



Union of Concerned Scientists

Citizens and Scientists for Environmental Solutions

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Regulatory Analysis and Development
USDA APHIS PPD
Station 3A-03.8
4700 River Road Unit 118
Riverdale, MD 20737-1238

Submitted via Federal eRulemaking Portal: Docket No. APHIS-2007-0016

RE: USDA APHIS draft environmental assessment and preliminary decision to deregulate Syngenta's genetically engineered ethanol corn

To whom it may concern:

The Union of Concerned Scientists (UCS) is grateful for the opportunity to comment on the USDA Animal and Plant Health Inspection Service's (APHIS's) draft environmental assessment on its proposed decision to grant nonregulatory status to Syngenta Seeds' corn variety, Event 3272, which has been genetically engineered to facilitate ethanol production.

UCS, the leading science-based nonprofit working for a healthy environment and a safer world, combines independent scientific research and citizen action to develop innovative, practical solutions and secure responsible changes in government policy, corporate practices, and consumer choices. A major goal of UCS's Food and Environment Program is to strengthen the regulatory system that applies to products of agricultural biotechnology.

BACKGROUND

On November 19, 2008, APHIS issued a *Federal Register* (FR) notice asking for public comment on its draft environmental assessment (EA) and preliminary decision to grant nonregulated status to Syngenta's genetically engineered (GE) Event 3272 corn (hereinafter "GE ethanol corn").¹ A June 4, 2009, FR notice announced a reopening of the comment period and summarized the comments the agency had received thus far.²

In addition, the June FR notice addressed one specific set of comments—those submitted by the Corn Refiners Association (CRA) questioning the agency's conclusion that the GE ethanol corn is not a plant pest.³ In responding to these comments, APHIS asserted two new conclusions on the jurisdiction of its plant pest regulatory program. These conclusions are that neither the GE ethanol corn plant nor the alpha-

¹ 73 Fed. Reg. 69602-04, November 19, 2008.

² 74 Fed. Reg. 26832-35, June 4, 2009.

³ Corn Refiners Association (CRA). 2009. Comments on proposed deregulation of Syngenta Seeds corn Event 3272, January 20, comment no. 0175.1 at www.regulations.gov/fdmspublic/component/main?main=DocketDetail&d=APHIS-2007-0016. The CRA (www.corn.org) is the national trade association representing the U.S. corn refining (wet milling) industry, which manufactures starches, sweeteners, corn oil, and animal feed ingredients from corn. Member companies include Archer Daniels Midland, Cargill, National Starch, and Corn Products International.

amylase enzyme meets the definition of a plant pest under the federal Plant Pest Act (PPA)⁴ and that as a result the agency has no regulatory authority over Syngenta's product. The argument made by the agency in support of its conclusion that the GE ethanol corn plant is not a plant pest could be made on behalf of most GE crops, and would effectively remove nearly all GE crops from PPA jurisdiction. Since the PPA is the primary authority under which the agency regulates GE crops,⁵ this move would effectively leave most GE crops unregulated.

After considering comments received from November 2008 through July 6, 2009, APHIS will decide whether to deregulate the new GE ethanol corn.⁶ A decision to grant nonregulated status means that the industrial corn variety would no longer be subject to the agency's regulatory authority and could be grown unfettered at commercial scale in the United States—free of any geographical or management restrictions.⁷

UCS submitted comments in January 2009 and is submitting the comments below in response to the June FR notice reopening the comment period.

GE ethanol corn

Syngenta's GE corn was developed with the hope of cutting costs in the production of ethanol from corn kernels. Developed solely as an industrial crop, GE ethanol corn is not intended for human consumption. If approved for nonregulated status, this product would be the first GE industrial crop commercialized for biofuel production. If this corn variety were widely adopted by farmers seeking to sell to ethanol manufacturing facilities, it could be planted on tens of millions of acres of U.S. farm land.

The GE ethanol corn was engineered to produce a new synthetic thermostable alpha-amylase designed to break down corn starch under the high-temperature conditions required for the dry-grind process of ethanol production.⁸ Usually the alpha-amylase necessary for the process is produced separately in a microbial system and added to batches of crushed corn during the liquefaction stage.⁹ The use of GE ethanol corn producing its own alpha-amylase, processed alone or with other varieties of corn, would obviate the need for exogenous enzyme.

The transgene for the alpha-amylase engineered into GE ethanol corn was patched together from selected sequences of three alpha-amylase genes obtained from three different microorganisms of the Archaeal

⁴ The Plant Pest Act was incorporated, along with the Noxious Weed Act, into the Plant Protection Act in 2000 (7 U.S.C. 7701 *et seq.*); APHIS is currently considering comments on proposed regulations implementing that authority (73 Fed. Reg. 60008-48).

⁵ PPA regulations governing GE plants at 7 CFR Part 340.

⁶ 74 Fed. Reg. 26835.

⁷ USDA APHIS. 2008. Syngenta Seeds, Inc., Alpha-Amylase Maize, event 3272, Draft Environmental Assessment (hereinafter "EA"), November 6, pp. 20-22. Document 2007-0016-0002 online at www.regulations.gov/fdmspublic/component/main?main=DocketDetail&d=APHIS-2007-0016.

⁸ Dry-grind processing is the predominant corn ethanol production process, with dry-mill plants accounting for nearly 85% of production capacity in 2007. EA, Appendix C, p. 74.

⁹ After corn kernels are ground to release water-insoluble starch molecules, the liquefaction process converts the starch to water-soluble fragments or dextrins. This step typically requires both high temperature cooking of the starch and the addition of thermostable microbial alpha-amylases that operate under high temperatures to break down the large starch molecules into smaller molecules called dextrins. Then, another microbial enzyme, beta-amylase (also called glucoamylase), is added to break down the dextrins into glucose molecules, which are converted to alcohol during the fermentation stage. (R.E. Warner and N.S. Mosier. 2007. Ethanol—Dry Grind Process. Sun Grant Initiative and University of Tennessee. Online at <http://bioweb.sungrant.org/Technical/Biofuels/Technologies/Ethanol+Production/Ethanol+Dry+Grind+Process/Default.htm>.)

order Thermococcales,¹⁰ which typically live in extremely hot waters. Archaeans¹¹ are a distinct type of microorganism discovered and described only in the last four decades. Because they are so different from other organisms, scientists place them in a new domain—Archaea—distinct from the better-known Bacteria and Eukaryote domains. A tissue-specific promoter ensures that most of the novel alpha-amylase gene is expressed in the corn kernel, where the enzyme is found at high levels, ranging up to 0.2 % of fresh weight.¹²

A second transgene engineered into the ethanol corn, originating from *Escherichia coli*, encodes the enzyme phosphomannose isomerase (PMI). The enzyme was used as a selectable marker during the genetic engineering process and is not expected to play a role in ethanol production. PMI is expressed throughout the plants' tissues at varying, but much lower,¹³ levels than the alpha-amylase.

Regulatory history—United States

Syngenta's industrial corn is subject to APHIS and Food and Drug Administration (FDA) oversight.

APHIS

APHIS oversees both field testing and commercialization of GE crops under the PPA.¹⁴ From 2002 to 2005, the agency acknowledged 14 Syngenta notifications for over 3200 acres of field tests of GE ethanol corn in at least 45 sites in 14 states and Puerto Rico.¹⁵ ¹⁶ On October 7, 2005, the company submitted a petition (APHIS petition # 05-280-01p) to APHIS requesting a determination of nonregulated status for GE ethanol corn. Deregulation would clear the way for commercial production and widespread use. That request is the subject of these comments.

FDA

Companies engineering food crops for human consumption typically volunteer to consult with the FDA on food safety issues under the agency's 1992 policy on GE foods.¹⁷ Even though GE ethanol corn is not intended for human consumption, Syngenta recognizes that it will be impossible to prevent contamination of the food supply with both the seeds and the pollen from its industrial corn. The company has

¹⁰ Syngenta. 2006. Petition for the Determination of Nonregulated Status, Maize Event 3272 (hereinafter "Petition"), September 10, p 23. Online at www.regulations.gov/fdmspublic/component/main?main=DocketDetail&d=APHIS-2007-0016, document ID 2007-0016-0004.

¹¹ Many archeans live in extreme environments, for example, near deep sea vents where temperatures are well over 100° C (212° F) or in extremely alkaline, acidic, or saline waters. ("Introduction to the Archaea" at www.ucmp.berkeley.edu/archaea/archaea.html)

¹² Petition, pp. 43-44.

¹³ The highest measurement is 8.5 µg/g fresh weight in pollen. Petition, pp. 43, 45.

¹⁴ Field testing at 7 CFR 340.3 and 4; commercialization at 7 CFR 340.6.

¹⁵ Under the notification process, an acknowledgement means that the company is allowed to plant the GE crop according to the specifications of the notification. Syngenta may or may not have planted all 3200 acres. Information on actual acres planted has not been released to the public.

¹⁶ Syngenta. 2007. "Response to APHIS/BRS review for technical completeness of Syngenta's petition for a determination of non-regulated status for corn event 3272, assigned APHIS number 05-280-01p." Letter from A. Tuttle, Syngenta, to N. Hoffman, USDA APHIS, January 10, p. 1, Table 1-1. Online at www.regulations.gov/fdmspublic/component/main?main=DocketDetail&d=APHIS-2007-0016, document ID 2007-0016-0004; Information Systems for Biotechnology. 2009. Field Test Release Applications in the U.S. Virginia Tech University. Online at www.isb.vt.edu/cfdocs/fieldtests1.cfm.

¹⁷ FDA. 1992. Statement of Policy: Foods Derived from New Plant Varieties; Notice. 57 Fed. Reg. 22984-23005. Even though FDA is charged with assuring the safety of the U.S. food supply, the agency has no authority to approve or deny marketing or to require submission of food safety data for most GE foods.

voluntarily consulted with the FDA on food safety risks posed by the new variety, completing the process in August 2007.¹⁸

Regulatory history—abroad¹⁹

Thus far, Syngenta has applied to 10 foreign countries for regulatory approvals for GE ethanol corn. Last year, three—Australia, New Zealand, and the Philippines—approved the variety for food and feed uses while Canada approved it for environmental (planting) as well as food and feed uses. Of the six remaining countries, the Republic of South Africa, the only African country to which Syngenta has applied, denied the company’s request and decisions are pending in Korea, Japan, Russia, Switzerland, and Taiwan. Syngenta appears not to have applied for any approvals in South American or Europe, other than its home base of Switzerland.

Environmental assessment: APHIS’s findings

Before GE ethanol corn can be granted nonregulated status, APHIS must satisfy requirements established under the PPA²⁰ and the National Environmental Policy Act (NEPA).²¹ The EA’s analysis of Syngenta’s request for deregulation is intended to inform the agency’s decision on whether nonregulated status should be granted under APHIS’s PPA regulations and its determination of whether a full environmental impact statement (EIS) is required under NEPA.

Under this process, the agency may grant nonregulated status if it: i) determines that the GE variety is not a plant pest and therefore should no longer be a regulated article under the PPA and ii) that the deregulated variety will have no significant impact on the environment and thus there is no need for the preparation of an EIS under NEPA. The agency determines whether an EIS is necessary before deciding whether to grant nonregulated status.²²

The draft EA concludes that the industrial corn “is unlikely to pose a plant pest risk; thus APHIS has no regulatory authority over [GE ethanol] corn and this GE corn variety is eligible for nonregulated status.”²³ The agency first sought public comment on this decision in its November FR notice.

In the June FR notice, APHIS provided a stunning new argument not advanced in the November document, nor in the 22 years of the existence of the APHIS PPA program, that would lead to the conclusion that the agency has no jurisdiction over the GE ethanol corn. (See section I of these comments for more detail.)

In its NEPA analysis, APHIS considered a number of potential environmental impacts before concluding that deregulation would have no significant impacts on human or animal health,²⁴ animal and plant communities and biodiversity,²⁵ and threatened or endangered species.²⁶

¹⁸ FDA. 2007. Biotechnology Consultation: Note to the File BNF No. 000095. Center for Food Safety and Applied Nutrition, August 7. Online at www.cfsan.fda.gov/~rdb/bnfm095.html; FDA. 2007. Biotechnology Consultation: Agency Response Letter BNF No. 000095. Center for Food Safety and Applied Nutrition, August 7. Online at www.cfsan.fda.gov/~rdb/bnfl095.html.

¹⁹ EA, pp. 7-8.

²⁰ 7 CFR Part 340.

²¹ 40 CFR Parts 1500-1508.

²² EA, p. 9.

²³ EA, p. 20.

²⁴ EA, p. 35.

²⁵ EA, p. 44.

²⁶ EA, p. 50.

SUMMARY OF UCS CONCLUSIONS/RECOMMENDATIONS

UCS urges APHIS to reject the application for the GE ethanol corn and consider the application under the new regulations now being developed under the Plant Protection Act. The jurisdictional issues raised by this application expose the legal deformities in the now defunct PPA and perfectly illustrate why the agency needed to ground the regulation of GE crops and other organisms on sounder legal authority. The agency should not use defective legal authority when a better alternative will soon be available. If it does go ahead under the PPA authority, the agency should withdraw its new interpretation of jurisdiction over GE plants and return to the interpretation that has been in place since 1987.

As we have argued before, we believe that APHIS should ban the outdoor production of all food crops genetically engineered to produce pharmaceutical and industrial substances, including the GE ethanol corn. Absent a ban, drugs and industrial chemicals, including the novel alpha-amylase produced by GE ethanol corn—products never intended for human consumption—will contaminate the food supply.

If it chooses not to set aside the GE ethanol corn application and consider it under its new Plant Protection Act regulations, the agency should fully comply with NEPA by preparing an EIS that details the significant economic and environmental impacts of widespread cultivation of the new variety. The draft EA fails to meet NEPA requirements in three important respects. First, it lacks sufficient data and analysis to support a conclusion that deregulation will not have a significant impact on the human environment. The agency does not adequately address the allergenicity concerns about the new alpha-amylase, which originated from three microorganisms to which people have not been exposed in either food or the environment. Second, the EA fails to consider the potential economic effects of large-scale production of GE ethanol corn, including impacts on U.S. corn processors and on corn exporters and growers if the variety were to contaminate shipments to any of the many countries that have not approved it. Third, APHIS only partially addresses alternatives to the GE ethanol corn, ignoring the availability of products that may offer significant advantages over the industrial corn for ethanol production.

Our detailed comments follow below.

UCS COMMENTS

I. UCS urges APHIS to set aside the application for the GE ethanol corn and consider the application under the new regulations now being developed under the Plant Protection Act.

As noted above, the Corn Refiners Association (CRA) submitted comments to APHIS opposing the deregulation of Syngenta's ethanol corn. The association made a strong case against deregulation based on the damage that the heat-stable amylase could do to products of the wet milling industry.²⁷ The CRA noted that “[a]lpha-amylase is detrimental to virtually all starch products and can be problematic at very low levels in applications dependent on high viscosity or where extended shelf-life is a requirement.”²⁸ It further noted that the EA prepared by APHIS had not considered the misdirection of ethanol corn to the corn wet milling industry, which “provides approximately seven billion pounds of corn starch to food and industrial consumers each year.”²⁹

²⁷ CRA. 2009. Comments, pp. 2-3.

²⁸ CRA. 2009. Comments, p. 2.

²⁹ CRA. 2009. Comments, p. 3.

In addition, the CRA advanced the legal argument that the alpha-amylase enzyme could be considered a plant pest because the enzyme would be expected to cause damage to plant products produced by wet milling.³⁰

The CRA argued that “the presence of alpha-amylase enzyme from [GE ethanol] corn delivered to a corn wet milling facility that produces manufactured and processed plant products could cause direct or indirect injury to these products.”³¹ This particular alpha-amylase, because it is active at high temperatures (unlike other enzymes used in the food industry), could be activated by a heating process during the manufacture of food products³² and, for example, reduce corn starch, which is used as a thickening agent, to liquid corn sugar.

The association claims that this kind of damage falls within the definition of a plant pest³³ and that the alpha-amylase fits the definition of a plant pest because it is a “living stage of an article similar to or allied with a bacterium or any article similar to or allied with a bacterium that can cause direct damage to a processed plant product” ... “if misdirected to corn wet milling facilities.”³⁴

Syngenta responded to the CRA after the close of the first comment period.³⁵ It did not challenge the corn refiners’ claims that the alpha-amylase could seriously damage the wet milling industry, but did rebut the legal argument that the enzyme itself met the definition of a plant pest.³⁶ Syngenta then went further and claimed that the GE ethanol corn plant itself did not fit the definition of a plant pest.³⁷

Surprisingly, in its June FR notice, APHIS agreed with Syngenta that the GE ethanol plant itself is not a plant pest because it is not a living stage of any of the eight entities listed in the definition of a plant pest.³⁸ Only one on the list is any kind of plant, in this case a parasitic plant.

APHIS makes it clear that “it cannot regulate GE plants outside the PPA’s plant pest definition in 7 USC 7702(14). This statutory definition provides specifically that only a parasitic plant can be a plant pest.”³⁹ In so doing, it offered a new interpretation of PPA authority that excludes practically all GE plants from PPA jurisdiction. (APHIS also agreed with Syngenta’s argument that the amylase enzyme is not a plant pest because it does not fit the “living stage” element of the plant pest definition,⁴⁰ but we will not comment further on this argument as it does not have widespread policy implications.)

The agency’s argument that GE ethanol corn is not a plant pest because it is not a parasitic plant applies to most, if not all, GE plants.

³⁰ CRA. 2009. Comments, p.2.

³¹ CRA. 2009. Comments, p. 2.

³² CRA. 2009. Comments, p. 3.

³³ 7 USC 7702(14): The term "plant pest" means any living stage of any of the following that can directly or indirectly injure, cause damage to, or cause disease in any plant or plant product: (A) A protozoan. (B) A nonhuman animal. (C) A parasitic plant. (D) A bacterium. (E) A fungus. (F) A virus or viroid. (G) An infectious agent or other pathogen. (H) Any article similar to or allied with any of the articles specified in the preceding subparagraphs.

³⁴ CRA. 2009. Comments, p. 1.

³⁵ Syngenta. 2009. Plant Protection Act analysis in reference to petition no. 05-280-01p, comment no. 0222.1 at [www.regulations.gov/fdmspublic/component/main?main=DocketDetail&d= APHIS-2007-0016](http://www.regulations.gov/fdmspublic/component/main?main=DocketDetail&d=APHIS-2007-0016).

³⁶ Syngenta. 2009. PPA analysis, p. 5-6.

³⁷ Syngenta. 2009. PPA analysis, pp. 8-9.

³⁸ 74 Fed. Reg. 26834.

³⁹ 74 Fed. Reg. 26834.

⁴⁰ 74 Fed. Reg. 26834.

To understand the implications of this legal conclusion, it is helpful to recall that APHIS brought GE plants under PPA jurisdiction in 1987 because it wanted to establish a pre-market review system for GE crops and other organisms and had no obviously suitable authority. No one believed that GE crops were especially likely to be plant pests in any conventional sense. Nevertheless, the agency built an elaborate regulatory regime under the PPA⁴¹ with interested parties sharing a tacit understanding that GE crops would be considered potential plant pests even though most clearly do not fit the strict definition set out in the act.⁴²

To give the scheme a semblance of rationality, APHIS decided to consider GE crops subject to regulation if there existed even a reason to believe they might be plant pests.⁴³ Under the regulations, plants would be so considered if they contained any genetic material from an organism that meets the definition of a plant pest.⁴⁴ The rationale was that a crop might carry genetic material derived from a plant pest, and that the presence of that DNA constitutes a reason to believe the engineered crop is a plant pest. Although tenuous from a scientific standpoint, it sufficed to bring virtually all GE crops under APHIS oversight.

The regulatory scheme does not grant commercial permits to GE crops, but instead deregulates them based on a conclusion that they are no longer considered plant pests. This conclusion is reached after examining substantial data packages submitted by the developer demonstrating that the crop poses no plant pest *risk*. The data packages contain information on a broad range of issues including potential weediness, flow of genes to wild relatives, impacts on non-target organisms, and other plant pest risks. At the end of the process, APHIS typically finds that a GE crop does not present a plant pest risk and therefore is no longer considered a regulated article under the PPA regulations.⁴⁵ Under this program, the agency has approved over 75 petitions requesting nonregulated status for GE plants since the early 1990s.⁴⁶

Developers of the vast majority of GE crops would be able to show that their products are not parasitic plants, do not meet the definition of a plant pest, and thus are not subject to APHIS oversight under PPA regulations. In such cases, developers would not need to follow PPA regulations for field trials nor would they need to collect and submit data in a deregulatory petition. They could ignore APHIS altogether or, as a courtesy, inform the agency that, like the Syngenta GE ethanol corn, their GE crops are not subject to PPA regulations because the crops are not parasitic plants.

Under this new jurisdictional interpretation, virtually any biotechnology company could choose to avoid regulation. In particular, developers with serious doubts about their prospects for approval may see this as an attractive opportunity to avoid having a product rejected by the agency. That may be what happened in this case. Syngenta may have become convinced that the strong objections of the corn refining industry would make it virtually impossible to deregulate the ethanol under the existing PPA process. Rather than face a denial of the application, the company may have sought to evade jurisdiction altogether.

⁴¹ 7 CFR Part 340.

⁴² 7 USC 7702(14).

⁴³ 7 CFR Part 340—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.

⁴⁴ 7 CFR 340.1.

⁴⁵ See, for example, a summary of the deregulatory process in a recent FR notice in which APHIS announced its determination of nonregulated status for a GE cotton variety: 74 Fed. Reg. 23987-88, May 22, 2009.

⁴⁶ USDA APHIS BRS. 2009. Petitions for nonregulated status granted. Online at www.aphis.usda.gov/brs/not_reg.html.

We do not take on the new interpretation of the PPA jurisdiction as a legal matter. The assertion that GE ethanol corn is not a plant pest is certainly arguable. But as a policy and regulatory matter, it would be extremely unwise for the agency to use this approach to approve this controversial application.

The jurisdictional issues raised by Syngenta's petition reveal the legal defects associated with the PPA and reinforce the need for APHIS to base the regulation of GE crops and other organisms on the more robust and sounder authority offered by the Plant Protection Act. The agency should not rely on flawed legal authority when a stronger option will soon be available. It should defer action on Syngenta's application and consider it anew once final regulations are promulgated under the Plant Protection Act.

If APHIS decides to proceed with this application under PPA authority, the agency should withdraw its new interpretation of GE crop jurisdiction and return to the interpretation established more than two decades ago.

The agency's shift in position on such a weighty matter throws the industry into chaos and undermines confidence in the oversight of GE crops both among the public and our trading partners.

II. If APHIS goes ahead with the application, the agency should fully comply with NEPA by preparing an EIS to illuminate the significant environmental impacts of widespread use of the GE ethanol corn before moving ahead with a decision to deregulate.

NEPA requires APHIS to prepare an EIS for major federal actions that significantly affect the quality of the human environment.⁴⁷ When an EIS is not categorically required or excluded, APHIS must prepare an EA, which lays out the data and analysis determining whether the effect on the environment is significant enough to require an EIS.⁴⁸ If an EA produces a finding of no significant impact, no EIS is required.

The draft EA on the GE ethanol corn fails to meet NEPA requirements because it does not provide sufficient data and analysis in a number of areas to support a conclusion that deregulation will not have a significant impact on the human environment. Our analysis, detailed below, leads to the conclusion that the NEPA analysis was deficient. Considering the precedent-setting nature of the application and the likely impact on an important industry, corn refining, we believe a proper analysis would lead to the conclusion that an EIS is required.

APHIS's analysis is deficient in several key areas, including the three we focus on below: allergenicity of the novel alpha-amylase, economic consequences of GE ethanol corn in food, and examination of alternatives to Syngenta's product in ethanol production.

A. APHIS has not provided sufficient data and analysis to support a conclusion that the novel alpha-amylase in GE ethanol corn will not have a significant impact on human health.

A major human health concern with Syngenta's novel product, as with most synthetic proteins which have been not been part of the human food supply, is the potential allergenicity of the alpha-amylase. After considering information from Syngenta and the FDA, APHIS concluded that the enzyme is not an allergenicity concern. However, UCS's assessment of this information and the agency's analysis of it leads us to question this conclusion. Adequately addressing allergenicity concerns is critical because, if

⁴⁷ Under NEPA, the human environment "include[s] the natural and physical environment and the relationship of people with that environment" (40 CFR 1508.14) and "[e]ffects include ecological (such as the effects on natural resources and on the components, structures, and functioning of affected ecosystems), aesthetic, historic, cultural, economic, social, or health, whether direct, indirect, or cumulative" (40 CFR 1508.8).

⁴⁸ 40 CFR parts 1500-1508, 7 CFR part 372.

the GE ethanol corn is widely adopted, the alpha-amylase will end up in the food supply. The fact that people have not been exposed previously to the protein will raise new exposure issues when consumers ingest it in food.

Food allergenicity is a complex process in which a person's immune system responds to specific proteins in food. Some proteins are well known as food allergens; however, the allergenicity status of most proteins is unknown. The only way to determine whether new proteins are food allergens is for people to ingest or inhale them. To avoid the serious health consequences, including death, that might result from testing for allergic responses in humans, regulators try to predict the allergenicity of proteins based on similarity between the novel protein and the biochemical characteristics of known allergens. Although these tests are relatively weak predictors, they are often the best available approaches.⁴⁹ If a new protein shares amino acid sequences or other biochemical characteristics with known allergens, it is considered to have allergenic potential.

1. APHIS did not demand sufficient data and analysis to address concerns about the potential allergenicity of the novel alpha-amylase.

The novel alpha-amylase in the GE ethanol corn comes from organisms that have never been in the food system and were only recently discovered by scientists. As such they raise red flags from an allergenicity point of view. The quality of the assessment of these concerns is inadequate.

APHIS' conclusion that the novel alpha-amylase is not likely to be an allergen relies on allergenicity tests submitted by Syngenta and the company's voluntary consultation with the FDA.⁵⁰

Syngenta's allergenicity testing

The allergenicity tests submitted by Syngenta do not provide sufficient information to determine whether or not the novel enzyme is likely to be allergenic. The submission falls far short of the lists of tests outlined in the Food and Agriculture Organization/World Health Organization (FAO/WHO) Expert Consultation on Allergenicity of Foods Derived from Biotechnology. The report from that consultation provided an authoritative list of tests appropriate for a protein, like the alpha-amylase, from organisms not known to be allergenic. The three major categories of tests are:

- Comparing amino acid sequences with those of known allergens,
- Determining digestibility of the protein in vitro in a pepsin resistance test (many allergenic proteins are resistant to digestion in simulated gastric fluids), and
- Analyzing the immunogenicity of the protein in animal models.⁵¹

Syngenta submitted adequate information comparing amino acid sequences, but the digestibility studies were of poor quality. The only information available on the pepsin resistance test is four sentences in the Syngenta petition⁵² and three sentences in an FDA document.⁵³ The APHIS EA provides no additional information.

⁴⁹ See, for example, FAO/WHO. 2001. Evaluation of Allergenicity of Genetically Modified Foods. Report of a Joint FAO/WHO Expert Consultation on Allergenicity of Foods Derived from Biotechnology, January 22-25. Online at <ftp://ftp.fao.org/esn/food/allergygm.pdf>.

⁵⁰ EA, p. 35.

⁵¹ FAO/WHO. 2001. Evaluation of allergenicity, Section 5.4, pp. 8-9. (The FAO/WHO guidelines recommend another step—serum screening—if there are sensitized people from whom serum can be obtained. For the microorganisms from which the alpha-amylase was obtained, there are no known sensitized people.)

⁵² Petition, p. 7, item 7 (3 sentences), p. 50, item 7 (1 sentence).

⁵³ FDA. 2007. Biotechnology Consultation. Note to the File, Section 4.3.1, paragraph 3.

Without more detail it is impossible to know if the data from the pepsin resistance test are valid. According to Fu et al. (2002),⁵⁴

[T]he digestion stability and thus the perceived allergenic potential of proteins, as determined by the in vitro digestion assays, may be influenced by the assay conditions used. Changes in pH or the relative amounts of enzymes and test proteins used in an assay may affect the relative digestibility measured.

The only information available concerning Syngenta's protocol for the digestibility test is that the alpha-amylase "protein purified from [GE ethanol corn] was incubated in SGF [simulated gastric fluid] at 37 °C for 0, 1, 5, 10, 20 and 30 minutes."⁵⁵ Far more is needed to judge the validity of the assay including protein concentrations, inclusion of standard test proteins, pepsin activity assays, and the makeup of protein/enzyme mixtures.⁵⁶ The appendix to these comments contains an excerpt from the FAO/WHO Expert Consultation concerning the details appropriate for a pepsin resistance test.

Syngenta submitted no results demonstrating lack of immunogenicity in animal models.

In summary, the paucity of information on the digestibility assay and the lack of an immunogenicity assessment make it impossible to conclude that the alpha-amylase is unlikely to become an allergen.

Syngenta's voluntary consultation with the FDA

APHIS also offers the completed the FDA consultation as evidence that the alpha-amylase is unlikely to be an allergenic protein.⁵⁷ However, the results of the consultation did not include any new data or more detailed analysis than that found in the EA. The application highlights the flaws in the FDA consultation process.

First, the FDA has no authority to require specific testing or data and must rely on a company's judgment as to what tests to conduct and what data to submit.⁵⁸ For example, the FDA could not require Syngenta to assess the immunogenicity of the new protein in an animal model, as recommended by the FAO/WHO Expert Consultation.

Second, the agency does not release detailed information on testing protocols or data generated to allow the public to make an independent judgment on the appropriateness and quality of the testing.

Third, the FDA does not conduct its own independent food safety assessment. Rather, it relies on the company's assessment and conclusions, as illustrated by the following excerpt from an agency summary of the Syngenta GE ethanol corn consultation:

Based on the safety and nutritional assessment *Syngenta has conducted*, it is our understanding that *Syngenta has concluded* that grain and forage from the new variety are not materially different in composition, safety, and other relevant

⁵⁴ T.-J. Fu, U.R. Abbott, and C. Hatzos. 2002. Digestibility of Food Allergens and Nonallergenic Proteins in Simulated Gastric Fluid and Simulated Intestinal Fluid—A Comparative Study. *Journal of Agricultural and Food Chemistry* 50:7154-60.

⁵⁵ Petition, p. 7, item 7.

⁵⁶ FAO/WHO. 2001. Pepsin resistance, Section 6.4, p. 13.

⁵⁷ EA, p. 35.

⁵⁸ D. Gurian-Sherman. 2003. Holes in the Biotech Safety Net: FDA Policy Does Not Assure the Safety of Genetically Engineered Foods. Center for Science in the Public Interest. Online at www.cspinet.org/new/pdf/fda_report_final.pdf.

parameters from grain and forage currently on the market, and that genetically engineered [ethanol] corn ... does not raise issues that would require premarket review or approval by FDA (emphasis added).⁵⁹

Fourth, the agency makes no judgment of its own on food risks. Rather, FDA merely indicates that it has no questions concerning the product, as this excerpt on GE ethanol corn indicates: “Based on the information Syngenta has presented to FDA, *we have no further questions* concerning grain and forage from [GE ethanol corn] at this time” (emphasis added).⁶⁰

UCS concludes that neither the EA, Syngenta’s petition, or the FDA consultation documents provide sufficient data, information, or analysis to address concerns about allergenicity. We are urging the FDA to assemble a panel of outside experts to consider the possibility that the new enzyme will present an allergenicity risk.

2. APHIS’s failure to allay allergenicity concerns is particularly critical because the presence of alpha-amylase in the food supply will raise new exposure issues for consumers not previously exposed to the protein or the organisms from which the protein was obtained.

The alpha-amylase will end up in the food system if the GE ethanol corn is widely adopted. A decision to deregulate GE ethanol corn would mean that the new variety could be grown anywhere in any amounts in the United States. APHIS would impose no geographic or management constraints.⁶¹ If the demand for ethanol corn continues to grow as it has in the past few years and if the GE variety is successful in supplanting current corn varieties destined for dry-mill grinding, then the new variety could be grown on 15 to 20 million or more acres each year.⁶²

Grown at such a scale, Syngenta’s voluntary plan to contain the industrial corn, growing and processing it in a so-called “closed loop” system,⁶³ will almost certainly fail to prevent widespread contamination of the food supply. As a result, GE ethanol corn could end up in corn tortillas, chips, syrup, flour, starch, and masa—and in thousands of processed foods made from these products. For example, corn syrup is used in manufacturing candies, soft drinks, breakfast cereals, baked goods, salad dressings, and a myriad other items on grocery shelves. Cornstarch is a component of cake, cookie, and pie mixes, and a host of other products where thickening is needed.

Syngenta’s “closed loop” plan, which APHIS would not require as a condition of deregulation, depends on contracts among the company, growers, and ethanol plants that prescribe methods and other requirements for cultivating, handling, and delivering GE ethanol corn to processing plants.⁶⁴ Despite the company’s intentions to confine the corn, the plan will fail, especially if the corn variety is grown at the scale noted above, for several reasons:

⁵⁹ FDA. 2007. Biotechnology Consultation. Note to the File

⁶⁰ FDA. 2007. Biotechnology Consultation: Agency Response Letter

⁶¹ EA, pp. 21-22.

⁶² APHIS notes that over 20% of the U.S. corn crop harvested from 86.5 million acres in 2007 (pp. 10, 12 and references cited therein), or approximately 17.3 million acres, went to ethanol production. That same year, with dry-mill plants accounting for over 83% of ethanol production capacity (Appendix C, p. 74, reference cited therein), roughly 14 million acres of corn were consumed in dry-mill production. Given expectations that corn ethanol production will dramatically increase in the years ahead (USDA Economic Research Service. 2006. USDA Agricultural Baseline Projections to 2015, OCE-2006-1, at www.ers.usda.gov/publications/oce061/oce20061.pdf, p. 4) and if dry-milling continues to account for about 85% of ethanol capacity, then the United States could see 15 to 20 million or more acres of corn going into dry-mill ethanol production annually.

⁶³ EA, pp. 25-26 and Appendix G, pp. 138-139.

⁶⁴ EA, Appendix G, pp. 138-139.

- **Cross pollination with food corn**
The most important flaw with the plan is that it contains no measures to control the spread of pollen. It is 100% certain that ethanol corn will cross pollinate with corn plants headed for the food supply. There will be no attempt—and indeed it would be impossible—to segregate the cultivation of millions of acres of ethanol corn beyond pollinating distance of food corn.
- **Human error**
A system involving thousands of growers, farm workers, and processing-plant employees growing millions of acres of GE ethanol corn and handling billions of bushels of corn kernels—all visually indistinguishable from corn destined for the food supply—will suffer countless instances of human error each year. Examples include inadvertently delivering ethanol corn to food grain elevators, accidentally planting ethanol corn seed in a food-corn field, accidentally spilling ethanol corn where it could show up the next year as volunteers in food corn or soybean crops.
- **Multiple points of vulnerability to contamination**
A 2004 UCS report prepared by six agricultural experts identified numerous points in the corn production system—from breeding through cultivation, handling, and processing—where GE industrial and drug-producing crops could contaminate the food supply.⁶⁵
- **Lack of government oversight or penalties for failure**
U.S. consumers will be dependent on *voluntary* actions by Syngenta, growers, and ethanol plant operators to protect the food supply.

Because people have never been exposed to the new protein or the organisms from which they originated in either food or the environment, the presence of the alpha-amylase in food products will raise new risk issues. First, the enzyme is produced from a chimeric transgene cobbled together from selected pieces of DNA from three donor microorganisms, about which scientists know little. Second, as noted above, the donor microorganisms are members of a group of recently discovered hyperthermophilic (extreme heat-loving) organisms so different from bacteria and eukaryotes that they have been placed in a new domain Archaea. Third, scientists have only recently begun to investigate the special properties of proteins from hyperthermophilic microbes that allow them to function under extremely high temperatures.⁶⁶ The EA did not consider the implications for allergenicity of these special properties.

B. The EA does not address potential economic impacts of widespread cultivation of GE ethanol corn.

The virtually assured contamination of the food supply with GE-ethanol corn will have economic implications, which APHIS failed to address. Under NEPA, the effects on the human environment that an agency must consider “include ecological . . . , aesthetic, historic, cultural, *economic*, social, or health, whether direct, indirect, or cumulative”(emphasis added).⁶⁷

⁶⁵ D. Andow, et al. 2004. *A Growing Concern: Protecting the Food Supply in an Era of Pharmaceutical and Industrial Crops*. Cambridge, Mass.: Union of Concerned Scientists. Online at www.ucsusa.org/assets/documents/food_and_agriculture/pharma_fullreport.pdf.

⁶⁶ S. Kumar and R. Nussinov. 2001. How Do Thermophilic Proteins Deal with Heat? *Cellular and Molecular Life Sciences* 58:1216-33.

⁶⁷ 40 CFR 1508.8.

Below we briefly discuss three of the potential economic impacts APHIS should have addressed in the draft EA. First, the detection of GE ethanol corn in exports to countries where the variety has not yet been approved has the potential to cause substantial losses to exporters, growers, and others in the corn supply chain, as illustrated, for example, by the impacts on growers and exporters of GE contaminants in rice in recent years.⁶⁸

Second, the corn refining industry has raised serious concerns about the impact of heat-stable alpha-amylases on the products of the wet milling industry.⁶⁹ These concerns were also acknowledged by the Food Standards Australia New Zealand (FSANZ) in its review of GE ethanol corn:

[T]he presence of corn containing a thermostable α -amylase may, in certain circumstances, affect the shelf life and quality of some finished food products. ... Should conditions be suitable for the [GE ethanol corn] α -amylase enzymes to act on the starch in a food, then these enzymes would change the final food's nutritional profile to one that contains a greater proportion of dextrins, disaccharides and monosaccharides. ... Such a change could be noticeable by consumers, through changes to the taste and texture of the final food.⁷⁰

New Zealand authorities did not approve the GE crop for planting but only for unintentional food and feed uses.

Third, finding the new variety in domestic food products—and in light of the grossly insufficient confinement measures proposed by Syngenta, it almost certainly will be found—could be costly to food companies and processors. The discovery of contaminating substances can cause enormous disruptions and costly remedies throughout the food chain, as demonstrated by the StarLink incident in 2000.⁷¹ The fact that the amylase was subject to a voluntary safety consultation at FDA will do little to reassure consumers who do not want industrial chemicals in their food.

C. APHIS failed to fully comply with a NEPA requirement to address alternatives.

APHIS partly fulfilled the NEPA requirement for an alternatives assessment. The EA compared the impacts of the use of GE ethanol corn, if it were deregulated, with the current use of microbial alpha-amylases in a number of areas.⁷² Based on Syngenta's economic analysis,⁷³ the agency concluded that replacing exogenous microbial alpha-amylases with the Syngenta product would reduce the costs and increase the efficiency of ethanol production. (The agency provided no independent economic analysis.)

The EA failed to examine other alternatives to GE ethanol corn besides exogenous, thermostable microbial enzymes. The agency should have evaluated other enzymes that may offer benefits well beyond those of GE ethanol corn. For example, ethanol producers are using two products—Stargen and BPX—which, according to the companies that market them, significantly shorten the production process by

⁶⁸ See, for example, D. Bennett. 2007. GM rice—proposed class action. *Delta Farm Press*, May 28. Online at <http://deltafarmpress.com/news/070528-class-action/index.html>.

⁶⁹ CRA. 2009. Comments.

⁷⁰ Food Standards Australia New Zealand (FSANZ). Explanatory Statement—Application A580—Food Derived from Amylase-Modified Corn, p. 11. Online at [http://fedlaw.gov.au/ComLaw/Legislation/LegislativeInstrument1.nsf/0/4B319CBFE94B75F9CA25740A000CA781/\\$file/A580GMcornES.pdf](http://fedlaw.gov.au/ComLaw/Legislation/LegislativeInstrument1.nsf/0/4B319CBFE94B75F9CA25740A000CA781/$file/A580GMcornES.pdf).

⁷¹ The costs of the StarLink incident ran into the hundreds of millions of dollars. (B. Lambrecht. 2001. *Dinner at the New Gene Café*. New York: St. Martin's Press, pp. 52-55.)

⁷² EA, pp. 20-47.

⁷³ EA, Appendix C, pp. 72-112.

eliminating the high-temperature liquefaction stage as well as the saccharification stage.⁷⁴ These products, which are commercially available, may offer significant advantages over both the standard exogenous alpha-amylases and Syngenta's product.

III. APHIS should ban the outdoor use of GE pharmaceutical and industrial food crops, including Syngenta's GE ethanol corn.

As discussed above, we believe that APHIS should delay Syngenta's petition for nonregulated status and consider the application under rules it is now developing under the Plant Protection Act.

We have urged that that rule establish a ban on the outdoor production of food crops genetically engineered for pharmaceutical and industrial purposes.⁷⁵ Without such a ban, the public can expect that the GE ethanol corn and other such crops, not intended for food products, will contaminate the food supply with drugs, plastics, and other industrial chemicals, many of which may be harmful to people.

Since the early 1990s, APHIS has allowed field testing of a number of crops—mostly food crops—genetically engineered to produce compounds not intended for food uses but for pharmaceutical and industrial purposes. Some examples include insulin, blood thinners, contraceptives, lubricating oils, paper-degrading enzymes, and plastics. So far, no drugs from GE crops have been approved by FDA. A few chemicals from industrial food crops have been commercialized for small-scale industrial uses (primarily for research purposes).

Most pharmaceutical and industrial varieties of food crops, like the GE ethanol corn, will be grown in close proximity to crops intended for the food supply and are visually indistinguishable from them. As a result, for a number of reasons given below and explained in more detail in a UCS report, *A Growing Concern: Protecting the Food Supply in an Era of Pharmaceutical and Industrial Crops*,⁷⁶ drugs and industrial chemicals from engineered food crops are likely to end up contaminating the food supply, even though they were never intended for human consumption.

A decision to deregulate ethanol corn would set an important precedent—allowing the commercialization of the first GE industrial crop for biofuel production and the first GE drug or industrial crop grown on an enormous scale—up to millions of acres each year. These millions of acres of ethanol corn would be grown alongside the millions of acres of corn intended for the food and feed supply and would certainly contaminate the corn destined for food markets. The precedent could open the doors to a flood of new, potentially dangerous non-food uses of GE food crops.

A ban on the outdoor use of GE food crops would not mean the death knell for the use of genetic engineering in the production of drugs or industrial chemicals. Proven approaches that would not threaten the food supply abound—engineered non-food crops used outdoors, GE food crops grown in confined greenhouses, and indoor fermentation systems employing GE microbes.⁷⁷ A ban would hasten the transition to these safer alternative production methods.

⁷⁴ J. Williams. 2006. Break It Down Now. *Ethanol Producer Magazine*, January. Online at www.ethanolproducer.com/article.jsp?article_id=319&q=&page=all.

⁷⁵ For more detail on UCS's argument in favor of a ban, see UCS. 2006. Position Paper: Pharmaceutical and Industrial Crops, October. Online at www.ucsusa.org/assets/documents/food_and_agriculture/ucs-position-pharma-and-industrial-crops.pdf.

⁷⁶ D. Andow, et al. 2004. *A Growing Concern*.

⁷⁷ See, for example, UCS. 2008. Sensible pharmaceutical production: safer, smarter alternatives to 'pharma' food crops grown outdoors. Online at www.ucsusa.org/food_and_agriculture/solutions/sensible_pharma_crops/sensible-pharma.

SUMMARY/CONCLUSIONS

The draft EA has not provided the data and analysis needed to support a conclusion that GE ethanol corn will not have a significant impact on the human environment. An EIS is needed for rigorous analysis to evaluate the possibility of allergenicity, determine likely exposure, describe and evaluate economic consequences, and explore alternatives. The GE ethanol corn variety should not be granted deregulatory status until that is done.

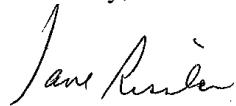
Also, in our view, with commercially feasible alternatives available, there is no need to adopt a product like Syngenta's GE ethanol corn that threatens a major industry like corn refining.

Finally, APHIS's jurisdictional discussion in the June FR notice exposes the legal defects in the PPA authority and points to the need for the agency to ground the regulation of GE crops and other organisms on sounder legal authority. The agency should not rely on a defective legal authority when a stronger option will soon be available.

Rather, APHIS should defer action on the GE ethanol corn and reconsider it under the rule currently being drafted under the Plant Protection Act. If it does go ahead under the PPA authority, APHIS should withdraw its new interpretation of jurisdiction over GE plants and return to the interpretation it has used since 1987.

Thank you for considering our comments.

Sincerely,



Jane Rissler, Ph.D.
Senior Scientist/Deputy Director, Food and Environment Program



Margaret Mellon, Ph.D., J.D.
Director, Food and Environment Program

APPENDIX: PEPSIN RESISTANCE TEST DETAILS

Source: Food and Agriculture Organization/World Health Organization (FAO/WHO). 2001. Evaluation of Allergenicity of Genetically Modified Foods. Report of a Joint FAO/WHO Expert Consultation on Allergenicity of Foods Derived from Biotechnology, January 22-25, Section 6.4, p. 13. Online at <ftp://ftp.fao.org/es/esn/food/allergygm.pdf>.

6.4. Pepsin Resistance

Purified or enriched expressed protein (non-heated and non-processed) should be subjected to pepsin degradation conditions using Standard Operating Procedures and Good Laboratory Practices (SOP/GLP). In addition, the expressed protein should be assessed in its principal edible form under identical pepsin degradation conditions to those used to examine the expressed protein. Both known non-allergenic (soybean lipoxygenase, potato acid phosphatase or equivalent) and allergenic (milk beta lactoglobulin, soybean trypsin inhibitor or equivalent) food proteins should be included as comparators to determine the relative degree of the expressed proteins pepsin resistance.

The protein concentrations should be assessed using a colorimetric assay (e.g., Bicinchoninic acid assay (BCA), Bradford Protein Assay, or equivalent protein assay) with bovine serum albumin (BSA) as a standard. Pepsin proteolytic activity should be assessed (Ryle). Enzyme/protein mixtures should be prepared using 500 µg of protein in 200 µL of 0.32% pepsin (w/v) in 30 mM/L NaCl, pH 2.0, and maintained in a shaking 37 C water bath for 60 minutes. Individual 500 microgram aliquots of pepsin/protein solution should be exposed for periods of 0, 15, 30 seconds and 1, 2, 4, 8, 15, and 60 minutes, at which time each aliquot should be neutralised with an appropriate buffer.

Neutralised protein solutions should be mixed with SDS-PAGE sample loading buffer with and without reducing agent (DTT or 2-ME) and heated for 5 minutes at 90°C. Samples containing 5µg/cm gel of protein should be evaluated using 10-20% gradient Tricine SDS-PAGE gels or equivalent gel system under both non-reducing and reducing electrophoretic conditions. Protein in the gels should be visualised by silver or colloidal gold staining procedures.

Evidence of intact expressed protein and/or intact fragments greater than 3.5 kDa would suggest a potential allergenic protein. Evidence of protein fragments less than 3.5 kDa would not necessarily raise issues of protein allergenicity and the data should be taken into consideration with other decision tree criteria.

For detection of expressed protein in an edible food source, a polyclonal IgG immunoblot analysis should be performed according to the laboratory procedures. The immunoblot analysis should be compared to the silver or colloidal gold stained SDS-PAGE gel and reflect the stained pattern of the expressed protein run under identical conditions.

The investigator should be aware of and consider the following precautions. Edible food sources may contain protease inhibitors or other substances that may promote or reduce protein degradation. Resulting fragments may not be reactive with the polyclonal IgG antibody source.

Finally, there is no absolute certainty that pepsin resistance or complete degradation of a protein will predict the allergenicity of novel proteins and must be taken into consideration with other decision tree criteria. Although the present pepsin resistance protocol is strongly recommended, it is recognized that other enzyme susceptibility protocols exist. Alternative protocols may be used for which adequate justification is provided. The producer is expected to take these results into consideration in combination with other decision tree criteria.

