



Position Paper: Pharmaceutical and Industrial Crops

INTRODUCTION

Most of the genetically engineered (GE) crops currently on the market are food or feed crops that have been modified for agronomic purposes—to better repel pests or to be compatible with chemical pesticides. A new generation of crops is now being modified for different purposes—to produce medicines or industrial compounds such as plastics. Many of these substances are being produced in corn and other food¹ crops visually indistinguishable from their non-industrial counterparts. Contamination of food crops with drugs or industrial chemicals could occur through seed mixing and cross-pollination. The potential contamination of food crops with the hundreds, if not thousands, of drugs or industrial compounds promised by this industry poses new and serious risks to the safety of the food system. Pharmaceutical and industrial compounds also pose potentially serious risks if released into the environment.

This paper details the position of the Union of Concerned Scientists (UCS) regarding federal policy on crops genetically engineered to produce pharmaceutical and industrial compounds. After careful analysis, we have concluded that current U. S. Department of Agriculture (USDA) regulations governing such crops, although stronger than they have been in the past, are still insufficiently stringent to assure the complete protection of the food supply in the United States. Moreover, the routes of contamination in existing commodity crop production systems are so numerous that even very strong regulatory systems may not be sufficient to prevent the contamination of the food system with crops genetically engineered to produce pharmaceutical and industrial compounds. Although it may be theoretically possible to design an adequate regulatory system, we believe it would be too complex to be implemented effectively by the USDA, the federal agency with primary authority over GE pharmaceutical and industrial crops.

Because of the vital importance of commodity food crops to agriculture, the U.S. economy, and our food system, UCS believes that rather than attempting to impose ever more elaborate restrictions on the growing of food crops engineered for pharmaceutical and industrial purposes, it would be better to ban such applications altogether.

UCS is also concerned about risks to the environment from the outdoor production of both food and non-food pharmaceutical and industrial crops. We are not, however, calling for a ban on all outdoor production of such crops. At present, we believe that the regulatory system probably could be strengthened sufficiently to reduce environmental risks to acceptable levels. We believe that our approach, which combines a ban on outdoor production in food crops with a tightening of regulations on production in non-food crops, warrants support from the broadest possible spectrum of stakeholders.

The effect of the ban would be either to encourage genetic engineers interested in pharma and industrial applications to shift from food crops to non-food crops, or, even better, to further

¹ For ease of reading, in this paper we will generally use the term “food” to encompass both food and animal feed. Unless we specify otherwise, the terms “food crops,” “food supply,” and “food system” encompass both food and feed.

develop completely enclosed production systems based on GE plant or animal cells, bacteria, fungi, or algae. Enclosed systems, which pose little or no threat to the food supply and the environment, have already been used successfully to produce drugs approved by the Food and Drug Administration (FDA).

In this paper, we provide background on the current status, potential benefits and risks, and federal regulation of pharmaceutical and industrial crops (referred to as “pharma/industrial crops”); offer two recommendations for strengthening federal oversight, including a ban on the outdoor production of food crops for such purposes; explain our rationale for a ban; and briefly discuss how such a ban would be implemented. In addition, we attach a document (“Frequently Asked Questions”) providing answers to a number of questions we expect to arise regarding the impacts of such a ban and our reasons for rejecting alternative regulatory approaches.

WHAT ARE PHARMA/INDUSTRIAL CROPS?

New molecular genetics techniques allow scientists to introduce genes brought in from a potentially vast array of organisms—including bacteria, viruses, fruit flies, and humans—into crops. Such crops are referred to as genetically engineered, bioengineered, or transgenic. Scientists began using these techniques more than twenty years ago to supplement traditional breeding methods. Thus far, they have created a wide variety of crops with novel traits in the laboratory, but only a few have achieved commercial success.

Pharma/industrial crops make up a new and distinct class of GE crops that are, in general, engineered for non-food purposes.² By non-food purposes, we mean for use as drugs and other disease-treating substances; for industrial purposes such as detergent and fiber manufacture, lubricants, and biofuels; and for specialty food/dietary purposes such as for food supplements, infant formula ingredients, and medical foods typically intended only for segments of the population with special medical needs or dietary requirements.

By contrast, crops engineered for food and feed purposes are modified for quality, production, or agronomic purposes. Food purposes include increased pest resistance and compatibility with herbicides, improved quality traits like increased levels of certain amino acids, and production characteristics like delayed ripening to reduce fruit damage during transportation. Only food or feed crops—those destined to be consumed by broad populations of humans or animals—can be engineered for food or feed purposes.

As an artificial technology not limited by natural breeding boundaries, genetic engineering vastly increases the potential number of plants with novel gene combinations compared with traditional breeding. Genetic engineering exploits this potential by moving beyond agronomic traits and endowing crops with the ability to produce substances like drugs, vaccines, and plastics. The possible number and diversity of such novel compounds are enormous.

² Rather than genetically engineer the crop itself to produce a drug, Large Scale Biology (LSB) spliced genes for pharmaceutical compounds into a plant virus (tobacco mosaic virus) and then infected a crop (tobacco) with the GE virus. The virus commandeered the tobacco plants’ manufacturing processes, forcing the production of virus-encoded pharmaceutical products. (Pollack, A. 2005. Biotech company closes after running out of cash. *New York Times*, December 24, 2005.)

Because genetic engineering is a new, not-well-understood technology, its products—whatever their intended purpose—are universally subject to more stringent regulations than traditionally bred counterparts. Concerns about GE crops often relate to the novelty of the imported genes and gene products, the high levels at which the gene products may be expressed, and the inability of genetic engineers to control the location of inserted genes within the genome.

Pharmaceutical and industrial compounds are of particular concern because they are being produced in GE plants that are not intended for the food supply. Many of these are designed to produce substances, often at high levels, that are toxic or bioactive. For practical reasons, most of the crops being engineered as pharma/industrial crops are food crops such as corn, soybeans, and rice, leading to concern that these pharma/industrial crops can contaminate the food supply, if they have not already done so.

UCS uses the term “pharma crops” to refer specifically to crops producing pharmaceutical compounds, that is, medical and veterinary substances like drugs and vaccines. We use the broader term “pharma/industrial crops” to encompass all crops genetically engineered for pharmaceutical, industrial, and specialty food purposes. In most cases, pharma/industrial crop products are expected to be extracted from the crop and used for various purposes. In other situations, the whole pharma/industrial plant or parts of it will be used. In relatively rare cases, the substances engineered into plants may have multiple uses.

As will be discussed below, the USDA currently has a similar but somewhat less expansive definition of pharma and industrial crops.

Brief history of the pharma/industrial crop industry

Since 1991, the USDA has approved at least 125 and perhaps 200 or more applications to grow GE pharma/industrial crops.³ More than 15 companies, along with several universities, have been involved in pharma/industrial crop production. Corn has been the crop of choice; others include soybeans, rice, tomato, barley, safflower, peas, and tobacco. Most pharma/industrial crop production has been in the form of relatively small field trials of tenths of an acre to tens of acres, although more than 300 acres of pharma rice were expected to be planted in the 2006 growing season.

So far, the FDA has not approved any substances produced in pharma crops as pharmaceuticals, although several are reportedly in clinical trials. Chemicals from several pharma/industrial food crops, for example, avidin, lactoferrin, lysozyme, and high oleic soybean oil, have been commercialized for small-scale industrial uses (primarily for research purposes).

Most pharma/industrial crops are indistinguishable from crops grown for food purposes, and many are grown in close proximity to those intended for human and animal consumption. As UCS demonstrated in its 2004 report *A Growing Concern*,⁴ the genes in pharma/industrial corn

³ The uncertainty about the number is a result of USDA policy allowing applicants to withhold information from the public as confidential business information.

⁴ Andow, D., H. Daniell, P. Gepts, K. Lamkey, E. Nafziger, and D. Strayer. 2004. *A Growing Concern: Protecting the Food Supply in an Era of Pharmaceutical and Industrial Crops*. Cambridge, MA: Union of Concerned Scientists. Online at www.ucsusa.org/food_and_environment/genetic_engineering/pharmaceutical-and-industrial-crops-a-growing-concern.html.

or soybean crops have numerous routes—both physical and biological—by which they can contaminate crops destined for food uses.

Worries about food crop contamination, which have dogged the industry from its inception, were confirmed in fall 2002 when the USDA discovered that ProdiGene, a pharma/industrial crop company, had allowed corn plants engineered to produce a veterinary drug (vaccine for pig diarrhea) to emerge as volunteers in a Nebraska soybean field. The company harvested the pharma corn along with the soybeans, and subsequently transported the contaminated soybeans to a grain elevator where thousands of bushels of commodity soybeans were contaminated. ProdiGene was also responsible for a separate incident that same fall, in which pharma corn in Iowa was suspected of having cross-pollinated with feed corn in adjacent fields.

Pharma/industrial crops in commerce or under development

The non-food uses of engineered crops encompass a range of diverse applications, including treating diseases, manufacturing detergents, producing energy, and supplementing diets. The major categories of purposes for which pharma/industrial crops have been engineered are briefly described below.

Pharmaceutical uses

Many crops are being developed to produce drugs or biologics for the diagnosis, treatment, or prevention of diseases in humans and animals. These pharmaceutical compounds include enzymes, hormones, anticoagulants, vaccines, and monoclonal antibodies targeted at a variety of diseases, such as cystic fibrosis and non-Hodgkin's lymphoma. (See Table 1.)

Industrial uses

Industrial uses of GE crops include manufacturing goods, producing fibers and lubricating oils, extracting and processing raw materials, and phytoremediation.⁵ Industrial compounds include enzymes and other proteins for use in manufacturing paper and plastics, tanning leather, mining and recovering minerals, and conducting experimental research. Examples of industrial enzymes produced in engineered corn are trypsin for making detergents and tanning leather and laccase for manufacturing detergents and paper. (See Table 1.) For some industrial purposes like tanning leather or manufacturing detergents, the new substances produced by the engineered plant are likely to be extracted and purified before use. For other applications, such as phytoremediation, the entire engineered crop may be used.

Crops may also be genetically engineered to facilitate the conversion of plants into fuels or enhance their usefulness for generating electricity. Scientists, for example, have introduced α -amylase into corn to facilitate the conversion of plant material into ethanol.

Although field tests began in the early 1990's, only a handful of pharma/industrial crops has been commercialized. These include DuPont's high oleic soybean variety, which has commercial industrial uses as a lubricant,⁶ and Calgene's high laurate canola, which had industrial oil applications. Both were originally developed and approved for food uses. Avidin, β -

⁵ Phytoremediation is the use of plants to remove or reduce contaminants in soils and sediments.

⁶ Cahoon, E.B. 2003. Genetic enhancement of soybean oil for industrial uses: prospects and challenges. *AgBioForum* 6:11-13; Glancey, J.L. et al. 1999. Development of a high oleic soybean oil-based hydraulic fluid. *Feedstocks* 4(2):1-2.

glucuronidase, aprotinin, trypsin, lactoferrin, and lysozyme—proteins produced in engineered food crops—have been commercialized for experimental research purposes.

Specialty food uses

Crops may be engineered to produce substances intended for a variety of specialty food uses. Examples include food additives, food colors, infant-formula ingredients, nutraceuticals and functional foods,⁷ medical foods,⁸ and dietary supplements.⁹

Multi-use substances

As mentioned above, some substances engineered into pharma/industrial crops may have two or more uses. For example, the enzyme trypsin, discussed earlier as an industrial chemical, also has pharmaceutical applications. The oils in high oleic soybeans have both food and industrial uses.

WHAT ARE THE POTENTIAL BENEFITS OF PHARMA/INDUSTRIAL CROPS?

The benefits of crops with such a vast array of potential uses are difficult to assess, particularly at this early stage in the industry's history. In general, if the crops are commercially successful, benefits can be assumed to accrue to companies that sell the products and to consumers that buy them. In addition, pharma/industrial crops might provide societal benefits beyond those obtained by companies and their customers. For example, they might help solve a national problem such as reducing dependence on fossil fuels or synthesizing drugs that cannot be produced by existing methods.

While acknowledging that pharma/industrial crops may generate commercial benefits, it is important to note the tendency for promoters of new technologies to inflate the benefits expected from their products. Pharma crops offer a good example of this tendency.

For example, a 2004 study from Virginia Polytechnic Institute and State University suggests that consumers as well as pharmaceutical companies could benefit from engineered drug-producing crops. The reasons cited were the speed with which new products can be brought to market, an increased variety of pharmaceutical products, and substantial savings from not investing in new buildings and equipment.¹⁰

⁷ The terms nutraceutical and functional food have been applied to foods or food components (for example, isolated vitamins, dietary supplements, herbal products) that may have health benefits. For more information, see www.extension.iastate.edu/Publications/PM1846.pdf.

⁸ The Orphan Drug Act defines a medical food as “a food which is formulated to be consumed or administered internally under the supervision of a physician and which is intended for the specific dietary management of a disease or condition for which distinctive nutritional requirements, based on recognized scientific principles, are established by medical evaluation.” For more information, see www.fda.gov/orphan/oda.htm.

⁹ According to the Dietary Supplement Health and Education Act (DSHEA), a dietary supplement is “a product taken by mouth that contains a ‘dietary ingredient’ intended to supplement the diet. The ‘dietary ingredients’ in these products may include: vitamins, minerals, herbs or other botanicals, amino acids, and substances such as enzymes, organ tissues, glandulars, and metabolites.... Whatever their form may be, DSHEA places dietary supplements in a special category under the general umbrella of ‘foods,’ not drugs, and requires that every supplement be labeled a dietary supplement.” For more information, see www.cfsan.fda.gov/~dms/ds-overview.html#what.

¹⁰ Kostandini, G. 2004. Potential impacts of pharmaceutical uses of transgenic tobacco: the case of human serum albumin and Gaucher's disease treatment. Masters Thesis, Virginia Polytechnic Institute and State University. Online at <http://scholar.lib.vt.edu/theses/available/etd-09152004-154300>.

So far, however, no pharma crop products have reached the pharmaceutical market, casting doubt on the claim of rapid market access. In addition, the potential differences in a pharma protein from crop to crop, as a result of uncontrollable outdoor growing conditions, may actually increase production costs.

Even if savings on buildings and equipment lowered production costs, there is no assurance they would result in lower drug prices for consumers. First, these expenses are only a minor factor in setting drug prices. Second, companies have many incentives not to pass the savings from reduced production costs along to consumers in the form of cheaper medicines. Moreover, some studies show that recent advances in closed-system technology have practically eliminated the cost difference between drug production in crops and cell culture systems.¹¹

There are also uncertainties about the recipients of economic benefits. Proponents sometimes contend that pharma crops will generate substantial economic benefits for farmers and rural America. A 2005 UCS report, *The Economics of Pharmaceutical Crops: Potential Benefits and Risks for Farmers and Rural Communities*,¹² examines and refutes these claims, pointing out that farmers are unlikely to benefit because of the small acreages involved and because growers' competition with each other to produce pharma crops will drive their profits down.

As with pharma crops, it is important to examine the claims for benefits of industrial crops critically, and look carefully at how the affected industries operate, alternatives to the new products, and the distribution of the benefits among sectors and groups.

In sum, pharma/industrial crops are likely to offer commercial benefits, but it is wise to take the often-grandiose claims of benefits with a grain of salt.

WHAT ARE THE RISKS OF PHARMA/INDUSTRIAL CROPS?

Risks, like benefits, are difficult to assess at this early stage of the technology. But it is possible to make some general statements about three broad kinds of risks posed by pharma/industrial crops: to human and animal health, to the environment, and to the economic interests of various stakeholders.¹³

Human and animal health risks

Pharma/industrial crops may be a health risk to humans and animals because compounds they produce could end up in the food or feed supply and harm people and animals that consume them.

¹¹ Agres, T. 2006. LSBC closing signals pharming trouble. *The Scientist*, January 17. Online at www.the-scientist.com/news/display/22969.

¹² Wisner, R. 2005. *The Economics of Pharmaceutical Crops: Potential Benefits and Risks for Farmers and Rural Communities*. Cambridge, MA: Union of Concerned Scientists. Online at www.ucsusa.org/food_and_environment/genetic_engineering/economics-of-pharmaceutical-crops.html.

¹³ For additional information on risks, see Freese, B. 2002. *Manufacturing Drugs and Chemicals in Crops: Biopharming Poses New Threats to Consumers, Farmers, Food Companies and the Environment*. Friends of the Earth and Genetically Engineered Food Alert. Online at www.foe.org/camps/comm/safefood/biopharm/BIOPHARM_REPORT.pdf.

These crops may contaminate food and feed crops in two ways.¹⁴ First, pollen from the pharma/industrial crops may be carried by wind, insects, or other animals to fields where food versions of the crops are grown. Second, visually indistinguishable pharma/industrial food crop seeds may accidentally mix, at various points in the production chain, with seeds of the same kinds of crops destined for food or feed markets.

The use of non-food crops such as tobacco can significantly reduce the potential for food supply contamination, but it does not completely eliminate the risk. For example, as a result of extreme weather events, pharma/industrial tobacco debris might end up in an adjoining alfalfa field and unintentionally contaminate the alfalfa harvest.

Most pharma/industrial crops will be engineered to produce compounds not normally found in food, for example, hormones, vaccines, diagnostic compounds, and plastics. Even products that are already part of the general food supply, such as cellulase, and/or those that are produced in humans and animals themselves, such as lactoferrin, may occur in higher amounts or in different forms in the pharma/industrial crops. As a result, humans and animals may be exposed to new proteins or altered forms or unaccustomed levels of proteins they normally produce or consume. Certain populations, including young children or elderly adults, may have special sensitivities to some of these compounds.

Most of the gene products of pharma/industrial crops are proteins that are new to the plant. These new proteins may be processed in ways that create new allergens or elicit other adverse immune system responses.¹⁵ In addition, the new proteins may have anti-nutritional,¹⁶ toxic, neurological, hormonal, or other harmful effects.

Pharma crop drugs, in particular, are designed to be biologically active in people or animals, and some may be toxic or harmful if accidentally ingested. Medicines intended to treat certain medical conditions could prove dangerous to people not suffering from those conditions. For example, blood thinners may harm people whose blood is normal or already too thin. Hormones are another serious concern if accidentally consumed because they produce significant physiological effects at very low doses. Some immunological effects may also occur at very low doses.

Plant-produced industrial compounds like biodegradable plastics and lubricants, dietary substances like the sweetener brazzein, or accumulated heavy metals may also be harmful if they contaminate the food supply.

Environmental risks

Regardless of their intended application, pharma/industrial crops grown outdoors also pose risks to the environment, by exposing grazing mammals, birds, reptiles, amphibians, soil and aquatic

¹⁴ Where plant viruses are engineered to produce drugs in infected crops (as in the case of Large Scale Biology's use of engineered tobacco mosaic virus to produce drugs in tobacco), the potential spread of the engineered virus to plants other than the pharma crop is another route by which food crops may be contaminated.

¹⁵ Prescott, V.E. et al. 2005. Transgenic expression of bean α -amylase inhibitor in peas results in altered structure and immunogenicity. *Journal of Agricultural and Food Chemistry* 53:9023-30.

van Ree, R. et al. 2000. β (1,2)-xylose and α (1,3)-fucose residues have a strong contribution in IgE binding to plant glycoallergens. *Journal of Biological Chemistry* 275(15):11451-58.

¹⁶ An anti-nutrient is a substance that interferes with or blocks nutrient metabolism or absorption.

organisms, and herbivorous and pollinating insects to potentially harmful compounds. Pharma/industrial transgenes may also spread to wild and weedy relatives of crop plants, widening the populations potentially exposed to biologically active compounds. Because they are toxic to insects or plant pathogens, some pharma/industrial compounds, if they are expressed in wild/weedy relatives, may make the relatives more fit or competitive, facilitating the spread of the pharma gene and possibly increasing weediness.

Economic risks

Processors, millers, retailers, exporters, and others in the food and feed industries have expressed concern about potentially adverse effects of pharma/industrial crop contamination on their products, brands, and markets. These concerns have been validated by a series of incidents involving the accidental mixing of unapproved genetically engineered crops, including pharma/industrial crops, with commodity versions of the same crops. The StarLink episode in 2000, for example, involved a nationwide recall of products that led to huge economic losses, estimated to have run into the hundreds of millions of dollars, for food processors and retailers, farmers, traders, and others in the food supply chains.¹⁷ Future contamination of food crops by pharma/industrial crops may cause similar disruptions and losses.

In formal comments on USDA rules for field testing of pharma/industrial crops, submitted in 2003, the Grocery Manufacturers Association and 10 other food industry organizations noted that “the food industry will not benefit from these new applications of plant biotechnology, but could be saddled with substantial losses and liabilities if the number and size of the failures of containment systems multiply.” In order to reduce the risk, they called on the department to adopt “a presumption against the use of food or feed crops for drug or industrial compound manufacturing.”¹⁸

In comments aimed at the FDA as well as the USDA, the same groups stated that:

[G]rowing drug crops is not commodity agriculture—it is open-air drug manufacturing. Regulators must acknowledge that they are not simply regulating a new kind of crop, but they are now charged with regulating something that has until now been outside the purview of the USDA permitting process—the regulation of drug manufacturing facilities. “Pharming” is not “farming;” it cannot be undertaken nor regulated in the same way as conventional crop agriculture....

The proposed guidance...fails to inspire confidence among U.S. food companies about the integrity of U.S. commodity supplies and the ability of current regulations to isolate and contain these products.¹⁹

¹⁷ Lambrecht, B. 2001. *Dinner at the New Gene Café*. New York: St. Martin's Press, pp. 52-55.

¹⁸ Grocery Manufacturers Association (GMA). 2003. RE: Docket No. 03-031-1. GMA comments on USDA bio-pharma permit regulations. Field testing of plants engineered to produce pharmaceutical and industrial compounds. March 10. Online at <http://www.gmabrands.com/publicpolicy/docs/comment.cfm?DocID=1135>.

¹⁹ GMA. 2003. RE: Food industry comments on proposed FDA regulations for plant-made pharmaceuticals. February 6. Online at <http://www.gmabrands.com/publicpolicy/docs/comment.cfm?DocID=1068>.

Other food industry organizations have taken an even stronger stand. The National Food Processors Association (NFPA),²⁰ for example, expressed the view that the food industry must have a “100% protection standard” against any contamination of the food supply.²¹ In 2003 comments to the USDA about what it called “plant made pharmaceuticals” (PMPs), NFPA said:

[G]iven a voice...NFPA would not have supported the use of food crops for the production of PMPs. The risk and impact of contamination to the food supply is simply too great, as the food industry learned through experiences with the commodity crop Starlink corn...NFPA strongly opposes the use of food crops to produce PMPs commercially without effective controls and procedures that ensure against any contamination of the food supply.²² (emphasis in original)

CURRENT REGULATION OF GE PHARMA/INDUSTRIAL CROPS

The regulatory scheme for pharma/industrial crops grows out of the existing federal framework for oversight of engineered organisms, originally put in place in the 1980’s and fleshed out in a series of subsequent regulations and policies. The framework currently encompasses about ten statutes, primarily those administered by three agencies, the USDA, the FDA, and the Environmental Protection Agency (EPA).

Below are highlights of the regulatory system as it currently applies to crops genetically engineered for food uses and pharma/industrial purposes.

Regulation of GE crops

Field tests

Prior to commercialization, GE crops are typically tested for several years in relatively small plots to assess performance under field conditions.

- The USDA oversees field tests of GE crops under the Federal Plant Protection Act (FPPA) through a system involving either simple notification to the USDA (for trials deemed to be lower-risk) or permits granted by the department (for higher-risk trials).²³ Under USDA rules, the term “field test” applies to any level of outdoor production—from tenths of an acre to thousands of acres—undertaken until the developer commercializes the crop.
- The EPA, under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), requires experimental use permits to field test crops genetically engineered for pesticidal purposes on more than 10 acres.

Commercialization

- The USDA allows the commercialization of GE crops (except pharma/industrial crops, as noted below) under a process styled as “deregulation” under the FPPA. Crop varieties that have been deregulated generally can be grown and sold without restrictions.

²⁰ In 2005, the NFPA changed its name to the Food Products Association, or FPA. FPA plans to merge with GMA in 2007.

²¹ National Food Processors Association (NFPA). 2003. News release, “No use of food or feed crops for plant-made pharmaceutical production without a ‘100% guarantee’ against any contamination, says NFPA,” February 6.

²² NFPA. 2003. RE: Docket No. 03-031-1. Field testing of plants engineered to produce pharmaceuticals and industrial compounds. 68 *Federal Register* 11337, March 10.

²³ The USDA’s permit authority derives from its ability to restrict the introduction and movement of plant pests under the Federal Plant Protection Act, 7 U.S.C. § 7701-7772.

- GE crops intended as food typically undergo voluntary food safety review in the context of a consultation with the FDA prior to going on the market.
- Pesticidal products produced by crops genetically engineered for pesticidal purposes must be registered by the EPA under FIFRA before they can be marketed.

Regulation of GE crops intended for pharma/industrial purposes: the USDA

In 1993, the USDA promulgated new regulations governing field tests of engineered plants. The new rules eliminated the requirement for a permit for almost all GE-crop trials and allowed them to be tested under a more lax notification process. Under the 1993 regulations, pharma crops were generally not eligible for the notification scheme and could only be planted after obtaining a USDA permit.²⁴ Industrial crops remained eligible for the notification regime until 2003, when the department also began requiring permits for their outdoor production.²⁵

Although more involved than simple notification, the USDA's permitting system was not rigorous, reflecting a benign view of the risks of pharma/industrial crops. The public and food industry reaction to the 2002 ProdiGene incidents forced the department to strengthen its oversight.

In a series of steps beginning in 2003, the USDA subjected field trials of pharma/industrial crops to increasingly stringent requirements as detailed in letters to affected companies and *Federal Register* notices.²⁶ In March 2006, the department consolidated its regulations and policies into a single document, "Draft Guidance for APHIS Permits for Field Testing or Movement of Organisms with Pharmaceutical or Industrial Intent,"²⁷ which we will refer to as "the Draft Guidance."

To implement these policies and requirements, the department defined GE crops based on intended use. As described in the Draft Guidance, the USDA requires a special (so-called Form 2000) permit for the outdoor production of all crops engineered for either pharmaceutical or industrial intent.

Developers who want to grow pharma/industrial crops outdoors must apply for a Form 2000 permit by submitting detailed explanations of the crop genetic engineering, the purpose and design of the proposed production, and methods to be employed to ensure confinement. Permit applications require the same information for proposed production of both pharma and industrial crops.

Upon approval of a proposal, the USDA issues a Form 2000 permit laying out conditions that developers must meet before, during, and after production. These include requirements for separating pharma/industrial crops from crops intended for food or feed use, cleaning production

²⁴ USDA APHIS. 1993. Genetically engineered organisms and products; notification procedures for the introduction of certain regulated articles; and petition for nonregulated status. *Federal Register* 58:7044-59, March 31.

²⁵ USDA APHIS. 2003. Introductions of plants genetically engineered to produce industrial compounds. *Federal Register* 68:46434-36, August 6.

²⁶ For example, USDA APHIS. 2003. Field testing of plants engineered to produce pharmaceutical and industrial compounds. *Federal Register* 68:11337-40, March 10; USDA APHIS. 2005. Introductions of plants genetically engineered to produce industrial compounds: final rule. *Federal Register* 70:23009-11, May 4.

²⁷ USDA APHIS. 2006. Draft guidance for APHIS permits for field testing or movement of organisms with pharmaceutical or industrial intent. March 31. Online at www.aphis.usda.gov/brs/pdf/Pharma_Guidance.pdf.

equipment, allowing government inspectors on the site, and post-harvest monitoring and land use restrictions.

Form 2000 permit conditions are generally the same whether a crop is engineered for pharmaceutical or industrial uses. However, requirements may vary depending on the biological characteristics of the crop and the details of the proposed production. For example, conditions specifying separation distances between pharma/industrial and food and feed crops may vary because crops differ in the distances their pollen may travel to cross pollinate other plants. Separation distances for recent pharma crop permits include two miles for safflower, a half mile for corn, and an eighth of a mile for field peas.²⁸

Finally, the USDA does not deregulate pharma/industrial crops and release them from permit conditions prior to commercialization as it does with other GE crops. Rather, the department continues to require permits regardless of the crops' commercial status.

Pharmaceutical crops

In the Draft Guidance, the USDA defines pharmaceutical crops as GE crops produced with pharmaceutical intent. It defines pharmaceutical intent as follows: "If commercialization of the product will require approval from FDA's Center for Biologics Evaluation and Research (for human biologics), Center for Drug Evaluation and Research (for human drugs), Center for Veterinary Medicine (for animal drugs), or USDA's Center for Veterinary Biologics (for animal biologics), then the organism is considered to have been engineered with pharmaceutical intent."²⁹

Industrial crops

Under the Draft Guidance, industrial crops are defined as follows: "[P]lants engineered to produce industrial compounds include those plants that meet the following three criteria: (1) The plants are engineered to produce compounds that are new to the plant; (2) the new compound has not been commonly used in food or feed; and (3) the new compound is being expressed for non-food, non-feed industrial uses. ... Industrial uses include, but are not limited to, detergent manufacturing, paper production, and mineral recovery."³⁰ The guidance indicates that plants engineered for phytoremediation purposes require Form 2000 permits when they are not intended for use as food.³¹

It is worth noting that the definition of industrial plants excludes (with the exception of those intended for phytoremediation) plants producing increased levels of naturally occurring substances and plants genetically engineered to contain substances that are "commonly" used in food. If the high oleic soybeans and or high laurate canola marketed in the 1990's for industrial oil purposes, for example, were to be developed today, they would probably not be subject to Form 2000 permit requirements because the genetic engineering merely increased the level of substances already present in the crops.

²⁸ USDA, APHIS. 2006. Supplemental permit conditions for release of safflower (permit 05-320-01r), corn (06-061-01r), and field peas (permit 05-355-02r). Online at www.aphis.usda.gov/brs/ph_permits.html.

²⁹ USDA APHIS. 2006. Draft guidance, p. 8.

³⁰ USDA APHIS. 2006. Draft guidance, pp. 8-9.

³¹ USDA APHIS. 2006. Draft Guidance, p. 9.

Although the USDA's definition of industrial crops would comfortably encompass most uses of engineered crops as biofuels or energy crops, the department has not announced specifically that energy crops would require Form 2000 permits. Even if the Draft Guidance were understood to cover energy crops in general, it would appear to exclude those crops engineered to produce higher amounts of naturally occurring substances, for example, enzymes to facilitate cellulose breakdown.

Specialty food crops

The USDA's Draft Guidance does not explicitly address the regulatory status of crop products destined for use as specialty foods, but appears to exclude most such crops from the requirement for a Form 2000 permit. Engineered food crops producing specialty foods would not be covered by the USDA's definition of pharmaceutical crops unless the expressed product were also going to be marketed as a human drug or biologic.

It seems likely that the USDA would consider dietary purposes in general to be "food" uses, which would avoid classification as an industrial crop. In line with this interpretation, the department added a new category of products to its pharma/industrial crop database³² in 2003—"value added protein for human consumption"—which appears to cover specialty food crops. So far only crops producing two compounds, lactoferrin and lysozyme, have been so classified by the USDA. According to USDA staff, the department does not require permits or impose special requirements on such crops and allows their production under the 1993 notification regulations that apply to most GE crops. Companies developing the lactoferrin and lysozyme products, however, are voluntarily submitting requests for permits to grow these crops.

Multi-use crops

In general, it appears that GE crops intended for pharmaceutical or industrial as well as food uses would be covered under the department's Draft Guidance and would be required to obtain Form 2000 permits.

Regulation of GE crops intended for pharma/industrial purposes: the FDA

Under the Federal Food, Drug, and Cosmetic Act (FFDCA), the FDA has strong authority to regulate the manufacture of pharmaceuticals, which could be used to oversee the growing of pharmaceutical crops. According to draft guidance published by the FDA in 2002, however, the agency has decided to rely on the USDA to oversee this phase of pharma crop production.³³

The food provisions of the FFDCA are generally not relevant for the oversight of pharmaceutical and industrial crops because most of the crops are not intended for use as foods.³⁴ But there is an important exception—the provision applying to indirect food additives. Under the FFDCA, food additives are defined to include not only substances that are intentionally added to foods but substances that become components of food indirectly. In relevant part, food additives are defined as:

³² USDA APHIS. 2006. Release permits for pharmaceuticals, industrials, value added proteins for human consumption, or for phytoremediation. Online at www.aphis.usda.gov/brs/ph_permits.html.

³³ Food and Drug Administration (FDA). 2002. Draft guidance for industry: drugs, biologics, and medical devices derived from bioengineered plants for use in humans and animals; availability. *Federal Register* 67:57828-29, September 12.

³⁴ The FFDCA defines "food" as "(1) articles used for food or drink for man or other animals, (2) chewing gum, and (3) articles used for components of any article." 21 U.S.C. § 321(f).

[A]ny [non-GRAS] 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....³⁵ (emphasis added)

Thus food additives may encompass substances, including chemicals and genes, the intended use of which may reasonably be expected to result in their *indirectly* becoming a component of food. The genes and expression products of pharmaceutical and industrial crops can become components of food via pollen transfer and seed mixing. These processes are ubiquitous and almost impossible to prevent, especially where food crops are used as pharmaceutical and industrial crops. Such substances would be considered indirect food additives unless generally regarded as safe (GRAS).

Substances can be demonstrated to be GRAS in two ways. The first is based on long use in the food system. Substances in the food system before 1958 and shown to be safe through either scientific procedure or experience based on common use in food³⁶ can be GRAS. But only rarely would the exact genes and expression products of chemicals intended for pharmaceutical or industrial use have been in the food supply in 1958. For substances not in the food supply in 1958, GRAS status requires that a substance be generally recognized, among qualified experts, as having been shown to be safe through scientific procedures.³⁷ For the most part, scientific studies on the food safety of pharma or industrial expression products would also be rare since the substances are not intended for food use.

Thus, the overwhelming majority of the genes and expression products of pharmaceutical and industrial crops are likely to meet the definition of indirect food additives. As such, those products would be subject to the same requirements as direct food additives, that is, manufacturers who want to sell them would have to submit food additive petitions to the FDA demonstrating that the products are safe.³⁸ Without such a petition, the food containing the substances would be considered adulterated³⁹ and could not legally be sold into interstate commerce.⁴⁰

So far, the FDA has not indicated whether it plans to treat the genes or expression products from pharmaceutical and industrial plants as indirect food additives. It has, however, said that the presence of non-food or non-feed materials originating from pharmaceutical crops could render food adulterated under the FFDCFA.⁴¹

³⁵ 21 U.S.C. § 321(s).

³⁶ 21 U.S.C. § 321(s).

³⁷ 21 U.S.C. § 321(s).

³⁸ A food additive is deemed to be “unsafe” for its intended use unless the Secretary of Health and Human Services (“the Secretary”) issues “a regulation prescribing the conditions under which such additive may be safely used.” 21 U.S.C. §§ 348(a)(2), (b)(1). A manufacturer obtains such a regulation by petitioning the FDA. 21 U.S.C. § 348(b)(1). The petition must set forth reports on the safety of the additive. 21 U.S.C. § 348 (b)(2).

³⁹ A food is deemed to be adulterated “... if it is or if it bears or contains ... any food additive that is unsafe within the meaning of section 348 of this title[.]” 21 U.S.C. § 342(a)(2)(C).

⁴⁰ The FFDCFA forbids the “[t]he introduction or delivery for introduction into interstate commerce of any food ... that is adulterated[.]” 21 U.S.C. § 331(a).

⁴¹ FDA. 2002. Draft guidance for industry

UCS RECOMMENDATIONS FOR REGULATING THE OUTDOOR PRODUCTION OF GE PHARMA/INDUSTRIAL CROPS

After considering the potential benefits and risks of pharma/industrial crops, including the vulnerability of the food supply to contamination, the Union of Concerned Scientists recommends that the USDA, at a minimum, take two steps that, in combination, will protect the food supply against pharma/industrial crop contamination and lessen the technology's impacts on the environment:

- #1. Ban the outdoor production of food crops genetically engineered for pharma/industrial purposes.**
- #2. Strengthen environmental risk assessments and controls on the outdoor production of non-food crops genetically engineered for pharma/industrial purposes.**

Each of these recommendations is discussed below.

Recommendation #1: The USDA should ban the outdoor production of food crops genetically engineered for pharma/industrial purposes.

Below we discuss our reasons for recommending a ban on the outdoor production of pharma/industrial food crops to protect the food supply and the potential implications, proposed scope, and implementation of such a ban.

Why is a ban necessary?

UCS believes that only a ban can achieve the necessary standard of complete protection of the food supply. Even if it were theoretically possible to create a regulatory system that offered complete protection from food pharma/industrial crops grown out of doors, we believe such an oversight system would be unmanageably complex and thus impossible for the USDA to implement.

Complete protection of the food supply is necessary.

Pharma/industrial substances vary in their effects, the levels at which they cause problems, and whether they remain active after ingestion. While many substances clearly represent a problem even at very low levels (for example, orally administered hormones), others may not. This suggests that some pharma/industrial products could be present in the food system without ill effects, and raises the question of whether the standard for protection ought to be complete prevention of contamination or reduction of contamination to "safe" or "acceptable" levels.

UCS believes the USDA should adopt the most stringent standard possible—complete protection of the food system—for three reasons:⁴²

1. **The discovery of a pharma/industrial substance in the food supply could have enormously disruptive effects regardless of the substance's effects or the levels at which it is found.**

The discovery of contaminating substances can cause disruption throughout the food chain as farmers, operators of grain elevators, wholesalers, food product manufacturers, and retailers attempt to clear the system of contaminated products. As noted above, the StarLink incident in 2000 demonstrated the potentially huge costs of such disruptions.

⁴² This discussion of the need for complete protection of the food supply from contamination by pharma/industrial crops is taken from the UCS report: Andow et al. 2004. *A Growing Concern*, pp. 10-11.

Contamination of food supplies by pharma/industrial substances poses especially large risks to retail food companies. Consumers who unwittingly ingest these products in foods are likely to direct their ire—and their lawsuits—against the companies that produced and sold the food. Apart from any legal liability, the publicity associated with such incidents could severely damage valuable brands. Purveyors of organic food products are at special risk because many consumers expect organic food to be free not only of pharma/industrial products but of *all* engineered genetic sequences and products.

Importantly, contamination can have negative economic consequences even if the substances involved do not cause demonstrable harm to consumers or are present below legal tolerances. For many consumers, the publicity surrounding the discovery of any amount of drugs in a well-known brand of breakfast cereal or taco shells would be more than enough reason to turn toward competitors' products. Such changes in consumer preferences can cost food companies millions of dollars.

A government policy aimed at ensuring “safe” levels of pharma/industrial genes in corn flakes would inevitably permit some level of pharma/industrial substances in foods/feeds—and a successful industry could mean thousands of such substances. We believe consumers and food companies alike simply will not accept a government program that sanctions drugs and plastics in the food system. Put another way, “Only Safe Levels of Drugs in U.S. Food” is untenable as a motto for the USDA’s pharma/industrial crop program. The only acceptable goal of such a program is to keep pharma/industrial substances out of food altogether.

Food companies are not the only entities at economic risk from pharma/industrial crop contamination. An incident involving the discovery of drug genes in food could also deliver a devastating blow to the future of food biotechnology, which is already under pressure.⁴³ Many consumers in other parts of the world are uneasy about GE food, and the discovery of pharma/industrial genes in grain destined for a country with a high level of consumer resistance could do serious harm to the agricultural biotechnology industry. As is the case for food companies, even if a biotech firm could demonstrate that its substances are only present in food at low or “safe” levels, this would not likely be enough to quell the uproar.

2. A regulatory system establishing tolerances for pharma/industrial substances would be a waste of resources.

A policy of reducing pharma/industrial crop contamination to acceptable levels would require a regulatory system to evaluate substances and establish tolerance levels designed to protect public health. Such a system, processing hundreds or even thousands of applications for pharma and industrial chemicals, would be expensive to set up and operate. It would require scientifically trained professionals to conduct food safety evaluations and other personnel to enforce requirements once they are set. This expenditure of professional and other resources is not justified, considering that none of the substances are intended for food use in the first place. It would be much more efficient to set up a system that prevents contamination completely.

3. Risk assessments are imperfect.

Even if the government did establish an expensive regulatory system, the public might still not

⁴³ *Nature Biotechnology*. 2004. Editorial: drugs in crops—the unpalatable truth. Volume 22, Number 2, February, p. 133.

be confident that the approved levels of pharma/industrial compounds did not threaten its health. The regulatory evaluations of compounds would be based on risk assessment, an imperfect science dependent on what is known about the chemical activity and toxicity of substances, the degree to which they are present in active or inactive form, and whether there are thresholds below which they are not harmful. Accurate assessment, therefore, requires an understanding of the connections between chemicals and a variety of disease or health-related end points. This understanding is incomplete at best. The emergence of harmful effects years after FDA approval of drugs demonstrates the difficulty of assessing risks.⁴⁴

In short, risk assessment science is not sufficiently robust to guarantee that all harmful chemicals will be screened from the food supply. In many cases, society must accept risk assessment as the best that can be done to inform regulatory decisions about chemical substances. That argument does not apply in this case.

For these reasons, we advocate complete prevention of contamination—a strict performance standard—as the goal of federal regulatory policy for pharma/industrial crops.

The USDA is unable to successfully implement the complex oversight system that would be required to meet the complete-protection standard.

As UCS discussed in detail in its 2004 report, *A Growing Concern*, pharma/industrial food crops are likely to contaminate the food supply under current production and regulatory systems, if they haven't done so already.

The existing regulatory regime, even as strengthened in recent years, is unlikely to prevent contamination. Many of the requirements—for example, a one-mile exclusion of pharma corn from other corn—are not stringent enough to totally prevent contamination.

Even if regulations were strengthened to a level that would theoretically completely protect the food supply, they would be enormously costly and complex to develop, put in place, and successfully implement. Such a regulatory regime would require new management systems, new regulations, an overhaul of the current oversight program, new equipment and technologies, and restrictions on farmers who do not grow pharma/industrial crops.

UCS believes it would be well beyond the USDA's capacity to ensure the successful operation of a new, complicated system. That conclusion is based on evidence of the department's inability to adequately implement its current regulatory system, which is relatively simple compared to the one that would be needed.

First, a December 2005 report from the USDA's Office of Inspector General (OIG) detailed significant deficiencies in the department's oversight of GE crop field tests, including trials of pharma/industrial crops. For example, the OIG found that the department failed to inspect

⁴⁴ See, for example, FDA. 2004. FDA issues public health advisory on Vioxx as its manufacturer voluntarily withdraws the product. *FDA News*, PO4-95, September 30. Online at <http://www.fda.gov/bbs/topics/news/2004/NEW01122.html>.

pharma/industrial crop fields as often as promised and to ensure proper and timely disposal of the crops after harvest.⁴⁵

Second, recent experience with the USDA indicates that serious deficiencies persist in its oversight system even though the department maintains that it has corrected many of the problems cited by the OIG.⁴⁶ This conclusion is based on analysis of documents received from the USDA in response to a Freedom of Information Act (FOIA) request that UCS submitted in January 2006. UCS asked for information on the department's monitoring of compliance with permit requirements for growing pharma/industrial crops outdoors, in particular, records on federal inspections of three fields (approximately 60 acres) of pharma rice grown by Ventria Bioscience in North Carolina in 2005. UCS also requested documents submitted by Ventria in compliance with permit requirements.

In response to the FOIA request, the USDA released documents⁴⁷ showing that it completed only three of five required inspections and failed to inspect the fields as promised during critical planting and harvesting events. The department also apparently allowed Ventria to ignore reporting requirements as the released documents contained only one of nine reports required from the company. Finally, the records showed no contact between the department and Ventria in the aftermath of Hurricane Ophelia, which passed close by the site in September 2005, a few weeks before harvest. Despite the fact that the severe weather might have spread pharma rice seeds into a nearby government-run rice-breeding plot, the USDA apparently showed no interest in the impact of Hurricane Ophelia on what was the most controversial and closely watched pharma crop production in 2005.

In summary, in light of the potential consequences of contamination events and the USDA's inability to prevent them, the best policy is for the USDA to ban the outdoor production of food crops that have been genetically engineered for pharmaceutical and industrial purposes and to support a research program to develop non-food crop and closed-system alternatives for pharma/industrial crop production.

Implications of the proposed ban

UCS recognizes that imposing a ban on the outdoor use of food crops is an extraordinary measure that may prove a short-term setback to the pharma/industrial crop industry, which to date has focused primarily on food crops. However, the effects of a ban may be ameliorated somewhat by the industry's recent move away from major food crops like corn toward increased use of the non-food crop tobacco.

UCS sees no workable alternative to a ban to effectively prevent ongoing and future contamination. A positive outcome, in addition to protecting the food supply, would be to encourage the industry to develop new GE non-food pharma/industrial crops and, even better, to

⁴⁵ USDA, Office of Inspector General, Southwest Region. 2005. Audit report: Animal and Plant Health Inspection Service controls over issuance of genetically engineered organism release permits. Audit 50601-8-TE, December. Online at www.usda.gov/oig/webdocs/50601-08-TE.pdf.

⁴⁶ USDA APHIS. 2006. Office of the Inspector General (OIG) report; frequently asked questions (FAQ). Online at www.aphis.usda.gov/brs/brs_oig.html.

⁴⁷ For more information, including documents released by USDA, see the following UCS web page: UCS uncovers lax USDA oversight of pharma crops. Online at www.ucsusa.org/food_and_environment/genetic_engineering/usda-ventria-oversight.html.

further develop systems based on plant cells, fungi, bacteria, or algae that could be grown in contained facilities. Such alternatives exist, and, unlike pharma crops, have already been used to produce FDA-approved pharmaceuticals.⁴⁸

A ban on food crops would not reduce risks to the environment as long as the industry's response was to shift from outdoor production of food crops to outdoor production of non-food crops. If, however, the ban led to a major shift toward indoor uses of GE crops, plant cells, or microbes, then a ban could also be a boon to the environment.

The attached document, "Frequently Asked Questions," provides additional information on the likely impacts of such a ban.

Scope of the proposed ban

UCS proposes that the USDA implement a ban on the outdoor production of food crops genetically engineered for pharma/industrial purposes. Such purposes include three major categories of uses: pharmaceutical, industrial (including fiber, biofuels, and energy crops), and specialty foods.

Below we define the terms food crops, outdoor production, food purposes, pharmaceutical purposes, industrial purposes, specialty food purposes, and multi-purpose crops. Our definitions of pharmaceutical and industrial crops are similar to but more expansive than those in the USDA's Draft Guidance.

Definitions

Food crops are vascular plants⁴⁹ grown for consumption by the general population of people and animals. Such crops include, among others, corn, soybeans, cotton, safflower, barley, rice, canola, alfalfa, fruits, and vegetables.

Non-food crops would include tobacco and other crops with no food uses and crops like jojoba with only rare food uses.

Outdoor production means any cultivation outside of fully enclosed structures such as greenhouses, buildings, or caves that would completely prevent the escape of pollen and seeds. The proposed ban would apply *only* to outdoor production.

Food purposes include improvement of agronomic performance, enhanced pest resistance, improved processing, altered composition, and related uses in crops intended for consumption by the general population of people or animals. Examples of such applications include genetic engineering to resist herbicides and insect and virus pests, increase yield, alter oil makeup of

⁴⁸ For additional information on alternative systems, see Freese, B. 2002. Alternatives to open-air biopharming, Appendix 5. In *Manufacturing Drugs and Chemicals in Crops: Biopharming Poses New Threats to Consumers, Farmers, Food Companies and the Environment*. Friends of the Earth and Genetically Engineered Food Alert. Online at www.foe.org/camps/comm/safefood/biopharm/BIPHARM_REPORT.pdf.

⁴⁹ A vascular plant is any plant containing food-conducting tissues (phloem) and water-conducting tissues (xylem), including plants that produce seeds (for example, corn, soybeans, and evergreen and oak trees) and ferns, but not mosses or algae.

seeds, or shorten processing time. Crops engineered for food purposes would *not* be subject to the proposed ban.

Pharmaceutical purposes would be assumed if crops were engineered to produce compounds that would have to be reviewed prior to commercialization as:

- Human biologics by the FDA Center for Biologics Evaluation and Research;
- Human drugs by the FDA Center for Drug Evaluation and Research;
- Animal drugs by the FDA Center for Veterinary Medicine; or
- Animal biologics by the USDA Center for Veterinary Biologics.

Industrial purposes encompass the production of compounds intended for manufacturing goods; processing raw materials; producing fiber, biofuels, and electricity; mining and recovering minerals; remediating contaminated soils; and conducting research.

Specialty food purposes include the production of compounds intended for consumption by segments of the human or animal population or subject to special FDA consideration. These include uses such as infant formula ingredients, dietary supplements, food additives, and medical foods.⁵⁰

Multi-purpose refers to those instances in which the same gene product has both food and pharmaceutical, industrial, or specialty food uses—as, for example, the high oleic acid compound mentioned above, which is an edible oil as well as a lubricant. Such crops present a challenge for the implementation of the ban. Should they be banned as pharma/industrial crops or allowed as food crops? The theory underpinning the ban is that intended use is a surrogate for the magnitude of the risk the substance presents to the food supply, that is, substances not intended for the food supply generally present a greater risk. Compounds that are genuinely intended for food purposes generally present lower risks. For purposes of the ban, we think the risk studies of the food use should prevail.

One way to think about it is to consider secondary uses that may arise after the product is on the market. Where a crop engineered with food or feed purpose is discovered to have a pharmaceutical, industrial, or specialty food use after it is on the market, it does not make sense to retroactively ban the crop. If it does not make sense to ban it retroactively, it similarly does not make sense to ban it if the pharmaceutical, industrial, or specialty food use is contemplated from the beginning. A crop should be assigned to the lower-risk category if its producer seriously intended it for a food use.

Thus, we propose that the ban *not* apply to crops engineered to produce a single protein intended for both food and pharmaceutical, industrial, or specialty food purposes. Such an exemption constitutes a temptation to assert multi-purpose in order to avoid the ban, but we believe that the requirement (discussed below) that applicants demonstrate to the USDA the technical feasibility of the food purposes will limit the use of the loop hole.

⁵⁰ FDA oversees infant formula ingredients, dietary supplements, and food additives under special regulatory provisions of the FFDCRA and has taken steps to regulate medical foods under the same act (FDA. 1996. Regulation of medical foods. *Federal Register* 61:60661-71, November 29). However, the agency has yet to promulgate medical foods regulations [Ross, S. 2000. Functional foods: the Food and Drug Administration perspective. *American Journal of Clinical Nutrition* 71(suppl):1735S-38S].

Where a crop is genetically engineered to express a single gene intended for both food and pharmaceutical, industrial, or specialty food purposes, the crop would be considered multi-purpose.

Although multi-purpose crops would *not* be subject to the ban, they, like non-food and feed crops, would be subject to the USDA's existing system for regulating pharma/industrial crops described in the Draft Guidance. In addition, as discussed above, genes and expression products from these crops should be considered indirect food additives, and the purveyors of the crops should be required to file formal food additive petitions demonstrating their safety for the food system.

In any case, the products would be subject to the FDA's voluntary consultation process.⁵¹

Implementation of the proposed ban

A key feature of the ban would be a requirement that prior to field testing producers of all GE crops declare the purpose for the genetic modification to the USDA. In response to a producer's declaration, the USDA would decide whether the crop were subject to the ban.

Before the first field trial of any GE food crop, a producer would declare in writing to the USDA the intended purpose for the genetic modification of the crop, that is, whether the crop is intended for food purposes or for pharmaceutical, industrial, or specialty food purposes. The producer would also document that the product of the genetic modification is consistent with the declared use. For example, adding a new gene to alter agronomic, nutritional, or production qualities would be consistent with a declaration of food purposes.

A producer of a multi-purpose crop would also document that the same new gene modifies the crop for both a food *and* a pharmaceutical, industrial, or specialty food purpose.

Currently, producers are required to provide similar information to the USDA in notifications and permit applications for field trials. The department provides a database organized in terms of the intended purposes of the genetic modifications for GE crop field trials conducted since 1987.⁵²

In response to a producer's declaration of intended purpose for a GE food crop, the USDA would decide whether the crop were subject to the ban, the department's pharma/industrial crop regulations, or the department's regulations for GE crops intended for food uses. Where USDA deems a crop "multiple use," it would not allow commercialization for any purpose until the completion of the FDA's consultation process for bioengineered food.

Recommendation #2: The USDA should strengthen controls on the outdoor production of non-food crops genetically engineered for pharma/industrial purposes.

Banning pharma/industrial food crops would substantially reduce the potential for contamination of the food supply—but would not eliminate the risk entirely, especially where non-food crops

⁵¹ FDA. 1992. Statement of policy: foods derived from new plant varieties. *Federal Register* 57:22984-23005, May 29.

⁵² Virginia Polytechnic and State University, Information Systems for Biotechnology. 2006. Field test releases in the U.S. Online at www.isb.vt.edu/cfdocs/fieldtests1.cfm.

were grown outdoors. There would still be opportunities for crop debris and seeds of non-food pharma/industrial crops to inadvertently mix with food crops. Non-food crops grown outdoors would also pose threats to the environment.

Under our proposal, the USDA would oversee non-food crops engineered for pharmaceutical, industrial, and specialty food purposes under its current system for regulating pharmaceutical and industrial crops. That system is theoretically capable of assessing risks to the environment and the food system and implementing control regimes to minimize risks. But we believe that the existing regulatory system should be strengthened considerably to better protect the food supply and the environment.

The USDA is currently preparing an environmental impact statement on its GE crop regulations under the National Environmental Policy Act.⁵³ UCS urges the department to take advantage of this process to strengthen its regulatory program to protect both the food supply and the environment from the risks of GE pharma/industrial non-food crops. For example, the USDA should increase the rigor of environmental assessments of pharma/industrial crop risks and lay out a new comprehensive, cradle-to-grave confinement and management system using elements of identity preservation systems, International Standards Organization systems, and Hazard Analysis Critical Control Points food safety systems.⁵⁴

The department should also institute a presumption against approval of the outdoor production of non-food pharma/industrial crops with sexually compatible wild or weedy relatives in the United States and non-food crops infected with a virus engineered to produce pharma/industrial compounds if that virus possesses a host range beyond the non-food crop.

SUMMARY

The Union of Concerned Scientists believes that GE food crops engineered for pharmaceutical, industrial, and specialty food purposes pose a sufficient threat to the safety of the U.S. food supply to warrant a federal ban on their outdoor production. While the limited ban we propose above is an extraordinary regulatory measure, it is also reasonable and pragmatic—especially in light of the USDA's inability to enforce current regulatory measures—and therefore deserves serious consideration. We believe that adoption of such a ban by the USDA would represent a major step in the direction of improved food safety and public health protection. UCS is also recommending that the department strengthen its controls on non-food crops engineered for pharmaceutical, industrial, and specialty food purposes.

Table 2 illustrates how our proposed pharma/industrial crop regulatory system would be implemented. The proposed system would apply existing regulations to the outdoor production of non-food crops that have been genetically engineered for pharmaceutical and industrial purposes. New regulations would be required to institute a ban on the outdoor production of food crops engineered for pharma/industrial purposes.

For more information about pharma and industrial crops, and to sign on to a petition to the USDA, visit www.ProtectOurFood.org.

⁵³ USDA APHIS. 2004. Environmental impact statement; introduction of genetically engineered organisms; notice of intent to prepare an environmental impact statement and proposed scope of study. *Federal Register* 69:3271-72, January 23.

⁵⁴ Andow et al. 2004. *A Growing Concern*, pp. 97-100.

Table 1. Selected examples of pharma/industrial substances produced in GE crops*

Use Category	Example	GE Crop	Development Status**	Source***
Pharmaceutical	Monoclonal antibody against tooth decay	Tobacco	Field tested, in Phase II clinical trials under FDA Investigational New Drug application	Planet Biotechnology
	Monoclonal antibody against herpes	Corn	Not available	Hegland
	Gastric lipase enzyme to treat cystic fibrosis	Corn	Field tested; Orphan Drug status, Phase I safety study, Phase IIa studies completed in Europe	Meristem Therapeutics
	Human contraceptive	Corn	Not available	McKie
	Vaccine against transmissible gastroenteritis virus in pigs	Corn	Field tested	ProdiGene
	Blood anticoagulant—hirudin (leech protein)	Canola	Grown commercially (Canada)	Giddings et al.
Industrial	High oleic acid oil—lubricant	Soybean	Grown commercially	Cahoon Glancey et al.
	Heat-stable α -amylase—degrade corn for ethanol production	Corn	Field tested; petition for commercialization pending at the USDA	Sheridan
	Fiber quality and strength altered	Cotton	Field tested	Virginia Tech University
	Laccase—manufacture paper	Corn	Field tested	Hood et al.
	Lactoferrin, lysozyme—research purposes	Rice	Field tested; grown commercially	Ventria, 2006a
Specialty food	Lactoferrin, lysozyme—medical food	Rice	Field tested	Ventria, 2006b
	Brazzein—food sweetener	Corn	Not available	Lamphear

*This table presents a sample of the crops reported to have been engineered to produce pharma/industrial compounds. The examples were obtained from a variety of sources, including company web sites, journal articles, and trade publications.

**Where information was not readily available, we have not conducted an exhaustive search to determine whether the crop/product has advanced beyond the laboratory stage to field trials, clinical trials, or commercial production. We do provide such information on a few of the crops.

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Table 2. Scheme for implementing the proposed USDA regulatory system for production of crops genetically engineered for pharma/industrial purposes

Type of GE crop		Purpose of genetic engineering <i>Example</i>	Production site		USDA regulation
Food	Non-food		Outdoor	Indoor	
X		Pharma/industrial <i>Produce a drug</i>	X		Ban
X		Food <i>Resist an herbicide</i>	X		Field trials and commercial production—current regulations for GE crops
X		Multi-purpose <i>Resist an herbicide and produce plastics (food and pharma/industrial)</i>	X		Field trials—current regulations for pharma/industrial crops Commercial production—current regulations for GE crops FDA’s consultation process must be completed before commercialization for either purpose Developer should file and the FDA should act on formal food additive petition before commercialization
	X	Pharma/industrial <i>Produce an industrial oil</i>	X		Field trials and commercialization—current regulations for pharma/industrial crop production
	X	Non-pharma/industrial <i>Produce larger fruit</i>	X		Field trials and commercial production—current regulations for GE crops
X		Pharma/industrial <i>Produce a drug</i>		X	None
X		Food <i>Resist an herbicide</i>		X	None
X		Multi-purpose <i>Resist an herbicide and produce plastics (food and pharma/industrial)</i>		X	None
	X	Pharma/industrial <i>Produce an industrial oil</i>		X	None
	X	Non-pharma/industrial <i>Produce larger fruit</i>		X	None