Crop Biotechnology: The Case for Product Stewardship

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ARTICLES

CROP BIOTECHNOLOGY: THE CASE FOR PRODUCT STEWARDSHIP

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As this year's spring planting season draws to a close, new questions are being raised about consumer acceptance of biotechnology crops. With millions of acres of genetically engineered corn, cotton, and soybeans in the ground, U.S. farmers are facing renewed resistance to biotechnology crops in overseas markets and increased scrutiny of agricultural biotechnology at home.

Regulation is designed to address both harm and liability. To the public, regulation provides assurance that a product is safe for its intended use. To the producer of the good and others in the chain of commerce, regulation provides assurance that appropriate safety standards have been met in bringing a product to market. These

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The views expressed in this article are the authors' alone and not necessarily those of their clients or employers.

assurances are particularly important when dealing with the introduction of a controversial, new technology. But even the best efforts by regulatory agencies may prove inadequate without the development and implementation of product stewardship programs by the private sector. This article will review the federal government's oversight programs, the key elements of a proactive product stewardship program, and the relationship between these two complimentary activities in addressing the commercialization of plant biotechnology.

I. THE SEEDS OF CONTROVERSY

Not all commercial applications of biotechnology have been met with resistance. It would be easy to conclude that products with obvious benefits to the consumer are the ones that get the best reception, but this would be far too simplistic an analysis. Clearly, timing is a factor, with early approvals drawing little public attention. The public's justifiable concern with anything that might affect the safety of the food supply is also certainly not to be underestimated. Novelty also plays an important role, providing fertile ground for the generation of misunderstanding, apprehension, and distrust in a general population that has little training in the science of genetics. A brief review will serve to illustrate the difficulty of predicting controversy in this developing field.

The first commercial application of modern biotechnology came in 1982, when the U.S. Food and Drug Administration ("FDA") approved a human insulin product for the treatment of diabetes.[1] Many other human pharmaceutical products followed, all with clear benefits to the consumer and little, if any, controversy. In 1990, the FDA took its first step into the realm of biotechnology foods and approved a genetically engineered enzyme, chymosin, for use in making cheese.[2] Although this product was the first of its kind, offered no obvious benefit to consumers, and was rapidly adopted by cheese producers as a substitute for rennet, chymosin attracted little attention let alone controversy.

In sharp contrast, three products under review by the federal government in the early 1990s drew fire from anti-biotechnology

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[1] *See* Drugs Composed Wholly or Partly of Insulin, 48 Fed. Reg. 16,704 (proposed Apr. 19, 1983) (to be codified at 21C.F.R. pts. 201, 429).

[2] *See* Direct Food Substances Affirmed as Generally Recognized as Safe; Chymosin Enzyme Preparation Derived From Escherichia Coli K-12, 55 Fed. Reg. 10,932 (March 23, 1990) (to be codified at 21 C.F.R pt. 184).

activists. The first was recombinant bovine somatotropin, also known as "rBST" or Posilac®, the first genetically engineered animal drug. When administered to lactating dairy herds, this protein hormone increases the production of milk that would ordinarily occur as a result of the cows' naturally occurring BST levels by as much as 10 to 20 percent.[3] Following a review of volumes of health and safety data, an extensive environmental assessment, public hearings and independent scientific peer review, the FDA approved rBST for sale in 1993.[4] Although it was the most exhaustively reviewed animal drug in the FDA's history and easily survived a court challenge,[5] opponents are still calling for a ban on its use. The second controversial product was the FLAVR SAVR™ tomato. Using recombinant DNA technology, scientists were able to alter the genetic structure of the plant so as to delay ripening of the fruit.[6] In spite of calls for additional study, the tomato successfully completed a lengthy FDA review process in 1994.[7] The tomato was sold without incident for several years with a special label voluntarily applied by the producer, although the product was never a commercial success due to its failure to meet consumer expectations. Numerous other fruits and vegetables with superior taste, texture, color, and other desirable properties have since been introduced without controversy.

The third product was the NewLeaf® potato. After inserting a gene from a common soil microorganism into a Russet Burbank potato, the plant was able to produce an insecticidal protein that provided protection from the Colorado potato beetle.[8] The naturally occurring form of the protein was used successfully in spray form by conventional and organic farmers for over 30 years without controversy. The approval in 1995 of the NewLeaf® potato was heralded by the U.S. Environmental Protection Agency ("EPA") as the first of many crops that would dramatically reduce farmers'

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[3] EXECUTIVE BRANCH OF THE FEDERAL GOVERNMENT, USE OF BOVINE SOMATOTROPIN (BST) IN THE UNITED STATES: ITS POTENTIAL EFFECTS 20-21 (1994). *See also* Animal Drugs, Feeds, and Related Products; Sterile Sometribove Zinc Suspension, 58 Fed. Reg. 59,946 (Nov. 12, 1993) (to be codified at 21 C.F.R pts. 510, 522).

[4] *See* Animal Drugs, Feeds, and Related Products; Sterile Sometribove Zinc Suspension, 58 Fed. Reg. 59,946 (Nov. 12, 1993) (to be codified at 21 C.F.R pts. 510, 522).

[5] *See* Stauber v. Shalala, 895 F. Supp. 1178 (1995).

[6] *See* Calgene, Inc.; Availability of Letter Concluding Consultation, 59 Fed. Reg. 26,647 (May 23, 1994).

[7] *See id.*

[8] *See* United States Environmental Protection Agency ("EPA"), Press Advisory, EPA Issues Registration and Approves Full Commercialization for Potato Plant-Pesticide (May 5, 1995).

dependence on chemical insecticides.[9] However, in spite of the potential environmental benefits, crops containing insecticidal proteins, which now include corn and cotton, have been among the most frequently attacked by environmental and consumer groups. As discussed in greater detail below, questions raised about the environmental safety of these crops have resulted in extraordinary regulatory controls imposed by the EPA and unprecedented product stewardship efforts by the companies involved.

II. ESTABLISHING A REGULATORY FRAMEWORK

A significant challenge posed by modern biotechnology was the potential regulation of new plant varieties produced by recombinant DNA techniques, one of several new methods developed by molecular biologists for moving desirable traits from one organism to another. Using these methods, researchers can identify the genetic material that produces a desirable trait, such as disease resistance, in one organism and then transfer that material to a second organism. If the gene transfer succeeds, it can result in a new "transgenic" plant with the same desirable trait as the donor organism. These products and the plants from which they are derived are commonly referred to as "genetically modified," although that phrase could be applied just as appropriately to plants and plant products that result from traditional plant breeding techniques.

As the federal government took up the challenge of regulating plant biotechnology in 1983, it was confronted with two extreme schools of thought: the "no regulation" school and the "no commercialization" school. The "no regulation" school made two principal arguments: first, plant biotechnology is simply an extension of conventional breeding techniques that have been used successfully for centuries with little or no regulation; and, second, regulation inhibits research and innovation and delays the realization of significant benefits.[10] On the other hand, the "no commercialization" school argued that until and unless all questions and doubts about a new technology were answered, it could not be trusted and had to be held in abeyance.[11] This is essentially the manner in which anti-

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[9] *See id. See also* Notice of Limited Plant Propagation Registration for a Plant-Pesticide, 60 Fed. Reg. 4910 (June 25, 1995). The product was developed by Monsanto Company.

[10] *See* Coordinated Framework for Biotechnology, 51 Fed. Reg. 23302, 23344-46 (1986). *See also* Proposal for a Coordinated Framework for Regulation of Biotechnology, 49 Fed. Reg. 50856 (proposed Dec. 31, 1984) (citing EPA Docket # OPTS 00049; USDA Docket # APHIS 00049; FDA Docket #84N-0431).

[11] *See* Coordinated Framework for Biotechnology, Fed. Reg. 23302, 23344-46. *See also*

biotechnology activists are urging the European Union to implement the "precautionary principle."[12]

In the end, the United States government chose a middle ground—it would regulate plant biotechnology, but not under a zero risk standard which would effectively preclude commercialization. On June 26, 1986, after public notice and comment,[13] the government issued its Coordinated Framework for Regulation of Biotechnology ("Coordinated Framework" or "Framework") under the auspices of the White House Office of Science and Technology Policy.[14] Responsibility for implementation of the Coordinated Framework fell to three lead agencies—the Department of Agriculture ("USDA"), the Food and Drug Administration ("FDA") within the Department of Health and Human Services, and the Environmental Protection Agency.

The Framework establishes a federal safety net under which all biotechnology products are subject to regulation under existing, product-based statutes. For example, plants remain subject to the USDA's jurisdiction while pesticides continue to be reviewed by the EPA. Over time, individual products or categories of products are eligible for exemption based on agency experience.[15] While acknowledging that then existing statutes were not drafted with biotechnology in mind, the decision not to seek new legislation was based in part on *Diamond v. Chakrabarty*, in which the Supreme Court upheld the patentability of a genetically engineered microorganism under the Patent Act originally drafted by Thomas Jefferson.[16]

During the nearly fifteen years following the Coordinated Framework's inception, the three lead agencies have cleared the way for hundreds of new agricultural, industrial, and health care products, including dozens of plants modified through modern

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Proposal for a Coordinated Framework for Regulation of Biotechnology, 49 Fed. Reg. 50856.

[12] *See* Frank B. Cross, *Paradoxical Perils of the Precautionary Principle*, 53 WASH. & LEE L. REV. 851 (1996) (noting that the precautionary principle "suggests that government should take precautions to protect public health and the environment, even in the absence of clear evidence of harm and notwithstanding the costs of such action").

[13] *See* Proposal for a Coordinated Framework for Regulation of Biotechnology, 49 Fed. Reg. 50,856 (proposed Dec. 31, 1984).

[14] *See* Coordinated Framework for Biotechnology, 51 Fed. Reg. 23302 (June 26, 1986).

[15] *See* Proposal for a Coordinated Framework for Regulation of Biotechnology, 49 Fed. Reg. at 50,858; Coordinated Framework for Biotechnology, 51 Fed. Reg. at 23,309.

[16] *See* Diamond v. Chakrabarty, 447 U.S. 303 (1980). *See also* Ex Parte Hibberd, 227 U.S.P.Q. 443 (BPAI, 1985). The Coordinated Framework did not address the protection of intellectual property rights in transgenic plants.

biotechnology. Decades of research have enabled plant specialists to apply their knowledge of genetics to improve crops such as corn, cotton, soybeans, potatoes, and canola. The researchers carefully monitor plants improved through biotechnology in laboratory, greenhouse, and field tests to ensure that improved crops are the same as traditional crops except for the addition of the beneficial traits. Products derived from traditional plant breeding, such as a stronger cotton fiber or heartier tomato hybrid, generally are not faced with any pre-market approval requirements from federal regulators. In sharp contrast, under the Coordinated Framework, a company interested in bringing a food, feed or fiber product to market, that results from modern microbiological techniques, might have to work its way through two or three different federal agencies.[17] This cautionary approach was adopted primarily in response to public perception rather than any inherent danger associated with the technology.

New plant products on the market today have brought significant benefits to farmers, consumers, and the environment. Some of the commercially available biotechnology crops include:

- High oleic soybeans, providing healthier cooking oils and processed foods with lower levels of saturated fat and trans-fatty acids;

- Produce with superior color, taste and texture and extended shelf life;

- Corn, cotton and potatoes protected against harmful insects, reducing the need to spray conventional pesticides;

- Corn, cotton, canola, soybeans, sugar beets, rice and flax modified to encourage environmentally friendly weed control practices that reduce soil erosion and chemical inputs;

- Squash, potatoes and papayas resistant to harmful viruses, reducing the need to spray conventional pesticides.

Benefits of future biotechnology products include plants resistant to drought and other extreme growing conditions, crops with improved

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[17] *See* Coordinated Framework for Biotechnology, 51 Fed. Reg. at 23,303.

nutritional value, allergen-free foods, plants used for production of pharmaceuticals, food and feed that can deliver a therapeutic dose of a vaccine or other biological, and plants that serve as an alternative source for oils and other petrochemical products.[18]

A. Regulation of Plants

The USDA has responsibility for safeguarding American agriculture and regulating organisms that pose a threat to plants. The USDA is typically the first stop for any company interested in developing a biotechnology plant. In particular, the recently enacted Plant Protection Act ("PPA")[19] and its predecessor statutes such as the Plant Pest Act[20] provide the USDA with the authority to regulate the movement into or within the United States of organisms that may endanger plant life and to prevent the introduction, dissemination or establishment of such organisms.[21] Based on this authority, the USDA established a permit system designed to ensure that new plant varieties receive a comprehensive review before they are ever planted in the field.[22] The implementing regulations prohibit the introduction of so-called "regulated articles" without a permit from the USDA's Animal and Plant Health Inspection Service ("APHIS").[23]

The APHIS rules do not regulate research of genetically engineered organisms in a laboratory or contained greenhouse, but come into play only when a person seeks to introduce genetically engineered organisms into the environment or interstate commerce.[24] A typical permit will cover small-scale field testing of a genetically engineered plant prior to commercialization. While APHIS automatically requires a permit if the donor or recipient organism is a known plant pest, it reserves the right to require a

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[18] *See* product benefit information, *at* http://bti.cornell.edu/research/reports/phuman.html (last visited Feb. 23, 2001); http://bti.cornell.edu/research/reports/pharming.html (last visited Feb. 23, 2001); http://www/betterfoods.org/Promise/Hunger/Hunger.htm (last visited Feb. 23, 2001); http://www/betterfoods.org/Promise/Environment/Environment.htm (last visited Feb. 23, 2001); http://www.ifpri.cgiar.org (last visited Feb. 23, 2001); http://www.bio.org/food&ag/approvedag98.html (last visited March 4, 2001).

[19] Plant Protection Act, Pub. L. No. 106-224, 114 Stat. 358, Title IV (2000).

[20] 7 U.S.C. §§ 150aa-jj (1994) (repealed 2000). The PPA supplements and extends the much older Plant Quarantine Act, 7 U.S.C. §§ 151-164, 166-167 (1994) (repealed 2000).

[21] Plant Protection Act, Pub. L. No. 106-224, §§ 411, 412, 114 Stat. 858, 440-43 (2000).

[22] *See* Introduction of Organisms and Products Altered or Produced Through Genetic Engineering Which Are Plant Pests or Which There Is Reason to Believe Are Plant Pests, 7 C.F.R. § 340.4 (2000).

[23] *Id.* § 340.1.

[24] *Id.* § 340.4.

permit for a product it has "reason to believe" is a plant pest.[25]

An application for the environmental introduction of a regulated article must be submitted to APHIS at least 120 days in advance of the proposed activity and must contain detailed information on such items as molecular biology, purpose and location of the proposed activity, safeguards to prevent escape and dissemination of plant pests, and differences between the modified organism and its unmodified parent.[26] Permit conditions will govern the actual release of the regulated article, including procedures for labeling and disposal, monitoring reports, and remedial measures to prevent the spread of plant pests.[27] If the applicant intends to import a regulated article or move the article in interstate commerce without conducting a field test or other activity that would result in an environmental introduction, the rules provide for a "limited permit" to be obtained under simplified procedures.[28]

APHIS has issued some 932 permits for genetically engineered organisms since the program began in 1987, primarily for small-scale field tests involving crop plants.[29] Based on its experience with the permit program, APHIS has provided a number of exemptions for articles which do not pose a plant pest risk. One of the more significant exemptions authorizes the introduction of certain regulated articles without a permit, provided that APHIS is notified in advance.[30] In order to qualify for the notification process, the regulated article must meet six eligibility criteria (e.g., introduced genetic material must not cause the introduction of an infectious entity) and six performance standards (e.g., field trials must be conducted so that regulated articles will not persist in the environment).[31]

Under the notification process, APHIS must either acknowledge that the designated introduction activity (i.e., import, interstate movement, or environmental release) is appropriate under notification or deny permission for introduction under notification.[32] To date, APHIS has acknowledged some 5,865 notifications for field

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[25] *Id.* § 340.1.

[26] *Id.* § 340.4(b).

[27] *See id.* § 340.4(f).

[28] *See id.* § 340.4(c).

[29] *See* USDA/APHIS web site, *at* http://www.nbiap.vt.edu/cfdocs/ISBtables.cfm (updated Jan. 23, 2000). During that same period, a total of 124 permit applications were withdrawn. *See id.*

[30] 7 C.F.R. § 340.3(a).

[31] *Id.* § 340.3(b).

[32] *See id.* § 340.3(e).

tests.[33] Another 353 have been denied, withdrawn, or otherwise voided.[34]

Another important exemption allows researchers to petition APHIS for a determination that an article should not be regulated as a plant pest. The rules contain detailed requirements for the data and information to be included in a petition for determination of "nonregulated status."[35] APHIS will publish a notice in the *Federal Register* and provide for a 60-day public comment period for each petition that meets the rules' eligibility criteria.[36] To date, APHIS has approved 52 out of 76 petitions submitted for nonregulated status; 24 others have been withdrawn or found to be incomplete or void, and three are now pending.[37]

Prior to issuing a permit for the introduction of a regulated article into the environment or making a determination of nonregulated status, APHIS must follow the requirements of the National Environmental Policy Act ("NEPA")[38] and prepare a publicly available environmental assessment, and where necessary, an environmental impact statement.[39] Before acknowledging the appropriateness of a notification or issuing a permit for an environmental release, APHIS must also coordinate with the state where the release is planned, including submitting a copy of the application or notification to the state department of agriculture for review.[40]

B. Regulation of Food

The Federal Food, Drug and Cosmetic Act ("FFDCA")[41] provides the FDA with broad regulatory authority over food and food ingredients. No particular statutory provision or regulation, however, deals expressly with food produced by biotechnology. The FDA's formal position concerning such foods, as expressed in the Coordinated Framework, is that the statute provides ample tools for the agency to apply to meet the challenges presented by novel foods and biotechnology.[42] This position was confirmed in 1992 with the

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[33] *See* USDA/APHIS web site, *supra* note 29.
[34] *See id.*
[35] *See* 7 C.F.R. § 340.6.
[36] *Id.* § 340.6(d)(2).
[37] *See* USDA/APHIS web site, *supra* note 29.
[38] 42 U.S.C. §§ 4321-4370 (1994).
[39] 7 C.F.R. § 372.5(b)(4).
[40] *Id.* §§ 340.3(e), 340.4(b).
[41] 21 U.S.C. §§ 301-395 (1994).
[42] *See* Statement of Policy for Regulating Biotechnology Products, 51 Fed. Reg. 23,309

publication of a comprehensive policy statement for foods derived from new plant varieties.[43]

Under the FDA's 1992 policy, biotechnology foods are not considered inherently dangerous and except in rare cases, should not require extraordinary pre-market testing and regulation.[44] The policy holds that biotechnology foods should be regulated just like ordinary foods unless they contain ingredients or demonstrate attributes that are not usual for the product.[45] According to the FDA, most food-related issues concerning products of biotechnology will involve the application of either section 402(a)(1)[46] or section 409[47] of the FFDCA.[48]

Section 402(a)(1) establishes a safety standard that may be triggered depending upon the circumstances presented by a given food or food constituent and provides the FDA with the authority to require, when necessary, pre-market approval of new food, foods developed by new techniques, or food ingredients.[49] This section is the FDA's primary enforcement tool for regulating the safety of whole foods, including foods derived from biotechnology plants. Any person who introduces food into interstate commerce is responsible for ensuring that the food does not run afoul of the provisions of section 402(a)(1).[50] The FDA has enforcement powers under the FFDCA authorizing it to seize adulterated food, enjoin its distribution, and prosecute those individuals responsible for its distribution.[51]

Under the FDA's 1992 policy, section 402(a)(1) applies to any substance that occurs unexpectedly in food at a level that may be

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(June 26, 1986).

[43] *See* Statement of Policy: Foods Derived from New Plant Varieties, 57 Fed. Reg. 22,984 (May 29, 1992). The FDA's current policy on the labeling of foods derived from new plant varieties is discussed in the same 1992 notice, 57 Fed. Reg. at 22,991, and in a separate notice, Food Labeling: Foods Derived from New Plant Varieties, 58 Fed. Reg. 25,837 (Apr. 28, 1993). Draft labeling guidance was issued in 2001. *See* Draft Guidance for Industry: Voluntary Labeling Indicating Whether Foods Have or Have Not Been Developed Using Bioengineering; Availability, 66 Fed. Reg. 4839 (Jan 18, 2001).

[44] *See* Statement of Policy: Foods Derived from New Plant Varieties, 57 Fed. Reg. at 22,985.

[45] *See* Statement of Policy: Foods Derived from New Plant Varieties, 57 Fed. Reg. at 22,985, 22,991-22,992.

[46] 21 U.S.C. § 342(a)(1) (1994).

[47] 21 U.S.C. § 348 (1994).

[48] *See* Statement of Policy: Foods Derived from New Plant Varieties, 57 Fed. Reg. at 22,985.

[49] *See id.* at 22,988.

[50] *Id.*

[51] 21 U.S.C. §§ 332-334 (1994).

"injurious to health."[52] This includes a naturally occurring toxicant whose level is unintentionally increased through genetic modification, as well as an unexpected toxicant that appears in the food for the first time.[53] The policy provides guidance to the food industry and plant breeders in the form of flow charts and other helpful instructions regarding prudent, scientific approaches to evaluating the safety of foods derived from new plant varieties, including the safety of the added substances that are subject to section 402(a)(1).[54]

Section 409 of the FFDCA authorizes the FDA to regulate "food additives," a term defined broadly to include "any substance the intended use of which results or may reasonably be expected to result, directly or indirectly, in its becoming a component... of any food . . ." and which is not generally recognized as safe for such use.[55] A food additive must be approved by the FDA prior to its being used in food, with the exception of a substance that is "generally recognized as safe" or "GRAS" by the scientific community.[56] The mechanism for securing agency approval is the submission of a food additive petition, which must contain data and information that shows that the additive will be safe for its intended use.[57] The petition is subject to public notice and comment.[58]

The 1992 policy makes it clear that the FDA will use section 409 to require food additive petitions in any case where safety questions exist sufficient to warrant formal pre-market review to ensure public health protection.[59] It also acknowledges that, in some cases, whole foods derived from new plant varieties might fall within the scope of section 409.[60] The FDA has rarely had occasion to review the safety of foods derived from traditionally-bred plants because these foods have been widely recognized and accepted as safe. Under the 1992 policy, genetic material transferred to plants through modern biotechnology is presumed to be GRAS.[61] The safety of substances

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[52] Statement of Policy: Foods Derived from New Plant Varieties, 57 Fed. Reg. at 22,990.

[53] *See id.*

[54] *See id.* at 22,991-22,992.

[55] 21 U.S.C. § 321(s) (1994).

[56] *See generally*, 21 U.S.C. §§ 342(a), 348 (1994).

[57] *Id.* § 348(b). The terms "safe" and "safety" have traditionally been defined by the FDA to provide for a "reasonable certainty" of no harm. 21 C.F.R. 170.3(i).

[58] *See id.*

[59] *See* Statement of Policy: Foods Derived from New Plant Varieties, 57 Fed. Reg. at 22,985.

[60] *See id.* at 22,990.

[61] *See id.*

found in food as a result of the presence of the transferred genetic material, referred to as "expression products," may not be as clear. Typical expression products would include carbohydrates, fats and oils. If the intended expression product differs significantly in structure, function, or composition from substances found ordinarily in food, or if the new substance has no history of safe use in food, such substance may not be GRAS and may require food additive regulation.[62] Once again, the 1992 policy provides useful guidance for evaluating the safety of food, including criteria and analytical steps for determining whether a product is a candidate for food additive regulation and whether FDA consultation is appropriate.[63] Ultimately, the food producer is held responsible for assuring the safety of its products by the FDA.

The 1992 policy encouraged developers of biotechnology foods to consult with the FDA prior to marketing their products, although these consultations were not required.[64] As a practical matter, companies developing new biotechnology food products have routinely consulted with FDA scientists as an integral part of their product stewardship programs. Through calendar year 2000, the FDA has conducted 49 final consultations under its 1992 policy,[65] the first involving the FLAVR SAVR™ tomato discussed earlier. A letter from the FDA acknowledging completion of the consultation process is evidence of a final consultation.[66] The letter provides assurance to potential customers that the product has been reviewed by federal food safety officials and also demonstrates that the developer has met the prevailing "standard of care" for such products.[67]

Following a series of public meetings, the FDA recently proposed to move from voluntary to mandatory review of biotechnology foods.[68] The proposed rule would require companies to provide notice of the intent to market a biotechnology food in the U.S. at

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[62] *See id.* at 22,985.

[63] *See id.* at 22,991-92.

[64] *Id.* at 22,989.

[65] *See* United States Department of Health and Human Services, United States Food and Drug Administration Center for Food Safety and Applied Nutrition, Foods Derived from New Plant Varieties Derived through Recombinant DNA Technology (Nov. 2000), *at* http://vm.cfsan.fda.gov/~lrd/biocon.html.

[66] *See* United States Food and Drug Administration, Center for Food Safety and Applied Nutrition, Guidance on Consultation Procedures: Foods Derived From New Plant Varieties (Oct. 1997), *at* http://www.cfsan.fda.gov/~lrd/consulpr.html.

[67] *See id.*

[68] *See* Premarket Notice Concerning Bioengineered Foods, 66 Fed. Reg. 4706 (proposed Jan. 18, 2001) (to be codified at 21 C.F.R. pts. 192, 592).

least 120 days prior to commercial distribution through the submission of a Pre-market Biotechnology Notice ("PBN").[69] The PBN would include data and information about the food and a narrative discussing the data and information.[70] The applicant must also agree to provide additional relevant data and information upon the Agency's request.[71] The public would have ready access to the PBN and the Agency's response to it.[72] The FDA would recommend that prospective applicants, prior to submitting a PBN, continue to make use of the consultation process to identify and discuss relevant safety, nutritional, or other regulatory issues regarding a biotechnology food.

C. Regulation of Pesticides

The Federal Insecticide, Fungicide, and Rodenticide Act ("FIFRA") is a licensing statute under which the EPA regulates the sale, distribution, and use of pesticides.[73] Intent is the single most important factor in deciding whether a substance is a "pesticide" for purposes of FIFRA.[74] For those substances that meet the statutory definition, their sale or distribution is prohibited in the absence of EPA approval.[75] The term "pesticide" is defined broadly to include, among other things, any substance intended to prevent, destroy, or repel undesirable insects, weeds, rodents, bacteria, or other living things that the EPA declares to be a pest.[76]

In order to be approved or "registered" under FIFRA, a pesticide must not cause "unreasonable adverse effects on the environment," which is defined to include ecological concerns as well as risks to human health.[77] Traditionally, this required the EPA to balance the potential adverse effects associated with the use of often inherently toxic compounds against the benefits of those compounds to the environment and to society in terms of factors such as an abundant, wholesome, and economical food supply.[78]

Any substance that is a pesticide under FIFRA is automatically

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[69] *Id.* at 4712.
[70] *See id.* at 4720.
[71] *Id.* at 4718.
[72] *Id.* at 4723.
[73] *See* 7 U.S.C. §§ 136, 136a-y. (1994).
[74] *Id.* § 136(u).
[75] *Id.* § 136j.
[76] *Id.* §§ 136(t) and (u).
[77] *Id.* § 136(bb).
[78] *See id.* (preceding the enactment of the Food Quality Protection Act of 1996, 110 Stat. 1489 (1996)).

subject to regulation under section 408 of the FFDCA, if used in the production of a food or feed crop.[79] Since 1996, the FFDCA has required the EPA to apply a safety-only standard when examining the potential dietary risks associated with residues of pesticides that may be found in food.[80] Section 408 of the FFDCA authorizes the EPA to issue regulations which permit residues of those pesticides in the food supply.[81] Maximum permissible residue levels for pesticides are referred to as "tolerances" and are set by rule for raw agricultural commodities, processed food, and animal feed under the same "reasonable certainty of no harm" standard that the FDA applies to food additives under section 409 of the FFDCA.[82] When residues are not anticipated or will not present any health or safety issues, an exemption from tolerance requirements can be granted by the EPA.[83] As with unapproved food additives, in the absence of a duly promulgated tolerance or exemption, or if the residue level detected in the food exceeds the tolerance, the food is deemed to be adulterated and subject to enforcement action under section 402 of the FFDCA.[84]

Modern genetic techniques permit the development of plants that produce their own pesticides or are otherwise resistant to insects, viruses and other plant pests. This capability is an extension of traditional plant breeding techniques that attempt to select the heartiest and most disease-resistant strains for use in producing hybrid seeds and plants. Following a lengthy review of regulatory options, in 1994 the EPA formally announced its intention to regulate the pesticidal substances in these plants, but not the plants themselves.[85] In effect, the Agency proposed an approach similar to that applied to "treated articles" such as insect protected lumber and mildew resistant paints.[86] As long as the pesticidal substance is registered for that use, the treated article itself is not subject to regulation by the EPA under FIFRA.[87] Residues of pesticidal

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[79] *See* 21 U.S.C. § 321(q) (1994).

[80] *See* 7 U.S.C. § 136(bb)(2); 21 U.S.C. § 346a(b)(2) (1994), as amended by the Food Quality Protection Act of 1996 (FQPA), 110 Stat. 1489 (1996).

[81] 21 U.S.C. § 346a(b).

[82] *See id.* § 346(a)(b)(2)(A)(ii); 21 C.F.R. 170.3(i).

[83] *Id.* § 346a(c).

[84] *Id.* § 342(a). Although the EPA is responsible for setting pesticide tolerances, food is subject to inspection and enforcement action by the FDA.

[85] *See* Plant-Pesticides Subject to the Federal Insecticide, Fungicide, and Rodenticide Act and the Federal Food, Drug, and Cosmetic Act, 59 Fed. Reg. 60,496 (Nov. 23, 1994).

[86] *See* Pesticide Registration and Classification Procedures, 40 C.F.R. § 152.25(a) (2000).

[87] *See id.*

substances anticipated in food or feed, however, would be subject to regulation under the FFDCA in the same manner as any other pesticide.

The EPA's 1994 proposals for "plant-pesticides" included a policy statement, regulations and a number of specific exemptions from the tolerance requirements that would ordinarily apply under the FFDCA.[88] The EPA recently moved to finalize a number of these proposals for regulating what the Agency now refers to as "plant-incorporated protectants."[89] As a practical matter, the Agency has been implementing the essential elements of the 1994 proposal in registration and tolerance decisions made since 1995.[90]

The EPA regulations typically proceed in two or three distinct stages, depending on the product involved. First, researchers interested in conducting large-scale field tests apply for an experimental use permit under section 5 of FIFRA.[91] Generally at this point small-scale field tests have already been conducted pursuant to a permit or notification under the USDA's plant pest program.[92] If granted, a FIFRA experimental use permit allows research to proceed, subject to monitoring requirements and under carefully controlled conditions that address such factors as the size and location of test plots, duration of plantings, and the use of cultivated crops, which generally are prohibited from entering the

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[88] *See* Plant-Pesticides, 62 Fed. Reg. 27,132 (proposed May 16, 1997) (to be codified at 40 C.F.R. pt. 180); Plant-Pesticides Nucleic Acids, 62 Fed. Reg. 27,142 (proposed May 16, 1997) (to be codified at 40 C.F.R. pt. 180); Plant-Pesticides Viral Coat Proteins, 62 Fed. Reg. 27, 149 (proposed May 16, 1997) (to be codified at 40 C.F.R. pt. 180); 59 Fed. Reg. 60,496 (1994); Plant-Pesticides Subject to the Federal Insecticide, Fungicide, and Rodenticide Act, 59 Fed. Reg. 60,519 (proposed Nov. 23, 1994) (to be codified at 40 C.F.R. pt. 152, 174); Plant-Pesticides Exemption from the Requirement of a Tolerance Under the Federal Food, Drug, and Cosmetic Act, 59 Fed. Reg. 60,535 (proposed Nov. 23, 1994) (to be codified at 40 C.F.R. pt. 180); Plant-Pesticides Exemption from the Requirement of a Tolerance Under the Federal Food Drug and Cosmetic Act for Nucleic Acids Produced in Plants, 59 Fed. Reg. 60,542 (proposed Nov. 23, 1994) (to be codified at 40 C.F.R. pt.180); Plant-Pesticides Exemption from the Requirement of a Tolerance Under the Federal Food, Drug, and Cosmetic Act for Viral Coat Proteins Produced in Plants, 59 Fed. Reg. 60,545 (proposed Nov. 23, 1994) (to be codified at 40 C.F.R. pt. 180).

[89] *See* Environmental Protection Agency, Final Rule, Regulations Under the Federal Insecticide, Fungicide, and Rodenticide Act for Plant-Incorporated Protectants (Formerly Plant-Pesticides), 66 Fed. Reg. 37772 (July 19, 2001).

[90] *See* NATIONAL RESEARCH COUNCIL, GENETICALLY MODIFIED PEST-PROTECTED PLANTS: SCIENCE AND REGULATION 30-32 (2000); U.S. EPA Fact Sheets for various plant-pesticides, *at* http://www.epa.gov/oppbppd1/biopesticides.factsheets (last visited March 4, 2001).

[91] *See* 7 U.S.C. § 136c(a) (1994). *See also* 40 C.F.R. § 172.3 (2000).

[92] *See* 7 C.F.R. § 340.4(d) (2000). *See also* Plant Protection Act, Pub. L. No. 106-224, 114 Stat. 358, Title IV (2000).

food supply.[93] The next stage, which applies to some but not all products, involves an application to the EPA for a registration that is limited to the production of propagative plant products such as seeds, tubers, corms, and cuttings.[94] The production of these plant reproductive materials is an integral step in the development of commercial plant varieties. The final stage involves submission to the EPA of an application for full commercialization of the plant-incorporated protectant.[95] Assuming the plant will be used for food or feed, the applicant must also petition for establishment of a tolerance or an exemption from tolerance requirements.[96]

D. Coordinated Review and Product Stewardship: A Case History of B.t. *Crops*

The EPA granted the first full registration for a plant-incorporated protectant on May 5, 1995.[97] The product was the NewLeaf™ potato, which contains genetic material that produces an insecticide within the plant itself.[98] The product was developed by transferring the genetic material needed to produce an insecticidal protein from a naturally occurring soil microorganism, *Bacillus thuringiensis* or "*B.t.*," to the potato.[99] After the genetic material is introduced, the protein is produced in minute quantities throughout the plant.[100] Conventional *B.t.* products have been registered for use as pesticides and sprayed on a variety of crops for decades, but timing the application of those sprays for maximum effect can pose problems for the grower.[101]

B.t. proteins are highly desirable pesticides because they

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93 40 C.F.R. §§ 172.3, 172.5, 172.8.

94 *See, e.g.*, Notice of Limited Plant Propagation Registration for a Plant-Pesticide, 60 Fed. Reg. 4910 (Jan. 25, 1995).

95 *See* 7 U.S.C. § 136a(c).

96 *See* 21 U.S.C. § 346a(a)(1), (d)(1) (1994).

97 U.S. EPA, Press Advisory, *supra* note 8. *See also* Notice of Limited Plant Propagation Registration for a Plant-Pesticide, 60 Fed. Reg. at 4910. The product was developed by the Monsanto Company.

98 U.S. EPA, Press Advisory, *supra* note 8. *See also* Notice of Limited Plant Propagation Registration for a Plant-Pesticide, 60 Fed. Reg. at 4910; U.S. EPA, *BACILLUS THURINGIENSIS* CRYIII(A) DELTA ENDOTOXIN AND THE GENETIC MATERIAL NECESSARY FOR ITS PRODUCTION IN POTATO (006432) (issued Apr. 2000), *at* http://www.epa.gov/oppbppd1/biopesticides/factsheets/fs006432t.htm [hereinafter, U.S. EPA, *B.t.* Fact Sheet].

99 U.S. EPA, Press Advisory, *supra* note 8.

100 *See id.*; Plant Pesticide Bacillus Thuringiensis CryIIIA Delta-Endotoxin and the Genetic Material Necessary for its Production Tolerance Exemption, 60 Fed. Reg. 21,725, 21,726 (May 3, 1995) (to be codified at 40 C.F.R. pt. 180).

101 *See* NATURAL RESEARCH COUNCIL, *supra* note 89, at 53.

specifically target insect pests such as the Colorado potato beetle.[102] In registering the protein for this use, the EPA found that it was nontoxic to mammals, birds, and most other insects, and would reduce the need for conventional pesticides.[103] The agency has since registered several other *B.t.* proteins for use in crop plants, including field corn, sweet corn, and cotton.[104] Technology companies have estimated that the combined cost to develop the products, conduct the appropriate scientific studies, and obtain the necessary clearances for the current *B.t.* crops exceeded $3 billion.[105]

The regulatory chronology of the NewLeaf™ potato illustrates how the developer of a single genetically engineered plant can be subject to four different regulatory programs administered by three different federal agencies. The review process for this one product spanned five years, from 1991-1995. The potato was initially field tested in small-scale plots under a permit granted by the USDA, followed by testing on a larger scale under an experimental use permit from the EPA.[106] Subsequently, the USDA reviewed data submitted by the developer and determined that the modified potato was not a plant pest and, therefore, was not considered a regulated article under the plant pest regulations.[107] The potato's developer then completed the consultation process with the FDA, having submitted information confirming that, other than the presence of the *B.t.* protein, the NewLeaf™ potato was not significantly different from any other Russet Burbank potato.[108] These actions cleared the

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[102] U.S. EPA, *B.t.* Fact Sheet, *supra* note 98.

[103] U.S. EPA, Press Advisory, *supra* note 7; Plant Pesticide Bacillus Thuringiensis CryIIIA Delta-Endotoxin and the Genetic Material Necessary for its Production Tolerance Exemption, 60 Fed. Reg. at 21,727; U.S. EPA, *B.t.* Fact Sheet, *supra* note 98.

[104] *See* NATURAL RESEARCH COUNCIL, *supra* note 90, at 33-35; EPA Fact Sheets for various *B.t.* plant pesticides, *at* http://www.epa.gov/oppbppd/biopesticides/factsheets (last visited March 4, 2001).

[105] *See* Memorandum of Points and Authorities in Support of the Motion to Intervene of American Crop Protection Association, Biotechnology Industry Organization, *B.t.* Registrants Task Force, and National Cotton Council at 5, Greenpeace International v. Browner, (No. 99-389 (LFO)).

[106] *See* APHIS Field Test Release Test Permit #91-050-02R, *at* http://www.nbiap.vt.edu; Receipt of Petition for Determination of Nonregulated Status for Genetically Engineered Potato Lines, 59 Fed. Reg. 61,866 (Dec. 2, 1994); Issuance of an Experimental Use Permit for Four Transgenic Plant Pesticides, 58 Fed. Reg. 33,815 (June 21, 1993).

[107] Availability of Determination of Nonregulated Status for Genetically Engineered Potato Lines, 60 Fed. Reg. 13,108, 13,109 (March 10, 1995).

[108] Under the FDA's 1992 Policy, the determination that a biotechnology food is not significantly different from a comparable food that results from conventional breeding techniques is needed in order to avoid possible regulation as a food additive. 57 Fed. Reg. 22990.

way for the review of health, safety, and environmental data and the eventual approval of applications for commercialization by the EPA. In addition to obtaining a registration of the *B.t.* protein as expressed in the potato under FIFRA, the applicant was also required to petition the EPA for a tolerance exemption for potential trace levels of the *B.t.* protein under the FFDCA.[109]

Although the EPA has approved the use of *B.t.* proteins in several crops, the registration actions have been conditioned on compliance with a host of requirements that imposed unique burdens on the companies and growers involved. In some cases, the EPA persuaded registrants to accept additional conditions years after the original product approval action.[110] Registrations for corn and cotton are subject to an ongoing reassessment scheduled for completion in 2001 when the underlying registrations will terminate if not extended by the agency.[111]

The EPA has methodically addressed each of the environmental concerns that have been raised with respect to the *B.t.* crops and, at this writing, has not found any basis to withdraw its approvals.[112] One of the principal concerns still under study by government, academia, and industry is the possibility that placing the *B.t.* protein in the plant where it is expressed at all times might accelerate the development of resistance to the protein in the pest population. To date the only documented case of resistance to the protein resulted from the use of the conventional *B.t.* sprays.[113] Nevertheless, the EPA has consulted with the USDA and panels of outside scientific advisors on the resistance issue and has mandated additional risk mitigation measures for *B.t.* crops to minimize the likelihood of insect resistance developing to *B.t.* products, conventional or

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[109] *See* Plant Pesticide Bacillus Thuringiensis CryIIIA Delta-Endotoxin and the Genetic Material Necessary for its Production Tolerance Exemption, 60 Fed. Reg. 21,725 (May 3, 1995) (to be codified at 40 C.F.R. pt. 180).

[110] *See, e.g.*, Response of the Environmental Protection Agency to Petition for Rulemaking and Collateral Relief Concerning the Registration of Certain Genetically Engineered Plants Expressing *Bacillus Thuringiensis* Endotoxins, Submitted by Petitioners Greenpeace International, et al. (Apr. 19, 2000) at 26, *at* http://www.epa.gov/oppbppd1/biopesticides/news/news-greenpeace.htm (discussing additional restrictions for *B.t.* field corn after its registration in 1997) [hereinafter, Response of the EPA]; U.S. EPA, *B.t.* Fact Sheet, *supra* note 98.

[111] *See* Time Extension for *B.t.* Corn and *B.t.* Cotton Plant-Pesticides Expiring Registrations, Registration and Process and Public Participation Opportunity, 65 Fed. Reg. 48,701 (proposed Aug. 9, 2000).

[112] *See id.*; Response of the EPA, *supra* note 110.

[113] *See* Response of the EPA, *supra* note 110, at 30, 34 (discussing the diamondback moth's resistance to *B.t.* as due to excessive and intensive use of *B.t.* foliar sprays).

genetically engineered.[114] These measures include post-market monitoring for resistance and the evaluation of new monitoring methods.[115] The majority of these new requirements have been applied to *B.t.* corn and cotton products and are included in insect resistance management ("IRM") plans that must be approved by the agency and implemented under the direction of the registrants.[116] In an excellent example of cooperative effort, the EPA has worked with corn growers and the producers of *B.t.* corn products through the Agricultural Biotechnology Stewardship Technical Committee, an industry-funded scientific group, to put strengthened IRM plans in place nationwide.[117]

III. THE ROLE OF PRODUCT STEWARDSHIP

Whether the product is a toaster or a sophisticated piece of magnetic resonance imaging equipment, proactive stewardship of a company's products and technologies is all about doing the right thing. The concept of product stewardship is not necessarily a new one, although it clearly goes well beyond the traditional commercial policy of "standing behind" one's product.

In its broadest terms, product stewardship can be thought of as the legal, ethical, and moral obligation to assess products and technologies to ensure that they are safe as well as socially and environmentally responsible. Stewardship includes the assessment, based on sound scientific principles, of the potential impact of a particular product or technology on human health and the environment, as well as those actions and principles necessary to protect the integrity and viability of a particular product or technology.

Not all stewardship efforts are necessarily confined to individual companies, nor should they be. Many activities are more appropriately industry-wide responsibilities, which are necessary or appropriate for the protection of products or technologies as a class. A good example of a pooling of resources to address scientific issues associated with the regulation of crop biotechnology can be found in

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[114] *Id.* at 17-27.

[115] *Id.*

[116] *Id.*

[117] *See* Time Extension for *B.t.* Corn and *B.t.* Cotton Plant-Pesticides Expiring Registrations, Registration and Process and Public Participation Opportunity, 65 Fed. Reg. at 48,703. The members of the Agricultural Biotechnology Stewardship Technical Committee are Aventis CropScience USA LP, Dow AgroSciences LLC, E.I. du Pont de Nemours & Company, Monsanto Company and Syngenta Seeds Inc.

the IRM stewardship efforts of *B.t.* corn producers discussed in the preceding section.

Many industries operate on the basis of voluntary consensus standards, including a broad array of standards developed by the American Society of Testing and Materials and other internationally recognized standard-setting organizations. Government agencies routinely recognize such standards and federal law requires agencies to use technical standards that are developed or adopted by voluntary consensus standards bodies unless it would be "inconsistent with applicable law or otherwise impractical."[118] The discussion that follows focuses primarily on the adoption of stewardship programs at the individual company level but can be used as a model for cooperative efforts among technology companies as well.

A. A Stewardship Organizational Model

The success of a corporate stewardship program depends on the existence of a Product Stewardship Council or other similar body that is fully integrated into the leadership structure of the business unit. This requires the commitment and active participation of management. The role of the Product Stewardship Council as ombudsman for good stewardship can only be effective with widespread awareness. The availability of the Council as a resource must be emphasized by management and actively promoted throughout the organization. Only then can a risk management process that is consistent with stewardship principles become the way of doing business. The discussion that follows examines the Product Stewardship Council in the context of a plant biotechnology company, although the same concepts can be applied in a variety of other settings involving the commercialization of new technologies.

There are two principal reasons for the creation of a Product Stewardship Council—structural and legal. In terms of organizational structure, the Council is designed to integrate the functional and staff team members identified to support the underlying business into an interdisciplinary team that is integral to the business. The team provides a direct, immediate, and global multidisciplinary resource on product and technology stewardship

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[118] *See* National Technology Transfer and Advancement Act of 1995, Pub. L. 104-113, § 12(d), 110 Stat. 782, (1996). The Office of Management and Budget ("OMB") has issued a guidance document on implementation of the requirements of this statute. *See* OMB Circular A-119, 61 Fed. Reg. 68,312 (Dec. 27, 1996).

issues and a forum for business, functional, and staff team alignment to address those issues. The Council should be designed to coordinate its activities with those of other product stewardship teams in other business and geographic sectors, and even in other companies.

From a legal perspective, the Product Stewardship Council must be empowered to ensure compliance with the letter and spirit of applicable regulatory requirements and to prevent potential product-related liabilities. Legal obligations in the U.S. include the submission of applications, notifications, data, and information in order to obtain the appropriate approvals and clearances from the USDA, the FDA, and the EPA under the Coordinated Framework.[119] Those obligations also extend to the post-market surveillance of agricultural biotechnology and crop derived products and to compliance with appropriate reporting requirements, such as those imposed by the EPA for plant-incorporated protectants.[120]

A properly functioning Product Stewardship Council needs a set of operating principles that have the support of company management and include all company stakeholders. Those operating principles must be sensitive to the conflicts that will inevitably arise when attempting to set the highest standards possible for good stewardship in light of the demands of the business and the new and rapidly advancing nature of science and technology with no long-standing historical precedent. Operating principles must encourage innovation and provide a resource for good stewardship solutions, finding a way through complex technical and legal issues. Finally, the operating principles need a policy orientation that allows the Council to focus on strategic issues and policies regarding the safety and stewardship of agricultural biotechnology products and technologies. A principal goal of the Council is to establish consensus on these strategic issues and policies, requiring alignment of various business, support, and functional staff plans and actions.

Examples of crop biotechnology stewardship issues include the following: risk assessment and risk management plans; biodiversity; seed quality and purity; protein safety, including potential for allergenicity; protein levels in food and feed; IRM plans for *B.t.* products and other plant-incorporated protectants; outcrossing and

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[119] *See* Coordinated Framework for Biotechnology, 51 Fed. Reg. 23302 (June 26, 1986). *See, eg.*, Statement of Policy: Foods Derived from New Plant Varieties, 57 Fed. Reg. 22,984 (May 29, 1992).

[120] *See* 40 C.F.R. § 159.195(c) (2000).

open pollination; identity preservation, product channeling, and trade. Risk management can address all of these issues and will be briefly discussed to illustrate the successful integration of sound stewardship principles.

A successful risk management process must be a fundamental part of the business culture, incorporated into each phase of product development and commercialization. Key elements of the risk management process include: identifying every potential source of harm (hazard); assessing the probability of occurrence of that harm (exposure); assessing the risk, if any, resulting from the potential combination of hazard and exposure; and the development of alternatives for the minimization and management of the assessed risks.

For products of agricultural biotechnology, the potential risks and risk management alternatives must be evaluated in the context of such factors as health, safety, environmental, and agricultural impacts; regulatory acceptance; public acceptance; market acceptance; and civil liability. Prior to commercialization of any new plant biotechnology product, the company would conduct a full, science-based risk assessment to identify and, to the extent possible, quantify every risk presented. Each risk would be reviewed in all relevant contexts, and an appropriate management plan would be established, including an effective plan to mitigate any risk that becomes a reality.

B. Crop Biotechnology Comes of Age

Much has been said and reported regarding the allegedly harmful effects of the rapid commercialization of biotechnology crops. However, the reality is far different. Since the first experimental field plots were planted in 1986, and the first commercial clearances for food crops were received in 1994 and 1995, biotechnology plants have been subject to intensive governmental, academic, and commercial oversight. Notwithstanding this intensive oversight, not a single instance of actual harm to health, safety, or the environment has ever been documented concerning a biotechnology crop currently on the market.

Perhaps the most highly visible allegation made against biotechnology crops concerned potential adverse effects of pollen from *B.t.* corn on the Monarch butterfly. It was not a surprise to scientists that Monarchs forcibly exposed to the *B.t.* protein might be harmed. One of the great benefits of *B.t.* is that, in contrast to conventional chemical insecticides, *B.t.* specifically targets

lepidopteran species and is harmless to most non-target animals, including beneficial species of insects.[121] The critical question was not whether non-target butterflies would be harmed if exposed, but whether they would ever be sufficiently exposed to be a cause for concern. Following initial studies in which Monarchs were exposed to *B.t.* pollen under laboratory conditions, the joint stewardship efforts of the *B.t.* corn producers helped fund research conducted by independent academic experts under actual field conditions.[122] The research was carried out in 1999 and 2000 under grants administered by the USDA. These studies, which have been submitted to the EPA, demonstrate that the level of exposure of Monarchs to *B.t.* corn pollen is insignificant.[123] The real enemies of the Monarch turn out to be habitat destruction in Mexico, the indiscriminate spraying of conventional pesticides, and the mowing of meadows rich in their favorite food source.[124]

Regulatory oversight and industry stewardship of crop biotechnology products, both pre-market and post-market, has occurred notwithstanding the fact that new conventionally bred varieties of food, feed, and fiber crops receive virtually no governmental oversight in the United States or any other nation. Moreover, the National Academy of Sciences ("NAS") has repeatedly held, most recently in an April 2000 report on pest-protected plants, that just because a plant is a product of biotechnology does not make it hazardous.[125] Specifically, the NAS has found: (1) no evidence that unique hazards exist either in the use of rDNA techniques or the movement of genes between unrelated organisms; (2) the risks associated with the introduction of rDNA engineered organisms are the same in kind as those associated with the introduction of unmodified organisms and organisms engineered

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121 *See* Response of the EPA, *supra* note 110, at 63-65.

122 *See* Issues Pertaining to the *B.t.* Plant-Pesticides Biopesticides Registration Action Document at IIC50-58, *available at* http://www.epa.gov/scipoly/sap [hereinafter, *B.t.* Plant-Pesticides Biopesticides Registration]. *See also* Backgrounder on Monarch Butterflies and *B.t.* Crops, *at* http://www.bio.org/food&ag/monarch.html (last visited March 2, 2001); Monarch Butterflies & *B.t.* Corn, *at* http://www.bio.org/food&ag/butterfly.htm (last visited March 2, 2001).

123 *See B.t.* Plant-Pesticides Biopesticides Registration, *supra* note 122. Backgrounder on Monarch Butterflies and *B.t.* Crops, *supra* note 122; *B.t.* Corn and Monarch Butterfly Factsheet (Apr. 28, 2000), *at* http://biotechknowledge.com/showlibsp.php3?uid=3287

124 *See* Mark Henderson, *The Threat That Never Was*, THE TIMES (London), Dec. 14, 2000. *See also*, Transcript, CBS Evening News, Dec. 22, 2000.

125 *See* NATIONAL RESEARCH COUNCIL, *supra* note 90, at 44-47 (citing and reconfirming NATIONAL ACADEMY OF SCIENCES, INTRODUCTION OF RECOMBINANT DNA-ENGINEERED ORGANISMS INTO THE ENVIRONMENT: KEY ISSUES (1987)).

by other methods; and (3) assessment of the risks of introducing rDNA-engineered organisms into the environment should be based on the nature of the organism and the environment into which it is introduced, not on the method by which it was produced.[126]

The foregoing is not meant to suggest that there are no risks associated with commercialization of biotechnology crops. Similarly, it would be foolhardy to imply that current regulatory programs and product stewardship efforts have achieved their objective and require no further improvement. On the contrary, it is the very nature of oversight of a rapidly developing technology that regulation and stewardship must be dynamic processes, always subject to reevaluation and modification based on new information and understanding. Indeed, the most recent report from the NAS contains several dozen recommendations concerning plants produced using genetic engineering as well as conventionally bred varieties,[127] and all three lead federal agencies have recently issued proposals intended to improve their oversight of biotechnology crops.[128]

Illustrating the need for proactive product stewardship and flexibility to respond to new information, one need look no further than the controversy surrounding StarLink™ corn that reached the mass media in the fall of 2000.[129] StarLink™ is one of several varieties of yellow corn protected against insect pests by a *B.t.* protein. In contrast to all other commercially approved plant-incorporated protectants, the EPA's initial approval for StarLink™ was limited to use for animal feed. This resulted from what the agency viewed as inconclusive studies on the potential for human allergic reactions to the unique StarLink™ protein.[130] In spite of regulatory restrictions and product stewardship plans designed to channel StarLink™ corn for animal feed use only, analyses of certain brands of taco shells and other finished human food products

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126 *Id.* at 44.

127 *See id.* at 177-80.

128 *See* Food and Drug Administration, Premarket Notice Concerning Bioengineered Foods, 66 Fed. Reg. 4706 (Jan. 18, 2001) (to be codified at 21 C.F.R. pts. 192, 592); Department of Agriculture, Request for Public Comment on How USDA Can Best Facilitate the Marketing of Grains, Oilseeds, Fruits, Vegetables, and Nuts in Today's Evolving Marketplace, 65 Fed. Reg. 71,272 (proposed Nov. 30, 2000) (to be codified at 7 C.F.R. chs. I, VIII); U.S. EPA, Plant-Incorporated Protectants (Formerly Plant-Pesticides), Supplemental Proposal, 66 Fed. Reg. 37855 (July 19, 2001).

129 *See generally*, U.S. EPA, Office of Pesticide Programs, Starlink Corn News Archive, *at* http://www.epa.gov/oppbppd1/biopesticides/otherdocs/starlink_news.htm (last visited Feb. 20, 2001) [hereinafter Starlink website].

130 *See id.*

revealed traces of StarLink™ genetic material, suggesting that StarLink™ corn had been commingled with varieties sold for human consumption.[131] While the matter is still under investigation, it appears that some modifications in the EPA approval process for plant-incorporated protectants and industry procedures for handling seed and harvested crops may be warranted.

The EPA announced, with industry support, that it will approve marketing of plant-incorporated protectants for the production of commodity grains only after all regulatory requirements have been met for both human and animal consumption.[132] Aventis CropScience, the producer of StarLink™, dramatically expanded its product stewardship program in an attempt to mitigate the adverse effects of the commingling of StarLink™ corn with other varieties. The StarLink™ registration previously granted by the EPA was voluntarily canceled by the company shortly after confirmation of the presence of traces of StarLink™ in the food supply.[133] Other measures taken by the company, in cooperation with the USDA, include providing compensation for losses suffered by corn growers and grain elevator owners.[134] The Biotechnology Industry Organization ("BIO"), which includes as members StarLink's™ producer as well as the producers of all other commercial *B.t.* crops, reaffirmed its commitment to safety and supported new steps to enhance the commercial introduction of seeds intended for production of commodity grain, food, and feed use.[135] Finally, various segments of the food and feed industries implemented stewardship programs to specifically address issues associated with StarLink™.[136]

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131 *See id.*

132 *See id.*

133 Notice of Receipt of Request for Cancellation of Registration of Bacillus thuringiensis (*B.t.*) subspecies tolworthi Cry9C and the Genetic Material Necessary for its Production in Corn, 66 Fed. Reg. 4825 (Jan. 18, 2001).

134 *See* Aventis CropScience Starlink Growers and Buffer Growers Claims Procedure for Losses Related to Starlink Corn, *at* http://www.us.cropscience.aventis.com/AventisUS/CropScience/stage/htm1/claimsprocedures1220.htm (updated Feb. 1, 2001); Aventis CropScience Elevators Claims Procedure for Losses Related to Starlink Corn, *at* http://www.us.cropscience.aventis.com/AventisUS/CropScience/stage/htm1/claimpolicyandformselevators1.htm (updated Jan. 12, 2001).

135 *See* Biotechnology Industry Organization, BIO Testifies at Senate Hearing on Biotech Food (Sept. 26, 2000), *at* http://www.bio.org/news/article.htm.

136 *See, e.g.,* National Grain and Feed Association web site, *at* http://www.ngfa.org/members/biotech/starlink.htm.

IV. CONCLUSION

It is essential that regulatory agencies operate on the basis of clear, consistent rules, coordinating their product reviews to the greatest extent possible given their individual statutory mandates. Building on the Coordinated Framework, agencies can issue revised regulations, policies, and guidelines as needed to meet changing product lines and new information. Rigorous, science-based safety assessments must be conducted for each new product or product category, first by the product developers and then by agency scientists. Conditions carefully tailored to address identified risks should continue to be placed on approvals where warranted, and approvals should always be subject to review based on new data and information from any credible source.

Proactive product stewardship will be critical to the relationship between the public and private sectors and, ultimately, to domestic and global public acceptance of the technology. Key stewardship goals include post-approval monitoring, customer education and training programs and the development of industry consensus standards. The expansion of existing cooperative efforts among growers, universities, government agencies, technology companies, and the food industry should be encouraged in order to promote these goals.

Few new technologies offer as much promise as the application of biotechnology to the production of food and feed crops worldwide. All stakeholders appear to agree that governmental oversight is appropriate, although it is clear that regulators and technology companies will face new challenges as the number and diversity of biotechnology crops continue to grow.