada, and the OECD Edinburgh Conference

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finding that they may be safely consumed in all cases even if, by the manufacturer's estimation, they are generally recognized as safe. For example, so little is known about how to measure the allergenic potential of novel proteins in foods that Congress or the FDA could reasonably conclude that food labels should contain information about GM content to allow persons with allergies to make informed decisions about whether to consume them. Thus, a labeling requirement for GM foods is easily justifiable under the health and safety rationale that the *Amestoy* court clearly acknowledged as appropriate under the First Amendment.

554. *See* Krebs, Chairman's Report, *supra* note 74, at 4 (concluding that "the strongly expressed demand for GM technology in developing countries casts substantial doubt on proposals for a worldwide moratorium made by some participants").

555. *See* Thomas O. McGarity, *Radical Technology-Forcing in Environmental Regulation*, 27 LOY. L.A. L. REV. 943 (1994).

have all concluded that it is no longer necessary to use antibiotic-resistance marker genes to achieve effective gene transfers in plants, and they have recommended that biotechnology companies phase out such markers.[556] This is a sound application of the precautionary principle, and it should be implemented as rapidly as possible.

An alternative to a product ban is a moratorium for the period of time required to accomplish some necessary intermediate step. Skeptics who do not favor an outright ban on GM foods might still demand a moratorium on the sale of some or all GM foods while the relevant government agencies put an adequate regulatory regime in place and while industry and academic scientists undertake the studies necessary to write detailed protocols for conducting appropriate safety studies. For example, a serious attempt to implement the precautionary principle might impose a moratorium on the marketing of GM foods in the United States pending the promulgation of adequate protocols for allergenicity testing and the implementation of an effective monitoring regime for GM foods in the marketplace.

2. Universal Pre-Market Approval—The recent Royal Society of Canada report suggested that "substantial equivalence" should not be employed as a threshold screening device through which GM foods are exempted from pre-market testing and review.[557] In particular, risk management decisions should be based upon thorough testing of GM plants for any adverse health or environmental effects.[558] The substantial equivalence concept could, however, prove useful as a benchmark of acceptable "background" risk.[559] The U.S.-EU Consultative forum recommended that all products of modern agricultural biotechnologies "be subject to a mandatory pre-market examination by the appropriate regulatory authorities and approved for sale only after they are found to meet the standard of presenting a reasonable certainty of no harm."[560] at least one major U.S. trade association has similarly taken the position that the fed-

556. OECD EDINBURGH RAPPORTEURS' SUMMARY, *supra* note 33, at 3.

557. ROYAL SOCIETY OF CANADA REPORT, 2001, *supra* note 14, at 206 (recommending that "those who are responsible for the regulation of new technologies should not presume its safety unless there is a reliable scientific basis for considering it safe").

558. *Id.* at 206 (suggesting that "the primary burden of proof is upon those who would deploy these food biotechnology products to carry out the full range of tests necessary to demonstrate reliably that they do not pose unacceptable risks").

559. *Id.* at 205 (suggesting that a GM plant should be approved for commercialization only after thorough testing has demonstrated that the GM food is substantially equivalent "in the types and magnitudes of health or environmental risks to those posed by the employment of its traditional, non-GM alternative").

560. EU-U.S. CONSULTATIVE FORUM, FINAL REPORT, *supra* note 149, at 8.

eral government should require manufacturers to "obtain clearances for new varieties in both the United States and in major export markets" before they are allowed to market GM food products in the United States.[561]

All of these recommendations share a common rejection of the substantial equivalence doctrine as a risk management policy and a preference for a regulatory process that more closely approximates the precautionary approach that Congress clearly envisioned when it enacted the Food Additive Amendments to the FDCA. FDA should implement these recommendations by abandoning the substantial equivalence justification for its liberal use of the GRAS concept and concluding that all GM foods contain food additives. Failing that, Congress should enact a "rifle shot" amendment to the FDCA providing that GM foods are food additives subject to the statutory approval process for those substances. Since both FDA in its food additive regulations and EPA in its tolerance setting actions apply the "reasonable certainty of no harm" test for product approval, this would ensure that all GM foods passed a safety-based threshold that did not allow the potential benefits of agricultural biotechnologies to overwhelm safety concerns.[562] Congress could alleviate FDA's understandable reluctance to launch a major new regulatory program with no new resources by requiring petitioners to pay application fees of sufficient magnitude to cover the cost of the approval process.

H. Monitoring and Enforcement

FDA has no systematic monitoring program in place to determine whether or not manufacturers and importers have been abusing the GRAS process. To protect consumers from further StarLink® episodes, FDA should establish a monitoring regime, similar to the regime currently in place for monitoring pesticide residues, for testing domestic and imported foods for the presence of GM food. FDA should begin by initiating (perhaps in a cooperative agreement with EPA) a monitoring program for GM

561. *Hearing Before the House Comm. on Agric. Subcomm. on Risk Mgmt., Research, and Specialty Crops*, 106th Cong. (Mar. 3, 1999) (testimony of Mike Yost, President, American Soybean Association).

562. *See* EU-U.S. CONSULTATIVE FORUM, FINAL REPORT, *supra* note 149, at 11 (taking the position that "[r]isk/benefit considerations should not be introduced until the basic threshold of reasonable certainty of no harm to human health has been reached").

pest-resistant plants using available tests for the presence of Bt endotoxins in food. The agencies should expand the program as tests for other proteins that are characteristic of GM foods become available. Since neither FDA nor EPA have adequate resources to conduct random testing of foods for the presence of illegal GM residues, Congress should allocate substantial additional resources to EPA and FDA for the purpose of monitoring and enforcement. Finally, both agencies may be able to come up with innovative ways for simplifying enforcement at the time that they conduct premarket clearance for GM plants. For example, EPA could require that the seeds for any GM pest-resistant plant that is not registered for general food use must be colored differently from normal seeds. It could even explore requirements that the GM plant itself be genetically engineered to ensure that the plant and all edible constituents are easily identified by color. Implementation of such innovative approaches could prevent future StarLink® fiascoes.

I. Retrospective Evaluation

Nearly all observers of the current regulatory regime in the United States believe that the government needs to do more to ensure that someone is undertaking long-term assessments of the health consequences of large-scale introduction of GM plants into the food supply. The Canadian Royal Society expert panel recommended the "development of mechanisms for after-market surveillance of GM foods incorporating a novel protein."[563] The U.S.-EU Consultative Forum recommended that "[g]overnments should undertake to develop and implement processes and mechanisms that will make it possible to trace all foods, derived from GMOs, containing novel ingredients or claiming novel benefits."[564] at this point, attempts to monitor for the presence of GM material in foods are facilitated by the presence of particular proteins and/or DNA in most GM foods that are detectable through relatively inexpensive monitoring techniques. EPA and FDA should

563. ROYAL SOCIETY OF CANADA REPORT, 2001, *supra* note 14, at 73.

564. EU-U.S. CONSULTATIVE FORUM, FINAL REPORT, *supra* note 149, at 12; *see also* LAPPE & BAILEY, *supra* note 14, at 134 (recommending establishment of a "formal tracking mechanism to ensure at least a statistically meaningful subset of transgenic crops entering the marketplace be closely followed, and that consumers who are at the end of the transgenic food chain be monitored for possible adverse effects").

insist at the time of pre-market approval that new GM foods are identifiable through similarly inexpensive analytical tests.[565]

CONCLUSIONS

Public trust is essential to the future of the agricultural biotechnology industry in the United States. While the benefits of agricultural biotechnology may never match the high expectations of its proponents, it can produce changes in the world food supply that will make all of our lives easier and healthier. But agricultural biotechnology poses potential risks to human health, some of which are well-known and largely avoidable, but many of which are poorly understood and unanticipated. The fact that agricultural biotechnology, like any ubiquitous modern technology, poses risks is, of course, no reason to deny society its benefits. Its potential risks are grounds, however, for proceeding ahead with humility and caution.

The public will not trust the agricultural biotechnology industry to establish and enforce its own health and environmental standards. Government must play a strong and highly transparent role in regulating the growth, processing and sale of GM foods. Unfortunately, the statutes that form the underlying foundation for the current federal regulatory regime were not enacted with biotechnology in mind and therefore leave several serious institutional and interpretational questions unresolved. More importantly, the agencies that have been administering the existing regulatory programs have relied far too heavily upon the "substantial equivalence" principle to allow the agricultural biotechnology industry to proceed full-speed-ahead with new products. The increased reluctance of consumers and major food processors and distributors to accept GM foods and the recent StarLink® fiasco suggest that significant changes in the current regulatory regime are in order.

The relevant regulatory agencies should not allow GM foods onto the market until the manufacturers have demonstrated with real scientific data, not broad and largely untestable assumptions, that there is a reasonable assurance that no harm will result to the people who eat those foods. The regulatory process should be

565. *See* OECD EDINBURGH RAPPORTEURS' SUMMARY, *supra* note 33, at 6 (urging further inquiry into the "practicalities of tracing GM food products throughout the food chain").

transparent so that watchdogs in the public interest groups can participate in and evaluate the decisions that the regulatory agencies reach. The agencies should have sufficient resources available, preferably from permit fees, to undertake serious evaluations of the data, to enforce the requirements that they impose, and to undertake retrospective evaluations of past decisions. Finally, consumers should, through fair and accurate labeling of GM foods, be given the right to choose whether or not to consume particular GM products. This may require significant changes in the agricultural distribution system to facilitate segregation of GM crops, and this may for a time increase the costs of both GM and non-GM foods. The alternative is a food distribution system that has lost its most valuable asset—the trust of the American consumer.