70218-1 5-12-1998 1/5

U.S. ENVIRONMENTAL PROTECTION AGENCY
Office of Pesticide Programs
Biopesticides and Pollution Prevention Division
(7511W) 401 M St., S.W.
Washington, D.C. 20460

EPA Reg. Number:	Date of Issuance:
70218-1	MAY 12 1998

NOTICE OF PESTICIDE:
__X__ Registration
_____ Reregistration

(under FIFRA, as amended)

Term of Issuance:
Unconditional Registration

Name of Pesticide Product:
StarLink™ Corn

Name and Address of Registrant (include ZIP Code):

Plant Genetic Systems (America) Inc.
7200 Hickman Road, Ste. 202
Des Moines, Iowa 50322

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.

This registration does not eliminate the need for continual reassessment of the pesticide. If EPA determines at any time, that additional data are required to maintain in effect an existing registration, the Agency will require submission of such data under section 3(c)(2)(B) of FIFRA.

This product is registered in accordance with FIFRA section 3(c)(5) and is subject to the following terms and conditions:

1. This registration will automatically expire on midnight May 30, 1999. After this registration has expired, no field corn seed that contain the pesticide product may be sold or planted. However, harvesting of such corn planted prior to May 30, 1999 is permissible subject to the terms of this registration. Plant Genetic Systems (America) is liable for the actions of its customers in regard to meeting the terms and limitations of this registration.

2. This registration is for field corn to be used only in animal feed, industrial non-food uses such as ethanol production, and seed increase. In addition, any corn grown within 660 feet of Cry9C corn must also be limited to use in animal feed and industrial non-food uses such as ethanol production. The acreage of corn planted may not exceed 109,000 acres for the animal feed and industrial uses and 11,000 acres for seed increase.

3. Plant Genetic Systems (America) must require that growers follow the USDA NC-205 guidelines for refuge for all Cry9C corn. These guidelines reflect the current knowledge base among USDA, academic, industry, and EPA scientists. Specifically, a 25% unsprayed or 40% sprayed non-Bt corn structured refuge in close proximity to the Bt crop is required. The refuge must be established within 1500-2000 feet of the Bt crop. Any insecticide treatment cannot include sprayable *Bt* products.

4. Plant Genetic Systems (America) must provide specific information through their technical bulletins, brochures, product labels, and educational presentations so that growers have the necessary tools to successfully implement an Insect Resistance Management (IRM) plan. A World Wide Web site on the internet would be a practical way to provide specific resistance management information. Included in this IRM information should be instructions on the appropriate use of the Bt plant-pesticides in a resistance

Signature of Approving Official:	Date:
[signature]	5/12/98

EPA Form 8570-6

management program, compatibility with existing Integrated Pest Management (IPM) programs, refuge deployment and management (including IPM options), monitoring, reporting of unusual pest damage, and any local any local and regional IRM considerations. The success of any IRM program will ultimately depend on growers who have the knowledge and tools to understand the problem of resistance and the steps that can be taken to combat it.

5. Plant Genetic Systems (America) must maintain a (confidential) database to track sales by units and location of Cry9C corn on a state and county-by-county basis. This material should be submitted annually (by January 31 of the year following each growing season) to the Agency on a Confidential Business Information (CBI) basis. As part of this report, Plant Genetic Systems (America) must provide an estimate of the acreage for Cry9C corn within each state.

6. Submit two copies of the revised final printed label for the record.

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.

Should you wish to amend your registration to remove the expiration date, you must do and submit status reports on the following.

1. In the study assigned MRID No. 442581-15 (Effects of Cry9C Corn on Predatory Non-Target Beneficial Insects and Endangered Species; Determination of Predatory Non-Target Beneficial Insect Study/Pollen Production Study) there was no consistent pattern of differences in abundance of predatory insects on the Cry9C versus the control corn plots throughout the growing season. Trapping height had no significant impact on the number of predators captured. Testing of larger plot sizes would, however, produce more significant results. Therefore, the beneficial insect monitoring should continue into the first few years of commercial use (provided the registration is amended to remove the expiration date) of the transgenic corn crops to confirm the small plot "no effects" findings.

2. Research to expand the knowledge base for the following pests that are or may be affected by Cry9C corn: European corn borer (ECB, *Ostrinia nubilalis* Hübner), southwestern corn borer (SWCB, *Diatraea grandiosella* Dyar),and black cutworm (BCW, *Agrotis ipsilon* Hufnagel). The February 1998 SAP meeting identified research needs for adult movement, pre- and post-mating dispersal, mating behavior, ovipositional patterns, fitness, and larval movement. This information is critical to the optimal design, placement, and evaluation of refugia.

3. A susceptibility study with the corn earworm (CEW, *Helicoverpa zea* Boddie) to determine if there are any fitness costs associated with exposure to Cry9C toxin. Submitted research has clearly indicated that there is little or no mortality of CEW associated with Cry9C. However, fitness costs, such as growth inhibition and delayed developmental time, may be an indication of toxicity and also a source of selection pressure. CEW is a pest of great concern in cotton growing areas since it is a pest of both corn and cotton and frequently moves from corn to cotton during the season. This creates the potential for multiple exposure to different Bt toxins between the two crops. Because of these resistance management concerns with CEW, a thorough investigation of all possible sources of resistance selection (including fitness costs) should be undertaken.

4. An examination of the Cry9C susceptibility of primary and secondary pests of corn including the SWCB, BCW, and southern corn stalk borer (SCSB, *Diatraea crambidoides* Grote). These insects have not yet been evaluated for susceptibility to the Cry9C toxin. Although these pests will not initially appear on the Cry9C corn label, they may still be affected by the Cry9C toxin and have an impact on resistance management. PGS has indicated in subsequent communications that susceptibility studies for SWCB have been planned and that SWCB and BCW may be added to the label in the future.

5. Verification of the high dose claimed for Cry9C corn using the guidelines established by the February 1998 SAP. The presence of a high dose of Bt toxin in transgenic crops is considered vital to the high dose/refuge strategy. Data cited by PGS seem to indicate that there is a high dose of toxin expressed in all Cry9C corn tissues except pollen, relative to the LC_{50} of first instar ECB larvae. However, given the importance of a "high dose," this claim should be further verified using the SAP guidelines. "High dose" was defined as 25 times the amount of toxin necessary to kill susceptible larvae. Five techniques were identified at the SAP meeting, of which at least two should be used to confirm a high dose. These were: 1) Serial dilution bioassays with artificial diet incorporating Bt plant tissue and non-Bt plant tissue of the same cultivar (control); 2) Bioassays with Bt plants that express 25 times less toxin than commercial Bt plants of the same cultivar; 3)

Surveys of large numbers of commercial Bt plants in the field--verify that the $LD_{99.99}$ for susceptibles is present and to also assure that 95% of heterozygotes will be killed; 4) Controlled infestations on the cultivar with insects of a known LC_{50}; 5) Bioassays on Bt plants with older instar larvae that are 25 times less susceptible–verify that 95% or greater are killed by the cultivar. The high dose should be verified throughout the growing season (not just at one point during the season) to cover all generations of corn pests.

6. Research on refuge deployment. Suggested areas of focus include the evaluation of: 1) in-field block or strip refuges; 2) external non-Bt corn refuges; and 3) alternate host crops as refuge.

7. Implement a resistance monitoring program that is not tied to a specific sales threshold and which uses the Field Failure Response Decision Tree submitted with your 5/1/98 response to our pre-acceptance letter. PGS proposes to monitor for resistance to Cry9C only in counties in which Cry9C corn accounts for at least 25% of the total corn grown. However, since the initial market penetration may be relatively low in the first few years of Cry9C corn availability, this type of monitoring plan may not provide an adequate sampling of the Cry9C corn distribution. Instead, a plan is recommended that will focus on both counties with a relatively high Cry9C corn distribution (not necessarily 25%) and also at a sufficient number of lower density sites to adequately represent the entire distribution region. The resistance monitoring plan should encompass all Cry9C susceptible pests, especially labeled pests. Resistance monitoring should be required in areas where the target pests are known to regularly overwinter. For ECB, this includes most of the United States, but for more migratory pests such as SWCB, monitoring can be focused on Southern overwintering sites (e.g. Texas).

8. Utilize a specific resistance monitoring program for all the target pests affected by Cry9C corn. Along these lines, PGS should collect baseline susceptibility data for the target pests of Cry9C corn, which can be helpful in documenting the extent and distribution of resistance. In addition, PGS must work to develop both a discriminating dose assay (to detect dominant resistance alleles) and a F_2 screen (to detect recessive resistance alleles) for each target pest. Current Agency requirements for other Bt corn products mandate the development of baseline susceptibility data and discriminating dose bioassays. These techniques may take time and research to develop. Until such time as these assays are available, PGS should utilize LC_{50} diet bioassays and leaf damage assays, which have also been mandated for previous Bt corn registrations. The use of in-field monitoring for pest damage and sentinel plots may also provide practical means of detecting resistance alleles. In their proposal, PGS does not clearly indicate the techniques, other than investigating reports of unexpected damage, that will be undertaken to monitor for resistance. Detecting shifts in the frequency of resistance genes through resistance monitoring can be an aggressive method to detect the onset of resistance before widespread crop failure occurs. As such, resistance monitoring is critical to the success of an IRM plan.

9. A full investigation regarding the potential for Cry9C cross resistance with CryIF, CryIIA, and CryIC for all of the pests of corn that may be susceptible to Cry9C (ECB, SWCB, BCW, possibly SCSB). CryIF shares a binding site with CryIA(a), CryIA(b), and CryIA(c), while CryIIA is found in some foliar Bt products and has shown broad cross resistance potential to CryIA in some cases. In addition, Cry9C is known to partially share a binding site with CryIC (a component of some microbial Bt products) in the beet armyworm (BAW, *Spodoptera exigua* Hübner) and ECB. Cross resistance, through shared binding sites or other mechanisms, is an area of major concern for resistance management. The PGS plan cites data which indicates that Cry9C does not share a binding site with CryIA(b) or CryIA(c) (the Bt toxins present in all other registered Bt corn products) in the diamondback moth (DBM, *Plutella xylostella* L.) and ECB. Due to these separate binding sites, there should be a relatively low potential for cross resistance between Cry9C and CryIA(b) or CryIA(c).

10. Provide to the Agency on an annual basis (by Januray 31 of the year following each growing season) a detailed (complete with study summaries, methods and protocols, and results) report of ongoing resistance management activities research. This report should be on a non-CBI basis.

Sincerely,

Janet L. Andersen

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

StarLink™ CORN

StarLink™ corn produces both an insecticidal protein, Cry9C from *Bacillus thuringiensis* subsp. *tolworthi*, for protection from European corn borer and a herbicide resistance protein, phosphinothricin acetyltransferase (PAT). PAT provides protection from the Liberty® herbicide (EPA Registration Number 45639-199), a selective herbicide that has glufosinate-ammonium as it's active ingredient.

StarLink™ corn are descended from corn plants transformed with vectors pRVA9909 and pDE110.

KEEP OUT OF REACH OF CHILDREN

CAUTION

Active Ingredient:	*Bacillus thuringiensis* subsp. *tolworthi* Cry9C protein and the genetic material necessary for its production in corn	0.9-4.7%†*
Inert Ingredients:	Substance produced by a marker gene and its controlling sequences in corn	0.2-1.6%†

† The percentages list the ingredient as a percent of the total plant protein on a dry weight basis.
* US Patents pending.

ACCEPTED
with COMMENTS
In EPA Letter Dated
MAY 12 1998
Under the Federal Insecticide, Fungicide, and Rodenticide Act as amended, for the pesticide registered under EPA Reg. No. 70218-1

EPA Registration No. **70218-1**
EPA Establishment Number: **070218-BEL-001**

DIRECTIONS FOR USE

It is a violation of Federal Law to use this product 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. All field corn containing the plant-pesticide that is sold or distributed by Plant Genetic Systems (PGS) or a cooperator or licensee of PGS, must be accompanied by informational material that contains the following:

StarLink™ corn contain a *Bacillus thuringiensis* subsp. *tolworthi* insecticidal protein, Cry9C and may only be used according to the instructions below for the control of the following insect:

European corn borer — *Ostrinia nubilalis* (Huber)

Do not use this corn until you have read the Bag Tag and the Grower's Guide.

Plant Genetic Systems (America), Inc.
7200 Hickman Road, Suite 202
Des Moines, Iowa 50322
Revised label: 7 May 98

Insect Resistant Management: To protect this important technology, a structured non-*Bt* corn refuge must be planted in close proximity (1500-2000 feet) to your StarLink™ corn fields. Specifically, a refuge of non-*Bt* corn equal to at least 25% of the total corn acres must be left unsprayed for control of European corn borer. If foliar sprays are applied for ECB control then at least 40% of the total corn acres must be planted to non-*Bt* corn.

Seed Production Uses: Seeds expressing the Cry9C protein should be planted at a maximum of 40,000 per acre on the site. Harvested seeds may be stored until a registration is granted for full commercial use. Any seeds, plants or plant materials in the StarLink™ plot, or within 660 feet of the plot, not used for seed production should be destroyed or can be used for animal feed or industrial (ethanol) purposes. None of the seeds, plants or plant materials in the StarLink™ plot, or within 660 feet of the plot, may be used for food uses or may enter international commerce.

Feed or Industrial Uses: Seeds expressing the Cry9C protein should be planted at a maximum of 40,000 per acre on the site. Any seeds, plants or plant materials in the StarLink™ plot, or within 660 feet of the plot, not used for seed production (see above) should be destroyed or can be used for animal feed or industrial (ethanol) purposes. None of the seeds, plants or plant materials in the StarLink™ plot, or within 660 feet of the plot, may be used for food uses or may enter international commerce.

STORAGE AND DISPOSAL

Seed Storage: Store in a cool dry place separate from conventional corn seed.

Seed and Plant Disposal: Any seeds, plants or plant materials in the StarLink™ plot, or within 660 feet of the plot, may be used for animal feed or industrial purposes or destroyed. None of the seeds, plants or plant materials in the StarLink™ plot, or within 660 feet of the plot, may be used for food uses or may enter international commerce.

Container Disposal: Do not reuse bag. Discard bag in trash. Ensure that the bag is completely empty of seed before disposal.

For Product Inquiry Information,
Call Toll Free: 1-888-GO-LIB-LINK
(1-888-465-4254)

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