1/24/97 PM 90 67979-1 P1/19

UNI. .D STATES ENVIRONMENTAL PROTEC\ .N AGENCY

JAN 24 1997

Dr. Rich Lotstein
Director of Regulatory Affairs
Novartis Seeds, Inc.
7500 Olson Memorial Hwy
Golden Valley, MN 55427

Dear Dr. Lotstein:

Subject: Application to Amend Your Full Commercial Use in Field Corn to Allow Limited Use in the South / Your Letter of 1/20/97
EPA Registration No. 67979-1

This registration is conditionally amended, to allow limited use in the South on 100,000 acres per anum where such acreage constitutes no more than 5% of the corn planted in any county that has more than 1000 acres of cotton, in accordance with FIFRA section 3(c)(7)(B) provided that you do the following terms and conditions.

1. Submit/cite all data required for registration of your product under FIFRA section 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 for the fiscal year in which the use of commercial field corn is conditionally registered, in accordance with FIFRA section 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.

3. This registration will automatically expire on midnight April 1, 2001. EPA will reevaluate the effectiveness of Novartis' resistance management plan before April 1, 2001, and decide whether to convert the registration to a non-expiring registration.

4. This registration is for field corn only.

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SYMBOL	7501W	7501W	7501W	7501W				
SURNAME	Mendelsohn	SOBIER	KOUGH	HUTTON				
DATE	1/23/97	1/23/97	1/23/97	1/28/97				

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*U.S. GPO: 1994-522-503/82085

5. Novartis will:

a. unless demonstrated to EPA's satisfaction that alternative resistance management practices are equally or more effective than a structured refugia, develop and submit to EPA a draft plan for "structured" refugia by 8/9/98 and a final plan by 1/31/99;

b. discuss the development and implementation of the plan and alternative resistance management practices with EPA throughout development and implementation; and

c. implement an EPA approved "structured" refugia plan or an EPA approved alternative resistance management plan no later than April 1, 2001.

6. Novartis will monitor for the development of resistance using baseline susceptibility data and/or a discriminating concentration assay when such an assay is available. Novartis will proceed with efforts to develop a discriminating concentration assay. Novartis will ensure that monitoring studies are conducted annually to determine the susceptibility of ECB and corn earworm (CEW) populations to the CryIA(b) protein. This resistance monitoring program will be developed to measure increased tolerance to *Bt* corn above the various regional baseline ranges.

Populations of ECB and CEW will be collected from representative distribution areas that contain Novartis' Bt corn plant-pesticide and monitored/screened for resistance, with particular focus on those areas of highest distribution. The results of 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 will instruct its customers (growers and seed distributors) to contact Novartis (e.g., via a toll-free customer service number) if incidents of unexpected levels of ECB and/or CEW damage occur. Novartis will investigate and identify the cause for this damage by local field sampling of plant tissue from corn hybrids that contain Novartis' Bt corn plant-pesticide and sampling of ECB & CEW populations, followed by appropriate *in vitro* and *in planta* assays. Upon Novartis' 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 by Novartis, Novartis will utilize the following to define a confirmed instance of ECB and/or CEW resistance:

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

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a. An LC_{50} in a standard CryIA(b) diet bioassay that exceeds the upper limit of the 95% confidence interval of the mean historical LC_{50} for susceptible ECB or CEW 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.

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 finds it appropriate to alter the criteria specified in the working definition, Novartis must obtain Agency approval in establishing a more suitable definition.

7. Novartis will report all instances of confirmed ECB & CEW resistance, as defined above, to the Agency within 30 days. Upon identification of a confirmed instance of ECB resistance Novartis 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 and/or CEW resistance, as defined above, Novartis 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, and (4) implement an action plan that is approved by EPA and that consists of some or all the following elements, as warranted:

a. Informing customers and extension agents in the affected area of ECB and/or CEW resistance,

b. Increasing monitoring in the affected area, and ensuring that local ECB or CEW populations are sampled on an annual basis,

c. Recommending alternative measures to reduce or control ECB or CEW 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 will voluntarily cease sale of all corn hybrids that contain Novartis' Bt corn plant-pesticide in the county experiencing loss of product efficacy and the bordering counties until an effective local management plan approved by EPA has been implemented. During the voluntary suspension period, Novartis 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 can resume sales in the affected county(ies).

8. Novartis will maintain a (confidential) database to track sales (units and location) of its Bt corn on a county-by-county basis. Novartis will provide annually, on a CBI basis, sales data for each state indicating the number of units of corn hybrids that contain Novartis' Bt corn plant-pesticide that were sold. As part of the overall sales report, Novartis will provide a listing of an estimate of the acreage planted with such states and counties with sales limitations detailed in item 11 of this letter. This information will be provided by January 31 of the year following each growing season.

9. Novartis will provide grower education. Novartis will agree to include an active partnership with such parties as: university extension entomologists and agronomists, consultants, and corn grower groups. Novartis 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 will inform the Agency as it develops, implements, and refines its communication strategies. In addition to grower communication vehicles, Novartis will also develop a Grower Guide consistent with the terms and conditions of this registration, to be distributed to all customers, that will include current information regarding resistance management and integrated pest management.

10. Novartis will develop a resistance management program that is acceptable to EPA and that includes the research and model development and testing specified in paragraph 10 a through f. Novartis will confer with the EPA as Novartis develops various aspects of its resistance management research program. Novartis agrees, as a condition of this registration, to submit

annually progress reports on or before January 31st each year on the following areas as a basis for developing a long-term resistance management strategy which include:

a. Novartis must submit by March 31, 1997, available research data on CEW relative to resistance development and Novartis' plans for producing resistance predictive models to cover regional management zones in the cotton belt based on *Helicoverpa zea* biology and cotton, corn, soybeans, and other host plants. These models must be field tested in the acreage allowed in item 11 of this letter and must be modified based on the field testing performed during the period of the conditional registration. EPA might modify the terms of the conditional registration based upon the field testing validation of the model and might require refugia in the future. EPA notes that there is some scientific work and even some models for H. zea on other crops in at least NC and TX that could be used for reference. EPA wants to be in close communication with Novartis as the model development and testing is ongoing. The requirement for development of resistance predictive models may be waived if Novartis provides the results of research that demonstrates resistance to CEW would have no significant impact on the efficacy of foliar Bt products and other Bt crops. Actual usage data of Btk on crops to control specific pests as well as successes and failures and field validated research would be necessary to support such a waiver request.

b. 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. A combination of a comprehensive literature review and research can fulfill this condition.

c. The feasibility of "structured" refuge options for ECB including both "block" refugia, "50-50 early/late season patchwork;" research needs to be done in both northern and southern areas on ECB as well as CEW.

d. Development of a discriminating concentration (diagnostic concentration) assay for field resistance (field screening) for ECB, CEW and other Lepidoptera pests of corn. Specific sampling locations will be established in each state to determine if increases in *Bt* toxin tolerance are occurring before crop failures develop. Increased tolerance levels need to be identified before field failure occurs. In monitoring for tunneling damage, the number of trivial tunnels may be less indicative of resistance development than the total extent of tunneling damage (e.g. length of tunnels). The extent of tunneling damage must be monitored as well as the number of tunnels.

e. Effects of corn producing the CryIA(b) delta endotoxin on pests other than ECB, including but not limited to CEW, fall armyworm, and the stalk borer complex.

f. 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. Possible high dose control exists for the first generation ECB in whorl stage, but not for later generation(s) on more mature corn plants. More data are needed on toxin expression in various parts of the plant at different stages plant development in regard to ECB, CEW and other secondary pests of corn (i.e. stalk borer complex, fall armyworm, and S.W. corn borer).

11. Novartis will ensure that in the combined states of Alabama, Arkansas, Georgia, Florida, Louisiana, North Carolina, Mississippi, South Carolina, Oklahoma (only the counties of Bryan, Caddo, Canadian, Garvin, and Grady), Tennessee (only the counties of Carroll, Chester, Crockett, Fayette, Franklin, Gibson, Hardeman, Hardin, Haywood, Henderson, Lake, Lauderdale, Lawrence, Lincoln, McNairy, Madison, Obion, Rutherford, Shelby, and Tipton), Texas, Virginia (only the counties of Greenville, Isle of Wright, Northampton, Southampton, Sussex, Suffolk) and Missouri (only the counties of Butler, Dunkin, Mississippi, New Madrid, Pemiscot, Scott, Stoddard) that the combined sale of this plant-pesticide in all the above states will not exceed the amounts required to plant 100,000 acres per anum. Further, Novartis will ensure that for the states and counties listed above that the amount sold will result in no more than 5% of the corn planted in any county with more than 1000 acres of cotton. Per item 8 of this letter Novartis will report all sales of this product by Novartis or its distributors annually to EPA no later than January 31st of the following year.

12. Collembola and *Daphnia magna* studies must be submitted by 5/14/97 for this active ingredient as already required in the seed increase registration and subsequent amendment dated 8/5/96.

13. Per your 1/20/97 letter, you will enforce the conditions of this registration among your customers via an electronic order allocation system. This system must provide the ability to restrict sales of *Bt*11 corn to a pre-determined quantity by county and track customer purchases by county and by Novartis Seeds assigned customer identity numbers.

14. Modify the draft label by replacing *"Bacillus thuringiensis* CryIA(b) delta-endotoxin and the genetic material necessary for its production" in the paragraph on page 2 beginning "All seed corn that contains..." with " *Bacillus thuringiensis* CryIA(b) delta-endotoxin and the genetic material (plasmid vector pZ01502) necessary for its production in corn."

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

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

Sincerely,

Janet L. Andersen, Director
Biopesticides and Pollution
Prevention Division (7501W)

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INSECT RESISTANT CORN

Bt Protein
Plant Pesticide Active Ingredient
for the Control of European Corn Borer in Corn

**(Pure form of the plant pesticide,
Bacillus thuringiensis subsp. *kurstaki* delta-endotoxin protein,
as expressed in corn cells)**

Active Ingredient:

Bacillus thuringiensis CryIA(b) delta-endotoxin and the genetic material (plasmid vector pZO1502) necessary for its production in corn	0.0002 - 0.0006% by seed weight

Inert Ingredient:

Substance produced by a marker gene and its controlling sequences in corn	< 0.0000001% by seed weight

Keep Out of the Reach of Children

CAUTION

Keep out of lakes, ponds or streams. Do not contaminate water by cleaning of equipment or disposal of wastes.

EPA Reg. No. 67979-1
EPA Est. No. 67979-IA-2

Novartis Seeds, Inc.
7500 Olson Memorial Highway
Golden Valley, MN 55427

ACCEPTED
with COMMENTS
In EPA Letter Dated
JAN 24 1997
Under the Federal Insecticide, Fungicide, and Rodenticide Act as amended, for the pesticide registered under EPA Reg. No. 67979-1

Directions for Use:

It is a violation of Federal law to use this product in a manner inconsistent with its labeling.

Novartis Seeds will ensure that in the combined states of Alabama, Arkansas, Florida, Georgia, Louisiana, North Carolina, Mississippi, South Carolina, Texas, Virginia (only the counties of Greensville, Isle of Wright, Northampton, Southampton, Sussex and Suffolk), Missouri (only the counties of Butler, Dunklin, Mississippi, New Madrid, Pemiscot, Scott and Stoddard), Oklahoma (only the counties of Bryan, Caddo, Canadian, Garvin and Grady) and Tennessee (only the counties of Carroll, Chester, Crockett, Fayette, Franklin, Gibson, Hardeman, Hardin, Haywood, Henderson, Lake, Lauderdale, Lawrence, Lincoln, McNairy, Madison, Obion, Rutherford, Shelby and Tipton), that the combined sale of corn seed containing this plant pesticide will not exceed the amounts required to plant 100,000 acres per annum. Further, Novartis Seeds will ensure that, for the states and counties listed above, the amounts sold will result in no more than 5% of the corn planted in any county having more than 1000 acres of cotton. Novartis Seeds will report all sales of this product by Novartis Seeds or its distributors annually to the EPA no later than January 31 of the following year.

Corn has been genetically modified to produce a *Bacillus thuringiensis* CryIA(b) delta-endotoxin protein for control of:

European corn borer	(*Ostrinia nubilalis*)

In addition, some control or suppression of the following corn pests can be provided:

Southwestern corn borer	*(Diatraea grandiosella)*
Corn earworm	*(Helicoverpa zea)*
Fall armyworm	*(Spodoptera frugiperda)*

All corn seed that contains the plant pesticide that is sold or distributed by Novartis Seeds or its distributors must be accompanied by informational material indicating the registration number (67979-1) and the active ingredient (*Bacillus thuringiensis* CryIA(b) delta-endotoxin and the genetic material necessary for its production), and stipulating that growers read the Grower Guide prior to planting the seed.

A Grower Guide must be distributed to all customers using seed containing the plant pesticide that will include instructions and recommendations regarding product use, insect resistance management, and integrated pest management.