

29964-3

05/18/2001

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U.S. ENVIRONMENTAL PROTECTION AGENCY
Office of Pesticide Programs
Biopesticides and Pollution Prevention Division (7511C)
1200 Pennsylvania Avenue NW
Washington, DC 20460

EPA Reg. Number:

29964-3

Date of Issuance:

MAY 18 2001

NOTICE OF PESTICIDE:

☒ Registration
☐ Reregistration

(under FIFRA, as amended)

Term of Issuance:

Conditional

Name of Pesticide Product:

Pioneer Brand Seed Corn with
Herculex I

Name and Address of Registrant (include ZIP Code):

Pioneer Hi-Bred International, Inc.
7250 NW 62nd Avenue
P.O. Box 552
Johnston, Iowa 50131-0552

Note: Changes in labeling differing in substance from that accepted in connection with this registration must be submitted to and accepted by the Biopesticides and Pollution Prevention Division prior to use of the label in commerce. In any correspondence on this product always refer to the above EPA registration number.

On the basis of information furnished by the registrant, the above named pesticide is hereby registered/reregistered under the Federal Insecticide, Fungicide and Rodenticide Act.

Registration is in no way to be construed as an endorsement or recommendation of this product by the Agency. In order to protect health and the environment, the Administrator, on his motion, may at any time suspend or cancel the registration of a pesticide in accordance with the Act. The acceptance of any name in connection with the registration of a product under this Act is not to be construed as giving the registrant a right to exclusive use of the name or to its use if it has been covered by others.

The registration application referred to above, submitted in connection with registration under § 3(c)(7)(C) 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 for this product to Mr. Owen Beeder of Registration Division (7505C) for the 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.
- 3) The subject registration will be limited to field corn originating from maize line 1507.

Signature of Approving Official:

(See second page for signature)

Date:

MAY 18 2001

4) The subject registration will automatically expire on midnight September 30, 2001. Prior to this date, EPA will determine whether to extend the expiration date, convert the registration to a non-expiring registration, or let the registration expire.

5) Several aspects of the Insect Resistance Management Plan will operate in synergy to promote grower compliance, however, the cornerstones of the compliance program must be the:

a) Grower Guides

Grower Guides and/or Product Use Guides must be submitted to the Agency at the time of distribution to growers. These Guides must be distributed to each seed customer and updated on an annual basis, as needed. The Guides provide complete information for growers regarding routine IRM practices that must be employed, and will be a primary educational and reference tool. Agreed-upon requirements and additional information that cannot be included in the Grower Guides for 2001 (e.g., because the requirements were enacted after printing and distribution of the Grower Guides) must be conveyed via supplemental communications to Pioneer Cry1F field corn seed customers.

b) Stewardship Agreement (grower agreement).

Each grower who purchases Pioneer Cry1F field corn seed must be required to sign a Stewardship Agreement, which will obligate the grower to follow the required IRM and non-target insect protection practices as specified in the Grower Guide/Product Use Guide and/or in supplements thereof.

c) A Strong and Multi-Pronged Grower Education Program.

A variety of methods must be employed to promote grower education and to continue to reinforce the need for adherence to all aspects of the IRM program.

d) Additional mechanisms must also be used to promote grower compliance, including:

Training of sales personnel, seed dealers and technical support staff. Coordination and reinforcement of IRM requirements through other organizations (e.g., NC-205, the Cooperative Extension Service, USDA, National Corn Growers Assn. (NCGA), American Crop Protection Assn., Biotechnology Industry Organization, crop consultants and other crop professionals).

6) Because a full understanding of the use of field corn near Karner blue butterfly habitats is currently under investigation, Pioneer Cry1F maize must not be sold in the following counties in 2001 where the Karner blue butterfly is known to exist in scattered populations: Illinois - Lake; Indiana - Porter and Lake; Michigan - Allegan, Lake, Monroe, Montcalm, Muskegon, Newaygo and Oceana; Minnesota - Anoka and Winona; New Hampshire - Merrimack; New York - Albany, Saratoga, Schenectady and Warren; Wisconsin - Adams, Barron, Burnett, Chippewa, Clark, Dunn, Eau Claire, Green Lake, Jackson, Juneau, Kenosha, Marquette, Menominee, Monroe, Oconto, Outagamie, Polk, Portage, Sauk, Shawano, Waupaca, Waushara, Wood. It must be stated in the Product Use Guide that Pioneer Cry1F corn will not be sold in these counties or distributed to anyone who will plant in these counties.

7) Stewardship Agreements/Grower Agreements will specify that growers must adhere to the refuge requirements as described in the Grower Guide/Product Use Guide and/or in supplements to the Grower Guide/Product Use Guide. Specifically, growers must plant a minimum structured refuge of at least 20% non-Bt corn. Insecticide treatments for control of European corn borer, corn earworm and/or

Southwestern corn borer may be applied only if economic thresholds are reached for one or more of these target pests. Economic thresholds will be determined using methods recommended by local or regional professionals (e.g., Extension Service agents, crop consultants). Instructions to growers will specify that microbial Bt insecticides must not be applied to non-Bt corn refuges.

8) For the 2001 growing season, grower agreements (Stewardship Agreements) for Pioneer Cry1F field corn grown in cotton-growing areas will specify that growers must adhere to the refuge requirements as described in the Grower Guide/Product Use Guide and/or in supplements to the Grower/Product Use Guide. Specifically, growers in these areas must plant a minimum structured refuge of 50% non-Bt corn. Cotton growing areas include the following States: 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 (except the counties of Carson, Dallam, Hansford, Hartley, Hutchinson, Lipscomb, Moore, Ochiltree, Roberts, and Sherman), Virginia (only the counties of Greensville, Isle of Wight, Northampton, Southampton, Sussex, Suffolk) and Missouri (only the counties of Butler, Dunkin, Mississippi, New Madrid, Pemiscot, Scott, Stoddard).

9) Requirements for refuge deployment will be described in the Grower Guides/Product Use Guides as described in Section D of the Industry IRM Plan submitted on April 19, 1999. Growers must continue to be required to plant only non-Bt corn in the refuge and to plant the refuge within ½ mile of their Pioneer Cry1F corn acreage. In regions of the corn belt where conventional insecticides have historically been used to control ECB and SWCB, growers wanting the option to treat these pests must plant the refuge within ¼ mile of their Pioneer Cry1F corn. Refuge planting options include: separate fields, blocks within fields (e.g., along the edges or headlands), and strips across the field. When planting the refuge in strips across the field, growers must be instructed to plant multiple non-Bt rows whenever possible.

10) Pioneer Hi-Bred will monitor for the development of resistance using baseline susceptibility data and/or a discriminating concentration assay when such an assay is available. Pioneer Hi-Bred will proceed with efforts to develop a discriminating concentration assay. Pioneer Hi-Bred will ensure that monitoring studies are conducted annually to determine the susceptibility of ECB and corn earworm (CEW) populations to the Cry1Ab 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 Pioneer Cry1F 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, Pioneer Hi-Bred will instruct its customers (growers and seed distributors) to contact Pioneer Hi-Bred (e.g., via a toll-free customer service number) if incidents of unexpected levels of ECB and/or CEW damage occur.

Upon exclusion of the causes specified in section 12a of this document, Pioneer Hi-Bred will investigate and identify the cause for this damage by local field sampling of plant tissue from corn hybrids that contain Pioneer Hi-Bred's Cry1F corn plant-pesticide and sampling of ECB & CEW populations, followed by appropriate in vitro and in planta assays. Upon Pioneer Hi-Bred's confirmation by immunoassay that the plants contain Cry1F 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 Pioneer Hi-Bred, Pioneer Hi-Bred 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

1. An LC50 in a standard Cry1F diet bioassay that exceeds the upper limit of the 95% confidence interval of the mean historical LC50 for susceptible ECB or CEW populations, as established by the ongoing baseline monitoring program. The source of Cry1F crystal protein standard for this bioassay will be *Bacillus thuringiensis* subspecies *aizawai*.
2. > 30% survival and > 25% leaf area damaged in a 5-day bioassay using Cry1F-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 Pioneer Hi-Bred finds it appropriate to alter the criteria specified in the working definition, Pioneer Hi-Bred must obtain Agency approval in establishing a more suitable definition.

The insect monitoring programs must include Southwestern corn borer (SWCB) and corn earworm (CEW), in addition to European corn borer (ECB). The program must focus monitoring in areas that typically have a high density of Bt corn or have historically been prone to high levels of corn borer pressure and where the refuge areas may more likely be treated with insecticides.

11) The current definition of confirmed insect resistance must be used as described in Section E of the Industry IRM Plan. Agency approval will be sought prior to implementation of any modified definition of confirmed insect resistance.

12) a) When field resistance has been demonstrated to have occurred, you must stop sale and distribution of Pioneer Cry1F corn in the counties where the field resistance has been shown until an effective local mitigation plan approved by EPA has been implemented. Pioneer Hi-Bred assumes responsibility for the implementation of resistance mitigation actions undertaken in response to the occurrence of resistance during the 2001 growing season. EPA interprets "suspected resistance" to mean, in the case of reported product failure, that the corn in question has been confirmed to be Cry1F corn, that the seed used had the proper percentage of corn expressing Cry1F protein, that the relevant plant tissues are expressing the expected level of Cry1F protein, that it has been ruled out that species not susceptible to the protein could be responsible for the damage, that no climatic or cultural reasons could be responsible for the damage, and that other reasonable causes for the observed product failure have been ruled out. The Agency does not interpret "suspected resistance" to mean grower reports of possible control failures, nor should extensive field studies and testing to fully scientifically confirm insect resistance be completed before responsive measures are undertaken.

12) b) Pioneer Hi-Bred will maintain a (confidential) database to track sales (units and location) of its Cry1F corn on a county-by-county basis. Pioneer Hi-Bred will provide annually, on a CBI basis, sales data for each state indicating the number of units of corn hybrids that contain Pioneer Hi-Bred's Cry1F corn plant-pesticide that were sold. As part of the overall sales report, Pioneer Hi-Bred will provide a listing of an estimate of the acreage planted within such states and counties with sales limitations. This information will be provided by January 31 of the year following each growing season.

13) Pioneer Hi-Bred will provide grower education. Pioneer Hi-Bred will agree to include an active partnership with such parties as: university extension entomologists and agronomists, consultants, and corn grower groups. Pioneer Hi-Bred will implement a grower education program (in part, as requested by Pioneer Hi-Bred, through the Grower Agreement setting forth any resistance management requirements) directed at increasing grower awareness of resistance management, in order to promote responsible product use. Insect Resistance Management educational materials for the 2001 growing season must be provided to the Agency as they become available for distribution. IRM educational materials must be developed and distributed at the same time that growers receive seed. Survey results and other available information must be used to identify geographic areas of non-compliance with insect resistance management plans. As described in the Industry IRM Plan submitted to EPA on April 19, 1999, an intensified grower education program will be conducted in these geographic areas prior to the following growing season. If individual non-compliant growers are identified, they must be prohibited from future purchases of Cry1F corn seed.

14) Pioneer Hi-Bred will confer with the EPA as Pioneer Hi-Bred develops various aspects of its resistance management research program. Pioneer Hi-Bred agrees, as a condition of this registration, to generate data and 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) Pioneer Hi-Bred must submit available research data on CEW relative to resistance development and Pioneer Hi-Bred's 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 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 refuge 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 Pioneer Hi-Bred as the model development and testing is ongoing. The requirement for development of resistance predictive models may be modified if Pioneer Hi-Bred 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 Bt 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" refuge, "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 SWCB. Sampling will be done in accordance with the Industry Plan to determine if increases in Cry1F 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 Cry1F 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.
- g) You must assess the feasibility of using the F2 screen, sentinel plots, and in-field screening kits to increase the sensitivity of resistance monitoring in 2001. By January 31, 2002, you must provide the Agency with the results from these investigations.
- h) You must implement a survey approach similar to the Iowa State University Bt Corn Survey (e.g., Pilcher and Rice, 1999) A statistically valid sample, as determined by Independent market research, of Bt corn growers in key states will be surveyed by a third-party. Bt corn growers will be included based upon a proportionately stratified random sample designed to balance the survey evenly across seed companies and geographies. In addition to demographic information, the survey will include questions related to insect resistance management such as:
- 1) What is your primary source of information on Bt corn?
 - 2) What percentage of your acres were planted to Bt corn this year?
 - 3) Are you following a recommended insect resistance management strategy?
 - 4) If you plant most of your acreage to Bt corn, are you likely to scout your non-Bt corn for economically damaging populations of corn borers?
 - 5) Did you treat your Bt corn acres with an insecticide?
 - 6) What planting pattern did you use for your refuge?
 - ° Planted Bt corn as one block in one field.
 - ° Planted Bt corn in one block in every field.
 - ° Split seed boxes in the planter and alternated every row or several rows with Bt and non-Bt corn in every field.
 - ° Planted Bt corn in large strips alternated with large strips of a non-Bt corn hybrid.
 - ° Planted Bt corn in an entire field and planted the border around the field with non-Bt corn.
 - ° Planted pivot corners to non-Bt corn with the irrigated area of the field planted to Bt corn.

- 15) A longer soil degradation study in actual field soil.

There is no evidence to indicate that prolonged exposure to trace amounts of Cry protein in the soil affects non-target organisms. The submitted data do not, however, sufficiently address the issue of residual Cry protein accumulation in the soil. The soil degradation study should be carried out for a longer period of time to determine the duration and the amount of residual Cry 1F protein in agricultural soil. Also, the soil used in the study should be actual field soil containing the microbial flora normally found in the field. This will give a more accurate rate of degradation of the Cry protein in the agricultural

environment because microbial populations in the rhizosphere are commonly 100 fold higher than in bulk soil. Bulk soil generally does not support populations of microorganisms as high as those in the rhizosphere or those in soils with high organic content (plant residues). In addition, field soil high in organic content should result in lower (if any) soil binding of Cry proteins. The details of the protocol for this study will be determined in further discussions between EPA and Pioneer. Pioneer must submit a final protocol for Agency review by August 31, 2001.

16) Confirmatory Monarch butterfly data.

An additional study submitted by Dow AgroSciences showed that Cry1F is non-toxic to neonate monarch butterfly larvae when fed a $\leq 10,000$ ng/mL diet dose. First instar larval weight and mortality were recorded after seven days of feeding. There was no mortality to monarchs fed 10,000 ng/mL diet, the highest rate tested. There was some growth inhibition at 10,000 ng/mL diet. Since pollen doses equivalent to 10,000 ng/mL diet are not likely to occur on milkweed leaves in nature, it can be concluded that Cry1F protein will not pose a risk to monarchs.

The conclusions should be confirmed by providing data showing that the amounts of Cry protein found in pollen on milkweed leaves in the field are at concentrations less than the 10,000 ng/mL diet used in this study. The NOEC of pollen on milkweed leaves also has to be determined.

17) Continuation of beneficial insect field monitoring.

The beneficial insect monitoring should continue into the first five years of commercial use of Cry1F corn crops to confirm the single season "no effects" findings and to gather data on long range non-target insect effects and abundance.

18) Analytical methods and method validation for the Cry1F protein in corn have been received. Cry1F DNA detection methods and method validation must be submitted. These data must be confirmed by an independent laboratory and by EPA. To support the EPA validation, you must provide samples, antibodies, and other required support to EPA's Laboratory in Ft. Meade, Maryland. Contact Susan Lawrence for additional information at (703) 308-8134.

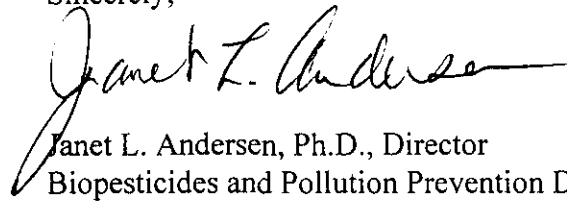
19) Modify the label so that the EPA Reg. No. is "29964-3." Submit five (5) copies of the revised final printed labeling before you release the product for shipment.

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

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

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Sincerely,

A handwritten signature in black ink, reading "Janet L. Andersen". The signature is fluid and cursive, with a long horizontal stroke at the end.

Janet L. Andersen, Ph.D., Director
Biopesticides and Pollution Prevention Division

Pioneer[®] brand seed corn with Herculex[™] I

Pure form of the plant-pesticide, *Bacillus thuringiensis* subsp. *aizawai* delta endotoxin protein as produced in corn cells. For control of European corn borer, Southwestern corn borer, Black cutworm, corn earworm, and Fall armyworm.

Active Ingredient:

Bacillus thuringiensis CryI F protein and the genetic material necessary for its production (plasmid insert PHI8999) in corn.<0.0010 - 0.235 %

*% total protein on a dry wt. basis as expressed in corn plant cells (whole plant)

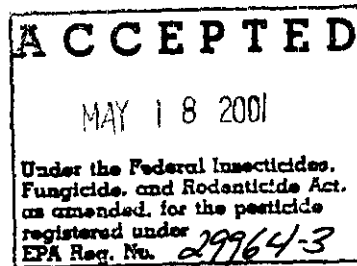
**KEEP OUT OF REACH OF CHILDREN
CAUTION**

EPA REG. NO.: 029964-G

EPA ESTABLISHMENT NUMBER: 029964-1A-001.

NET CONTENTS: _____

Pioneer Hi-Bred International, Inc.
Regulatory Sciences and Resources
7250 NW 62nd Avenue
Johnston, IA 50131



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DIRECTIONS FOR USE

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

The plant-pesticide product should be used as specified in the terms and conditions of the registration.

Corn has been transformed to express a *Bacillus thuringiensis* subsp. *aizawai* (*B.t.a.*) delta-endotoxin protein for control of the European corn borer (*Ostrinia nubilalis*) and other lepidopteran pests.

Routine applications of insecticides to control European corn borer are unnecessary when corn containing the *B.t.a.* delta-endotoxin protein is planted.

Growers are instructed to read information on insect resistance management.

CROP	INSECTS CONTROLLED
Field corn	Black cutworm Corn earworm European corn borer Fall armyworm Southwestern corn borer

EPA Accepted: __/__/__