Bacillus thuringiensis Cry3Bb1 Protein and the Genetic Material Necessary for its Production (Vector ZMIR13L) in Event MON863 Corn (006484) Fact Sheet

I. Description of the Active Ingredient

- **Pesticide Name:** Bacillus thuringiensis Cry3Bb1 Protein and the Genetic Material Necessary for its Production (Vector ZMIR13L) in Event MON863 Corn
- **EPA Registration Number:** 524-528
- **Date Registered:** February 24, 2003
- **Trade and Other Names:** Corn Event MON863, YieldGard RootwormT
- **OPP Chemical Code:** 006484
- **Basic Manufacturer:**

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

- **Type of Pesticide:** Plant-Incorporated Protectant
- **Uses:** Field Corn
- **Target Pest(s):** Corn Rootworm

II. Background

EPA has conditionally registered the Monsanto Company's new active ingredient, Bacillus thuringiensis Cry3Bb1 protein and the genetic material necessary for its production (vector ZMIR13L) in Event MON863 corn. The Agency has determined that the use of this pesticide is in the public interest and that it will not cause any unreasonable adverse effects on the environment during the time of conditional registration.

At 80 million planted acres, corn is the largest crop grown in the U.S. and accounts for 20% of total agricultural cropland. Over the past 5 years, conventional insecticides have been applied to between14 to 18 million acres of corn to control CRW. This single corn pest accounts for 1 out of every 7 insecticide applications to agricultural crops. Infested acreage is increasing due to extended diapause and behavior modification as CRW lays its eggs in soybean fields which are planted in rotational corn. The acres infested with CRW is expected to grow 2.6% per year and, by 2013, to total 39 million acres.

In assessing the potential benefits from MON 863, EPA compared the efficacy of MON 863 to other chemical controls for CRW, evaluated the human health and environmental benefits compared to registered alternatives, estimated the grower benefits, and estimated the chemical pesticide use reduction from adoption of MON 863. EPA made a determination that the registration of MON 863 was in the public interest and that the benefits outweigh the risks.

The MON863 registration and the Cry3Bb1 tolerance exemption under 40 CFR Part 180.1214 have been extended. The MON863 registration is currently set to expire on July 31, 2006. The Cry3Bb1 tolerance exemption no longer has a time limitation.

Top of Page

III. Science Assessment

Product Characterization

Event MON863 corn was produced by transforming corn tissue via a method employing bombardment of particles coated with DNA (Vector ZMIR13L) which contained both the cry3Bb1 and nptII genes. The cry3Bb1 and nptII genes were stably introduced into the corn genome as one intact copy. Ranges of Cry3Bb1 protein levels in MON863 in microgram Cry3Bb1 protein per gram of fresh weight tissue were 30-93 (leaf), 49-86 (grain), 30-93 (pollen), 3.2-66 (root), and 13-54 (above ground whole plant). Monsanto is being required to submit expression data in terms of dry weight, as the amount of protein present in the given tissue.

Cry3Bb1 protein is a delta-endotoxin from Bacillus thuringiensis spp. kumamotoensis and has activity against certain beetles. The wild-type cry3Bb1 gene was modified to enhance the protein's activity against the corn root worm complex. The nptII gene encodes neomycyin phosphotransferase II and was used as a marker protein to identify the corn tissue that had been transformed with ZMIR13L.

Adequate information was submitted to show that the Cry3Bb1 test material derived from microbial cultures was biochemically and functionally similar to the protein produced by the plant-incorporated protectant ingredients in corn. Production of microbially produced protein was used to obtain sufficient material for testing.

Top of Page

Human Health Assessment

Data demonstrate a lack of mammalian toxicity at high levels of exposure (well above exposure levels that are reasonably anticipated in corn) to the pure Cry3Bb1 proteins. Gross necropsies performed at the end of the three acute oral toxicity studies in mice indicated no findings of toxicity attributed to exposure to the test substance. LD50 s were greater than 2,700; 2,980; and 3,780 mg Cry3Bb1 protein/kg body weight (highest doses tested).

The potential for the Cry3Bb1 proteins to be food allergens is minimal. Data demonstrate that the Cry3Bb1 protein is rapidly degraded by gastric fluid in vitro. Further, a comparison of amino acid sequences of known allergens and toxins uncovered no evidence of any homology with Cry3Bb1.

A tolerance exemption exists under 40 CFR 180.1214 (for Bacillus thuringiensis Cry3Bb1 protein and the genetic material necessary for its production in corn) that includes Event MON863.

The extraction and detection method submitted in support of 40 CFR 180.1214 is adequate for analysis of Cry3Bb1 protein in corn grain. However, Monsanto is required to submit method validation data by an independent laboratory, as well as reagents to the EPA's Office of Pesticide Programs Ft. Meade Laboratory for their validation of the method. In addition, to assure that grain handlers have a test method in place prior to harvest, Monsanto must make available Cry3Bb1 strip tests to grain handlers. EPA further understands that these are 'qualitative' test kits and that Monsanto is in discussions with USDA/GIPSA about providing methodology and reagents for their use in developing a validated 'quantitative' method for MON 863.

Top of Page

Environmental Assessment

The Agency has conducted an environmental hazard assessment of the Cry3Bb1- producing corn lines. The general topics covered include gene flow to related wild plants, development of weediness, effects on wildlife, and fate of Cry3Bb1 proteins in the environment. The assessment is based on data submitted to the Agency during the development of the corn lines, additional data submitted for registration, FIFRA Scientific Advisory Panel (SAP) recommendations, consultations with scientific experts, and public comments received by the Agency.

The Agency assesses the toxicity of Cry3Bb1 protein to representatives of potentially exposed non-target

organisms by a tiered testing system using single species maximum hazard dose laboratory data using mortality as the end point. The toxicity of the Cry3Bb1 protein has been evaluated following challenge of several species of invertebrates including: adult and larval honey bees, a parasitic hymenopteran (Nasonia), green lacewings, lady beetles, collembola, monarch butterfly, and earthworms. Reproductive and developmental observations were also made on collembola, honeybee and lady beetle larva maturation studies. The August, 2002 SAP (as well as several public comments) however, found the green lacewing and parasitic wasp studies lacking and recommended testing of alternative species. Although Bt Cry proteins are very specific in their activity to only certain insect species, the Agency has examined the potential toxicity of Cry3Bb1 protein to birds, fish, and mammals. After evaluating all of the data, the SAP report, and the public comments, the Agency has concluded that no unreasonable adverse effects on non-target organism are expected from Cry3Bb1 protein produced in field corn for the duration of this conditional registration. However, some additional non-target insect studies are needed as confirmatory data and EPA has concluded that it is appropriate for long term environmental effects to be assessed by appropriately designed field monitoring during the initial years of the Cry3Bb1 corn registration.

EPA has determined that the use of Cry3Bb1 in field corn will not cause adverse effects to threatened or endangered species. The Cry3Bb1 protein appears to be specifically toxic to Chrysomelid beetles and currently there are no Chrysomelid species listed on the endangered species list. The habitats of endangered/threatened beetle species do not overlap with corn fields. For endangered aquatic beetles, EPA considered the amount of corn pollen in water. Even using the extremely conservative estimate that 100% of the corn pollen was deposited on the water, the concentration of Cry3Bb1 in pollen was several orders of magnitude below the toxic level for any insect.

At present, the Agency is aware of no identified significant adverse effects of Cry3Bb1 proteins on the abundance of non-target beneficial organisms in any population in the field, whether they are pest parasites, pest predators, or pollinators. Field testing and field census data submitted to the Agency show minimal to undetectable changes in the beneficial insect abundance or diversity. In corn fields, the densities of predatory and non-target insects are generally higher on Cry3Bb1 corn than non-Bt corn primarily because the Cry3Bb1 corn is not subjected to the same number of applications of nonspecific pesticides. Two year invertebrate abundance studies do not show a shift in the biodiversity in Cry3Bb1 corn, except in cases where the predators are dependent on the pest insect as prey. In contrast, treatment with chemical pesticides, when studied, had significant effects on the total numbers of insects and on the numbers within the specific groups. To date, the available field test data show that compared to crops treated with conventional chemical pesticides, the transgenic crops have no detrimental effect on the abundance of non-target insect populations. However, annual insect monitoring of representative commercial fields will continue for long term biodiversity effects assessment.

The Agency believes that cultivation of Cry3Bb1 corn may result in fewer adverse impacts to non-target organisms than result from the use of chemical pesticides. Under normal circumstances, Cry3Bb1 corn requires substantially fewer applications of chemical pesticides. This should result in fewer adverse impacts to non-target organisms because application of nonspecific conventional chemical pesticides is known to have an adverse effect on non-target beneficial organisms found living in the complex environment of an agricultural field. Many of these beneficial organisms are important integrated pest management controls (IPM) for secondary pests such as aphids and leafhoppers. The overall result of cultivation of corn expressing Cry3Bb1 proteins is that the number of chemical insecticide applications for non-target pest control is reduced for management of multiple pest problems

The movement of transgenes from Cry3Bb1 host plant into weeds and other crops has also been considered. The Agency has determined that there is no significant risk of gene capture and expression of Cry3Bb1 protein by wild or weedy relatives of corn in the U.S., its possessions or territories. The fate of Cry3Bb1 protein in soils and indirect effects on soil biota have also been evaluated. Test data show that most of the Cry protein deposited into soil is quickly degraded, although a residual amount may persist in biologically active form for a much longer period of time. It is also reported that the same degree of Bt Cry protein persistence takes place in soils that have been exposed to repeat Bt spray applications when compared to soil exposed to a growing Bt crop. Limited data do not indicate that Cry proteins have any measurable effect on microbial populations in the soil. Horizontal gene transfer from transgenic plants to soil bacteria has not been demonstrated. Published studies of

Bt Cry protein in soil show no effect on bacteria, actinomycetes, fungi, protozoa, algae, nematodes, springtails or earthworms. In addition, new plants planted in soil containing Bt Cry protein do not take up the Bt protein.

The Agency has sufficient information to believe that there is no risk from the proposed uses of Cry3Bb1 corn to non-target wildlife, aquatic and soil organisms. However, after consultation with the FIFRA Scientific Advisory Panel in August, 2002 and from several public comments, the Agency is requesting additional data. The supplementary studies would provide additional weight to support the Agency's conclusions. Refer to section C for additional details on the Agencies assessment and requirement for additional data.

Top of Page

Insect Resistance Management

Corn expressing the Cry3Bb1 protein is intended to provide protection against certain species of the corn rootworm (CRW) including the western corn rootworm (Diabrotica virgifera virgifera), northern corn rootworm (D. barberi) and Mexican corn rootworm (D. virgifera zea). Monsanto acknowledges that a robust and practical IRM plan will require time to develop and they are proposing a three-year interim plan. An interim plan was submitted by Monsanto because they believe growers need to be able to grow MON 863 corn for a period of time so that important information can be generated and growers can be provided an understanding of corn rootworm IRM requirements.

It should be noted that previous IRM assessments for Plant-Incorporated Protectants (PIPs) needed to consider the potential for resistant organisms feeding upon the PIP affecting the performance of registered microbial Bt pesticides against those organisms. In the case of CRW, there are no registered microbial or PIP products for the control of this organism at this time. Likewise, cross-resistance to Cry proteins in other PIPs or microbial products is not an issue.

Monsanto submitted many documents in support of their proposed IRM plan. An IRM plan for MON 863 corn dated June 20, 2000 was submitted to the Agency. An amended IRM plan dated January 8, 2002 was submitted to the Agency intended to supercede the previous submission. Additional preliminary research dated February 20, 2001 was submitted to the Agency. A FIFRA Scientific Advisory Panel (SAP) was convened in August 2002. The August 2002 SAP comments regarding Monsanto’s interim IRM plan were documented in a memorandum from Paul Lewis to Marcia Mulkey dated November 6, 2002. In response to the SAP, Monsanto submitted additional information to EPA on December 13, 2002. This additional information, along with additional clarifications provided to the Agency by Dr. Michael Caprio on December 20, 2002, Dr. David Andow on December 23, 2002 and Dr. Fred Gould on February 12, 2003 were incorporated into the final review.

A 20% non-Bt corn refuge is sufficient for a 3 year interim period while additional information is being gathered. The non-Bt corn refuge should be planted as continuous blocks adjacent to the MON 863 fields, as perimeter strips, or as non-transgenic strips planted within the transgenic field. A 20% non-Bt corn refuge is necessary to produce an adequate number of CRW susceptible to the Cry3Bb1 protein. Considering the limited movement of CRW larvae, planting refuges close to transgenic fields in large blocks is preferred to narrow strips. If a 20% refuge is planted as row strips within a corn field, then the strips must consist of at least 6 to 12 consecutive rows.

Seed and granular insecticide treatments to control CRW larvae are acceptable on refuge acres. However, it is not acceptable to treat refuges for adult CRW control as these treatments may diminish the effectiveness of the refuge. If growers spray their corn fields with insecticides to control pests other than CRW, all acres (Bt and non-Bt) should be treated identically. Bt fields and the non-Bt refuge acres should be treated with identical agronomic practices such as irrigating all corn (Bt and non-Bt) at the same time. To ensure the production of similar numbers of CRW, Bt and non-Bt corn should be planted in fields with similar backgrounds. For example, if MON 863 hybrids are planted on continuous corn fields then the non-Bt refuge should be planted on continuous corn fields or both should be planted on first-year corn acres. Non-Bt refuges should not be planted on first year corn fields if the MON 863 hybrids are planted on rotated fields.

Additional research is needed to establish a long-term IRM strategy for MON 863 corn. The August 2002 SAP recognized areas of research recommended by the NCR 46 and identified ten additional areas needing further investigation for a basic scientific assessment. EPA is requiring studies on pest biology and genetics, if possible, the development of resistant laboratory colonies, evaluation of other IRM options, improved computer models, affect of MON 863 on CRW fitness, and additional information monitoring for resistance and mitigation/remedial action. Details of the research needs are in the IRM chapter and the requirements are listed in the terms and conditions of the registration.

Top of Page

Benefits

In assessing the potential benefits from MON 863, EPA compared the efficacy of MON 863 to other chemical controls for CRW, evaluated the human health and environmental benefits compared to registered alternatives, estimated the grower benefits, and estimated the chemical pesticide use reduction from adoption of MON 863. EPA made a determination that the registration of MON 863 was in the public interest and that the benefits outweigh the risks.

MON 863 corn is as effective or more effective than chemical insecticides in protecting corn roots from CRW larval feeding damage, based on the review of the submitted field efficacy studies. Without MON 863 or conventional insecticides, CRW can reduce yields from up to 9 to 28%. Considering all of the efficacy studies reviewed using MON 863 and non-transgenic corn, MON 863 generally experienced less root damage, often significantly less root damage, from southern, northern, and western corn rootworm than a non-transformed control hybrid even when the non-transformed corn was treated with registered soil insecticides. Less root damage has been shown to be correlated with better yields.

MON 863 corn offers practical advantages to corn growers over the current registered alternatives. It can be planted early for a longer growing season and potentially higher yield, while ensuring adequate CRW protection throughout the growing season. In addition, growers should be able to plant their crop more quickly because they won't have to continually have to stop and refill the insecticide boxes. MON 863 seeds can also have seed treatments that will allow even greater control of other associated pests such as wireworm, grub, maggots, and cutworms. Thus, growers will have multi-pest protection while carrying out insect control in essentially a single step at planting. All of these advantages to planting MON 863 corn are practical, easier, and safer for the grower. Planting MON 863 corn will save the grower money in application, insecticide, labor, fuel, equipment, storage and disposal costs (since there will be no insecticide containers needed for CRW control). Plus, MON 863 is labeled for general use and will replace current reliance on restricted use products. MON 863 will provide the grower and other occupational workers greater safety, protect water bodies from run-off, and mitigate spray-drift and potential impacts on local non target organisms, such as bird populations.

Based on the Agency's review of the submitted studies, the 50-year history of safe use of Cry proteins in U.S. agriculture, and comparable results to studies of other proteins in the Cry3 class, EPA has determined that there is a reasonable certainty of no harm resulting from exposure to this protein. MON 863 corn presents no unreasonable risks to humans during any stage of its life cycle, from production, handling, storage, ingestion, to disposal. Cry3Bb1protein has no toxic effects on mammals, and is not likely to induce allergic or hypersensitive responses based on results in all appropriate tests. MON 863 is less toxic than all of the major insecticides currently used to control CRW damage.

All of the major chemicals used for CRW control can cause adverse environmental effects under conditions of normal use. Fifteen products are labeled as "toxic," 6 as "highly toxic," 1 as "very highly toxic," and 14 as "extremely toxic" to birds, fish and other wildlife. EPA has identified 10 insecticides used in agriculture as the most toxic to birds and 3 are currently used to control the corn rootworm (carbofuran, phorate and methyl parathion). In contrast, the Cry3Bb1 protein has no toxic effects on non-target organisms based on results in all appropriate tests. In addition, Cry3Bb1 is degraded rapidly in the soil (reducing non-target exposure). The Cry3Bb1 protein is expressed by the corn plant; thus, reducing the exposure to non-target organisms from

application spillage. In addition, Cry3Bb1 has a narrow target range (beetles of the family Chrysomelidae). The family Chrysomelidae contains no known endangered species. To date, there have been no functional receptors for Cry proteins on intestinal cells of fish, birds, or mammals. As labeled, MON 863 corn poses less risk to the environment than the registered alternatives.

Cumulative grower benefits are projected to be $49.2 million for the three year period 2003 to 2005. The time necessary to develop corn hybrids containing Cry3Bb1 and the time necessary to obtain full European Union approval are key factors affecting the growth rate in benefits. At full commercial maturity when offerings are available for all infested acreage, annual grower benefits are predicted to be $110 million per year. Grower benefits are defined as the difference between the value of MON 863 and it's cost. The value is based on expected yield improvements, reduced costs for insecticides, and practical benefits related to a more flexible and safer product for growers to use than the alternatives. Average grower benefits are estimated to be $6.56/acre which is about 2% of gross income. Crop budgets suggest a net return per acre for corn (not including land charges) of around $60 per acre so MON 863 has the potential to increase profits by 10%. The benefit estimates include all economic costs, such as out of pocket plus opportunity costs. This includes an estimated MON 863 technology fee as well as costs of market acceptance and refuge requirements unique to genetically-modified organisms (GMO's).

Pesticide use reduction projections indicate that as MON 863 CRW-protected corn adoption increases in the next three years, acre treatments will be reduced extensively for all chemical insecticides used currently to control CRW. The greatest use reductions are seen in both the organophosphate and synthetic pyrethroid classes. By 2005, approximately 1.5 million acre treatments of organophosphate insecticides, 1.9 million acre treatments of synthetic pyrethroid insecticides, 0.1 million acre treatments of carbamate insecticides, and 0.5 million acre treatments of other chemical insecticides including members of the phenyl pyrazole class (e.g., fipronil) will be reduced based on current projections. By 2007, the extent of insecticide use reduction will be even greater, approximately 2.5 million acre treatments of organophosphate insecticides, 3.5 million acre treatments of synthetic pyrethroid insecticides, 0.1 million acre treatments of carbamate insecticides, and 0.9 million acre treatments of other chemical insecticides are expected to be reduced.

Top of Page

IV. Terms and Conditions of the Registration

EPA Registration Number 524-528

Monsanto is required to do the following as terms and conditions of the registration.

1. The subject registration will automatically expire on midnight July 31, 2006.

2. The subject registration will be limited to Bacillus thuringiensis Cry3Bb1 Protein and the Genetic Material Necessary for its Production (Vector ZMIR13L) in Event MON863 Corn use in field corn.

3. Submit/cite all data required for registration of your product under FIFRA § 3(c)(5) when the Agency requires registrants of similar products to submit such data.

4. Submit production information for this product to Mr. Owen Beeder of Office of Pesticide Programs, Registration Division (mail code 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 December 15, following the and of the preceding fiscal year.

5. Submit independent laboratory method validation (under Harmonized Guideline 860.1340) to complete the database for Cry3Bb1 corn within 12 months of the date of registration. Provide to the EPA laboratory (Ft. Meade, MD) methodology and/or reagents necessary for validation of a Cry3Bb1 analytical method within

6 months of the date of registration. The extraction and detection method as described for Cry3Bb1 protein appears to be adequate for analysis of Cry3Bb1 protein in corn grain. However, this method must be validated by both an independent laboratory and the EPA Biological and Economic Analysis Division laboratory before it can be considered a valid method. In addition, to assure that grain handlers have a test method in place prior to harvest, Monsanto must make available Cry3Bb1 strip tests to grain handlers and demonstrate to the Agency this provision prior to September 2003. EPA understands that these are 'qualitative' test kits and that Monsanto is in discussions with USDA/GIPSA about providing methodology and reagents for their use in developing a validated 'quantitative' method for MON 863 and that this transfer of materials will take place once registration occurs.

Top of Page

6. Submit expression data in terms of dry weight, as the amount of protein present in the given tissue. Tissues for which expression data must be provided include: leaf, root, pollen, seed, and whole plant. In addition, data for each of these tissues should be provided for young plants in rapid growth, during flowering, and mature plants before harvest when that part of the plant is present. Data obtained for roots should also include typical times when corn rootworm would be feeding. Data are due within 24 months of the date of registration.

7. Submit field degradation studies evaluating accumulation and persistence of Cry3Bb1 in several different soils in various strata. Representative fields must have been planted with MON863 and include both conventional tillage and no-till samples and be harvested under typical agronomic conditions. Sampling must continue until the limit of detection is reached. Studies should include soils with high levels of a variety of clays. Both ELISA and insect bioassays need to be conducted and compared to determine if Cry3Bb1 is accumulating or persisting in soil samples. A protocol is due within 90 days of the date of registration, and a progress report is due within one year of the date of registration. A final report is due two years from the date of registration.

8. Submit laboratory toxicity tests with Orius insidiosus (minute pirate bug), and carabid (ground beetle), within 24 months of the date of registration, provided the registration is amended to extend the registration date. Protocols are due within 120 days of the date of registration. We note that further investigation of the biology and life cycle of the red milkweed beetle demonstrates that there will be little or no exposure of larvae under natural conditions. Although adults may be exposed to Bt corn pollen while feeding on milkweed leaves, Bt is typically less toxic to adults than larvae. There is also no protocol for rearing red milkweed beetles in the laboratory and the development of such a laboratory assay would be difficult due to the red milkweed beetle’s long development time. Therefore, on October 1, 2003, the Agency granted Monsanto’s request and the waived requirement for conducting a red milkweed beetle study set forth in the notice of registration.

9. Full-scale field or semi-field studies with appropriate end points and statistical power must be conducted. Submit intermediate and multi-year non-target organism field studies with statistical power. You must submit final results to field studies previously summarized in MRID No.456530-03 (The carabid and nematode data are of particular interest.) and annual reports each year of this registration every April 30th.

10. Submit a six week broiler dietary study with 60% - 70% MON 863 corn in the diet that is of appropriate duration to represent the start and growing periods of the test species. Balanced diets should be formulated according to the National Research Council guidelines ("Nutrient Requirements of Poultry," Ninth Revised Edition, 1994) with the energy requirements of the test species being met by the inclusion of corn in the diet to assess hazards from chronic exposure of wild or domesticated fowl. A protocol for poultry studies must be submitted within 90 days of the date of registration with a final report submitted 18 months after approval of the protocol.

Top of Page

11. Submit the following insect resistance management/pest biology data. Protocols and data sets identified in Monsanto's 12/13/2002 letter must be submitted within 90 days of the date of registration. A progress report must be submitted by January 31, 2004. The final reports must be submitted by January 31, 2006.

    - Research regarding adult and larval movement and dispersal, mating habits, ovipositional patterns, number of times a female can mate and fecundity.
    - Research to determine if IRM strategies designed for WCRW and NCRW are appropriate for MCRW
    - Research regarding the mechanism of potential resistance of CRW to MON 863 is necessary to develop an appropriate long-term IRM strategy. Monsanto must attempt to develop resistant CRW colonies to aid in determining selection intensity.
    - Research regarding the effect of WCRW ovipositing in soybean prior to overwintering and extended diapause in NCRW on an IRM strategy needs further investigation.
    - Detailed summaries of the four data-sets identified in Monsanto's December 13, 2002 letter should be submitted to the Agency to support their conclusion that the initial resistance allele frequency is ? 0.01.
    - Baseline susceptibility studies currently underway should be continued for WCRW and initiated for NCRW and monitoring techniques such as discriminating dose concentration assays need to be thoroughly investigated for their feasibility as resistance monitoring tools.

Top of Page

12. BPPD strongly urges Monsanto to submit data and information cited in the benefits assessment to help measure the impacts and potential benefits of the use of MON 863 corn on a wide scale. [Note that this is not a required term or condition of the registration.]

13. Monsanto must implement the following Insect Resistance Management Program:

    The required IRM program for Cry3Bb1 Bt corn has the following elements:

    1. Requirements relating to creation of a non-Cry3Bb1 Bt corn refuge in conjunction with the planting of any acreage of commercial Cry3Bb1 Bt corn;
    2. Requirements for the registrants to prepare and require Cry3Bb1 Bt corn users to sign "grower agreements" which impose binding contractual obligations on the grower to comply with the refuge requirements;
    3. Requirements for the registrants to develop, implement, and report to EPA on programs to educate growers about IRM requirements;
    4. Requirements for the registrants to develop, implement, and report to EPA on programs to evaluate and promote growers' compliance with IRM requirements (the Cry3Bb1 Compliance Assurance Program (CAP) must integrate with the CAP already approved for MON810, EPA Registration Number 524-489);
    5. Requirements for the registrants to develop, implement, and report to EPA on monitoring programs to evaluate whether there are statistically significant and biologically relevant changes in target insect susceptibility to Cry3Bb1 protein in the target insects;
    6. Requirements for the registrants to develop, and if triggered, to implement a "remedial action plan" which would contain measures the registrants would take in the event that any insect resistance was detected as well as to report on activity under the plan to EPA;
    7. Submit annual reports on sales(by state and county), IRM grower agreements results, compliance, and educational program on or before January 31st each year beginning in 2004.

a. Refuge Requirements

Grower agreements (also known as stewardship 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.

- Refuge planting options include: refuge acres should be planted as blocks adjacent to MON 863 corn fields or as in-field strips.
- External refuges must be planted adjacent to Cry3Bb1 MON 863 fields.
- When planting the refuge in strips across the field, refuges must be at least 6 rows wide, preferably 12 consecutive rows wide.
- Insecticide treatments for control of corn rootworm larvae may be applied. Instructions to growers will specify that insecticides labeled for control of corn rootworm adults cannot be applied while adults are present in the refuge unless the Cry3Bb1 field is treated in a similar manner.

b. Grower Agreements

1. Persons purchasing the Bt corn product must sign a grower agreement. The term "grower agreement" refers to any grower purchase contract, license agreement, or similar legal document.
2. The grower agreement and/or specific stewardship documents referenced in the grower agreement must clearly set forth the terms of the current IRM program. By signing the grower agreement, a grower must be contractually bound to comply with the requirements of the IRM program.
3. The registrant must develop a system (equivalent to what is already approved for MON 810, EPA Reg. No. 524-489) which is reasonably likely to assure that persons purchasing the Bt corn product will affirm annually that they are contractually bound to comply with the requirements of the IRM program. The proposed system will be submitted to EPA within 90 days from the date of registration.
4. The registrant must use grower agreements and submit to EPA within 90 days from the date of registration a copy of that agreement and any specific stewardship documents referenced in the grower agreement. If Monsanto wishes to change any part of the grower agreement or any specific stewardship documents referenced in the grower agreement that would affect either the content of the IRM program or the legal enforceability of the provisions of the agreement relating to the IRM program, thirty days prior to implementing a proposed change, the registrant must submit to EPA the text of such changes to ensure that it is consistent with the terms and conditions of the amendment.
5. The registrant must establish a system (equivalent to what is already approved for MON 810, EPA Reg. No. 524-489) which is reasonably likely to assure that persons purchasing the Bt corn sign grower agreement(s), and must provide within 90 days from the date of the registration a written description of that system.
6. The registrant shall maintain records of all Bt corn grower agreements for a period of three years from December 31st of the year in which the agreement was signed.
7. Beginning on January 31, 2004 and annually thereafter, the registrant shall provide EPA with a report showing the number of units of its Bt MON863 corn seeds sold or shipped and not returned, and the number of such units that were sold to persons who have signed grower agreements. The report shall cover the time frame of the twelve-month period covering the prior August through July.
8. The registrant must allow a review of the grower agreements and grower agreement records by EPA or by a State pesticide regulatory agency if the State agency can demonstrate that confidential business information, including names, personal

information, and grower license number, will be protected.

Top of Page

c. IRM Education and IRM Compliance Monitoring Programs

1. Monsanto must design and implement a comprehensive, ongoing IRM education program designed to convey to Bt MON863 corn users the importance of complying with the IRM program. The program shall include information encouraging Bt MON863 corn users to pursue optional elements of the IRM program relating to refuge configuration and proximity to Bt MON863 corn fields. The education program shall involve the use of multiple media, e.g. face-to-face meetings, mailing written materials, EPA reviewed language on IRM requirements on the bag or bag tag, and electronic communications such as by Internet, radio, or television commercials. Copies of the materials will be provided to EPA for its records. The program shall involve at least one written communication annually to each Bt MON863 corn user separate from the grower technical guide. The communication shall inform the user of the current IRM requirements. Monsanto shall coordinate its education programs with educational efforts of other registrants and other organizations, such as the National Corn Growers Association and state extension programs.
2. Annually, the registrant shall revise, and expand as necessary, its education program to take into account the information collected through the compliance survey required under paragraph 6] and from other sources. The changes shall address aspects of grower compliance that are not sufficiently high.
3. Beginning January 31, 2004 and annually thereafter, the registrants must provide a report to EPA summarizing the activities carried out under the education program for the prior year and the plans for their education program during the current year. The registrant must either submit a separate report or contribute to the report from the industry working group (ABSTC).
4. The registrant must design and implement an ongoing IRM compliance assurance program designed to evaluate the extent to which growers purchasing its MON863 Bt corn product are complying with the IRM program and that takes such actions as are reasonably needed to assure that growers who have not complied with the program either do so in the future or lose their access to the MON863 Bt corn product. The registrant shall coordinate with other Bt corn registrants in designing and implementing its compliance assurance program and integrate the Cry3Bb1 CAP with the CAP already approved for MON810, EPA Registration Number 524-489. The registrant must prepare and submit within 90 days of the date of registration a written description of their compliance assurance program including a summary of the program implemented in the 2003 growing season. Other required features of the program are described in paragraphs 5] - 15] below.

Top of Page

5. The registrant must establish and publicize a "phased compliance approach," i.e., a guidance document that indicates how the registrant will address instances of non-compliance with the terms of the IRM program and general criteria for choosing among options for responding to any non-compliant growers. The options shall include withdrawal of the right to purchase MON863 Bt corn for an individual grower or for all growers in a specific region. An individual grower found to be significantly out of compliance two years in a row would be denied sales of the product the next year. Similarly, seed dealers who are not fulfilling their obligations to inform/educate growers of their IRM obligations will lose their opportunity to sell MON863 Bt corn.
6. The IRM compliance assurance program shall include an annual survey of a statistically

representative sample of Bt corn growers conducted by an independent third party. The survey shall measure the degree of compliance with the IRM program by growers in different regions of the country and consider the potential impact of non-response. The sample size and geographical resolution may be adjusted annually, based upon input from the independent marketing research firm and academic scientists, to allow analysis of compliance behavior within regions or between regions. The sample size must provide a reasonable sensitivity for comparing results across the U.S.

7. The survey shall be designed to provide an understanding of any difficulties growers encounter in implementing IRM requirements. An analysis of the survey results must include the reasons, extent, and potential biological significance of any implementation deviations.
8. The survey shall be designed to obtain grower feedback on the usefulness of specific educational tools and initiatives.
9. The registrant shall provide a preliminary summary of their findings by November 15 and a final written summary of the results of the prior year's survey (together with a description of the regions, the methodology used, and the supporting data) to EPA by January 31 of each year. The registrant shall confer with EPA on the design and content of the survey prior to its implementation.
10. Annually, the registrant shall revise, and expand as necessary, its compliance assurance program to take into account the information collected through the compliance survey required under paragraphs 6] through 8] and from other sources. The changes shall address aspects of grower compliance that are not sufficiently high. The registrant must confer with the Agency prior to adopting any changes to a previously approved CAP.
11. The registrant shall train its representatives who make on-farm visits with MON863 Bt corn growers to perform assessments of compliance with IRM requirements. In the event that any of these visits result in the identification of a grower who is not in compliance with the IRM program, the registrant shall take appropriate action, consistent with its "phased compliance approach," to promote compliance.
12. The registrant shall carry out a program for investigating legitimate "tips and complaints" that its growers are not in compliance with the IRM program. Whenever an investigation results in the identification of a grower who is not in compliance with the IRM program, the registrant shall take appropriate action, consistent with its "phased compliance approach."
13. If a grower, who purchases MON863 Bt corn for planting, was specifically identified as not being in compliance during the previous year, the registrant shall visit with the grower and evaluate whether that the grower is in compliance with the IRM program for the current year.
14. Beginning January 31, 2004 and annually thereafter, Monsanto shall provide a report to EPA summarizing the activities carried out under their compliance assurance program for the prior year and the plans for the compliance assurance program during the current year. The report will include information regarding grower interactions (including, but not limited to, on-farm visits, verified tips and complaints, grower meetings and letters), the extent of non-compliance, corrective measures to address the non-compliance, and any follow-up actions taken.
15. The registrant and the seed corn dealers for the registrant must allow a review of the compliance records by EPA or by a State pesticide regulatory agency if the State agency can demonstrate that confidential business information, including the names, personal information, and grower license number of the growers will be protected.

Top of Page

d. Insect Resistance Monitoring

The Agency is imposing the following conditions for this product

1. The registrants will monitor for resistance and/or trends in increased tolerance for corn rootworm. Sampling should be focused in those areas in which there is the highest risk of resistance development. You must submit a protocol within 90 days of the date of registration.
2. The registrant shall provide to EPA a description of its resistance monitoring plan by January 31, 2004. The description shall include: sampling (number of locations and samples per locations), sampling methodology, bioassay methodology, standardization procedures, detection technique and sensitivity, and the statistical analysis of the probability of detecting resistance.
3. The registrant must follow up on grower, extension specialist or consultant reports of less than expected results or control failures for the corn rootworm. The registrant will instruct its customers (growers and seed distributors) to contact them (e.g., via a toll-free customer service number) if incidents of unexpected levels of damage occurs from these target pests. The registrant will investigate all damage reports submitted to the company or the company's representatives. See Remedial Action Plans section below.
4. A report on results of resistance monitoring and investigations of damage reports must be submitted to the Agency annually by April 30th each year for the duration of the conditional registration.

e. Remedial Action Plans

A Remedial Action Plan covering both suspected and confirmed resistance for corn rootworm must be submitted by 1/31/2004. If resistance is confirmed, all MON863 acres (including MON863 Bt fields and non-MON863 Bt refuges) must be treated with insecticides targeted at CRW adults as well as larvae.

Top of Page

Annual Reports:

The registrant will provide annual reports to EPA on its Cry3Bb1 PIP expressed in corn based on the following table.

Report	Description	Due Date
Annual Sales	Reported by county and state summed by state	January 31st each year beginning in 2004
Grower Agreement	Number of units of Bt corn seeds shipped or sold and not returned, and the number of such units that were sold to persons who have signed grower agreements	January 31st each year beginning in 2004
Grower Education	Education program completed previous year and plan for next year	January 31st each year beginning in 2004
Proposed Compliance Plan	Written description of Compliance Assurance Program	90 Days of the Date of Registration

Compliance Assurance Plan	Compliance Assurance Program Activities and Results	January 31st each year starting in 2004
Compliance	To include annual survey results and plans for the next year Preliminary survey report November 15th each year and full report	January 31st each year thereafter
Insect Resistance Monitoring	Submission of protocol	90 Days of the Date of Registration
Insect Resistance Monitoring	Description of the program including sampling (number of locations and samples per locations), sampling methodology, bioassay methodology, standardization procedures, detection technique and sensitivity, and the statistical analysis of the probability of detecting resistance.	January 31, 2004

Top of Page

Additional reports are due as described in the following table:

Report	Description	Due Date
IRM Grower Agreements	Proposed system to assure growers sign grower agreements	90 Days of the Date of Registration
IRM Affirmation Plan	System to assure annual affirmation by growers of their IRM obligations	90 Days of the Date of Registration
Changes to Grower Agreement and/or IRM documents	Current grower agreement(s) and any specific stewardship documents	At least 30 days before any changes related to IRM are expected to be imposed.
Insect Resistance Monitoring Results	Results of monitoring and investigations of damage reports	April 30th each year

Top of Page

V. Additional Contact Information:

Ombudsman, Biopesticides and Pollution Prevention Division (7511P)
Office of Pesticide Programs
Environmental Protection Agency
1200 Pennsylvania Avenue, NW
Washington, D.C. 20460