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66736-1

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Page 1 of 8

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

MAR 17 1998

Mr. Richard Lotstein
Director, Regulatory and Government Affairs
Novartis Seeds, Inc. - Field Crops - NAFTA
P.O. Box 12257
Research Triangle Park, N.C. 27709-2257

Dear Mr. Lotstein:

Subject: Application to Amend Your Event 176 Bt Corn Registration to Allow Its
Additional Use in Popcorn
EPA Reg. No.: 66736-1

The amendment application referred to above, submitted in connection with registration under § 3(c)(7)(B) of the Federal Insecticide, Fungicide, and Rodenticide Act, as amended, is acceptable provided that you do the following terms and conditions.

- 1) Submit/cite all data required for registration of your product under FIFRA § 3(c)(5) when the Agency requires all registrants of similar products to submit such data.
- 2) Submit production information (80 kilogram units of seed produced) for this product (both popcorn and field corn) for each fiscal year in which this product is conditionally registered, in accordance with FIFRA § 29. The fiscal year begins October 1 and ends September 30. Production information will be submitted to the Agency no later than November 15, following the end of the preceding fiscal year. Submit this information to Owen Beeder, EPA/ OPP (7505C) ,401 M St., S.W. Wash., D.C. 20460.
- 3) This registration will automatically expire on midnight April 1, 2001. EPA will reevaluate the effectiveness of Novartis Seeds (Field Crops)'s resistance management plans before April 1, 2001 and decide whether to convert the registration to a non-expiring registration.
- 4) Novartis Seeds (Field Crops) will do the following regarding structured refugia:

a) For the popcorn use, Novartis Seeds (Field Crops) and/or its licensees will require popcorn growers to sign a ~~consultation~~ agreement that binds the grower to

SYMBOL	implement a structured refuge for insect resistance management when planting					
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Novartis Seeds' Event 176 Bt popcorn. The contract will state that popcorn growers who do not comply with this requirement will not be sold Event 176 Bt popcorn the following year;

b) For the popcorn use, the contractual agreement will state that popcorn growers must follow the recommendations for structured refuges presented in the NC 205 report prepared by the Research and Extension Entomologists of the North Central Regional Research Project (e.g., 20-30% of the corn acreage will be non-Bt corn, or in continuous corn areas where European corn borers are typically sprayed with insecticides, 40% of the corn acreage will be non-Bt corn; the refuge must be within 1/2 mile of the Bt popcorn fields). Specifically, the recommendations set forth in the NC-205 report will be followed (Ostlie, K.R., W.D. Hutchinson, and R.L. Hellmich, 1997. *Bt Corn and European Corn Borer*. NCR Publication 602);

c) For the popcorn use, the land that comprises the required refuge may consist of any non-Bt field corn or non-Bt popcorn acreage;

5) Novartis Seeds (Field Crops) will monitor for the development of resistance using baseline susceptibility data and/or a discriminating concentration assay when such an assay is available. Novartis seeds (field crops) will continue efforts to develop a discriminating concentration assay. Novartis seeds (field crops) will ensure that monitoring studies are conducted annually to determine the susceptibility of ECB populations to the CryIA(b) protein. Populations of ECB will be collected from representative distribution areas of the registrant's Event 176-derived hybrids, with particular focus on those areas of highest distribution. The results of such monitoring studies will be communicated to the Agency on an annual basis, by January 31 of the year following the population collections for a given growing season.

In addition, Novartis Seeds (Field Crops) will instruct their customers (growers and seed distributors) to contact Novartis Seeds (Field Crops) (e.g., via a toll-free customer service number) if incidents of unexpected levels of ECB damage occur. Novartis seeds (field crops) will investigate and identify the cause for this damage by local field sampling of plant tissue from their hybrids and sampling of ECB populations, followed by appropriate *in vitro* and *in planta* assays. Upon Novartis Seeds (Field Crops)'s confirmation by immunoassay that the plants contain CryIA(b) protein, bioassays will be conducted to determine whether the collected ECB population exhibits a resistant phenotype.

Until such time that a discriminating concentration assay is established and validated, Novartis seeds (field crops) will utilize the following to define a confirmed instance of ECB resistance:

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Progeny from the sampled ECB population will exhibit both of the following characteristics in bioassays initiated with neonates:

- a. An LC50 in a standard CryIA(b) diet bioassay that exceeds the upper limit of the 95% confidence interval of the mean historical LC50 for susceptible ECB populations, as established by the ongoing baseline monitoring program. The source of CryIA(b) crystal protein standard for this bioassay will be *Bacillus thuringiensis* subsp. *kurstaki* strain HD1-9.
- b. > 30% survival and > 25% leaf area damaged in a 5-day bioassay using CryIA(b)-positive leaf tissue under controlled laboratory conditions.

Based upon continued experience and research, this working definition of confirmed resistance may warrant further refinement. In the event that Novartis Seeds (Field Crops) find it appropriate to alter the criteria specified in the working definition, Novartis Seeds (Field Crops) must obtain Agency approval in establishing a more suitable definition.

6) Novartis Seeds (Field Crops) will report all instances of confirmed ECB resistance, as defined above, to the Agency within 30 days. Upon identification of a confirmed instance of ECB resistance Novartis Seeds (Field Crops) will take the following immediate mitigation measures:

- a. notify customers and extension agents in the affected area,
- b. recommend to customers and extension agents in the affected area the use of alternative control measures to reduce or control the local ECB population, and
- c. recommend to customers and extension agents in the affected area that crop residues be incorporated into the soil following harvest, to minimize the possibility of overwintering of ECB.

Within 90 days of a confirmed instance of ECB resistance, as defined above, Novartis seeds (field crops) will: (1) notify the Agency of the immediate mitigation measures that were implemented, and (2) submit to the Agency a proposed long-term resistance management action plan for the affected area, (3) work closely with the Agency in assuring that an appropriate long-term resistance management action plan for the affected area is implemented, (4) and implement an action plan that is approved by EPA and that consists of some or all the following elements:

a. Informing customers and extension agents in the affected area of ECB resistance,							
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- b. Increasing monitoring in the affected area, and ensuring that local ECB populations are sampled on an annual basis,
- c. Recommending alternative measures to reduce or control ECB populations in the affected area,
- d. Implementing a structured refuge strategy in the affected area based on the latest research results. The implementation of such a strategy will be coordinated by the Agency with other registrants.
- e. If the above elements are not effective in mitigating resistance, Novartis seeds (field crops) will voluntarily cease sale of all of Novartis seeds (field crops)' CryIA(b) corn in the county experiencing loss of product efficacy to this active ingredient and the bordering counties until an effective local management plan approved by EPA has been implemented. During the voluntary suspension period, Novartis Seeds (Field Crops) may sell and distribute in these counties only by obtaining EPA approval to study resistance management in those counties. The implementation of such a strategy will be coordinated by the Agency with other registrants.

If EPA agrees that an effective resistance management plan has been implemented which mitigates resistance, Novartis Seeds (Field Crops) can resume sales in the affected county(ies).

7) Novartis Seeds (Field Crops) will maintain a database to track its sales (units and location) of Event 176-derived corn (both field and popcorn) on a county-by-county basis, to the extent that such data are available. Novartis seeds (field crops) will provide annually sales data for each state indicating the number of units of Event 176-derived hybrids that it sells. This information will be provided by January 31 of the year following each growing season.

8) Novartis Seeds (Field Crops) will provide grower education. Novartis Seeds (Field Crops) will include an active partnership with such parties as: university extension entomologists and agronomists, consultants, and corn grower groups. Novartis Seeds (Field Crops) will implement a grower education program directed at increasing grower awareness of resistance management, in order to promote responsible product use. As specific resistance management recommendations are developed (e.g., as a result of ongoing research or experience) these will be incorporated, as appropriate, into the various grower communication and educational media. Novartis Seeds (Field Crops) will inform the Agency as they develop, implement, and refine their communication strategies. In addition to grower communication vehicles, Novartis Seeds (Field Crops) will also develop a Grower

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resistance management and integrated pest management.

9) Novartis Seeds (Field Crops) will develop a resistance management program that is acceptable to EPA and that includes the research specified in paragraph 9, a. through e., of this section. It will confer with EPA as it develops various aspects of that program and will submit annual progress reports to EPA including results and conclusions from research and the scientific literature as they become available in the research areas listed in paragraph 9, a. through e. of this section. Novartis Seeds (Field Crops) will conduct the research specified in paragraph 9, a. through e., and any other research that is included in the program that EPA accepts. Novartis Seeds (Field Crops) will use the research as a basis to develop a long-term resistance management strategy.

- a. ECB pest biology and behavior including adult movement and mating patterns, larval movement, survival on silks, kernels, and stalks, and overwintering survival and fecundity on non-corn hosts.
- b. The feasibility of "structured" refuge options for ECB including both "block" refugia, "50-50 early/late season patchwork", and other possibilities.
- c. Development of a discriminating concentration (diagnostic concentration) assay for field resistance (field screening) for ECB.
- d. Effects of corn producing the CryIA(b) δ -endotoxin on pests other than ECB, such as corn earworm; and the stalk borer complex.
- e. The biology of ECB resistance including receptor-mediated resistance and its potential effect on population fitness, as well as the effects on insect susceptibility to other Cry proteins.

If these conditions are not complied with, the registration will be subject to cancellation in accordance with FIFRA § 6(e). Your release for shipment constitutes acceptance of these conditions.

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A stamped copy of the label is enclosed for your records.

Sincerely,

Janet L. Andersen

Janet L. Andersen, Ph. D.
Director
Biopesticides and Pollution
Division (7511W)

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PESTICIDE ACTIVE INGREDIENT

Bacillus thuringiensis
European Corn Borer Control Protein

Pure form of the Plant Pesticide, *Bacillus thuringiensis* CryIA(b) delta-endotoxin protein as produced in corn cells.

Active Ingredient:

Bacillus thuringiensis CryIA(b) delta-endotoxin and the genetic material necessary for its production (pCIB4431 in corn) 0.0001 - 0.0018%*

Inert Ingredient:

A substance produced by a marker gene and its controlling sequences in corn ≤ 0.0009%*

*Percent of total plant protein on a dry weight basis

Keep Out of Reach of Children

CAUTION

EPA Reg. No. 66736-1

EPA Est. 66736-NC-001

Novartis Seeds, Inc. - Field Crops - NAFTA
3054 Cornwallis Road
P.O. Box 12257
Research Triangle Park, NC 27709-2257

ACCEPTED
with COMMENTS
In EPA Letter Dated
MAR 17 1998
Under the Federal Insecticide,
Fungicide, and Rodenticide Act
as amended, for the pesticide
registered under EPA Reg. No.
66736-1
66736-1

Directions for Use;

It is a violation of Federal law to use this in a manner inconsistent with its labeling. Keep out of lakes, ponds or streams. Do not contaminate water by cleaning of equipment or disposal of wastes.

Corn has been genetically modified to produce a *Bacillus thuringiensis* CryIA(b) delta-endotoxin protein for control of the European corn borer (*Ostrinia nubilalis*).

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Field Corn and Popcorn

All field corn and popcorn containing the plant-pesticide that is sold or distributed by Novartis Seeds, or a cooperator or licensee of Novartis Seeds, must be accompanied by informational material that contains the following:

- 1) "This hybrid [inbred] produces a *Bacillus thuringiensis* CryIA(b) protein that provides significant protection against European corn borer (*Ostrinia nubilalis*). Routine insecticide applications should not be necessary under typical conditions to prevent yield loss caused by first- and second-generation infestations of this pest. The CryIA(b) insecticidal protein, together with the genetic material necessary for its production in corn, is approved under EPA Reg. No. 66736-1."
- 2) "This hybrid [inbred] also produces a protein that increases its tolerance to the herbicide glufosinate ammonium. *Glufosinate ammonium is not recommended for use on this hybrid [inbred]*. If you plant a glufosinate-resistant crop in the next growing season, please note that volunteer plants from this corn hybrid [inbred] may not be controlled by a glufosinate ammonium herbicide."
- 3) Informational material accompanying hybrid field corn or popcorn seed sold for commercial plantings must also state: "Prior to planting this hybrid, carefully read this information and the Grower Guide for [brand name] ECB Protected Corn Hybrids [or ECB Protected Popcorn Hybrids]. The Guide includes instructions and recommendations regarding product use, insect resistance management and integrated pest management. If you have not received a copy or would like additional copies, please call (toll free) [telephone number]."

For popcorn only, the informational material must additionally state: "Note the requirement for planting a refuge of non-*Bt* corn, to equal at least 20 - 30% of the total corn acres where foliar insecticides are not applied for control of European corn borer (ECB), or at least 40% of the total corn acres where foliar insecticides are applied for ECB control. The refuge must be within one-half mile of the *Bt* popcorn."

The registration of this pesticide product for use in field corn and popcorn will automatically expire on midnight of April 1, 2001. After this registration has expired, no field corn or popcorn seed or plants that contain the pesticide product may be planted, grown or harvested.

* Among other things, the Grower Guide shall state that the level of insect protection can vary depending on environmental factors and seed purity.