

FEDERAL REGULATION OF GENETICALLY ENGINEERED FOOD ADDITIVES AND PESTICIDES

BY WARREN AUSUBEL †

INTRODUCTION

Biotechnology, which enables scientists to modify a cell's genetic structure,¹ has significant potential to yield beneficial advances in such diverse areas as agriculture,² medicine,³ and pollution control.⁴ The

© 1989 *High Technology Law Journal*

† J.D. 1988, University of Pennsylvania Law School; B.A. 1983, University of Chicago.

1. Biotechnology has been defined as "the application of biological systems in organisms to technical and industrial processes." Proposal for a Coordinated Framework for Regulation of Biotechnology Notice, 49 Fed. Reg. 50,856, 50,906 (1984) [hereinafter Proposed Coordinated Framework]. Biotechnology employs techniques of genetic engineering, such as recombinant DNA (rDNA), recombinant RNA (rRNA), and cell fusion. Coordinated Framework for Regulation of Biotechnology, 51 Fed. Reg. 23,302, 23,302 (1986) [hereinafter Coordinated Framework]. These techniques allow for the introduction of genes into microorganisms, plants, and higher animals. Anderson & Cuthbertson, *Safety Testing of Novel Food Products Generated by Biotechnology and Genetic Manipulation*, 5 BIOTECHNOLOGY AND GENETIC ENGINEERING REVIEWS 369, 370 (1987). For example, the gene for rat growth hormone has been inserted into mice to increase their size. Palmiter, Brinster, Hammer, Trumbauer, Rosenfeld, Birnberg & Evans, *Dramatic Growth of Mice That Develop from Eggs Microinjected with Metallothionein - Growth Hormone Fusion Genes*, 300 NATURE 611 (1982).

In this paper, the terms "biotechnology" and "genetic engineering" will be used interchangeably to denote those processes which alter a cell's genetic structure or composition.

2. See Brill, *Safety Concerns and Genetic Engineering in Agriculture*, 227 SCIENCE 381, 381 (1985) (genetic engineering may lead to the development of plants which are more resistant to pests, and which utilize fertilizers more efficiently); M. MANTEGAZZINI, THE ENVIRONMENTAL RISKS FROM BIOTECHNOLOGY 23, 73 (1986) (use of genetic engineering to produce animal growth hormones and plant herbicide resistance is likely to have significant impacts in agriculture).

3. See Note, *An Overview of FDA Regulation of Biotechnology Derived Products: Dealing with the Collision of Science and Society*, 11 RUTGERS COMPUTER & TECH. L.J. 501, 502-03 (1985) (discussion of drugs and medical tests which may be developed through biotechnology).

4. See Korwek & De La Cruz, *Federal Regulation of Environmental Releases of Genetically Manipulated Microorganisms*, 11 RUTGERS COMPUTER & TECH. L.J. 301, 307 (1985) (discussion of use of genetically engineered microorganisms to treat liquid and solid wastes); Regal, *Models of Genetically Engineered Organisms and Their Ecological Impact*, in ECOLOGY OF BIOLOGICAL INVASIONS OF NORTH AMERICA 111 (H. Mooney & J. Drake eds. 1986) (biotechnology industry may promote advances in pollution management, chemical engineering, mining, and other areas); M. MANTEGAZZINI, *supra* note 2,

application of genetically engineered products, however, may pose substantial ecological and health risks. It is conceivable, for instance, that genetic material engineered into organisms might subsequently be transmitted by the engineered organism to indigenous species.⁵ Such unintended genetic transfers could have serious impacts on the environment. For example, genetic material engineered into crop plants to produce resistance to herbicides could perhaps be transmitted from the crop plants to weeds.⁶

The Federal Government has sought to address the possible hazards posed by biotechnology through the Coordinated Framework.⁷ In

at 28-29 (use of biotechnology to treat soil and water contaminated with pollutants may produce major benefits for society).

5. See generally Lenski, *The Infectious Spread of Engineered Genes*, in APPLICATION OF BIOTECHNOLOGY: ENVIRONMENTAL AND POLICY ISSUES 99-126 (J. Fowle III ed. 1987) (discussion of mechanisms by which DNA can be transmitted from one organism to another).

6. *Id.* at 102. Based on current knowledge, however, it is uncertain how frequently such situations might occur. *Id.* at 107. See also MANTEGAZZINI, *supra* note 2, at 4 ("There has been insufficient research to evaluate the mediating influence of environmental factors . . . on the survival, establishment and growth of, and genetic transfer by, genetically engineered bacteria.").

7. The Federal Government has published several policy statements and regulatory guidelines on the use of biotechnology. See 52 Fed. Reg. 22,892-914 (1987) (current USDA regulations regarding genetically engineered plant pests); Coordinated Framework, 51 Fed. Reg. 23,302-50 (1986) (published by OSTP) (policy statements by the FDA, EPA, USDA, Occupational Safety and Health Administration (OSHA), and the National Institutes of Health (NIH) regarding their respective roles in the regulation of biotechnology and biotechnology products); 51 Fed. Reg. 23,352-93 (1986) (USDA notice proposing regulations on (1) the introduction of genetically engineered organisms which are or may be plant pests, and (2) agricultural biotechnology research); 50 Fed. Reg. 47,174-95 (1985) (revised index of U.S. laws and regulations applicable to biotechnology, and notice of the establishment of the Biotechnology Science Coordinating Committee (BSCC), a committee within the organizational structure of the Federal Coordinating Council for Science, Engineering and Technology (FCCSET). FCCSET, in turn, is housed within OSTP. The purpose of the BSCC is to facilitate cooperation among federal agencies on emerging scientific issues); 49 Fed. Reg. 50,856-77 (1984) (index of U.S. laws and regulations related to biotechnology compiled by the Office of Science and Technology Policy (OSTP), an Executive Office); Proposed Coordinated Framework, 49 Fed. Reg. 50,878-907 (1984) (published by OSTP) (statements of policy regarding the regulation of biotechnology products issued by the Food and Drug Administration (FDA), the Environmental Protection Agency (EPA), and the Department of Agriculture (USDA)).

In addition, the NIH has issued several regulatory guidelines regarding DNA research. See generally Jaffe, *Inadequacies in the Federal Regulation of Biotechnology*, 11 HARV. ENVTL. L. REV. 491, 493, 496-500 (1987). These guidelines, however, only affected NIH-funded research. *Id.* Additional discussions of the NIH guidelines can be found in Naumann, *Federal Regulation of Recombinant DNA Technology: Time for a Change*, 1 HIGH TECH. L.J. 61, 65-70 (1986); Note, *Designer Genes That Don't Fit: A Tort Regime for Commercial Releases of Genetic Engineering Products*, 100 HARV. L. REV. 1086, 1087-89 (1987); Note, *supra* note 3, at 505-06.

order to provide for safety concerns, the Coordinated Framework supplies a regulatory scheme which distributes the regulation of biotechnological products among various federal agencies. The Federal Government intends to regulate biotechnology, in large part, under existing laws and regulations, rather than develop new statutory and regulatory standards to address biotechnology.⁸ Thus, in general, products of biotechnology will be subject to regulations and statutory standards which originally were promulgated to address products produced through processes other than genetic engineering.⁹

Commentators, however, have criticized the Coordinated Framework for its establishment of an administrative, bureaucratic solution to the risks posed by biotechnology.¹⁰ The federal regulatory structure has been faulted for being confusing and ill-defined on biotechnology issues, and has been considered inefficient and costly because of its reliance on a case-by-case adjudicative style of rulemaking, which requires the governmental decision-makers to have a high degree of expertise. Plainly, it will be expensive and time-consuming for government officials to develop sufficient knowledge of biotechnology as the field grows and as more proposals are submitted to the Government for review.¹¹ The EPA, in fact, has already acknowledged that it lacks scientific data on significant aspects of biotechnology.¹²

8. "Upon examination of the existing laws available for the regulation of products developed by traditional genetic manipulation techniques, the working group concluded that, for the most part, these laws as currently implemented would address regulatory needs adequately." Coordinated Framework, 51 Fed. Reg. 23,303 (1986).

9. The Federal Government justified this approach in the Coordinated Framework on the ground that the use of existing health and safety laws would provide more immediate protection and certainty for industry than would new legislation. In addition, the Federal Government indicated that a new unitary statutory framework did not seem feasible because too many federal agencies would be needed to regulate the great variety of products produced through biotechnology. *Id.*

10. See generally Note, *supra* note 7, at 1087-92; Jaffe, *supra* note 7, at 528-43.

11. See, e.g., *Environmental Implications of Genetic Engineering: Hearings before the Subcomm. on Investigations and Oversight and the Subcomm. on Science, Research and Technology of the House Comm. on Science and Technology, 98th Cong., 1st Sess.* 131-32 (1983) (statement of Dan R. Clay, Acting Assistant Adm'r., Office of Pesticides and Toxic Substances, U.S. Env'tl. Protection Agency) ("EPA's programs and staffs in general have little experience evaluating the safety of living organisms. Oversight of biotechnology is opening an entirely new area of responsibility for us. It will require extensive training of existing staff and recruitment of personnel with skills we have not previously required.").

12. See REPORT OF THE STUDY GROUP ON BIOTECHNOLOGY, ASSESSING EPA'S BIOTECHNOLOGY RESEARCH AND INFORMATION NEEDS (1986) (released by the EPA's Science Advisory Board), discussed in Note, *supra* note 7, at 1092 (EPA possesses scant scientific data on several scientific issues which concern biotechnology, including the survival and growth of genetically engineered organisms in the environment, and the possibilities that genetic material will be transferred from engineered to indigenous organisms).

In addition, the Coordinated Framework may cause uncertainty as to which agency has regulatory responsibility for future biotechnology products. Because current laws and regulations generally fail to directly address biotechnology issues, there may be instances in which no federal agency has clear jurisdiction for the regulation of a genetically engineered product.¹³ For example, the NIH Guidelines regulating rDNA research only apply to institutions which receive NIH grants. Thus, private companies which conduct rDNA research without NIH funding are not subject to the NIH regulations.¹⁴ On the other hand, possible overlaps in jurisdiction among the federal agencies involved in the regulation of biotechnology may lead to the development of inter-agency conflicts. Such a conflict has existed between the NIH and the FDA regarding the regulation of clinical human trials and drug testing for human gene therapy, a treatment whereby patients are injected with genetic material.¹⁵

To remedy these problems associated with the current regulatory framework on biotechnology, it has been proposed that a "super-agency" be created to regulate genetic engineering.¹⁶ Alternatively, it has been suggested that the tort system should be modified to enable parties to bring lawsuits and obtain relief for harms caused by genetic engineering.¹⁷ Instead of advocating such comprehensive changes in the legal framework governing biotechnology products, this paper will examine the regulation under the current regulatory structure of two particular products of biotechnology, namely, genetically engineered food additives and pesticides which are introduced into the genetic structure of food. Accordingly, Part I of this paper sets out the statutory framework for the regulation of these bioengineered substances.

Since, in general, new statutes and regulations have not been enacted to address the problems posed by the use of these products of biotechnology, the present legal framework to which conventional, non-bioengineered food additives and pesticides are subject will apply to the genetically engineered forms of these substances. This article focuses on

13. Cf. N.Y. Times, Oct. 8, 1988, at 1, col. 4 (discussion of case in which government regulatory agencies failed to prevent Norelco from marketing a product which contained a probable carcinogen).

14. See Naumann, *supra* note 7, at 68-69, 93; Note, *supra* note 7, at 1088.

15. See Naumann, *supra* note 7, at 71, 80-81, 93. See also *Foundation on Economic Trends v. Heckler*, 756 F.2d 143 (D.C. Cir. 1985), discussed in Naumann, *supra* note 7, at 82-88 (discussion of a disagreement between the NIH and a separate DNA advisory committee regarding the approval of proposed experiments which involved the release of genetically engineered bacteria into the environment).

16. Naumann, *supra* note 7, at 90-96.

17. Note, *supra* note 7, at 1092-1105.

the substantive and procedural provisions of existing federal laws under which bioengineered food additives and pesticides will be reviewed.

Essentially, the Federal Government regulates food additives and pesticides under two laws, the Federal Food, Drug, and Cosmetic Act (FFDCA),¹⁸ and the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA).¹⁹ Of these two statutes, the FFDCA is the more encompassing, as it includes under its purview pesticides as well as food additives, whereas FIFRA only covers pesticides. The FFDCA, moreover, provides for a more complex system of safety regulations than does FIFRA. Under FIFRA, substances are reviewed under a single risk/benefit standard. The FFDCA, however, contains several different safety standards.

These FFDCA safety standards can be organized into two broad categories. The first category is comprised of general standards, under which substances are considered to be either added or endogenous to a food. The FFDCA provides separate standards for each type of substance. The second category contains special standards for the regulation of food additives, unavoidably added substances, and pesticides.

Because food additives and pesticides are specifically addressed in these Special Standards, the bioengineered forms of these substances should be regulated under these standards. This is significant for two reasons. First, the Special Standards, unlike the General Standards, allow the Government to review the use of a substance before it is marketed. The General Standards basically permit the FDA to act only after the substance has been introduced into commerce. Second, within the special standard for food additives is the Delaney Clause, under which the Federal Government is obligated to restrict the use of carcinogenic substances in food. This paper argues in Part II that in the interest of public health, genetically engineered food additives and pesticides should be subjected to the tougher safety provisions contained in the Special Standards. Moreover, because the presence of carcinogenic additives and pesticides in food has reached dangerous levels, the Government should adopt a policy which encourages the use of biotechnology techniques to manufacture non-carcinogenic food additives and pesticides.

I. STATUTORY FRAMEWORK

Under current federal law, foods and food additives are regulated by the FDA under the FFDCA.²⁰ The FFDCA bans the introduction or

18. 21 U.S.C. §§ 301-92 (1982).

19. 7 U.S.C. §§ 136-136y (1982).

20. The FFDCA additionally provides for the regulation of pesticides present on raw and processed foods. 21 U.S.C. §§ 346a, 348 (1982). Significant responsibility for the regulation of pesticides is also placed with the EPA under FIFRA.

delivery into interstate commerce of "misbranded" or "adulterated" food.²¹ The term "misbranded" is defined in Section 403 of the FFDCA. In general, this section proscribes the use of misleading labeling and packaging, as well as false representations as to the quality of food.²² Section 402 defines "adulteration" as the addition of poisonous or deleterious substances to food.²³

Two specific misbranding provisions, one dealing with false and misleading labeling,²⁴ the other concerning "standards of identity,"²⁵ are clearly implicated by the alteration of the genetic make-up of a food. Since the misleading labeling problem has received little attention and the standards of identity provision will not be a likely basis for FDA

The FFDCA also delegates certain responsibilities to the EPA. Under Reorganization Plan No. 3 of 1979, 35 Fed. Reg. 15,623 (1970), reprinted in 42 U.S.C.A. § 4321 app. at 524-525 (West 1977), the EPA has the duty to promulgate pesticide regulations under the FFDCA and monitor their compliance, but the FDA enforces pesticide regulations.

Thus, the FDA has the primary authority to regulate the safety of foods and food additives, but the FDA and the EPA share the authority to regulate pesticides.

21. 21 U.S.C. § 331(a)-31(c) (1982).

22. *Id.* § 343.

23. *Id.* § 342.

24. 21 U.S.C.A. § 343(a)(1) (West Supp. 1988).

Genetic engineering raises mislabeling issues because a food's genetic structure may be changed to such an extent that it no longer resembles its progenitor, and thus, arguably, should not be labeled with the name of the progenitor. However, possible labeling problems which may arise as use of genetic engineering techniques increase have received little attention. Gibbs & Kahan, *Federal Regulation of Food and Food Additive Biotechnology*, 38 ADM. L. REV. 1, 20 (1986).

25. 21 U.S.C. §§ 341, 343(g) (1982).

This misbranding provision is infringed when a food fails to comply with the appropriate "standard of identity" promulgated by the FDA. *Id.* Standards of identity are regulations set by the FDA which identify a food, set a standard of quality for a food, or establish standards for fill of containers. *Id.* § 341. The FFDCA, however, prohibits the FDA from setting standards of identity for most fresh and dried fruits and vegetables. *Id.* In fact, the only fruits or vegetables for which standards of identity are allowed under the Act are avocados, cantaloupes, citrus fruits, and melons. Gibbs and Kahan, *supra* note 24, at 21 n.97. Even for these foods, however, the FDA has not set standards of identity. See 21 C.F.R. §§ 103 (Quality standards for food without identity standards), 130 (Food standards: general), and 564 (Definitions and standards for animal foods). Therefore, the provision regarding standards of identity forms an unlikely basis for FDA regulatory action on bioengineered products.

This inability to set standards of identity also creates some enforcement problems under the adulteration standard. One of several grounds for finding adulteration involves a finding that a food is missing valuable constituents normally present. 21 U.S.C. § 342(b)(1) (1982). Thus, such food can only be seized if the valuable constituents of the food have been defined in FDA regulations. Since there is no standard of identity for most fresh fruits and vegetables, the FDA probably would be unable to regulate bioengineered food additives and pesticides under this particular provision. See generally Comment, *Regulation of Genetically Engineered Foods Under the Federal Food, Drug, and Cosmetic Act*, 33 AM. U.L. REV. 899, 906 (1984).

action, we will now turn our attention to the FFDCa adulteration provision.

The FDA policy statement in the Coordinated Framework suggests that certain adulteration standards contained in the FFDCa, Sections 402 and 409, are likely to be invoked in the regulation of biotechnology.²⁶ Section 402 contains the General Adulteration Standard for endogenous and added substances, whereas Section 409 contains the Special Standard applied to food additives.²⁷ These statements clearly establish that the FDA intends to utilize the General and certain Special Standards contained in the FFDCa to regulate biotechnology.

The next section examines in depth the application of these standards to the regulation of genetically engineered food additives and pesticides.

II. APPLICATION OF THE FFDCa ADULTERATION PROVISION TO GENETICALLY ENGINEERED FOOD ADDITIVES AND PESTICIDES

The FFDCa essentially provides two categories of regulation for adulterated food.²⁸ The first category is a general regulation, which covers food adulterated by both endogenous and added substances.²⁹ A food will be considered adulterated if it contains an endogenous substance which "ordinarily renders" the food injurious to health.³⁰ This safety standard is weaker than the "may render" test which is applied to added substances.³¹

The second category of regulation consists of Special Standards for particular sources of adulteration, including food additives,³² unavoidably added substances,³³ and pesticides.³⁴ These provisions enable the FDA to place restrictions, known as tolerances, upon a substance before it is used.³⁵ In contrast, the General Adulteration Standard was enacted

26. Coordinated Framework, 51 Fed. Reg. 23,312-13 (1986).

27. The FDA also indicated that in general, other FFDCa sections, when relevant, could be applied to regulate biotechnology. *Id.*

28. 21 U.S.C. § 342(a) (1982).

29. *Id.* § 342(a)(1).

30. *Id.*

31. *See United States v. 2,116 Boxes of Boned Beef*, 516 F. Supp. 321 (1981). *See infra* note 37 and accompanying text.

32. 21 U.S.C. §§ 342(a)(2)(C), 348 (1982).

33. 21 U.S.C. §§ 342(a)(2)(A), 346 (1982). *See also* 39 Fed. Reg. 42,743-44 (1974) (discussing scope of § 406); Rosenkranz, *FDA Regulation of Environmental Contaminants After Community Nutrition Institute v. Young*, 41 FOOD DRUG COSM. L.J. 330, 341-53 (1986) (analysis of the scope of § 406).

34. 21 U.S.C. §§ 342(a)(2)(B), 346a (1982).

35. *See infra* note 60 and accompanying text.

to enable the FDA to seize adulterated food after it is marketed.³⁶ By imposing restrictions upon a substance prior to marketing, the Special Adulteration Standards provide greater safety protection in the regulation of biotechnology since there is less of a risk that adulterated products will be introduced into the marketplace. Nevertheless, it is clear that the legal framework governing genetically engineered food additives and pesticides includes both the General Adulteration Standard contained in Section 402 and the tolerance standards which pertain to food additives and pesticides.

A. General Regulation of Adulteration

1. REGULATION OF ENDOGENOUS AND ADDED SUBSTANCES: SECTION 402(a)(1)

Section 402(a)(1) provides that a food will be deemed to be adulterated "[i]f it bears or contains any poisonous or deleterious substance which *may render* it injurious to health."³⁷ If, however, the substance is "not an added substance such food shall not be considered adulterated under this clause if the quantity of such substance in such food does not *ordinarily render* it injurious to health."³⁸ Thus, under Section 402(a)(1), the "may render" standard implicitly applies only to added substances, whereas the "ordinarily render" standard pertains to endogenous substances.³⁹

The "may render" standard for added substances is more protective of consumer health and safety than the "ordinarily render" test for endogenous substances. To meet the "may render" standard, the FDA does not have to show that the food caused actual injury for the food to be considered adulterated. Rather, the FDA need only show that a reasonable possibility of injury to health may be caused by the food.⁴⁰ Moreover, special vulnerabilities of segments of the population (aged,

36. See *infra* note 61 and accompanying text.

37. 21 U.S.C. § 342(a)(1) (1982) (emphasis added).

38. *Id.* (emphasis added).

39. Substances which would be evaluated under the "ordinarily render" standard are oxalic acid, a toxin which is present in spinach and rhubarb, and caffeine, which naturally occurs in coffee and cocoa. Merrill & Schewel, *FDA Regulation of Environmental Contaminants in Food*, 66 VA. L. REV. 1357, 1367-68 & n.48 (1980). Examples of "added" substances are mercury when present in swordfish, *United States v. Anderson Seafoods, Inc.*, 622 F.2d 157 (5th Cir. 1980), and salmonella in eggs, *United States v. 1200 Cans, Pasteurized Whole Eggs*, 339 F. Supp. 131 (N.D. Ga. 1972).

40. See, e.g., *Flemming v. Florida Citrus Exchange*, 358 U.S. 153, 160-61 (1958), *reh'g denied*, 358 U.S. 948 (1959); *United States v. Lexington Mill & Elevator Co.*, 232 U.S. 399, 406-11 (1914). See also 42 Fed. Reg. 52,814 (1977) (discussion of "may render" standard).

sick, etc.) are considered in the determination of the health risks posed by the food.⁴¹

For the "ordinarily render" standard, the FDA must prove that the endogenous substance in question renders the food injurious when consumed by ordinary consumers in ordinary amounts.⁴² This standard, however, has rarely been contested in actions before the FDA and the courts, perhaps because manufacturers are wary of engaging in litigation in which their defense would be that the food is only slightly injurious.⁴³

Whether the "may render" or "ordinarily render" provision applies to a food is dependent upon whether the deleterious substance is "added" or not. However, "added" in Section 402(a)(1) is nowhere defined in the FFDCA. One view of Section 402(a)(1) is that a substance is "added" if it is incorporated into a food as the result of any human intervention, whether direct or indirect.⁴⁴ For example, a court has found that mercury present in swordfish was artificially introduced and attributable to human intervention.⁴⁵

The FDA, however, has gone beyond the "human intervention" definition of "added." The FDA regulations state that all poisonous and deleterious substances are "added" within the meaning of the FFDCA unless they are "naturally occurring." "Naturally occurring" substances are "inherent natural constituent[s] of a food."⁴⁶ Substances which are the result of "environmental, agricultural, industrial, or other contamination" cannot be considered "naturally occurring;" rather the FDA deems them to be added.⁴⁷

41. *Lexington Mill*, 232 U.S. at 411. See also Rosenkranz, *supra* note 33, at 339.

42. *United States v. 1,232 Cases Am. Beauty Brand Oysters*, 43 F. Supp. 749 (W.D. Mo. 1942). See Rosenkranz, *supra* note 33, at 339 & n.56 (discussion of "ordinarily render" standard).

43. Comment, *supra* note 25, at 904-05 & nn.33 & 34. The weakness of the "ordinarily render" standard is highlighted by the fact that many toxicants found naturally in foods (e.g., oxalic acid in spinach) would not survive an action under the "may render" standard, but would survive under the "ordinarily render" standard. *Id.* at 915 n.98.

44. *Continental Seafoods, Inc. v. Schweiker*, 674 F.2d 38 (D.C. Cir. 1982); *United States v. Anderson Seafoods, Inc.*, 622 F.2d 157 (5th Cir. 1980). See generally Gibbs & Kahan, *supra* note 24, at 12 & n.59; Comment, *supra* note 25, at 905 & n.36.

45. *Anderson Seafoods*, 622 F.2d 157 (5th Cir. 1980). Moreover, the D.C. Circuit has ruled that the existence of salmonella in shrimp was at least due in part to human intervention, and thus the salmonella was considered to be "added" under § 402(a)(1). *Continental Seafoods*, 674 F.2d 38 (D.C. Cir. 1982).

Another example of a substance's presence in food that results from indirect human intervention is lead in milk. See 39 Fed. Reg. 42,743 (1974).

46. 21 C.F.R. §§ 109.3(c-d), 509.3(c-d) (1988).

47. *Id.* §§ 109.3(c), 509.3(c).

This definition deems substances to be added which are introduced to food either through human intervention or through actions of the environment. For instance, a toxic substance, aflatoxin, which is produced by a bacterial mold that grows naturally on crops, is deemed to be "added" by the FDA because the presence of aflatoxin on crops is the result of environmental or agricultural phenomena. On the other hand, the toxin oxalic acid is not considered to be "added" when present in spinach because this toxin is produced as a result of the genetic structure of spinach, not environmental or agricultural influences. Thus, the FDA's interpretation of the term "added" seems to turn on whether the substance is introduced through internal or external processes.⁴⁸

Generally, the FDA's definition of "added" appears to be accepted by the courts. In *Continental Seafoods*, the D.C. Circuit refused to rule on the validity of the regulation which contained this definition.⁴⁹ In a recent Supreme Court case, *Young v. Community Nutrition Institute*,⁵⁰ the Court indicated that aflatoxin is in fact "added." Other federal district and circuit court cases which preceded *Young* also have supported the FDA's interpretation of "added."⁵¹

2. BIOTECHNOLOGY APPLICATIONS

The issue posed by Section 402(a)(1) is which standard, "may render" or "ordinarily render," should apply to food which contains genetically engineered products. Such substances are "added" in the sense that they are produced by human intervention, but not "added" in that they are part of the genetic make-up of the plant.

A similar question is raised regarding hybridized food. Hybridization, like genetic engineering, alters the genetic composition of a plant through human intervention. The FDA, however, has never brought an enforcement action against any food on the theory that a breeding program added a new substance.⁵² Such a position is sensible, because if

48. See Rosenkranz, *supra* note 33, at 340.

49. *Continental Seafoods*, 674 F.2d at 42 n.14.

50. 476 U.S. 974, 106 S.Ct. 2360 (1986).

51. See Rosenkranz, *supra* note 33, at 340.

52. Gibbs & Kahan, *supra* note 24, at 17; Comment, *supra* note 25, at 916. Genetic alterations produced through breeding can be dangerous. For instance, a new American potato cultivar, the "Lenape," had to be removed from commerce in 1970 because it contained unusually high levels of glycoalkaloid. Sinden, Sanford & Webb, *Genetic and Environmental Control of Potato Glycoalkaloids*, 61 AM. POTATO J. 141, 146 (1984).

In Germany, some years ago, a new breed of grape was discovered to have produced teratogenic damage in chickens. The grapes were intended to be used for winemaking, but apparently were not used because of these toxic effects. See Breider, *Toxikologische Probleme in der Zuchtung Physiologisch Resistenter Kulturpflanzen*, 67 DEUTSCHE LEBENSMITTEL-RUNDSCHAU 67 (1971).

every act of human cultivation sufficed to implicate the "may render" standard, then the only foods not containing added substances would be wild foods.⁵³

Arguably, biotechnology techniques should not be construed under Section 402(a)(1) as are hybridization and breeding, because genetic engineering does constitute greater human intervention. In fact, in the Coordinated Framework, the FDA suggested that substances produced through genetic engineering could be subject to the "may render" standard.

[If] the quantity of the constituent exceeds the amount that normally would be present because of some technological adjustment to the product, that excess quantity may also be viewed as "added substance" within the meaning of the Section [402(a)(1)]. . . . Similarly, if a food produced by new biotechnology contains, as a result of the production process, a harmful or deleterious substances [sic] not contained ordinarily in the food, the food could be in violation of the section.⁵⁴

Finally, a highly toxic compound, cucurbitacin, was found in types of squash grown in California and Alabama during the summer of 1981. Rymal, Chambliss, Bond & Smith, *Squash Containing Toxic Cucurbitacin Compounds Occurring in California and Alabama*, 47 J. FOOD PROT. 270 (1984). These toxic squash, which apparently were produced through breeding techniques, were detected because cucurbitacin has an extremely bitter taste. *Id.* at 270-71.

53. The "may render" standard, which applies to added substances in food, was originally formulated in the statute that preceded the FFDCA, the Pure Food Act of 1906, ch. 3915, 34 Stat. 768, *repealed by* FFDCA of 1938, ch. 675, § 902(a), 52 Stat. 1040, 1059. It has been observed that the "may render" standard contained in the Pure Food Act and the FFDCA was not intended to cover substances introduced into food through breeding techniques. "Because traditional breeding methods were already in existence before [1938], . . . Congress obviously did not perceive that the mere cultivation or use of traditional selective breeding techniques available at that time were acts of human intervention that would bring a food within the reach of the may render standard." Comment, *supra* note 25, at 916 n.103.

54. Coordinated Framework, 51 Fed. Reg. 23,312 (1986). The statement in the first sentence quoted here is supported by 21 C.F.R. §§ 109.3(d), 509.3(d) (1988), which provide that when a natural substance is increased to abnormal levels through intervening acts, the substance is viewed as "added" to the extent of the increase. In construing 21 C.F.R. § 109.3(d), the court in *United States v. Anderson Seafoods, Inc.*, 622 F.2d 157, 161 (5th Cir. 1980), held that the "may render" standard applies to all of a deleterious substance whenever any part of that substance is shown to have been introduced by man. This ruling may have consequences in the area of biotechnology as genetic engineers develop techniques to increase the amount of toxins which a plant normally produces.

For an example of a plant genetically engineered to contain a toxin not ordinarily present, see Hilder, Gatehouse, Sheerman, Barker & Boulter, *A Novel Mechanism of Insect Resistance Engineered into Tobacco*, 330 NATURE 160 (Nov. 12, 1987) (genetically engineered tobacco, which contained a gene that encoded a cowpea trypsin inhibitor, had enhanced resistance to insect pests).

The FDA policy statement in the Coordinated Framework, however, did not address whether the FDA intends to make a distinction between the progenitor plant which was genetically engineered, and the progeny, which received the new genetic material naturally.⁵⁵ This gap in the policy statement poses a problem. To regulate the progenitor under the "may render" standard while regulating the progeny under the "ordinarily render" standard would plainly not make sense if the goal of regulation is to provide protection, because both would have the same genetic make-up and therefore pose the same risks. Moreover, the practical problems involved in determining a plant's parentage could make such a distinction unworkable.⁵⁶ Thus, there exist compelling reasons for the FDA to adopt the position that the "may render" standard applies to the progeny, as well as to the genetically engineered progenitors.⁵⁷

In summary, it appears that the FDA views genetically engineered substances in food to be "added" under Section 402(a)(1), and that such food could be subjected to an enforcement action under the "may render" standard. This is a prudent position because if bioengineered substances were viewed as endogenous, the weaker "ordinarily render" standard would then apply to food which contained such substances. However, the FDA statement in the Coordinated Framework that manufacturers of bioengineered substances could be subject to the tougher "may render" standard may not have that much significance for the regulation of genetically engineered food additives and pesticides. As previously emphasized, the FDA has indicated its intention to invoke existing statutory provisions when relevant to biotechnology. These existing provisions include Section 409, which is the FFDCA tolerance standard that pertains to food additives.⁵⁸ Thus, because the FDA usually applies the FFDCA tolerance standards to regulate food additives and pesticides instead of Section 402(a)(1), the FDA should invoke these same standards for the regulation of genetically engineered food additives and pesticides.

The next section analyzes the application of the tolerance standards contained in the FFDCA to the regulation of genetically engineered food additives and pesticides.

55. See Comment, *supra* note 25, at 917 n.107 (discussion of the techniques of seeding and grafting).

56. See *id.* at 918 n.108 (noting that courts will have difficulty in determining the parentage of seized plants).

57. Perhaps the Coordinated Framework is comparing both the progenitor and the progeny to the natural form of the food. In that case, the FDA would apply the "may render" standard to both the progenitors and the progeny.

58. See *supra* note 27 and accompanying text.

B. Application of Tolerance Standards to Genetically Engineered Food Additives and Pesticides

The advantage of the tolerance standards in the FFDCa which cover food additives (§ 409), unavoidably added poisons (§ 406), and pesticides (§ 408),⁵⁹ is that they enable the FDA to regulate these substances before the food enters the market.⁶⁰ In contrast, under the General Adulteration Standard contained in Section 402(a)(1), the FDA can generally proscribe the use of a substance only after (1) the substance has been introduced into interstate commerce, and (2) the FDA proves that the substance "may render" or "ordinarily render[s]" the food injurious.⁶¹ The burdens associated with this *post hoc* regulatory approach motivated Congress to amend the FFDCa to provide a pre-approval framework for food additives.⁶²

59. See *supra* notes 33-35.

60. Section 409 of the FFDCa states that a "food additive shall . . . be deemed to be unsafe . . . unless . . . its use or intended use are [sic] in conformity with . . . a regulation . . . prescribing the conditions under which such additive may be safely used." 21 U.S.C. § 348(a) (1982). These food additive regulations are commonly known as "tolerances." If the FDA has not issued a tolerance for a food additive, a food containing such an additive will be deemed adulterated under § 402(a)(2)(C), 21 U.S.C. § 342(a)(2)(C), unless the FDA has granted an exemption to the tolerance requirement. *Id.* § 348(a)(1).

Section 406 provides that when a "poisonous or deleterious substance . . . is so required or cannot be so avoided, the Secretary shall promulgate regulations limiting the quantity therein or thereon to such extent as he finds necessary for the protection of public health . . ." *Id.* § 346.

Section 408 states that "[t]he Administrator shall promulgate regulations establishing tolerances with respect to the use in or on raw agricultural commodities of poisonous or deleterious pesticide chemicals . . . as safe for use, to the extent necessary to protect public health." *Id.* § 346a(b).

Promulgated tolerances are located in 21 C.F.R. §§ 172-180, 193, 561 (1988) (substances covered by § 409 of the FFDCa); 21 C.F.R. §§ 109.15, 109.30 (1988) (§ 406 tolerance); 40 C.F.R. § 180 (1987) (§ 408 tolerances).

61. 21 U.S.C. §§ 334(a)(1), 342(a)(1) (1982). See also 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, 194-95 (1978) ("By itself, [Section 402(a)(1)] gives the agency no authority to evaluate or approve the safety of a substance before it is 'added' to food."). However, Section 701(a) empowers the FDA to enact regulations through informal rulemaking "for the efficient enforcement" of the FFDCa. 21 U.S.C. § 371(a) (1982). Thus, it is arguable that the FDA could promulgate regulations which explicate the "ordinarily render" and "may render" standards. See Rosenkranz, *supra* note 33, at 350-51.

62. See S. Rep. No. 2422, 85th Cong., 2d Sess., reprinted in 1958 U.S. CODE CONG. AND ADMIN. NEWS 5300, 5300 (Senate report for the Food Additives Amendment of 1958, which added § 409 to the FFDCa) ("[U]nder existing law the Federal Government is unable to prevent the use in foods of a poisonous or deleterious substance until it first proves that the additive is poisonous or deleterious. To establish this proof through experimentation . . . may require 2 years or even more. . ."). For example, in *United States v. An Article of Food Consisting of Cartons of Swordfish*, 395 F. Supp. 1184 (S.D.N.Y. 1975), the Government took samples of swordfish in January and February of

The General Adulteration Standard, however, theoretically covers all the substances to which the tolerance standards pertain. The FDA has stated that Section 402(a)(1) "is deliberately cumulative with the provisions relating to establishment of tolerances for food substances referenced in Section 402(a)(2)."⁶³ However, if a tolerance is issued, then the FDA deems Section 402(a)(1) to be pre-empted.⁶⁴

The Section 406 tolerance clause, as previously noted, concerns the regulation of unavoidably added substances. However, both pesticides and food additives can be regulated under Section 406 tolerances, provided that they are unavoidable and that the FDA cannot issue tolerances for these substances under Sections 408 and 409. The FDA has stated that "when a tolerance for an unavoidable pesticide cannot be issued under the criteria of section 408 of the act, section 406 is available to control its use."⁶⁵ Regarding food additives, the FDA indicated that "the tolerance-setting provisions of section 406 of the act . . . deal with those unavoidably added poisonous or deleterious ingredients that could not meet the high standards for issuance of a regulation under the authority of section 409 of the act."⁶⁶

1971 to analyze them for mercury content. The government determined that the fish were contaminated with mercury, but did not seize them until July, 1971. The government sought to condemn the fish under 21 U.S.C. § 334 and claimed that the fish were adulterated under the "may render" standard. 395 F. Supp. at 1185. The District Court decision, however, granting the Government's motion for summary judgment was not issued until June 1975, over four years after the samples were taken.

63. 39 Fed. Reg. 42,743 (1974). Court decisions have supported this claim. In *Young v. Community Nutrition Institute*, 476 U.S. 974 (1986), the Court ruled that the FDA need not enact Section 406 tolerances, and instead can rely on the General Adulteration Standard contained in Section 402(a)(1). Moreover, *United States v. Goodman*, 486 F.2d 847 (7th Cir. 1973), held that the EPA has discretion under the FFDCA not to issue tolerance standards under Section 408, which pertains to pesticides.

64. "[T]he language in Sections 406, 408(a), [and] 409(a) . . . of the act grant[] an exemption from section 402(a)(1) . . . if a regulation under one of those sections is in effect." 39 Fed. Reg. 42,745 (1974).

65. *Id.*

66. *Id.* at 42,744.

Section 406 provides that tolerance levels will be set "to the extent to which the use of such substance is required or cannot be avoided . . . , 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 (1982). This language indicates that Section 406 tolerances are set on a risk/benefit basis. See generally *Rosenkranz, supra* note 33, at 351-52. In contrast, Section 409 provides for a more rigorous examination of the substance's health hazards. See *infra* notes 114-139 and accompanying text (discussion of safety standards contained in § 409). Thus, the Section 406 standard provides the Government more flexibility to register hazardous substances for use.

Section 408 tolerances for pesticides are also set on a risk/benefit basis. See *Regulation of Pesticides in Food: Addressing the Delaney Paradox Policy Statement, Notice*, 53 Fed. Reg. 41,104, 41,106 (1988) [hereinafter *Delaney Clause Notice*]. It is not altogether clear how a pesticide could fail to meet the criteria set out in Section 408 yet satisfy the risk/benefit standard in Section 406.

Thus, Sections 402(a)(1) and 406 are viewed by the FDA as being safety valves in its regulation of food additives and pesticides. Section 402(a)(1) is deemed to be pre-empted whenever tolerances are issued, and according to the FDA, pesticides and food additives are subject to Section 406 tolerances only if tolerances cannot be issued under Sections 408 and 409. The FDA, however, rarely resorts to the Section 406 tolerance provision.⁶⁷ On the other hand, thousands of tolerances have been issued for pesticides and food additives under Sections 408 and 409.⁶⁸

Clearly, Sections 408 and 409 are more relevant for the regulation of food additives and pesticides than Section 406. Therefore, because the FDA has stated that it intends to invoke existing federal law to regulate biotechnology products the Section 408 and 409 tolerance provisions logically will be the focal point for the regulation of genetically engineered pesticides and food additives.

In the past, the FDA has indicated that tolerances should not be established where "technological or other changes are foreseeable in the near future that might affect the appropriateness of the tolerance."⁶⁹ In such situations where the technological data are in a state of flux, the FDA would establish administrative guidelines called "action levels," to define the acceptable level of the substance.⁷⁰ The reason the FDA favored the establishment of action levels in "state of flux" situations was that it would issue action levels without complying with standard notice and comment rule-making procedures.⁷¹ In this way, the FDA could avoid the burdens of rule-making, yet still set forth standards of adulteration.⁷²

Nevertheless, this action level program was recently invalidated in *Community Nutrition Institute v. Young*.⁷³ The FDA claimed that action

67. Only one formal Section 406 tolerance has ever been issued. 21 C.F.R. §§ 109.15, 109.30 (1988) (Section 406 tolerance for PCBs). This dearth is due to the fact that the FDA must follow burdensome rule-making procedures to promulgate a Section 406 tolerance. See § 701(e), 21 U.S.C. § 371(e) (1982). See also Rosenkranz, *supra* note 33, at 352 & n.123 (FDA took over a decade to promulgate the PCB tolerance). Basically, Section 701 provides for notice and comment procedures, a public hearing, and judicial review regarding the promulgation of tolerances set under Section 406.

68. See *supra* note 60. See also NAT'L RESEARCH COUNCIL, REGULATING PESTICIDES IN FOOD 35-36 (1987) [hereinafter NAS report].

69. 21 C.F.R. § 109.6(b)(3) (1988).

70. 21 C.F.R. §§ 109.4(b), 109.6(a),(c) (1988).

71. See 42 Fed. Reg. 52,817 (1977). See generally Rosenkranz, *supra* note 33, at 357-58 (discussion of FDA's action level rule). Notice and comment requirements are provided by the Administrative Procedure Act (APA), 5 U.S.C. § 553 (1982).

72. The FDA's authority to issue action levels was based on the General Adulteration Standard and the tolerance standards, as well as other FFDCA provisions. See 21 C.F.R. § 109.6(d) (1988) (authority to set action levels based on §§ 306, 402(a), 406, 408, 409, and 701 of the FFDCA).

73. 818 F.2d 943 (D.C. Cir. 1987).

levels were merely nonbinding statements of agency policy. Therefore, the FDA was allowed under an exception contained in the Administrative Procedures Act (APA) to avoid notice and comment requirements.⁷⁴ The court disagreed and held that action levels were substantive rules which could have binding effect only if they were issued in compliance with the notice and comment requirements in the APA.⁷⁵ Since the ability to establish action levels without notice and comment procedures was the feature that distinguished action levels from tolerances, the extent to which the FDA will implement action levels in the future is unclear. This is true not only for the FDA's regulation of substances produced by conventional means, but also for products produced through biotechnology.

Consequently, the current framework for the regulation of genetically engineered food additives and pesticides is essentially comprised of the Section 408 and 409 tolerance standards. The next sections of this article explore how these products of biotechnology will be reviewed under these tolerance standards.

1. SECTION 409

a. Statutory Provisions

The FFDCA defines the term "food additive" as "any substance the intended use of which results or may reasonably be expected to result, directly or indirectly, in its becoming a component or otherwise affecting the characteristics of any food . . . if such substance is not generally recognized . . . [as] safe . . ."⁷⁶ Pesticides on raw agricultural commodities are excluded from the definition of "food additive."⁷⁷

Such pesticides are regulated on a separate statutory basis (Section 408) from food additives (Section 409). By implication, however, pesticide residues on processed foods are considered to be food additives.⁷⁸

74. 5 U.S.C. § 553(b)(3)(A) (1982) (exception to notice and comment requirement for "interpretative rules [and] general statements of policy.").

75. 818 F.2d at 949.

76. § 201(s), 21 U.S.C. § 321(s) (1982). See also 21 C.F.R. § 170.3(e) (1988) (definition of food additive).

77. 21 U.S.C. § 321(s)(1) (1982). Other substances are also excluded from the definition of "food additive." See *id.* § 321(s)(3)-(5) (exemption from food additive definition for color additives, substances used in accordance with certain prior approvals, and new drugs for animals).

78. See, e.g., *United States v. Ewig Bros. Co.*, 502 F.2d 715, 722 (7th Cir. 1974) ("Before processing, DDT is a 'pesticide chemical' on a raw product; after processing, it is an 'additive.'"), *cert. denied*, 420 U.S. 945 (1975).

Foods become processed when they are converted from their raw form into a new product.⁷⁹

The food additive definition is very broad. Although the definition in the statute uses the phrase "intended use," food additives need not be intentionally used.⁸⁰ The "intended use" element of the definition merely requires that the substance's presence in a food not be accidental and unforeseeable.⁸¹ Thus, it has been held that substances which "migrate" into food through contact are food additives.⁸²

A food additive cannot be used unless a tolerance, or an exemption to the tolerance requirement, is issued by the FDA.⁸³ The FDA may issue a Section 409 tolerance after a manufacturer submits a food additive petition (FAP) to the FDA.⁸⁴ The petition has to contain data on the "chemical identity and composition of the food additive," the substances used in the synthesis of the food additive, and "[t]he amount of the food additive proposed for use," as well as data which examine the safety of the food additive.⁸⁵

Not all substances which become components of food are deemed to be food additives. The food additive definition contains an exception for substances which are "generally recognized as safe" (GRAS).⁸⁶ The FDA has not compiled a complete list of the substances it considers to satisfy the GRAS exception.⁸⁷ Manufacturers, moreover, do not have to procure FDA approval for the use of a GRAS substance, or even notify the FDA of the proposed use.⁸⁸ If a manufacturer uses a substance on the assumption that it is GRAS, the manufacturer faces liability under the regulations only if the FDA later decides the substance is not

79. For example, tomato juice and tomato paste are processed foods made from raw tomatoes. See *infra* notes 161-163 and accompanying text (discussion of processed foods).

80. 39 Fed. Reg. 42,744 (1974).

81. *Id.*

82. *Id.* See also *infra* note 110 and accompanying text (discussion of migration).

83. See *supra* note 60.

84. Section 409(b), 21 U.S.C. § 348(b) (1982). 21 C.F.R. §§ 171.1-.130 (1988) describe the requirements for submission of FAPs. It has been estimated that approval for a direct food additive takes five to seven years. McNamara, *FDA Regulation of Food Substances Produced by New Techniques of Biotechnology*, 42 FOOD DRUG COSM. L.J. 50, 53 (1987). Moreover, under FDA regulations, the FDA on its own may propose the issuance of a food additive tolerance. 21 C.F.R. § 170.15 (1988).

85. 21 C.F.R. § 171.1(c) (1988).

86. See *supra* note 77 and accompanying text.

87. 21 C.F.R. § 170.30(d) (1988). Lists of GRAS substances are located in 21 C.F.R. §§ 182, 184 & 186.

88. FDA Statements of General Policy or Interpretation, 39 Fed. Reg. 34,172, 34,188 (1974) ("Section 409 . . . does not require that a food manufacturer consult with, or obtain the approval of, the Food and Drug Administration, before using a food ingredient on the ground that it is GRAS for the use involved."); McNamara, *supra* note 84, at 51.

GRAS.⁸⁹ However, if the FDA does decide that the substance is in fact a food additive which is not covered by a tolerance or an exemption, foods containing such substances will be considered unsafe under Section 409, and thus adulterated under Section 402(a)(2)(C).⁹⁰ The FFDCA provides that persons who introduce adulterated food into interstate commerce can be subject to criminal penalties,⁹¹ and the food can be seized in an action for condemnation by the FDA.⁹²

GRAS status can be established either through experience based on common use of the substance prior to 1958, or through scientific procedures.⁹³ General recognition of safety based on the common use provision will ordinarily be established through generally available data.⁹⁴ To establish GRAS status through scientific procedures, a petitioner must submit the same scientific evidence that is required for the approval of a food additive, as well as provide published studies which support the petition.⁹⁵

The FDA can initiate a review of a substance's GRAS status based on new information.⁹⁶ For instance, the FDA can initiate a review of substances whose GRAS status was based on common use prior to 1958 if those substances have been "significantly altered" by (1) commercial processes introduced into use after 1957, or by (2) breeding or selection after 1957.⁹⁷ The term "selection" refers to the spontaneous genetic changes which occur through generations as species adapt for survival in their environment. Breeding and hybridization are forms of artificial selection because the breeder selects as parents of the next generation those animal or plants which possess desired qualities.⁹⁸ Clearly, the FDA's use of the term "selection" refers to the process of artificial selection.

At one time, the FDA proposed that "significant alteration" should be defined as a 10% or greater increase in a toxicant, or a 20% or greater

89. McNamara, *supra* note 84, at 52 n.9. See also 21 C.F.R. § 170.38(b) (1988) (regulation stating that the FDA may propose that a substance is not GRAS).

90. See 21 C.F.R. § 170.38(a) (1988).

91. 21 U.S.C. § 333 (1982).

92. *Id.* § 334.

93. 21 U.S.C. § 321(s) (1982).

94. 21 C.F.R. § 170.30(c) (1988).

95. *Id.* § 170.30(b).

96. *Id.* § 170.30(l).

97. *Id.* § 170.30(f)(1-2). This regulation supports the FDA's prerogative to affirm a substance's GRAS status after the review.

98. See, e.g., P. Moody, INTRODUCTION TO EVOLUTION 11 (2d ed. 1962); Andow, Levin & Harwell, *Evaluating Environmental Risks from Biotechnology: Contributions of Ecology*, in APPLICATION OF BIOTECHNOLOGY: ENVIRONMENTAL AND POLICY ISSUES 130 (J. Fowle III ed. 1987).

reduction in a nutrient.⁹⁹ However, it never adopted these criteria, leaving uncertain the degree of change that would lead the FDA to review a substance's GRAS status.¹⁰⁰

Hybridization and breeding do not seem to affect the status of a GRAS substance. Neither the FDA nor the courts have distinguished the GRAS status of hybrids from that of conventional pre-existing crops.¹⁰¹ The FDA, however, could make such a distinction if the hybrid were significantly different from pre-existing crops.¹⁰²

b. Biotechnology Application

The Coordinated Framework appears to deal with food additives differently than GRAS substances for the purpose of biotechnology. In the Coordinated Framework, the FDA indicated that for every substance produced by rDNA, a new FAP must be approved, even though a similar substance has been approved as a food additive.¹⁰³ On the other hand, the Coordinated Framework also intimated that a GRAS substance would not necessarily lose its status merely because it was produced through biotechnology.

Comments questioned whether a GRAS substance (including microbes) could lose its GRAS status solely because it was produced or modified by new biotechnology. The answer is yes, if the new substance (and its contaminants) have been altered in such a way that it can no longer be generally recognized by qualified experts to be safe. In this instance, the substance would be a food additive and the provisions of Section 409 would apply.¹⁰⁴

Plainly, the second sentence in this statement contains the implication that GRAS status might not be lost if the bioengineered substance had not changed to the extent envisioned by the FDA in this passage.¹⁰⁵

99. Spiher, *The Growing of GRAS*, 10(3) HORT. SCIENCE 241 (1975).

100. Gibbs & Kahan, *supra* note 24, at 16 n.80.

101. Telephone interview with Jim Maryanski, scientist, Center for Food Safety, FDA (Jan. 9, 1989) (agricultural varieties have not in the past been subject to pre-market approval); Comment, *supra* note 25, at 920.

102. See *supra* note 98 and accompanying text.

103. "Substances that are used in animal feeds, other than drugs, and that are produced by recombinant DNA technology, are considered to be food additives and require approval of a separate food additive petition (FAP), even though a similar substance is currently approved as a food additive." Coordinated Framework, 51 Fed. Reg. 23,311 (1986). It seems likely that if the FDA espouses this view for bioengineered substances in animal feeds, it would have similar or heightened concern for such substances in human food. See McNamara, *supra* note 84, at 58.

104. Coordinated Framework, 51 Fed. Reg. 23,313 (1986).

105. See also McNamara, *supra* note 84, at 58-59 (FDA statement in the Coordinated Framework indicates products of biotechnology might retain GRAS status).

The FDA thus did not provide a clear scheme for the review of bioengineered substances in the Coordinated Framework. It alternatively indicated that bioengineered substances might require the submission of FAPs, and, contrarily, that bioengineered substances could be considered GRAS. Perhaps the FDA's policy statement in the Coordinated Framework means that if a bioengineered substance is to be used as a food additive, a new FAP must be submitted even though the substance is essentially the same as a conventional, approved food additive. If the manufacturer, however, claims the substance is GRAS, the manufacturer may not be under a burden to submit a petition for GRAS affirmation,¹⁰⁶ as this is not required under ordinary circumstances. As noted above, the FDA allows manufacturers to use a GRAS substance without procuring FDA approval, or even notifying the FDA of the proposed use of the substance.¹⁰⁷

The FDA policy statement in the Coordinated Framework leaves open the possibility that a genetically engineered substance could be used in food production without being subjected to prior governmental review. The potential to circumvent pre-market regulation is undesirable in light of the unknown effects of biotechnology on health and safety. Arguably, it is appropriate to apply the GRAS exception to food products which have established their safety through experience based on significant prior use. The government's resources are best allocated to the examination of substances which pose likely health hazards, not to substances which have not created health risks over time. Genetically engineered products should be reviewed by the Federal Government before reaching the marketplace precisely because we have so little experience with biotechnology products and their effects on the public health.

Manufacturers clearly have strong incentives to procure governmental approval for genetically engineered substances before introducing them into commerce. As previously noted, if a substance asserted by a manufacturer to be GRAS is later judged by the FDA to be a food additive, the manufacturer could face criminal and civil liability under the FFDCA.¹⁰⁸ Nevertheless, the GRAS loophole should be closed in the context of biotechnology because a manufacturer, for whatever reason, might choose to take advantage of the GRAS provision and market a product without governmental approval or adequate analysis for health and safety hazards. Leaving such discretion to a private entity creates an intolerable risk.

106. 21 C.F.R. §§ 170.35(a), 570.35(a) (1988) (regulations stating that any interested person may submit a petition for GRAS affirmation).

107. See *supra* note 88 and accompanying text.

108. See *supra* notes 90-91.

Moreover, the FDA has the legal basis to assert, if it chooses to do so, that genetically engineered products used in food production are food additives and thus subject to the pre-approval framework. This legal basis is founded on the FDA's broad authority to determine when a substance is or is not a food additive. For instance, in *Monsanto v. Kennedy*,¹⁰⁹ the court ruled that the FDA has the authority to determine that substances which "migrate" into food from the food's container are food additives, "so long as [the substance's] presence in food can be predicted on the basis of a meaningful projection from reliable data."¹¹⁰ The FDA, therefore, has the discretion to apply the literal terms of the definition of "food additive" in the FFDCA. The court similarly noted that the FDA also has discretion to determine whether or not a substance is GRAS.¹¹¹

Because the FDA has broad authority to determine that substances which migrate into food are food additives, it has sufficient authority to rule that a bioengineered substance is a food additive when introduced into a food. Such an interpretation of the food additive definition in the FFDCA is arguably reasonable and legally supportable.¹¹²

Aside from the pre-approval issue, another reason biotechnology products should be construed to be food additives is that food additives are subject to the Delaney Clause in Section 409, which restricts the use of carcinogenic substances in food.¹¹³ The Delaney Clause provides that "no additive shall be deemed to be safe if it is found to induce cancer when ingested by man or animal."¹¹⁴ GRAS substances, however, are not subject to the Delaney Clause because by definition they are not food additives, and thus outside the ambit of Section 409.

109. 613 F.2d 947 (1979).

110. *Id.* at 955. The process of migration referred to in this case is based on the second law of thermodynamics, which indisputably predicts that whenever two substances come into contact, they will tend to diffuse, or migrate, into each other.

111. *Id.* at 956.

112. "[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 [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. NRDC*, 467 U.S. 837, 843-44 (1984). See also *Scott v. FDA*, 728 F.2d 322, 324 (6th Cir. 1984) ("The FDA's interpretation of the Food, Drug, Cosmetic Act is entitled to considerable deference.").

113. Section 409 provides two safety clauses: the Delaney Clause which restricts the use of carcinogenic substances in food; and the General Safety Clause which applies to non-carcinogenic additives and carcinogenic impurities. The Delaney Clause involves a stricter standard for FDA approval. This stricter standard makes application of the Delaney Clause to bioengineered food substances more desirable from a consumer safety viewpoint than the weaker standard embodied in the General Safety clause. See *infra* note 128 and accompanying text.

114. 21 U.S.C. § 348(c)(3)(A) (1982).

The Delaney Clause has traditionally been considered to create a complete prohibition on the use of carcinogenic food additives.¹¹⁵ FDA attempts to read in a *de minimis* exception to the Delaney Clause to allow for the use of minimally carcinogenic additives have so far been unsuccessful.¹¹⁶ The EPA, however, recently issued a *de minimis* interpretation of the food additive Delaney Clause. The EPA announced that it will read the Delaney Clause to allow the use of carcinogenic pesticides in processed foods which pose a "negligible risk" to health, which the EPA has defined as a one in a million chance of getting cancer over a 70-year lifetime of use.¹¹⁷ In light of the FDA's failed attempts to read in a *de minimis* interpretation, this regulation is of questionable legal validity.¹¹⁸

A distinction, however, has been made between the additive and the impurities present in the additive. In *Scott v. FDA*,¹¹⁹ the court held that the Color Additive Delaney Clause¹²⁰ does not apply to impurities, and thus color additives can contain carcinogenic impurities which pose insignificant risks. The *Scott* court based its ruling on the fact that the Delaney Clause literally only applies to the additive, not to impurities or constituents contained in the additive.¹²¹ Thus, in *Scott*, it was decided that although the color additive D & C Green No. 5 contained a carcinogenic impurity, p-toluidine, the additive itself was not carcinogenic and consequently the additive was found to be safe under the Delaney Clause.¹²²

115. See NAS report, *supra* note 68, at 13, 22, 26.

116. See *Public Citizen v. Young*, 831 F.2d 1108 (D.C. Cir. 1987) (color additive amendment's Delaney Clause does not contain an implicit *de minimis* exception). See also *Public Citizen v. Bowen*, 833 F.2d 364 (D.C. Cir. 1987) (challenge to FDA's proposed *de minimis* interpretation of the food additive Delaney Clause dismissed because the FDA's proposal was not finalized). After *Bowen*, the FDA withdrew the proposal to apply a *de minimis* reading to the food additive Delaney Clause.

117. Delaney Clause Notice, 53 Fed. Reg. 41,112 (1988). The EPA sets the FFDCA tolerances for pesticides, and thus has the responsibility to set food additive tolerances for pesticides under § 409. See *supra* note 20 (EPA responsibilities under the FFDCA).

118. See, e.g., *EPA Sets New Policy on Pesticide Cancer Risks*, 242 SCIENCE 366 (Oct. 21, 1988) ("[I]n adopting the new policy, EPA is skating on thin legal ice. It appears to be proposing a flexible interpretation of one of the most unbending provisions in the nation's food laws -- the infamous Delaney Clause . . ."). Cf. Strauss, *Reaffirming the Delaney Anticancer Clause: The Legal and Policy Implications of an Administratively Created De Minimis Exception*, 42 FOOD DRUG COSM. L.J. 393, 428 (1987) (concluding that the FDA does not have the legal authority to implement a *de minimis* policy under the Delaney Clause).

119. 728 F.2d 322 (6th Cir. 1984).

120. 21 U.S.C. § 376(b)(5)(B) (1982).

121. 728 F.2d at 324-25.

122. *Id.*

This exception to the Delaney Clause, which has come to be known as the "constituents policy," has apparently been construed by the FDA to apply to food additives as well.¹²³ Moreover, the EPA has applied the constituents policy in the area of pesticide tolerance setting under Section 409 in cases where a non-oncogenic pesticide contained oncogenic nonfunctional constituents.¹²⁴

Because the Delaney Clause does not apply to these constituents, both the FDA and the EPA assess the health risks posed by constituents under the General Safety Clause, the other safety clause contained in Section 409. Under the current regulatory framework, the Delaney Clause applies to carcinogenic additives, whereas the General Safety Clause applies to non-carcinogenic additives and to carcinogenic impurities. The General Safety Clause provides that "[n]o such regulation shall issue if a fair evaluation of the data . . . fails to establish that the proposed use of the food additive . . . will be safe."¹²⁵ Although GRAS substances are technically not covered by the General Safety Clause, they too are required, by definition, to be "safe." Thus, the FDA applies the same safety analysis in its regulation of GRAS substances when affirmation is sought as is applied to food additives under the General Safety Clause.¹²⁶

The General Safety Clause does not require absolute certainty of safety. Rather, "[s]afety requires proof of a reasonable certainty that no harm will result from the proposed use of an additive."¹²⁷ Thus, the General Safety Clause embodies a non-absolute, non-zero risk standard.

The FDA has formulated a set of guidelines describing the scientific standards which must be met by sponsors of food additive petitions.¹²⁸ Essentially, under the guidelines, the FDA determines whether the additive meets the "reasonable certainty" test for safety by computing an "acceptable daily intake" (ADI) figure which is the amount of the

123. See Strauss, *supra* note 119 at 410-11.

124. See EPA, Notice on Tolerances for the Pesticide Dicamba, 49 Fed. Reg. 47,481 (1984) [hereinafter Dicamba Notice]; NAS report, *supra* note 68, at 88, 90, 94-95, 206-08 (discussion and use of EPA's interpretation of the constituents policy).

125. 21 U.S.C. § 348(c)(3) (1982).

126. See 21 C.F.R. § 170.30(b) (1988) ("General recognition of safety based upon scientific procedures shall require the same quantity and quality of scientific evidence as is required to obtain approval of a food additive.").

127. S. Rep. No. 2422, 85th Cong., 2d Sess. (1958), reprinted in 1958 U.S. CODE CONG. AND ADMIN. NEWS 5300, 5305 (Senate report for the Food Additive Amendment of 1958, which added § 409 to the FFDC). See also 21 C.F.R. §§ 170.3(i), 570.3(i) (1988) ("Safe" defined to require "reasonable certainty . . . that the substance is not harmful").

128. FDA, TOXICOLOGICAL PRINCIPLES FOR THE SAFETY ASSESSMENT OF DIRECT FOOD ADDITIVES AND COLOR ADDITIVES IN FOOD (1982). This publication is otherwise known as the "REDBOOK." See Notice on the Use of the Food Additive Aspartame, 49 Fed. Reg. 6,672, 6,674-75 (1984) [hereinafter Aspartame Notice] (discussion of the REDBOOK); 47 Fed. Reg. 46,141 (1982) (notice that the REDBOOK is available to the public).

additive that can be safely consumed on a chronic basis with a reasonable certainty of safety.¹²⁹ To arrive at this figure, the FDA determines the no observable effect level (NOEL), which is the highest dose level of the substance at which no adverse effect is observed in animal studies. The NOEL figure is then divided by a safety factor, usually 100, to arrive at the ADI.¹³⁰ The FDA then computes an "estimated daily intake" (EDI) figure, which is based on studies of consumption patterns of various population subgroups.¹³¹ Under this methodology, the ADI generally must exceed the EDI for the additive to satisfy the safety standard contained in the General Safety Clause.¹³² The EPA uses a similar calculation to evaluate pesticides under the General Safety Clause.¹³³

Even though carcinogenic constituents are considered under the General Safety Clause, they are not evaluated under the ADI/EDI standard. This is because of the notion that any level of a carcinogen is unsafe.¹³⁴ Thus, it would be a contradiction in terms to compute an "acceptable daily intake" for a carcinogen. Instead, both the FDA and the EPA use risk assessment models to assess harms posed by carcinogenic constituents under the General Safety Clause, and carcinogenic additives under the Delaney Clause. Risk assessment models are based on animal bioassay data and allow for the computation of an upper-bound estimate of human cancer risks created by a substance.¹³⁵

129. Aspartame Notice, 49 Fed. Reg. 6,678 (1984).

130. 21 C.F.R. § 170.22 (1988) ("[A] food additive for use by man will not be granted a tolerance that will exceed 1/100th of the maximum amount demonstrated to be without harm to experimental animals.").

131. Aspartame Notice, 49 Fed. Reg. 6,678 (1984).

132. *Id.*

133. See NAS report, *supra* note 68, at 31-33, 35. Instead of computing an EDI figure, the EPA uses the term "theoretical maximum residue concentration" (TMRC), which is the functional equivalent of the EDI. The ADI must exceed the TMRC for a tolerance to be issued for the pesticide. *Id.* at 32.

134. "There is no adequate evidence that there is a safe level of exposure for any carcinogen Unfortunately, scientists have not yet developed any way to measure a person's individual risk. Exposure to a low level of a carcinogen thus has to be considered a risk for everyone." NAT'L INST. OF HEALTH PUB. NO. 84-2039, EVERYTHING DOESN'T CAUSE CANCER (1984).

135. NAS report, *supra* note 68, at 33. Scientists have criticized the principle underlying risk assessment models, that human cancer risks can be determined through analysis of experiments on animals:

Extrapolation from the results of rodent cancer tests done at high doses to effects on humans exposed to low doses is routinely attempted by regulatory agencies when formulating policies attempting to prevent future cancer. There is little sound scientific basis for this type of extrapolation, in part due to our lack of knowledge about mechanisms of cancer induction, and it is viewed with great unease by many epidemiologists and toxicologists.

Ames, Magaw & Gold, *Ranking Possible Carcinogenic Hazards*, 236 SCIENCE 271 (1987).

Conversely, use of risk assessment models has also been defended on the grounds that (i) it is useful in setting priorities on the use of agency resources; (ii) it enables agencies to engage in risk/benefit balancing when required by law; (iii) it has become embedded in the regulatory structure; and (iv) limitations in toxicological testing methods virtually compel the use of risk assessment procedures. Scheuplein, *Risk Assessment and Food Safety: A Scientist's and Regulator's View*, 42 FOOD DRUG COSM. L.J. 237, 240-41 (1987).

The FDA has taken the position that constituents which pose an additional lifetime oncogenic risk of less than one in one million will be considered safe.¹³⁶ The EPA apparently applies a "low potential risk" test, which it has not defined further.¹³⁷ The EPA has only applied the constituents policy to an impurity which had a oncogenic risk rate of 1 in 100 million.¹³⁸

Thus, in this complex regulatory framework established for the analysis of health hazards posed by the use of food additives and pesticides, there exist some differences in opinion between the FDA and the EPA about specific safety standards. Besides the disagreement between the FDA and the EPA regarding the constituents policy, the FDA and the EPA have also taken different interpretations of the Delaney Clause. The FDA is currently applying the traditional zero-risk standard, whereas the EPA has adopted a negligible risk standard.¹³⁹

While this regulatory structure potentially allows for a rigorous examination of the health hazards posed by food additives and pesticides, the GRAS provision provides a possible loophole. As previously emphasized, food substances asserted to be GRAS by manufacturers can bypass scrutiny under these safety standards.¹⁴⁰ This is so because substances claimed to be GRAS can be used without governmental review. The GRAS provision thus constitutes the blind spot of this regulatory structure. However, even when the GRAS substance is reviewed because either the FDA or a manufacturer seeks to formalize its status, the toughest regulatory standard that will be applied is a non-zero risk standard. Significantly, there does not exist a Delaney Clause standard for GRAS substances. Thus, the FDA could possibly approve as GRAS a food substance that had a negligible carcinogenic risk rate. In fact, GRAS substances in use prior to 1958 that were approved under the common use provision clearly carry carcinogenic risk rates.¹⁴¹ However, the FDA has not yet granted GRAS status to any substance that it was required to approve on the basis of scientific evidence which had a carcinogenic risk rate. FDA adherence to this position, however, may change in the future.¹⁴²

136. NAS report, *supra* note 68, at 207.

137. See Dicamba Notice, 49 Fed. Reg. 47,482 (1984).

138. *Id.*

139. See *supra* notes 115-18.

140. See *supra* note 88 and accompanying text.

141. See Ames, Magaw & Gold, *supra* note 135, at 271 (discussion of carcinogens naturally present in fruits and vegetables).

142. Cf. *Public Citizen v. Young*, 831 F.2d 1118, 1119-20 (D.C. Cir. 1987) (discussion of possibility that GRAS substances can carry trivial carcinogenic risks).

It is presently unclear how the lack of an applicable anti-cancer clause for GRAS substances will affect the Federal Government's regulation of bioengineered substances. Thus far, no manufacturer has developed a carcinogenic pesticide or food additive through genetic engineering techniques. Manufacturers in the future, however, may produce such products. Given the uncertain effects genetic engineering may produce, it would be prudent if the FDA were to adopt a policy which prohibited manufacturers of genetically engineered substances from claiming GRAS status for their products. Under such a policy, all genetically engineered food substances and pesticides used on processed foods would necessarily be regulated as food additives. The benefit of this policy would be that these substances would be reviewed by the government prior to their commercial use and scrutinized under the Delaney Clause for carcinogenic risks.

Pesticides used solely on raw agricultural products, however, cannot be subject to the Section 409 provision because they are explicitly excluded from its purview under the food additive definition. In the FFDCA, pesticides present only on raw foods are subject to a different provision, Section 408.¹⁴³ FIFRA also provides a basis for the regulation of pesticides. The next section examines the regulatory standards provided by Section 408 and FIFRA.

2. THE REGULATORY STANDARDS PROVIDED BY SECTION 408 AND FIFRA

Section 402(a)(2)(B) declares that raw agricultural commodities will be deemed adulterated if they contain pesticides held to be unsafe under Section 408.¹⁴⁴ Section 408 in turn provides that if a pesticide on a raw agricultural commodity is not GRAS, then it is considered unsafe unless the EPA has issued a tolerance, or exempted the pesticide from the tolerance requirement.¹⁴⁵

Section 408 expressly contains a risk/benefit standard.¹⁴⁶ To determine under Section 408 the risks posed by the use of pesticides, the EPA distinguishes non-oncogenic pesticides from oncogenic pesticides. For non-oncogenic pesticides, the EPA uses the same ADI/TRMC

143. See *supra* note 78 and accompanying text.

144. 21 U.S.C. § 342(a)(2)(B) (1982). The term "pesticide" is defined as "any substance which, alone, in chemical combination or in formulation with one or more other substances, is a pesticide within the meaning of the Federal Insecticide, Fungicide, and Rodenticide Act . . . and which is used in the production, storage, or transportation of raw agricultural commodities." 21 U.S.C.A. § 321(q) (West Supp. 1988).

145. 21 U.S.C. § 346a(a) (1982). As a general rule, pesticides are not GRAS for the purposes of § 408. 40 C.F.R. § 180.2(a) (1987).

146. See *supra* note 66.

methodology which is used to evaluate non-oncogenic pesticides under Section 409.¹⁴⁷ For oncogenic pesticides, the EPA relies upon risk assessment models to determine the oncogenic risk posed by the pesticide.¹⁴⁸ As explained above, this is the same methodology the EPA uses to evaluate pesticides under the Delaney Clause.¹⁴⁹

The regulation of pesticides, however, does not rest solely on FFDCA standards. Pesticides also must be registered by the EPA under FIFRA for the uses which are proposed by the manufacturer.¹⁵⁰ Pesticides may be registered for use if they generally will not cause "unreasonable adverse effects on the environment."¹⁵¹ This provision has been defined to address "any unreasonable risk to man or the environment; taking into account the economic, social, and environmental costs and benefits of the use of . . . [the] pesticide."¹⁵² Thus, FIFRA resembles Section 408 of FFDCA in that both implement a risk/benefit balance for the evaluation of pesticides.¹⁵³ Both, moreover, allow for the use of carcinogenic pesticides.¹⁵⁴

In general, however, the EPA will not issue a Section 408 tolerance if the pesticide has a oncogenic risk rate higher than one in ten thousand.¹⁵⁵ On the other hand, pesticides which have risk rates of one in one million or lower will generally receive Section 408 tolerances.¹⁵⁶ This policy regarding tolerance approvals is significant for FIFRA regulation because if the pesticide will be applied to food, the EPA will not register the pesticide under FIFRA until the necessary FFDCA tolerances have been granted.¹⁵⁷

Under this regulatory framework, a pesticide manufacturer has two different types of standards to meet, depending on the types of foods to which the pesticide will be applied. If the pesticide will be applied solely to crops which are not considered to have processed forms, then the pesticide need only meet the risk/benefit standards contained in

147. See NAS report, *supra* note 68, at 31-35.

148. *Id.*

149. See *supra* note 125 and accompanying text.

150. See NAS report, *supra* note 68, at 23.

151. FIFRA, 7 U.S.C. § 136a(c)(5)(C) (1982).

152. *Id.* § 136(bb).

153. EPA has listed data requirements for the registration of pesticides under FIFRA in 40 C.F.R. §§ 158.20 - 158.170 & 162.1 - 162.177 (1987). Data generally required concern the product's chemical properties, its effectiveness, and health hazards posed by the use of the pesticide.

154. See NAS report, *supra* note 68, at 19, 25, 34.

155. *Id.* at 34.

156. *Id.*

157. Delaney Clause Notice, 53 Fed. Reg. 41,105 (1988); NAS report, *supra* note 68, at 23.

Section 408 and FIFRA.¹⁵⁸ If, however, the pesticide will be applied to crops which will yield processed products, then the manufacturer will also have to satisfy the EPA's negligible risk standard for carcinogens under the Delaney Clause. This standard requires that the pesticide have a risk rate of one in one million or lower.¹⁵⁹

Crops which have processed forms are those which can be converted into sauces, juices, etc.¹⁶⁰ Under current EPA guidelines, most fruits and vegetables, and all meat, milk, poultry, and pork products are not considered to have processed forms.¹⁶¹ However, tomatoes, apples, potatoes, grapes, and citrus fruits are considered to have processed forms.¹⁶² Using genetic engineering techniques, scientists have already succeeded in introducing a pesticidal substance, *Bacillus thuringiensis* endotoxin genes (BT), into tomatoes.¹⁶³ Thus, the Government may someday be faced with the regulation of a genetically engineered pesticide under Section 409, because tomatoes, as noted above, have processed forms. Currently, the BT product is not up for review because no manufacturer has yet indicated it is ready to market the product. In this particular case, the Delaney Clause will pose no bar, because BT is not carcinogenic. In the future, however, crops may be subjected to genetically engineered pesticides which are carcinogenic.

The development of carcinogenic pesticides through genetic engineering techniques would exacerbate the EPA's already difficult task of reducing the amount of carcinogenic residues in food. The National Academy of Sciences, for instance, has estimated that there exist at least fifteen foods which have oncogenic risk rates greater than 1 in 10,000 after treatment with pesticides.¹⁶⁴ The highest risk rate belonged to tomatoes, which have a risk rate of 8.75 in 10,000, which, astonishingly, is higher than risk rates for many, if not most, pesticides currently in use. Moreover, it has been estimated that approximately 2,500 Section

158. See *supra* notes 135-41 and accompanying text.

159. See *supra* note 117 and accompanying text.

160. See NAS report, *supra* note 68, at 62 (discussion of several forms of processed apples); Delaney Clause Notice, 53 Fed. Reg. 41,122 (1988) (discussion of processed form of tomatoes).

161. See NAS report, *supra* note 68, at 6, 10. EPA defines processed foods in a non-regulatory companion to 40 C.F.R. § 158, Subpart K, entitled "Pesticide Assessment Guidelines Subdivision O: Residue Chemistry." For a discussion of these guidelines, see NAS report, *supra* note 68, at 42.

162. NAS report, *supra* note 68, at 10.

163. Hilder, Gatehouse, Sheerman, Barker & Boulter, *supra* note 54, at 161; Gould, *Genetic Engineering, Integrated Pest Management and the Evolution of Pests*, 3 TRENDS IN ECOLOGY AND EVOLUTION, 6 TRENDS IN BIOTECHNOLOGY (Apr. 1988) (special combined issue) at S15. As its name suggests, the BT endotoxin gene acts to synthesize a chemical, known as BT endotoxin, which is pesticidal.

164. NAS report, *supra* note 68, at 78.

408 tolerances and 30 Section 409 tolerances exist for pesticides which have been found to be oncogenic in test animals.¹⁶⁵ Although the Delaney Clause is supposedly triggered whenever new information shows that a pesticide is carcinogenic, the EPA has not invoked the Clause to revoke any pesticide tolerance.¹⁶⁶ This EPA policy has led to the situation whereby new, safer (although carcinogenic) pesticides are barred under the Delaney Clause, whereas the older, more carcinogenic pesticides are continued in use.

Biotechnological processes should be used to help solve the problem of carcinogenic residues in food, rather than exacerbate it. Therefore, the EPA should adopt a policy which discourages the use of bioengineering to produce genetically engineered carcinogenic pesticides. In the Coordinated Framework, however, the EPA did not address this issue. Instead, the EPA focused on the regulation of genetically engineered microorganisms, not the introduction of pesticidal genetic material into plants.¹⁶⁷ Thus, it remains an open question what policies the EPA will seek to advance in its regulation of genetically engineered pesticidal substances introduced into crops.

III. CONCLUSIONS

The various statutory provisions can be summarized as follows:

<i>Provision</i>	<i>Standard 402(a)(1)</i>
	Added substances -- "may render" standard.
	Endogenous substances -- "ordinarily render" standard.
408	Risk/Benefit
	Non-oncogenic pesticides -- ADI/TMRC Standard.
	Oncogenic pesticides -- generally approved if risk below 1 in 1 million.
409	General Safety Clause:
	Additives and pesticides -- ADI/EDI-TMRC standard.
	Constituents -- 1 in 1 million standard by FDA, "low potential risk" standard by EPA.
	Delaney Clause:
	Zero risk standard by FDA;
	<i>De minimis</i> risk standard by EPA.

With regard to biotechnology, the FDA indicated in the Coordinated Framework that it considers the "may render" standard applicable

165. *Id.* at 36.

166. Delaney Clause Notice, 53 Fed. Reg. 41,108-09 (1988).

167. See Coordinated Framework, 51 Fed. Reg. 23,313-36 (1986) (EPA statement of policy on the use of microbial products of biotechnology).

to natural substances in food increased through genetic engineering, as well as to new substances introduced into the food.¹⁶⁸ The FDA position on how bioengineered substances would be reviewed under the food additive and GRAS regulations is less clear.

However, there exist strong justifications for supporting the position that the FDA and the EPA should consider bioengineered substances used in food as food additives. First, food additives, unlike GRAS substances, are subject to the Delaney Clause's prohibition of carcinogens.¹⁶⁹ Even if the EPA successfully adopts a negligible risk standard under the Clause, such a standard will be more stringent than the GRAS provisions which do not specifically provide for the prohibition of carcinogens. Plainly, a negligible risk standard is better than no standard. Although the FDA currently will not approve a substance as GRAS if it is carcinogenic,¹⁷⁰ it might attempt to do so in the future. Without an applicable anti-carcinogen clause barring its way, the FDA might be successful in promulgating such a policy. In fact, the FDA arguably would have a stronger legal basis in promulgating a negligible risk standard for carcinogenic GRAS substances than for food additives since the Delaney Clause only applies to the latter.¹⁷¹

The other major reason for considering bioengineered substances as food additives is that if they were to be considered GRAS substances, manufacturers could use them without FDA approval or knowledge. Whereas food additives are generally subject to the pre-approval framework set out in Section 409, GRAS substances can be used by manufacturers without any prior contact with the FDA.¹⁷² Only if the FDA subsequently rules that the substance is not GRAS will manufacturers face liability under the FFDCFA.¹⁷³

The FDA stated in the Coordinated Framework that it did not need to establish additional administrative procedures to deal with biotechnology issues.¹⁷⁴ Rather, it preferred to review biotechnology questions on a case-by-case basis. The EPA, moreover, did not provide a statement of policy concerning the regulation of pesticidal substances incorporated into plants through genetic engineering techniques. Thus, because no new provisions have been provided by either agency, the regulatory framework applied to bioengineered food additives and pesticides will be

168. See *supra* note 54 and accompanying text.

169. See *supra* note 114 and accompanying text.

170. See *supra* note 142 and accompanying text.

171. See *supra* note 114 and accompanying text.

172. See *supra* note 88 and accompanying text.

173. See *supra* note 89 and accompanying text.

174. Coordinated Framework, 51 Fed. Reg. 23,309.

essentially the same as that applied to such substances produced using conventional methods.

The Federal Government currently faces the difficult task of reducing carcinogenic residues present in food. Biotechnology techniques may prove to be very helpful in the development of products which could be used to eliminate the current reliance on carcinogenic pesticides and additives. The Federal Government should therefore adopt policies which would encourage the biotechnological development of such non-carcinogenic products.

