524-552

3/19/2009

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

1/13

MAR 19 2009

Ms. Margaret Wideman
Regulatory Affairs Manager
Monsanto Company
800 North Lindbergh Blvd
St. Louis, MO 63167

Dear Ms. Wideman:

Subject: Your September 4, 2008 Amendment Request to Amend the Insect Resistance Management Terms and Conditions for MON 88017 x MON 810
EPA Registration No. 524-552

The amendment referred to above, submitted in connection with registration under section 3(c)(7)(A)of the Federal Insecticide, Fungicide, and Rodenticide Act, as amended, are acceptable subject to the following comments.

Insect Resistance Management:

The listed IRM terms and conditions are being modified as follows.

1) Under 6a Refuge Requirements, the statement "These refuge requirements do not apply to seed increase/propagation of inbred and hybrid corn seed" is replaces with "These refuge requirements do not apply to seed propagation of inbred and hybrid corn seed corn up to a total of 20,000 acres per county and up to a combined U.S. total of 250,000 acres per PIP active ingredient per registrant per year."

2) Under 6d Insect Resistance Monitoring and 6e Remedial Action Plans, the Cry1Ab-related portions are removed and replaced by 6f below.

Thus, under 6d1, the statement "For the Cry1Ab portion of the product, you will monitor for resistance and/or trends in increased tolerance for European corn borer, Southwestern corn borer, and corn earworm. Sampling should be focused in those areas in which there is the highest risk of resistance development." is removed. Under 6d6, the phrase "by April 30th of each year for lepidopteran insects" is removed. Under 6e, the statement "The October 15, 2001 Remedial Action Plan for Responding to Resistance in European Corn Borer, Corn Earworm and/or Southwestern Corn Borer must be used for suspected and confirmed resistance of these pests." is removed.

Further the 6d. and 6e. headings are modified to read as 6d. Cry3Bb1 Insect Resistance Monitoring and 6e. Cry3Bb1 Remedial Action Plans.

CONCURRENCES

SYMBOL ▶	7511	7511P						
SURNAME ▶								
DATE ▶	3/19/09	3/19/09						

6f. Cry1Ab Insect Resistance Monitoring

The Agency is imposing the following conditions for this product:

The registrant will monitor for resistance to its lepidopteran-resistant Bt corn. The monitoring program shall consist of two approaches: (1) focused population sampling and laboratory testing; and (2) investigation of reports of less-than expected control of labeled insects. Should field-relevant resistance be confirmed, an appropriate resistance management action plan will be implemented.

(1) Focused Population Sampling

The registrant shall annually sample and bioassay populations of the key target pests *Ostrinia nubilalis* (European corn borer; ECB), *Diatraea grandiosella* (Southwestern corn borer; S WCB), and *Helicoverpa zea* (corn earworm; CEW). Sampling for the target pests will be focused in areas identified as those with the highest risk of resistance development (e.g., where lepidopteran-active Bt hybrids are planted on a high proportion of the corn acres, and where the insect species are regarded as key pests of corn). Bioassay methods must be appropriate for the goal of detecting field-relevant shifts in population response to lepidopteran resistant Bt corn and/or changes in resistance allele frequency in response to the use of Bt corn and, as far as possible, should be consistent across sampling years to enable comparisons with historical data.

The number of populations to be collected shall reflect the regional importance of the insect species as a pest, and specific collection regions will be identified for each pest. For ECB, a minimum of 12 populations across the sampling region will be targeted for collection at each annual sampling. For SWCB, the target will be a minimum of six populations. For CEW, the target will be a minimum of 10 populations. Pest populations should be collected from multiple corn-growing states reflective of different geographies and agronomic conditions. To obtain sufficient sensitivity to detect resistance alleles before they become common enough to cause measurable field damage, each population collection shall attempt to target 400 insect genomes (egg masses, larvae, mated females, and/or mixed-sex adults), but a successful population collection will contain a minimum of 100 genomes. It is recognized that it may not be possible to collect the target number of insect populations or genomes due to factors such as natural fluctuations in pest density, environmental conditions, and area-wide pest suppression.

The sampling program and geographic range of collections may be modified as appropriate based on changes in pest importance and for the adoption levels of lepidopteran-resistant Bt corn. The Agency shall be consulted prior to the implementation of such modifications.

The registrant will report to the Agency before August 31 each year the results of the population sampling and bioassay monitoring program.

Any incidence of unusually low sensitivity to the Bt protein in bioassays shall be investigated as soon as possible to understand any field relevance of such a finding. Such investigations shall proceed in a stepwise manner until the field relevance can be either confirmed or refuted, and results of these shall be reported to the Agency annually before August 31. The investigative steps will include:

1. Re-test progeny of the collected population to determine whether the unusual bioassay response is reproducible and heritable. If it is not reproducible and heritable, no further action is required.

2. If the unusual response is reproducible and heritable, progeny of insects that survive the diagnostic concentration will be tested using methods that are representative of exposure to Bt corn hybrids under field conditions. If progeny do not survive to adulthood, any suspected resistance is not field relevant and no further action is required.

3. If insects survive steps 1 and 2, resistance is confirmed, and further steps will be taken to evaluate the resistance. These steps may include:

- determining the nature of the resistance (*i.e.,* recessive or dominant, and the level of functional dominance);
- estimating the resistance-allele frequency in the original population;
- determining whether the resistance-allele frequency is increasing by analyzing field collections in subsequent years sampled from the same site where the resistance allele(s) was originally collected;
- determining the geographic distribution of the resistance allele by analyzing field collections in subsequent years from sites surrounding the site where the resistance allele(s) was originally collected.

Should field-relevant resistance be confirmed, and the resistance appears to be increasing or spreading, the registrant will consult with the Agency to develop and implement a case-specific resistance management action plan.

(2) Investigation of Reports of Unexpected Levels of Damage by the Target Pests:

The registrant will follow up on grower, extension specialist or consultant reports of unexpected levels of damage by the lepidopteran pests listed on the pesticide label. The registrant will instruct its customers to contact them if such incidents occur. The registrant will investigate all legitimate reports submitted to the

company or the company's representatives.

If reports of unexpected levels of damage lead to the suspicion of resistance in any of the key target pests (ECB, SWCB, and CEW), the registrant will implement the actions described below, based on the following definitions of *suspected resistance* and *confirmed resistance.*

Suspected resistance

EPA defines *suspected resistance* to mean field reports of unexpected levels of insect feeding damage for which:

- the corn in question has been confirmed to be lepidopteran-active Bt corn;
- the seed used had the proper percentage of corn expressing Bt protein;
- the relevant plant tissues are expressing the expected level of Bt protein; and
- 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 that there could be no other reasonable causes for the damage.

The Agency does not interpret *suspected resistance* to mean grower reports of possible control failures or suspicious results from annual insect monitoring assays, nor does the Agency intend that extensive field studies and testing be undertaken to confirm scientifically the presence of insects resistant to Bt corn in commercial production fields before responsive measures are undertaken.

If resistance is *suspected,* the registrant will instruct growers to do the following:

- Use alternative control measures in the Bt corn fields in the affected region to control the target pest during the immediate growing season.
- Destroy Bt corn crop residues in the affected region within one month after harvest with a technique appropriate for local production practices to minimize the possibility of resistant insects over-wintering and contributing to the next season's target pest population.

Additionally, if possible, and prior to the application of alternative control measures or destruction of crop residue, the registrant will collect samples of the

insect population in the affected fields for laboratory rearing and testing. Such rearing and testing shall be conducted as expeditiously as practical.

Confirmed resistance

EPA defines *confirmed resistance* to mean, in the case of field reports of unexpected levels of damage from the key target pests, that all the following criteria are met:

- There is >30% insect survival and commensurate insect feeding in a bioassay, initiated with neonate larvae, that uses methods that are representative of exposure to Bt corn hybrids under field conditions (ECB and SWCB only).

- In standardized laboratory bioassays using diagnostic concentrations of the Bt protein suited to the target pest in question, the pest exhibits resistance that has a genetic basis and the level of survivorship indicates that there may be a resistance allele frequency of ≥ 0.1 in the sampled population.

- In standardized laboratory bioassays, the LC_{50} exceeds the upper limit of the 95% confidence interval of the LC_{50} for susceptible populations surveyed both in the original baselines developed for this pest species and in previous years of field monitoring.

(3) Response to Confirmed Resistance in a Key Target Pest as the Cause of Unexpected Levels of Damage in the Field

When field resistance is *confirmed* (as defined above), the following steps will be taken by the registrant:

- EPA will receive notification within 30 days of resistance confirmation;

- Affected customers and extension agents will be notified about confirmed resistance within 30 days;

- Monitoring will be increased in the affected area and local target pest populations will be sampled annually to determine the extent and impact of resistance;

- If appropriate (depending on the resistant pest species, the extent of resistance, the timing of resistance, and the nature of resistance, and the availability of suitable alternative control measures), alternative control measures will be employed to reduce or control target pest populations in the affected area. Alternative control measures may include advising customers and extension agents in the affected area to incorporate crop residues into the soil following harvest to minimize the possibility of over-wintering insects, and/or applications of chemical insecticides;

- Unless otherwise agreed with EPA, stop sale and distribution of the relevant lepidopteran-active Bt corn hybrids in the affected area immediately until an effective local mitigation plan approved by EPA has been implemented;

- The registrant will develop a case-specific resistance management action plan within 90 days according to the characteristics of the resistance event and local agronomic needs. The registrant will consult with appropriate stakeholders in the development of the action plan, and the details of such a plan shall be approved by EPA prior to implementation;

- Notify affected parties (e.g. growers, consultants, extension agents, seed distributors, university cooperators and state/federal authorities as appropriate) in the region of the resistance situation and approved action plan; and

- In subsequent growing seasons, maintain sales suspension and alternative resistance management strategies in the affected region(s) for the Bt corn hybrids that are affected by the resistant population until an EPA-approved local resistance management plan is in place to mitigate the resistance.

A report on results of resistance monitoring and investigations of damage reports must be submitted to the Agency annually by August 31st each year for the duration of the conditional registration.

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 of Cry1Ab corn constitutes acceptance of these conditions.

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

Sincerely,

Sheryl K. Reilly, Ph.D., Chief
Microbial Pesticides Branch
Biopesticides and Pollution
Prevention Division (7511P)

MON 88017 x MON 810

Rootworm- and Corn Borer-Protected Corn Seed
(OECD Unique Identifier: MON-88Ø17-3 × MON-ØØ81Ø-6)

This product is effective in controlling corn leaf, stalk and ear damage caused by corn borers and root feeding damage caused by corn rootworm larvae.

Active Ingredient:

Bacillus thuringiensis Cry3Bb1 protein and the genetic material necessary for its production (Vector ZMIR39) in event MON 88017 corn (OECD Unique Identifier: MON-88Ø17-3)..... 0.0071 - 0.015%

Bacillus thuringiensis Cry1Ab delta-endotoxin and the genetic material necessary for its production (Vector PV-ZMCT01) in event MON 810 corn (OECD Unique Identifier: MON-ØØ81Ø-6).....0.0011 - 0.0017%

Other Ingredients:

Substance produced by a marker gene and the genetic material necessary for its production (Vector ZMIR39) in event MON 88017 corn (OECD Unique Identifier: MON-88Ø17-3).....0.0038 - 0.007%

Percentage (wt/wt) on a dry weight basis for whole plant (forage).

CAUTION

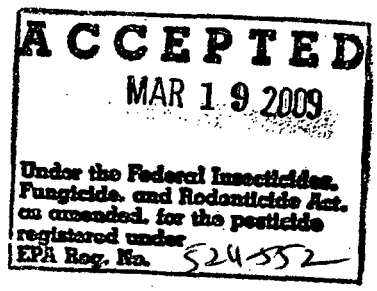
KEEP OUT OF REACH OF CHILDREN

NET CONTENTS_____

EPA Registration No. 524-552

EPA Establishment No. 524-MO-002

Monsanto Company
800 North Lindbergh Blvd.
St. Louis, MO 63167



DIRECTIONS FOR USE

It is a violation of Federal law to use this product in any manner inconsistent with this labeling. The following information regarding commercial production must be included in the MON 88017 x MON 810 Technology Use Guide (IRM Guide).

MON 88017 x MON 810 protects corn crops from leaf, stalk, and ear damage caused by corn borers and root damage caused by corn rootworm larvae. In order to minimize the risk of these pests developing resistance to MON 88017 x MON 810 corn, an insect resistance management plan must be implemented which includes planting of a structured refuge.

This plant-incorporated protectant may be combined through conventional breeding with other registered plant-incorporated protectants that are similarly approved for use in combination, through conventional breeding, with other plant-incorporated protectants to produce inbred corn lines and hybrid corn varieties with combined pesticidal traits.

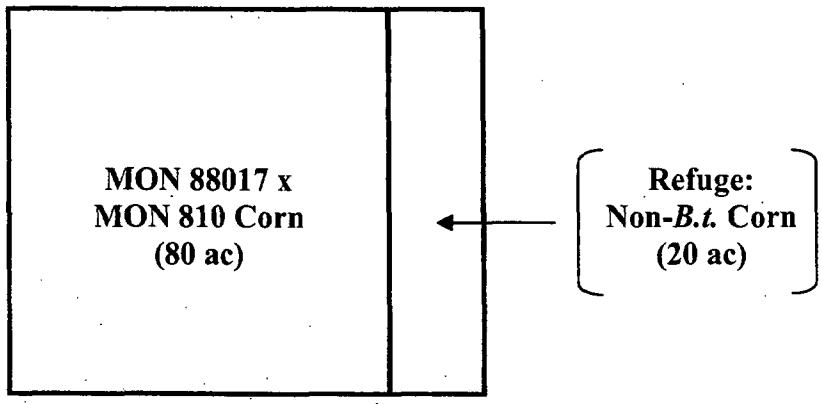
INSECT RESISTANCE MANAGEMENT

Corn Belt / Noncotton Growing Region Refuge Requirements

For MON 88017 x MON 810 corn grown in noncotton growing regions of the United States, two options for deployment of the refuge are available to growers.

The first option is planting a common refuge for both corn borers and corn rootworms. The common refuge must be planted with corn hybrids that do not contain *Bacillus thuringiensis* (*B.t.*) technologies for the control of corn borers or corn rootworms. The refuge area must represent at least 20% of the grower's corn acres (i.e., sum of MON 88017 x MON 810 acres and refuge acres; refuge area must contain 20 acres of corn for every 80 acres of MON 88017 x MON 810 corn planted). It can be planted as a block within or adjacent (e.g., across the road) to the MON 88017 x MON 810 field, perimeter strips (i.e. strips around the field), or in-field strips. If perimeter or in-field strips are implemented, the strips must be at least 4 consecutive rows wide. The common refuge can be treated with an insecticide to control rootworm larvae and other soil pests. The refuge can also be treated with a non-*B.t.* foliar insecticide for control of late season pests if pest pressure reaches an economic threshold for damage; however, if rootworm adults are present at the time of foliar applications then the MON 88017 x MON 810 field (acres) must be treated in a similar manner. Economic thresholds will be determined using methods recommended by local or regional professionals (e.g., Extension Service agents, crop consultants, etc.). A schematic of one common refuge deployment option is shown below:

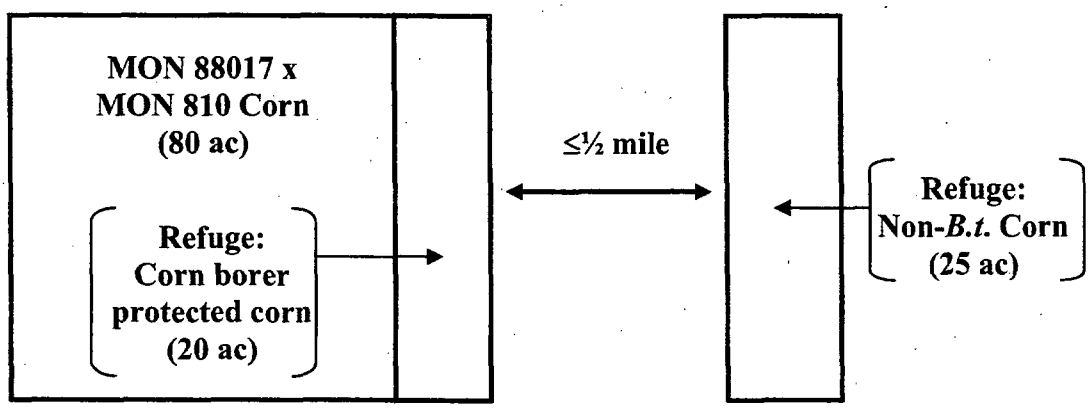
Common Refuge



The second option is planting separate refuge areas (e.g., two refuge areas, a double refuge, paired refuge areas) for corn borers and corn rootworms. The corn borer refuge must be planted with corn that is not a lepidoteran-protected *B.t.* hybrid, must represent at least 20% of the grower's corn acres, and must be planted within ½ mile of the MON 88017 x MON 810 field. The corn borer refuge can be treated with an insecticide for corn rootworm larval control, or a non-*B.t.* foliar-applied insecticide for corn borer control if pest pressure reaches an economic threshold for damage.

The corn rootworm refuge must be planted with corn that is not a corn rootworm-protected *B.t.* hybrid, but can be planted with *B.t.* hybrids that control corn borers. The corn rootworm refuge must represent at least 20% of the grower's corn acres (i.e., corn rootworm refuge must contain 20 acres of corn for every 80 acres of MON 88017 x MON 810 corn planted) and can be planted as a block within or adjacent to the MON 88017 x MON 810 field, strips around the field, or in-field strips. The corn rootworm refuge can be treated with an insecticide to control rootworm larvae and other soil pests. The refuge can also be treated with a non-*B.t.* foliar insecticide for control of late season pests; however, if corn rootworm adults are present at the time of foliar applications then the MON 88017 x MON 810 field must be treated in a similar manner. A schematic of one separate refuge option with the corn rootworm refuge planted as a block within the field and the corn borer refuge planted within a ½ mile of the MON 88017 x MON 810 field is shown below:

Separate-Refuge Option
{Two-Refuge Option, Double-Refuge Option, Paired-Refuge Option}

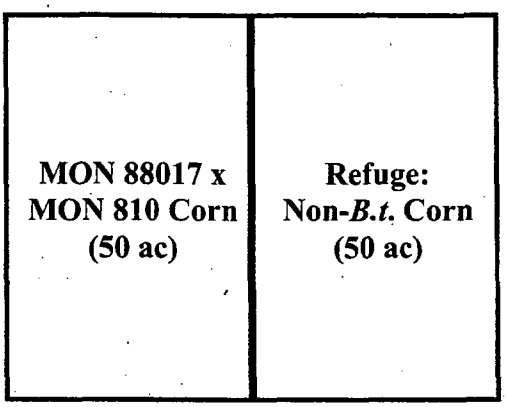


Corn/Cotton Growing Area (Cotton Growing Area) Refuge Requirements

For MON 88017 x MON 810 corn grown in cotton growing areas of the U.S. the common refuge and separate refuge options (e.g., two-refuge options, double-refuge options, paired-refuge options) are also available, however, the refuge area is larger. Cotton growing areas include the following states: Alabama, Arkansas, Florida, Georgia, Louisiana, North Carolina, Mississippi, South Carolina, Oklahoma (only the counties of Beckham, Caddo, Comanche, Custer, Greer, Harmon, Jackson, Kay, Kiowa, Tillman, and Washita), Tennessee (only the counties of Carroll, Chester, Crockett, Dyer, Fayette, Franklin, Gibson, Hardeman, Hardin, Haywood, Lake, Lauderdale, Lincoln, 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 Dinwiddie, Franklin City, Greensville, Isle of Wight, Northampton, Southampton, Suffolk City, Surrey, and Sussex), and Missouri (only the counties of Dunkin, New Madrid, Pemiscot, Scott, and Stoddard).

The first option is planting a common refuge for both corn borers and corn rootworms. The common refuge must be planted with corn hybrids that do not contain *B.t.* technologies for the control of corn rootworms or corn borers. The refuge area must represent at least 50% of the grower's corn acres (i.e., refuge must contain 50 acres of non-*B.t.* corn for every 50 acres of MON 88017 x MON 810 corn planted). It can be planted as a block within or adjacent to the MON 88017 x MON 810 field, strips around the field, or in-field strips. If perimeter or in-field strips are implemented, the strips must be at least 4 consecutive rows wide. The common refuge can be treated with an insecticide to control rootworm larvae and other soil pests. The refuge can also be treated with a non-*B.t.* foliar insecticide for control of late season pests if pest pressure reaches an economic threshold for damage; however, if rootworm adults are present at the time of foliar applications then the MON 88017 x MON 810 field must be treated in a similar manner. A schematic of one common refuge deployment option is shown below:

Common Refuge

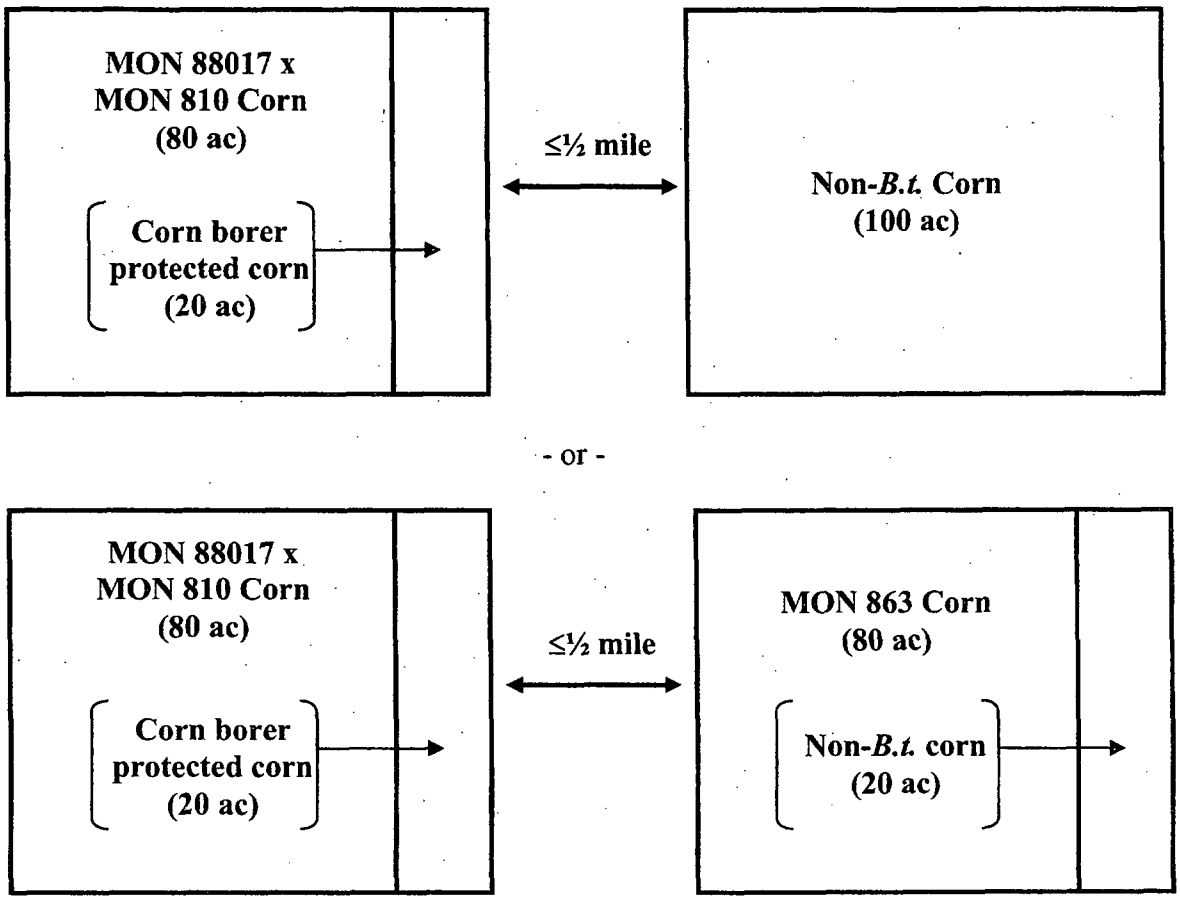


The second option is planting separate refuge areas (e.g., two refuge areas, double refuge areas, paired refuge areas) for corn borers and corn rootworms. The corn borer refuge must be planted with corn that is not a lepidopteran-protected *B.t.* hybrid, must represent at least 50% of the grower's corn acres (i.e., must contain 50 acres of corn for every 50 acres of lepidopteran-protected corn planted), and must be planted within ½ mile of the MON 88017 x MON 810 field. The corn borer refuge can be treated with an insecticide for corn rootworm larval control, or a non-*B.t.* foliar-applied insecticide for corn borer control if pest pressure reaches an economic threshold for damage. Economic thresholds will be determined using methods recommended by local or regional professionals (e.g., Extension Service agents, crop consultants, etc.).

The corn rootworm refuge must be planted with corn that is not a rootworm-protected *B.t.* hybrid, but can be planted with *B.t.* hybrids that control corn borers. The corn rootworm refuge must represent at least 20% of the grower's corn acres (i.e., corn rootworm refuge must contain 20 acres of corn for every 80 acres of MON 88017 x MON 810 corn planted) and be planted as a block within or adjacent to the MON 88017 x MON 810 field, strips around the field, or in-field strips. The corn rootworm refuge can be treated with an insecticide to control rootworm larvae and other soil pests. The refuge can also be treated with a non-*B.t.* foliar insecticide for control of late season pests; however, if rootworm adults are present at the time of foliar applications then the MON 88017 x MON 810 field must be treated in a similar manner. Schematics for two separate-refuge options with the corn rootworm refuge planted as a block within the MON 88017 x MON 810 field and the corn borer refuge planted as a block within a ½ mile of the MON 88017 x MON 810 field are shown below:

Separate-Refuge Option

{Two-Refuge Option, Double-Refuge Option, Paired-Refuge Option}



Grower agreements will specify that growers must adhere to the refuge requirements that will be described in the Technology Use Guide (IRM Guide) for MON 88017 x MON 810 corn or other applicable product use documents. Growers who fail to comply with the IRM requirements risk losing access to the product.

These refuge requirements do not apply to seed propagation of inbred and hybrid corn seed up to total of 20,000 acres per county and up to a combined U.S. total of 250,000 acres per PIP active ingredient per registrant per year.

CORN INSECTS CONTROLLED OR SUPPRESSED

Field corn has been genetically transformed to produce the *B.t.* Cry1Ab and Cry3Bb1 proteins for the control or suppression of the following lepidopteran and coleopteran insects, respectively:

European corn borer (*Ostrinia nubilalis*)
Southwestern corn borer (*Diatraea grandiosella*)
Southern cornstalk borer (*Diatraea crambidoides*)
Sugarcane cornstalk borer (*Diatraea saccharalis*)
Corn earworm (*Helicoverpa zea*)
Fall armyworm (*Spodoptera frugiperda*)
Stalk borer (*Papaipema nebris*)

Western corn rootworm (*Diabrotica virgifera virgifera*)
Northern corn rootworm (*Diabrotica barberi*)
Mexican corn rootworm (*Diabrotica virgifera zeae*)

MON 88017 x MON 810 is a product of Monsanto's research program offering unique genetic characteristics for specific grower needs and may be protected by one or more of the following U.S. Patents: 5,164,316, 5,196,525, 5,352,938, 5,352,605, 5,359,142, 5,424,412, 5,484,956, 5,554,798, 5,641,876, 5,717,084, 5,728,925, 5,804,425, 5,859,347, 5,593,874, 6,025,545, 6,063,597, 6,083,878, 6,180,774, 6,331,665, 7,064,248, 7,227,056 and RE39247.