

BIOPESTICIDES REGISTRATION ACTION DOCUMENT
Preliminary Risks and Benefits Sections

***Bacillus thuringiensis* Plant-Pesticides**

U.S. Environmental Protection Agency
Office of Pesticide Programs
Biopesticides and Pollution Prevention Division

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I. Overview

A. Executive Summary

EPA has undertaken a comprehensive, preliminary reassessment of the time limited registrations for all *Bacillus thuringiensis* (*Bt*) corn and cotton plant-pesticides that will be reviewed for registration renewal in the fall of 2001. This reassessment has been designed to assure that the decisions on the renewal of the corn and cotton registrations are based on the most current health and ecological data (including recently reviewed non-target impact data) and incorporates recommendations made by the March 1995, February 1998, and December 1999 FIFRA Scientific Advisory Panel (SAP) and the findings of the 1999 National Academy of Sciences (NAS) report on *Genetically Modified Pest-Protected Plants*. The June 2000 SAP report has not yet been received, but will be considered when this assessment is finalized. Also included in this assessment is the data that supports the registration of the NatureMark *Bt* potato as well as data developed in support of a number of plant-pesticides that are no longer produced or will not be seeking registration renewal. In the interest of assuring a truly comprehensive review, it is EPA's intention to present and assess the full range of data and information available.

The complete reassessment document is fashioned after the Agency's traditional Reregistration Eligibility Document (RED). This format was selected to present the data and findings in a format that is familiar to the registrants, the users and the general public. The *Bt* Plant-Pesticides Biopesticides Registration Action Document (BRAD) Preliminary Risk and Benefits Sections document has five major sections:

1. Product Characterization
2. Human Health Assessment
3. Ecological Assessment
4. Insect Resistance Management
5. Benefits.

The Executive Summary includes one additional section, Other Considerations.

1. Product Characterization:

The characterization data provided by the registrants continue to provide adequate product information to guide subsequent risk assessment. Product characterization is critical to understanding the way in which the registered products were created and the unique characteristics that need to be individually assessed for each *B. t.* plant-pesticide. This section provides information on the specific transformation systems that were used for each product, the characterization of the DNA insert, the inheritance and stability characteristics of the product line, and the protein characterization and levels of *Bt* protein expression for the various plant tissues. Specific information and data for each of the registrations seeking renewal are included in tabular and descriptive formats.

2. Human Health Assessment

The assessment confirms EPA's original findings that there are no unreasonable adverse effects from these products. The human health assessment for the *Bt* plant-pesticides draws heavily on the science and toxicology of proteins. All *Bt* plant-pesticides are proteins and for the majority of proteins currently registered, the source bacterium has been a registered microbial pesticide which has been approved for use on food crops without specific restrictions. The *Bt* proteins approved for use in food are expected to behave as would be expected of a dietary protein. The microbial pesticides have a long history of safe use without adverse health or environmental effects. Several types of data are required for the *Bt* plant-pesticides in order for the Agency to make the "reasonable certainty of no harm finding." The data are evaluated in order to determine that (1) the protein behaves as would be expected of a dietary protein breaking down rapidly in digestive fluids; (2) the protein is not structurally related to any known food allergen or protein toxin; and (3) the protein does not display any oral toxicity when administered at high doses. In this section of the assessment, product specific data are addressed for each of the following areas: in vitro digestion assay, heat stability and amino acid sequence homology comparisons, and acute oral toxicity, including mutagenicity and developmental toxicity, subchronic toxicity and chronic exposure and oncogenicity. Product specific information is also addressed for immune system effects, endocrine effects, dose response and dietary risk characterizations. The rationale is presented for why any dietary protein, including the *Bt* proteins, would not be expected to raise concerns for subchronic and chronic effects such as mutagenicity, oncogenicity and developmental toxicity. A discussion of immune system effects, endocrine effects and dietary and non-dietary risk characterization is included for each product as would be found in any assessment for a pesticide chemical's food tolerance determination since implementation of the FQPA amendments to the FFDCFA.

3. Ecological Assessment

Gene flow to wild species through outcrossing is not a concern for any of the registered *Bt* plant-pesticides. Considering all of the information available, the weight of evidence indicates no unreasonable adverse effects of *Bt* Cry proteins expressed in plants to non-target wildlife, plants or beneficial invertebrates. EPA is, however, continuing to review and participate in research and review of the pertinent scientific literature for the purpose of continually refining the Agency's ecological risk assessment of the *Bt* crop registrations. In the event that any data indicate unexpected long range population, community or ecosystem effects, the Agency will take immediate and appropriate action.

The ecological assessment section of this document focuses heavily on evaluating the impacts of *Bt* plant-pesticides on non-target species. EPA recognizes that there has been considerable public concern about the potential for these products to have significant and unintended consequences for non-target species such as the monarch butterfly. This assessment relies not only on the original data developed in support of the *Bt* registrations, but additionally, on data recently developed and

submitted to EPA under a Data Call-In (DCI) requirement and recently published literature. Specific data is cited for concerns related to gene outcrossing and weediness, fate in soils and potential indirect effects on soil biota, direct effects on non-target species including mammals, avian and aquatic species, insects, lepidoptera, and endangered species.

4. Insect Resistance Management

Available data indicate that after five years of commercialization, no reported insect resistance has occurred to the *Bt* toxins expressed either in *Bt* potato, *Bt* corn, or *Bt* cotton products. The Agency believes that the existing IRM plan for *Bt* potato is adequate to mitigate Colorado potato beetle resistance. The existing IRM plan for *Bt* corn (strengthened for the 2000 growing season) is adequate to mitigate European corn borer resistance in areas infrequently using insecticides, but may need improvements to mitigate corn earworm and other stalk-boring pests. The existing IRM plan for *Bt* cotton (already strengthened for the 2001 growing season) may need improvements in refuge size and deployment to mitigate tobacco budworm, cotton bollworm, and pink bollworm resistance.

Bt insect resistance management (IRM) is key to assuring that the target pests do not build up an immunity or resistance to the individual plant-pesticides. An IRM plan grounded in sound and current science will prolong the utility of the *Bt* pesticides and will guard against unintended consequences such as those discussed in the ecological assessment. EPA has identified seven elements that are critical to a solid IRM plan. These include (1) knowledge of pest biology and ecology, (2) appropriate dose expression strategy, (3) appropriate refuge, (4) resistance monitoring and remedial action plan should resistance occur, (5) employment of integrated pest management (IPM), (6) communication and education strategies on use of the product, and (7) development of alternative modes of action. This section of the reassessment presents and evaluates the existing IRM requirements for each product and presents alternatives that may extend the life of this technology.

5. Benefits

EPA believes that significant benefits accrue to growers, the public, and the environment from the availability and use of certain *Bt* plant-pesticides. Direct benefits to growers for *Bt* corn, cotton, and potatoes has likely exceeded \$100 million in 1999. Cotton had the highest per acre grower benefits and the largest reduction in conventional pesticide use. *Bt* corn increases yield over non-*Bt* corn when the insect pests reach damage levels. This section outlines how those benefits are defined and evaluated. Specific information on grower cost savings, increased yields, reduced conventional pesticide use, benefits to wildlife, etc. is presented by product.

6. Other Considerations

Earlier this summer, Novartis Seeds, Inc. and Mycogen Seeds c/oDow AgroSciences LLC came to the Agency indicating that as part of their business plans they would be phasing out their Event 176 corn products. Novartis Seeds and Mycogen Seeds c/o Dow AgroSciences LLC Event 176 Cry1Ab

corn registrations will expire on April 1, 2001 and on June 30, 2001, respectively. Existing stocks for these products must be used before or during the 2003 growing season. EPA has determined that allowing use of existing stocks for Event 176 *Bt* corn products through the 2003 growing season will not result in unreasonable adverse effects and the plant-pesticides will be gone from the environment long before resistance would have been predicted to develop. Both registrants will be required to comply with any increased IRM requirements that may result from this reassessment for any existing stocks.

B. *Bt* Corn Plant-Pesticides

1. Bt11, Cry1Ab, *Bt* Corn

OPP Chemical Code: 006444

Pesticide Name: *Bacillus thuringiensis* Cry1Ab Delta-Endotoxin and the Genetic Material Necessary for Its Production (Plasmid Vector pZ01502) in Corn

Trade and Other Names: Bt11, YieldGard®, Attribute™

Uses: Full Commercial Use in Field Corn and Sweet Corn

Registrants:

Novartis Seeds, Inc. -Field Crops - NAFTA
P.O. Box 12257
Research Triangle Park, NC 27709-2257

Novartis Seeds, Inc. - Vegetables - NAFTA
600 N. Armstrong Place
Boise, Idaho 83704

2. MON810, Cry1Ab *Bt* Corn

OPP Chemical Code: 006430

Pesticide Name: *Bacillus thuringiensis* Cry1Ab Delta-Endotoxin and the Genetic Material Necessary for Its Production in Corn

Trade and Other Names: MON 810, Yieldgard®

Uses: Full Commercial Use in Field Corn

Registrant: Monsanto Company
700 Chesterfield Parkway North
St. Louis, MO 63198

3. CBH351, Cry9C *Bt* Corn

OPP Chemical Code: 006466

Pesticide Name: *Bacillus thuringiensis* subspecies *tolworthi* Cry9C Protein and the Genetic Material Necessary for Its Production in Corn

Trade and Other Names: StarLink™

Uses: Full Commercial Use in Field Corn Grown for Feed or Industrial Uses Only (e.g., Ethanol Production)

Registrant: Aventis CropScience USA LP
2 T.W. Alexander Drive
Research Triangle Park, NC 27709

C. *Bt* Cotton Plant-Pesticides

Cry1Ac *Bt* Cotton

OPP Chemical Code: 006445

Pesticide Name: *Bacillus thuringiensis kurstaki* Delta-Endotoxin as Produced by the Cry1Ac Gene and Its Controlling Sequences as Expressed in Cotton.

Trade and Other Names: BollGard®

Uses: Full Commercial Use in Cotton with Geographic Limitations Due to Weedy Relatives

Target Pest(s): Cotton bollworm, tobacco budworm & pink bollworm

Registrant: Monsanto Company
700 Chesterfield Parkway North
Saint Louis, Missouri 63198

D. *Bt* Potato Plant-Pesticides

Cry3A *Bt* Potato

OPP Chemical Code: 006432

Pesticide Name: *Bacillus thuringiensis* Cry3A Delta-Endotoxin and the Genetic Material Necessary for its Production in Potato

Trade and Other Names: NewLeaf®

Uses: Full Commercial Use in Potatoes

Target Pest(s): Colorado Potato Beetle

Registrant: Monsanto Company
700 Chesterfield Parkway North
Saint Louis, Missouri 63198

E. *Bt* Plant-Pesticides Use, Registration Approval History, and Tolerance Listings

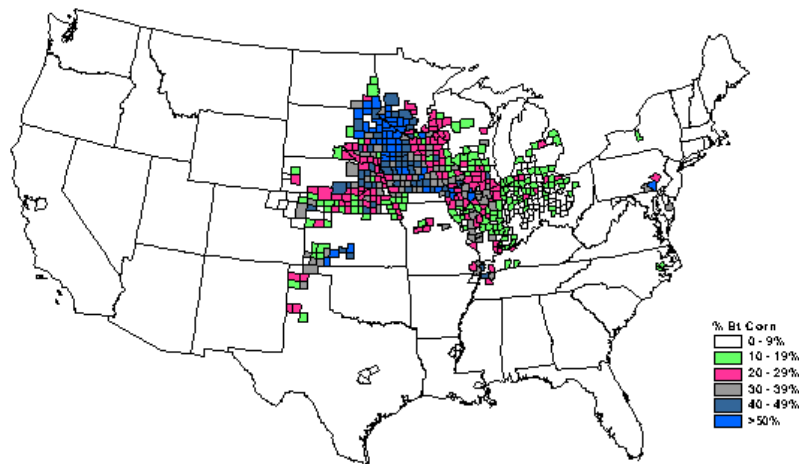
1. Use History

a) *Bt* Corn

EPA estimates adoption of *Bt* field corn was 0.4 million acres (1%) in 1996, 4.4 million acres (6%) in 1997, 14.5 million acres (18%) in 1998, and 19.8 million acres (26%) in 1999, the last year for which EPA has firm data.

The following map was provided to the Agency by the Agricultural Biotechnology Stewardship Technical Committee (2000), from data compiled by FSI, Inc.

Figure 1. U.S. Distribution of *Bt* Corn*



* Represents the percentage of total corn acreage planted to *Bt* corn hybrids in counties in which > 50,000 total acres of corn were planted. (Source: *Bt* corn industry sales data as compiled by FSI, Inc., 1999)

b) *Bt* Cotton

The Bollgard acreage and percent of cotton acreage planted to Bollgard (provided by Monsanto in its annual sales reports) from 1996-1999 is summarized on a state-by-state level below. The 1996-2000 Beltwide Cotton Insect Loss Reports produced by Mississippi State provide additional detailed use data and are found at <http://www.msstate.edu/Entomology/Cotton.html>.

Bollgard acreage in each state 1996-1999

State	Bollgard®Acreage			
	1996	1997	1998	1999
Alabama	348,810	251,784	306,535	398,683
Arizona	53,290	175,537	207,713	197,911
Arkansas	166,881	113,490	111,818	173,652
California	618	9,868	29,129	91,705
Florida	52,836	55,030	53,377	45,249
Georgia	375,744	533,340	508,842	693,288
Louisiana	157,411	202,080	244,616	382,839
Mississippi	443,986	410,333	506,149	746,163
Missouri	498	592	519	6,254
New Mexico	393	2,693	20,869	12,263
North Carolina	20,519	21,027	77,490	274,312
Oklahoma	11,772	7,103	11,459	69,545
South Carolina	53,864	91,891	71,894	176,149
Tennessee	10,833	17,431	57,649	390,245
Texas	98,819	186,654	276,520	458,694
Virginia	86	37	1,876	6,300
U.S. Total	1,796,390	2,078,890	2,486,493	3,585,437

c. *Bt* Potato

Although no specific reporting requirements were required as part of this registration in 1995, EPA recommended the continued development of a data base to monitor the use of the genetically modified potatoes and correlate possible resistant reports with the use sites. Based on three-year averages, about 1 million acres of fall potatoes are planted in the U.S. annually. According to information provided in Monsanto/NatureMark's annual status reports and meetings with the Agency, about 10,000 A (or 1% of the total) in 1996 and 25,000 A (or 2.5% of the total) in 1997 were planted in *Bt* potatoes (marketed as NewLeaf® Russet Burbank and NewLeaf® Superior and NewLeaf® Atlantic varieties) in the U.S.

Acreage information was gathered from 94 of 112 total customers in 1996. The proportion of NewLeaf® potatoes on these farms ranged from 0.1% to 69% of total potato acreage. Farm size ranged from less than 500 to 5000 acres. About 50,000 acres (<4%) of *Bt* potatoes were planted in 1998 and 1999. *Bt* potatoes were marketed as NewLeaf® Russet Burbank, Superior, Atlantic, and Shepody varieties.

2. Registration and New Use Approval History

In 1995, EPA approved the registration of the *Bt* potato, *Bt* corn, and *Bt* cotton products. Often a full commercial registration was preceded with what is called a "seed increase" registration which allowed for the product to be increased in quantity without full commercial release. Limited sales and use occurred in 1995. Five of the eleven products/uses (the Novartis Seeds' Event 176 Cry1Ab corn product has both field corn and popcorn uses) registered have been voluntarily cancelled or are being phased out. MON 801 was voluntarily cancelled in 1998. Dekalb Cry1Ac *Bt* corn is not being sold in the United States at this time and is undergoing voluntary cancellation. Novartis and Mycogen Seeds c/o Dow AgroSciences LLC have decided not to renew their Event 176 Cry1Ab corn registrations and these registrations will expire on April 1, 2001 and on June 30, 2001. Existing stocks for these products must be used before or during the 2003 growing season.

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Date	<i>Bt</i> Crop	Company	EPA Reg. No(s)
May 1995 - Seed Increase October 1995 - Full Commercial	Cry3A Potatoes	Monsanto	524-474
March 1995 - Seed Increase August 1995 - Full Commercial Note: Registrations Expire 4/1/01 and Will Not Be Extended	Event 176 Cry1Ab Field Corn	Novartis	66736-1
March 1995 - Seed Increase August 1995 - Full Commercial Note: Registrations Expire 6/30/01 and Will Not Be Extended	Event 176 Cry1Ab Field Corn	Mycogen Seeds c/o Dow AgroSciences LLC	68467-1
March 1998 - Full Commercial Note: Registration Expires 4/1/01 and Will Not Be Extended	Event 176 Cry1Ab Popcorn	Novartis	66736-1
March 1995 - Seed Increase May 1995 - Full Commercial	Cry1Ac Cotton	Monsanto	524-478
May 1996 - Seed Increase August 1996 - Full Commercial	Bt 11 Cry1Ab Field Corn	Novartis	67979-1
February 1998 - Full Commercial	Bt 11 Cry1Ab Sweet Corn	Novartis	65268-1
December 1996 - Full Commercial	MON810 Cry1Ab Corn	Monsanto	524-489
May 1996 - Seed Increase May 1998 - Voluntary Cancellation	MON 801 & MON 810 Cry1A(b) Corn	Monsanto	524-492
March 1997 - Full Commercial Note: Voluntary Cancellation Requested 4/18/2000 Pending FIFRA Section 6(f) Comment Period (Ends 12/11/2000)	Cry1Ac Corn	DeKalb/Monsanto	69575-2
May 1998 - Full Commercial for feed use only	Cry9C Corn	Aventis CropScience USA LP	264-669

3. Food Clearances/Tolerance Exemptions

The following tolerance exemptions allow the use of the listed plant-pesticides in food and/or feed. The Cry9C tolerance exemption is limited to corn used for feed only.

- a) *Bacillus thuringiensis* **Cry3A** delta-endotoxin and the genetic material necessary for its production are exempted from the requirement of a tolerance when used as a plant-pesticide in **potatoes**. [40 CFR 180.1147; 60 FR 21728, May 3, 1995]
- b) *Bacillus thuringiensis* **Cry1Ab** delta-endotoxin and the genetic material necessary for its production (plasmid vector pCIB4431) in corn is exempt from the requirement of a tolerance when used as a plant-pesticide in the raw agricultural commodities of **field corn, sweet corn, and popcorn**. [40 CFR 180.1152; 60 FR 42446, Aug 16, 1995]
- c) *Bacillus thuringiensis* subspecies *kurstaki* **Cry1Ac** delta-endotoxin and the genetic material necessary for its production in all plants are exempt from the requirement of a tolerance when used as plant-pesticides in **all plant raw agricultural commodities**. [40 CFR 180.1155; 62 FR 17722, Apr. 11, 1997]
- d) *Bacillus thuringiensis* **Cry1Ab** delta-endotoxin and the genetic material necessary for its production in all plants are exempt from the requirement of a tolerance when used as plant-pesticides in **all plant raw agricultural commodities**. [40 CFR 180.1173; 61 FR 40343, Aug 2, 1996]
- e) *Bacillus thuringiensis* subspecies *tolworthi* **Cry9C** protein and the genetic material necessary for its production in corn is exempted from the requirement of a tolerance for residues, only in **corn used for feed; as well as in meat, poultry, milk, or eggs resulting from animals fed such feed**. [40 CFR 180.1192; 63FR 28258, May 22, 1998]