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January 19, 2009

Regulatory Analysis and Development
USDA APHIS PPD
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Submitted via Federal eRulemaking Portal: Docket No. APHIS-2007-0016

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

UCS is submitting these comments in response to a November 19, 2008, *Federal Register* notice[1] announcing the availability of an environmental assessment (EA) and preliminary APHIS decision to grant nonregulated status to Syngenta's genetically engineered (GE) Event 3272 corn (hereinafter "GE ethanol corn"). After receiving comments on the EA and preliminary decision, the agency will decide whether to deregulate the new GE ethanol corn. 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.[2]

Environmental assessment: APHIS's findings

Before GE ethanol corn can be granted nonregulated status, APHIS must satisfy requirements established under the federal Plant Pest Act (PPA)[3] and the National Environmental Policy Act (NEPA).[4] The EA's

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[1] 73 Fed. Reg. 69602-04.
[2] 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.
[3] 7 CFR 340.6. The Plant Pest Act was supplanted by 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).
[4] 40 CFR Parts 1500-1508.

analysis of Syngenta's request for deregulation is intended to support the agency's determination of whether nonregulated status should be granted under APHIS's PPA regulations and whether a full environmental impact statement (EIS) is required under NEPA.

Under the PPA 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 and ii) that the deregulated variety will have no significant impact on the environment. Once it has received and considered public comments, the agency will determine whether an EIS is necessary before deciding whether to grant nonregulated status.[5]

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."[6] In other words, the agency's preliminary decision, upon which it is seeking public comment, is to deregulate the GE ethanol corn.

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,[7] animal and plant communities and biodiversity,[8] and threatened or endangered species.[9]

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 the corn 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.

Specifically, 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.[10] 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.[11] The use of GE ethanol corn containing 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 Archaean

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[5] EA, p. 9.
[6] EA, p. 20.
[7] EA, p. 35.
[8] EA, p. 44.
[9] EA, p. 50.
[10] 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.
[11] 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,[12] which typically live in extremely hot waters. Archaeans[13] 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 specific promoter ensures that most of the novel alpha-amylase is expressed in the corn kernel, where it is found at high levels, ranging up to 0.2 % of fresh weight.[14]

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,[15] 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.[16] From 2002 to 2005, the agency acknowledged[17] 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.[18]

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. That request is the subject of these comments.

FDA
Companies engineering food crops for human consumption typically volunteer to consult with the Food and Drug Administration (FDA) on food safety issues under the agency's 1992 policy on GE foods.[19] Even though GE ethanol corn is not intended for human consumption, Syngenta apparently recognizes that it will be impossible to prevent contamination of the food supply with its industrial corn. The

[12] 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.
[13] 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)
[14] Petition, pp. 43-44.
[15] The highest measurement is 8.5 µg/g fresh weight in pollen. Petition, pp. 43, 45.
[16] Field testing at 7 CFR 340.3 and 4; commercialization at 7 CFR 340.6.
[17] 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.
[18] 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.
[19] 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.

company has voluntarily consulted with the FDA on food safety risks posed by the new variety, completing the process in August 2007.[20]

Regulatory history—abroad[21]

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 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.

SUMMARY OF UCS CONCLUSIONS/RECOMMENDATIONS

UCS urges APHIS to ban the outdoor production of GE ethanol corn and other food crops genetically engineered to produce pharmaceutical and industrial substances. Absent a ban, drugs and industrial chemicals, including GE ethanol corn—products never intended for human consumption—will contaminate the food supply.

If it rejects a ban, the agency should fully comply with NEPA by revising the draft EA or preparing an EIS that details the significant 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 allay 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 corn exporters and growers if the variety were to contaminate shipments to 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.

Finally, UCS recommends that APHIS delay action on this precedent-setting application until after Obama-appointed officials are in place and have had an opportunity to review federal oversight of GE crops.

Our detailed comments follow below.

UCS COMMENTS

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

APHIS should deny Syngenta's petition for nonregulated status and implement a ban on the outdoor production of food crops genetically engineered for pharmaceutical and industrial purposes.[22] Without

[20] 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.

[21] EA, pp. 7-8.

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 1990's, 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 are 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*, [23] 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.

Recognizing that these crops, as a class, pose greater risks than most other GE crops, APHIS for years has regulated them more stringently.[24] UCS urges APHIS to step in now—while the industry is in an early stage of development and economic repercussions would be relatively minor—and institute a ban to fully protect the food supply from contamination by drugs and industrial chemicals. This needs to be done immediately before potentially hundreds of engineered food crops—producing any number of pharmaceuticals and industrial chemicals—are grown on millions of acres each year amidst the corn, soybeans, and other crops destined to feed people.

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.[25] A ban would hasten the transition to these safer alternative production methods.

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[22] 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.

[23] 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.

[24] USDA APHIS. 2008. Guidance for APHIS Permits for Field Testing or Movement of Organisms Intended for Pharmaceutical or Industrial Use, July 9. Online at www.aphis.usda.gov/brs/pdf/Pharma_Guidance.pdf.

[25] 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.

II. If APHIS rejects a ban, the agency should fully comply with NEPA by preparing either a more detailed EA or 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.[26] When an EIS is not categorically required or excluded, the department 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.[27] 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 APHIS should prepare at least a new EA. Considering the precedent-setting nature of the application, we believe it is likely a new EA 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 conclude that the issue has not been resolved. Putting the allergenicity concern to rest is critical for two reasons. If 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 certain way to know 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.[28] If a new protein shares amino acid sequences or other biochemical characteristics with known allergens, it is considered to have allergenic potential.

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[26] 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).

[27] 40 CFR parts 1500-1508, 7 CFR part 372.

[28] 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/es/esn/food/allergygm.pdf.

1. ***Our analysis of APHIS's position leads us to conclude that the agency has not provided the data and analysis needed to allay concerns about the potential allergenicity of the novel alpha-amylase.***

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 consultation with FDA.[29]

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 Food and Agriculture Organization/World Health Organization (FAO/WHO) Expert Consultation on Allergenicity of Foods Derived from Biotechnology provides 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.[30]

Syngenta submitted information on the first two kinds of tests. However, for the digestibility assay, the company provided few details. In fact, the only information available on the pepsin resistance test is four sentences in the Syngenta petition[31] and three sentences in an FDA document.[32] The APHIS EA provides no additional information.

Without more detail on the pepsin resistance test, it is impossible to know if the data from the test are valid. Detailed information is critical because, according to Fu et al. (2002),[33]

> "the 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 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 ºC for 0, 1, 5, 10, 20 and 30 minutes."[34] 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.[35] The appendix to these comments contains an excerpt from the FAO/WHO Expert Consultation concerning the details appropriate for a pepsin resistance test.

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[29] EA, p. 35.

[30] 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.)

[31] Petition, p. 7, item 7 (3 sentences), p. 50, item 7 (1 sentence).

[32] FDA. 2007. Biotechnology Consultation. Note to the File, Section 4.3.1, paragraph 3.

[33] 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.

[34] Petition, p. 7, item 7.

[35] FAO/WHO. 2001. Pepsin resistance, Section 6.4, p. 13.

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 consultation with FDA

APHIS also offers the completed FDA consultation as evidence that the alpha-amylase is unlikely to be an allergenic protein.[36] However, because the consultation process is flawed in several respects, it does not allay concerns about allergenicity.

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.[37] 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 FDA 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 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).[38]

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).[39]

UCS concludes that neither the EA, Syngenta's petition, or the FDA consultation documents provide sufficient data, information, or analysis to allay concerns about allergenicity.

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

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[36] EA, p. 35.
[37] 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.
[38] FDA. 2007. Biotechnology Consultation. Note to the File
[39] FDA. 2007. Biotechnology Consultation: Agency Response Letter

the United States. APHIS would impose no geographic or management constraints.[40] 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.[41]

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,[42] 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.[43] 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:

- 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.

[40] EA, pp. 21-22.
[41] 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.
[42] EA, pp. 25-26 and Appendix G, pp. 138-139.
[43] EA, Appendix G, pp. 138-139.

- 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.[44]

- 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 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 we 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.[45] 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).[46]

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.[47]

Second, 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.[48] The fact that the amylase was subject to a voluntary safety

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[44] 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.

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

[46] 40 CFR 1508.8

[47] 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.

[48] 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.)

consultation at FDA will do little to reassure consumers who do not want industrial chemicals in their food.

Third, consumer reactions to altered shelf life and stability of certain food products may impact processors and retailers. The Food Standards Australia New Zealand (FSANZ) review of GE ethanol corn acknowledges the problem:

> "[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."[49]

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.[50] Based on Syngenta's economic analysis,[51] 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 enzymes that may go well beyond the putative benefits 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 eliminating the high-temperature liquefaction stage as well as the saccharification stage.[52] These products, which are commercially available, may offer significant advantages over both the standard exogenous alpha-amylases and Syngenta's product.

Summary/conclusion

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. A revised EA or an EIS is needed for rigorous analysis to exclude the possibility of allergenicity, determine likely exposure, detail economic consequences, and explore alternatives. The GE ethanol corn variety should not be granted deregulatory status until that is done.

Finally, in our view, with commercially feasible alternatives available, there is no need to adopt a risky product like Syngenta's GE ethanol corn, which may never deliver its promised benefits and is likely to contaminate the country's most valuable commodity crop, corn.

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[49] 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.

[50] EA, pp. 20-47.

[51] EA, Appendix C, pp. 72-112.

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

III. In any event, APHIS should delay its decision on this precedent-setting application until the Obama administration has had an opportunity to review APHIS's approach to the regulation of GE crops, and especially pharmaceutical and industrial crops.

As noted above, Syngenta's petition is the first for a food crop engineered for biofuel purposes. It should not be granted nonregulated status on its own merits, but more importantly should not be deregulated while the agency is considering a new regulatory scheme for GE crops, including a new policy for GE pharmaceutical and industrial crops.[53] Like many other decisions favoring industry over the public interest, this one is being pushed forward just as the Bush administration is leaving office. APHIS should not move ahead with a decision on Syngenta's product until newly appointed agency are in place and have an opportunity to put their own stamp on the direction of biotechnology regulation, including pharmaceutical and industrial crops. Under such a schedule, a decision on this important, precedent-setting application would be consistent with the Obama administration policy on GE crop oversight.

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

[53] APHIS issued a proposed rule for public comment in the *Federal Register* on October 9, 2008 (73 Fed. Reg. 60008-48).

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.