StarLink (Cry9C) Corn Factsheet

What is Cry9C corn?

Registered to AgrEvo (now Aventis CropScience) under the trade name of StarLink in 1998, Cry9C corn is the latest variety of Bt corn to be developed for commercial use. StarLink corn produces Cry9C protein, a plant pesticide for which there is no history of human dietary exposure. Because Cry9C has several properties characteristic of food allergens, it is presently not permitted in corn for human consumption, but rather only in feed corn. In April of 1999, AgrEvo petitioned the EPA to permit Cry9C “in or on all raw agricultural commodities” (i.e. for human consumption). The EPA has not yet ruled on this petition due to concern about Cry9C’s potential allergenicity.

How are Bt corn varieties such as StarLink regulated?

The EPA’s role:
The Cry endotoxins in Bt corn are regulated as “plant pesticides” by the EPA. The EPA is required by law to determine the maximum allowable levels of pesticide residues in or on foods – known as “food tolerances.” The Agency may also grant an exemption from the food tolerance requirement if it finds that there is a “reasonable certainty” that aggregate exposures to the residue will not cause harm. In the case of Cry9C protein, EPA granted an exemption limited to corn for animal feed, meat and other products derived from animals fed such feed, as well as corn for industrial uses.

The FDA’s role:
The FDA is charged with preventing adulterated foods (whether domestic or imported) from reaching the market. A food is considered adulterated if it contains a substance that may make the food injurious to human health, or if it contains unapproved additives or pesticides. Thus, a primary responsibility of the FDA is enforcing the food tolerances for pesticides (including plant pesticides such as Cry9C) set by the EPA. The FDA has the power to remove adulterated foods from the market and to impose sanctions on food producers.

At present, the FDA does not require premarket safety testing of the great majority of genetically engineered (GE) foods, regarding them as “substantially equivalent” to their natural precursors. In effect, biotech companies are put on the honor system as to whether they have done the proper safety assessments and testing. Although FDA policy calls for “particular attention” to potentially allergenic proteins introduced by genetic engineering1, an FDA spokesperson has disclaimed all responsibility for assessment of the allergenic potential of Cry9C, stating that EPA has “the regulatory responsibility and authority to evaluate food safety issues for crops such as Bt corn that are genetically engineered to express pesticidal traits (Cry9C)...”2 Thus, although the FDA does not have the authority to approve the use of Cry9C in food, it is required to enforce the safety standards set by the EPA for Cry9C.

Regulatory History of StarLink Corn

* Application for registration of StarLink corn filed by Plant Genetic Systems3 (PGS): 8/8/97
* PGS requests an exemption from the requirement of a tolerance for Cry9C residues “in or on all raw agricultural commodities” 9/19/97
* EPA grants a temporary exemption from the tolerance requirement for Cry9C residues, restricting it as follows: “only in corn used for feed; as well as in meat, poultry, milk or eggs resulting from animals fed such feed” 4/10/98
* StarLink corn approved for use as animal feed and for industrial uses 5/22/98
* AgrEvo resubmits petition to the EPA to expand exemption to cover Cry9C residues “in or on all raw agricultural commodities” 4/7/99
* Public comment period for input on expanding the exemption: 12/21/99 – 2/22/00
* Friends of the Earth and Genetically Engineered Food alert reveal that StarLink has contaminated the food supply 9/18/00
* Aventis cancels its registration of StarLink corn at the urging of the EPA (meaning that StarLink can no longer be planted for any agricultural purpose) 10/12/00
* AgrEvo requests time-limited exemption for StarLink in processed foods; EPA

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2 Letter from Rudaina Alrefai, Division of Product Policy, Office of Premarket Approval, Center for Food Safety and Applied Nutrition, FDA to Richard Caplan. August 1, 2000
3 PGS was taken over by AgrEvo; AgrEvo was then taken over by Aventis, the current registrant.
announces scientific review of new evidence (source: EPA press release) 10/30/00
* EPA releases Scientific Advisory Panel report noting that there is a medium likelihood that StarLink is an allergen. 12/05/00
* Federal Register notice concerning the April 2001 filing by Aventis of a petition to the EPA to establish a tolerance of 20 ppb of Cry9C in corn 6/20/01
* EPA announces that based on the Scientific Advisory Panel’s recommendations, “establishing a tolerance (legal residue limit) of StarLink in human food products is not currently supported.” 7/27/01

Background on Cry9C Protein

What is Cry9C protein?
Cry9C is one of a family of crystalline (Cry) proteins known as endotoxins that are produced by *Bacillus thuringiensis* (Bt), a naturally occurring soil bacterium. Of more than 60 known Cry proteins, the genes that express three of them (Cry1Ab, Cry1Ac, Cry9C) have been spliced into different varieties of corn to produce what is generically known as “Bt corn,” which then produces the respective Cry protein in its tissues. When certain moths, butterflies and beetles (such as the European corn borer and Monarch butterfly larva) eat corn tissue containing a Cry endotoxin, the substance disrupts their digestive systems and kills them. Cry9C protein is produced by the most recently developed variety of Bt corn, StarLink, which was registered to AgrEvo (now Aventis) in 1998 (see “Regulatory History”).

What makes Cry9C protein different than other Cry proteins?
* Unlike other Cry proteins, Cry9C is heat-stable and also resistant to degradation in gastric juices. These two properties are generally considered the most important indicators of potential allergenicity [See “Quote Sheet” below]

* There is no known history of human dietary exposure to the Cry9C protein. In contrast, people have been exposed to other Cry proteins for many years in the form of Bt sprays.

* In the other Bt corn varieties, the Cry protein is expressed primarily in the plant’s leaves and pollen. StarLink corn produces substantial levels of Cry9C in kernels and roots as well as leaves. In fact, the Cry9C concentration in corn kernels is 10 to over 400 times as high as that of the Cry proteins produced by other varieties of Bt corn.⁴

Why is Cry9C permitted in feed corn?
The EPA determined that consumption of the meat, eggs or milk from animals fed Cry9C corn would be unlikely to cause an allergic reaction because human dietary exposure to Cry9C via animal feed use is anticipated to be “minimal to nonexistent.” However, the EPA admits that “finite residues” of Cry9C could be present in meat, milk or eggs derived from animals fed Cry9C corn. The Agency does not appear to have conducted or be aware of any direct measurements of Cry9C in products derived from animals fed Cry9C corn.⁵

What is a food allergen and how does it elicit an allergic response?
Many food allergens are proteins that are fairly stable to digestion or only partially broken down. The protein or its fragments migrate across the intestinal wall and stimulate immune cells known as lymphocytes. Lymphocytes stimulate the production of the IgE antibodies that are specific for each allergen. Eventually, subsequent exposures to the allergen leads to release of biochemicals known as histamines and prostaglandins. These chemicals, in an effort to protect the body, cause the typical allergic symptoms of respiratory distress, running nose and stuffiness, swelling, and skin rashes.⁶ Occasionally, even minute quantities of food allergens can cause

⁴ Dr. Allan Felsot, “Insecticidal Genes: Part 2,” Agrichemical and Environmental News, No. 168, April 2000, Table 2, p. 4.
more serious reactions. “With peanut allergies, ingestion of nanogram [= one one-billionth of a gram] quantities can cause anaphylaxis.”

Quotes from the EPA and the Scientific Advisory Panel on the Potential Allergenicity of Cry9C

The EPA conducted a review of AgrEvo’s studies on StarLink corn and Cry9C, concluding that much of AgrEvo’s data are “…either inconclusive, or indicate that Cry9C exhibits some characteristics of known allergens.”

“… it is not possible for the Agency to determine that there is a lack of allergenic potential from Cry9C based upon the available information.”

The EPA then submitted the matter to its Scientific Advisory Panel (SAP) for further clarification of Cry9C’s potential allergenicity. Both the EPA and the SAP emphasize that food allergenicity is a poorly understood phenomenon. In particular, little is known of either the sensitization process by which people first acquire allergies, or how to predict whether a novel protein is or could become an allergen.

According to the SAP, the best indicators of allergens are precisely those properties possessed by Cry9C: “When considering characteristics of food allergen proteins, the best available criteria presently known are: 1) heat stability and 2) resistance to digestion.” Though far from perfect, “…these properties can be used as screening tools…”

Other indicators of potential allergenicity are less reliable:

1) The EPA criticized AgrEvo’s rat study purporting to show that Cry9C is not allergenic: “The brown Norway rat model is not a validated test for food allergy at this point and the study submitted is significantly flawed…”

2) Comparison of the suspected allergen’s structure or function to known allergens is of little use: “In the hundreds of allergens characterized, there does not appear to be a biochemical property or amino acid sequence motif in these proteins that will prove helpful in determining the potential allergenicity of a novel protein.”

The SAP concludes that: “…well designed scientific studies are not available to critically assess Cry9C as a potential food allergen.”

Meanwhile, food allergies are on the rise: “There is a conceived perception by the public and expressed in the medical literature that there is an increase in allergenicity to foods and food products…”

Consumption of food allergens can cause mild to serious reactions in sensitive individuals “…ranging from gastrointestinal upset to, rarely, anaphylactic shock.”

The EPA appears to support the labeling of food products that contain allergenic proteins. For those with food allergies: “…being able to identify and avoid the offending food is critical, including being able to identify the ingredients in processed food that may contain such ingredients.”

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9 SAP Report, p. 6.
12 SAP Report, p. 11.
14 Ibid., p. 12.