524-552

7/2/2013

1/16

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
Washington, D.C. 20460

JUL - 2 2013

OFFICE OF CHEMICAL SAFETY
AND POLLUTION PREVENTION

Diane Ruezinsky, Ph.D.
Regulatory Affairs Manager
Monsanto Company
1300 I Street, NW, Suite 450 East
Washington, DC 20005

Re: MON 88017 x MON 810
EPA Registration No. 524-552
Amendment to conditions of registration
Submission dated 03/26/2013
Decision No. 477188

The amendment referred to above, submitted in connection with registration under Section 3(c)(7)(A) of the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), is acceptable only as an extension to the current conditional, time-limited registration and provided that you comply with the updated terms and conditions as described in this letter.

1) The subject registration will automatically expire at midnight on September 30, 2015.

2) The subject registration will be limited to Cry3Bb1 [*Bacillus thuringiensis* Cry3Bb1 protein and the genetic material necessary for its production (vector PV-ZMIR39) in event MON 88017 corn (OECD Unique Identifier: MON-88Ø17-3)] x Cry1Ab [*Bacillus thuringiensis* Cry1Ab protein and the genetic material necessary for its production (vector PV-ZMCT01) in event MON 810 corn (OECD Unique Identifier: MON-ØØ81Ø-6)] for use in field corn.

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

4) Submit/cite all data, determined by EPA to be acceptable and required to support the individual plant-incorporated protectants in MON 88017 and MON 810, within the time frames required by the terms and conditions of EPA Registration Numbers 524-551 and 524-489, respectively.

5) 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 registered plant-incorporated protectants to produce inbred corn lines and hybrid corn varieties with combined pesticidal traits.

6) You must commit to implement an Insect Resistance Management (IRM) Program, consisting of the following elements:

- Requirements relating to creation of a refuge for the Cry3Bb1 and Cry1Ab components that meet the requirements of the individual traits. The refuge for both traits may be combined by planting non-*Bacillus thuringiensis* (*Bt*) corn as the refuge, or the refuge for each trait may be planted separately. In the latter case, corn rootworm-resistant *Bt* corn may be planted in the lepidopteran refuge for the Cry1Ab component, and lepidopteran-resistant *Bt* corn may be planted in the corn rootworm refuge for the Cry3Bb1 component.

- Requirements for Monsanto Company (Monsanto) to prepare and require MON 88017 x MON 810 users to sign grower agreements that impose binding contractual obligations on growers to comply with the refuge requirements.

- Requirements for Monsanto to develop, implement, and report to EPA on programs to educate growers about IRM requirements.

- Requirements for Monsanto to develop, implement, and report to EPA on programs to evaluate and promote growers' compliance with IRM requirements.

- Requirements for Monsanto to develop, implement, and report to EPA on monitoring programs to evaluate whether there are statistically significant and biologically relevant changes in susceptibility to the Cry3Bb1 and Cry1Ab proteins in the target insects.

- Requirements for Monsanto to develop and, if triggered, to implement a remedial action plan that would contain measures Monsanto would take in the event that any field-relevant insect resistance was detected, as well as to report on activity under the plan to EPA.

- Requirements for Monsanto to maintain and provide the Agency, upon request, the number of units sold by state and county, IRM grower agreement results, and substantive changes to educational programs for the previous growing season, within three months of the request.

- Requirements for Monsanto, on or before August 31st of each year, to submit reports on resistance monitoring.

a. Refuge Requirements for MON 88017 x MON 810

These refuge requirements do not apply to seed increase/propagation of inbred and hybrid seed corn up to a total of 20,000 acres per county and up to a combined United States (U.S.) total of 250,000 acres per plant-incorporated protectant (PIP) active ingredient per registrant per year.

When on-farm assessments identify non-compliance with refuge requirements for one or more *Bt* corn products, additional educational material and assistance will be provided by Monsanto to help these growers meet the refuge requirements across their farming operations.

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.

Corn Belt/Non-Cotton-Growing Area Refuge Requirements

For MON 88017 x MON 810 grown in non-cotton-growing areas 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 *Bt* 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). It must 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 a soil-applied or seed-applied insecticide to control rootworm larvae and other soil pests. The refuge can also be treated with a non-*Bt* 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. Economic thresholds will be determined using methods recommended by local or regional professionals (e.g., Extension Service agents or crop consultants).

The second option is planting separate refuge areas for corn borers and corn rootworms. The corn borer refuge must be planted with corn that is not a lepidopteran-protected *Bt* hybrid, must represent at least 20% of the grower's corn acres (i.e., sum of MON 88017 x MON 810 acres and corn borer refuge acres), and must be planted within ½ mile of the MON 88017 x MON 810 field. The corn borer refuge can be treated with a soil-applied or seed-applied insecticide for corn rootworm larval control, or a non-*Bt* 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 or crop consultants). The corn rootworm refuge must be planted with corn that is not a corn rootworm-protected *Bt* hybrid, must represent at least 20% of the grower's corn acres (i.e., sum of MON 88017 x MON 810 acres and corn rootworm refuge acres), and must 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 corn rootworm refuge can be treated with a soil-applied or seed-applied insecticide to control rootworm larvae and other soil pests. The refuge can also be treated with a non-*Bt* 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. Economic thresholds will be determined using methods recommended by local or regional professionals (e.g., Extension Service agents or crop consultants).

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

For MON 88017 x MON 810 grown in cotton-growing areas of the United States, the common refuge and separate 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 Dunklin, 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 *Bt* technologies for the control of corn borers or corn rootworms. The refuge area must represent at least 50% of the grower's corn acres (i.e., sum of MON 88017 x MON 810 acres and refuge acres). It must 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 a soil-applied or seed-applied insecticide to control rootworm larvae and other soil pests. The refuge can also be treated with a non-*Bt* 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. Economic thresholds will be determined using methods recommended by local or regional professionals (e.g., Extension Service agents or crop consultants).

The second option is planting separate refuge areas for corn borers and corn rootworms. The corn borer refuge must be planted with corn that is not a lepidopteran-protected *Bt* hybrid, must represent at least 50% of the grower's corn acres (i.e., sum of MON 88017 x MON 810 acres and corn borer refuge acres), and must be planted within ½ mile of the MON 88017 x MON 810 field. The corn borer refuge can be treated with a soil-applied or seed-applied insecticide for corn rootworm larval control, or a non-*Bt* 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 or crop consultants). The corn rootworm refuge must be planted with corn that is not a corn rootworm-protected *Bt* hybrid, must represent at least 20% of the grower's corn acres (i.e., sum of MON 88017 x MON 810 acres and corn rootworm refuge acres), and must 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 corn rootworm refuge can be treated with a soil-applied or seed-applied insecticide to control rootworm larvae and other soil pests. The refuge can also be treated with a non-*Bt* 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. Economic thresholds will be determined using methods recommended by local or regional professionals (e.g., Extension Service agents or crop consultants).

b. Grower Agreements for MON 88017 x MON 810

1) Persons purchasing MON 88017 x MON 810 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) Monsanto must continue to integrate this amended registration into the current system used for its other *Bt* corn plant-incorporated protectants, which is reasonably likely to assure that persons purchasing MON 88017 x

MON 810 will affirm annually that they are contractually bound to comply with the requirements of the IRM program.

4) Monsanto must continue to use its current grower agreement for MON 88017 x MON 810. 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 (30) days prior to implementing a proposed change, Monsanto must submit to EPA the text of such changes to ensure that it is consistent with the terms and conditions of this amended registration.

5) Monsanto shall maintain records of all MON 88017 x MON 810 grower agreements for a period of three (3) years from December 31st of the year in which the agreement was signed.

6) Monsanto shall make available upon request records of the number of units of MON 88017 × MON 810 corn seed sold or shipped and not returned, and the number of such units that were sold to persons who have signed grower agreements, for the previous growing season, within three months of the request.

7) Monsanto 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 numbers of the growers, will be protected.

c. IRM Education and IRM Compliance Monitoring Programs for MON 88017 x MON 810

1) Monsanto must continue to implement and enhance (as set forth in paragraph 17 of this section) a comprehensive, ongoing IRM education program designed to convey to MON 88017 x MON 810 users the importance of complying with the IRM program. The program shall include information encouraging MON 88017 x MON 810 users to pursue optional elements of the IRM program relating to refuge configuration and proximity to MON 88017 x MON 810 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 MON 88017 x MON 810 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 organizations, such as the National Corn Growers Association and state extension programs.

2) Annually, Monsanto shall revise, and expand as necessary, its education program to take into account the information collected through the compliance survey, required under paragraph 6–8 of this section, and from other sources. The changes shall address aspects of grower compliance that are not sufficiently high.

3) Within three months of EPA request, Monsanto shall provide copies of grower education materials and information on grower education activities including any substantive changes to these materials and activities conducted either individually or as part of a report from the industry working group, Agricultural Biotechnology Stewardship Technical Committee (ABSTC).

4) Monsanto must continue to implement and improve an ongoing IRM compliance assurance program designed to evaluate the extent to which growers purchasing MON 88017 x MON 810 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 Monsanto's *Bt* corn products.

Monsanto shall coordinate with other *Bt* corn registrants in improving its compliance assurance program and continue to integrate this amended registration into the current compliance assurance program used for its other *Bt* corn plant-incorporated protectants. Other required features of the program are described in paragraphs 5–23 of this section.

5) Monsanto must maintain and publicize a "phased compliance approach" i.e., a guidance document that indicates how it 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 after the first year of non-compliance. While recognizing that for reasons of difference in business practices there are needs for flexibility between different companies, Monsanto must use a consistent set of standards for responding to non-compliance. An individual grower found to be significantly out of compliance two (2) years in a row would be denied access the next year to Monsanto's *Bt* corn products for which the grower is required to plant a separate structured refuge. Similarly, seed dealers who are not fulfilling their obligations to inform/educate growers of their IRM obligations will lose their opportunity to sell *Bt* corn.

6) The IRM compliance assurance program shall include an annual survey, conducted by an independent third party[1], of a statistically representative sample of growers of MON 88017 x MON 810 who plant the vast majority of all corn in the United States and in areas in which the selection intensity is greatest. The survey shall consider only those growers who plant 200 or more acres of corn in the Corn Belt and who plant 100 or more acres of corn in corn-cotton areas. 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 independent marketing research firms 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 United States.

7) The survey shall be designed to provide an understanding of any difficulties growers encounter in implementing IRM requirements. An analysis of 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) Monsanto shall provide 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, on or before January 31st of each year. Monsanto shall confer with other registrants and EPA on the design and content of the survey prior to its implementation.

10) Annually, Monsanto shall revise, and expand as necessary, its compliance assurance program to take into account the information collected through the compliance survey, required under paragraphs 6–8 of this section, and from other sources. The changes shall address aspects of grower compliance that are not sufficiently high. Monsanto must confer with EPA prior to adopting any changes.

11) Monsanto shall conduct an annual on-farm assessment program. Monsanto shall train its representatives who make on-farm visits with MON 88017 x MON 810 growers to perform assessments of compliance with IRM requirements. There is no minimum corn acreage size for this program. Therefore, growers will be selected for this program from across all farm sizes. In the event that any of these visits result in the

[1] A third party is classified as a party other than Monsanto, the grower, or anyone else with a direct interest in IRM compliance for *Bt* corn.

identification of a grower who is not in compliance with the IRM program, Monsanto shall take appropriate action, consistent with its phased compliance approach, to promote compliance.

12) Monsanto shall carry out a program for investigating legitimate tips and complaints that MON 88017 x MON 810 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, Monsanto shall take appropriate action, consistent with its phased compliance approach.

13) If a grower, who purchases MON 88017 x MON 810 for planting, was specifically identified as not being in compliance during the previous year, Monsanto shall visit with the grower and evaluate whether the grower is in compliance with the IRM program for the current year.

14) Annually, Monsanto shall provide a report to EPA summarizing the activities carried out under its compliance assurance program for the prior year and the plans for the compliance assurance program during the current year. Within one (1) month of submitting this report to EPA, Monsanto shall meet with EPA to discuss its findings. 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. The report must inform EPA of the number of growers deemed ineligible to purchase *Bt* corn seed on the basis of continued non-compliance with the insect resistance management refuge requirements. Monsanto may elect to coordinate information with other registrants and report collectively the results of compliance assurance programs.

15) Monsanto and the seed corn dealers for Monsanto 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 numbers of the growers, will be protected.

16) Monsanto may coordinate with other registrants in designing and implementing its compliance assurance program.

17) Monsanto will enhance the refuge education program throughout the seed delivery channel by:

i. Ensuring sales representatives, licensees, seed dealers, and growers recognize the importance of correct refuge implementation and potential consequences of failure to plant the required refuge; and

ii. Continuing to include the refuge size requirement on all MON 88017 x MON 810 seed bags or bag tags. The MON 88017 x MON 810 label accepted by EPA must include how this information will be conveyed to growers via text and graphics.

18) Monsanto will focus the majority of on-farm assessments on regions with the greatest risk for resistance by:

i. Using Bt corn adoption, pest pressure information, and other available information to identify regions where the risk of resistance is greatest; and

ii. Focusing approximately two-thirds of on-farm assessments on these regions, with the remaining assessments conducted across other regions where MON 88017 x MON 810 is used.

19) Monsanto will use its available MON 88017 x MON 810 sales records and other information to refine grower lists for on-farm assessments of their compliance with refuge requirements by:

i. Identifying for potential on-farm assessment growers whose sales information indicates they have purchased MON 88017 x MON 810 but may have purchased little or no refuge seed from Monsanto, licensees, or affiliated companies.

20) Monsanto will contract with third parties to perform on-farm assessments of compliance with refuge requirements:

i. The third-party assessors will conduct all first-time on-farm assessments, as well as second-year on-farm assessments, of those growers found out of compliance in a first-time assessment.

21) Annually, Monsanto will refine the on-farm assessment program for MON 88017 x MON 810 to reflect the adoption rate and level of refuge compliance for MON 88017 x MON 810.

22) Monsanto will follow up with growers who have been found significantly out of compliance under the on-farm assessment program and are found to be back in compliance the following year:

i. All growers found to be significantly out of compliance in a prior year will annually be sent additional refuge assistance information for a minimum of 2 years by Monsanto, a seed supplier, or a third-party assessor, after completing the assessment process.

ii. Monsanto will conduct follow-up checks on growers found to be significantly out of compliance within 3 years after they are found to be back in compliance.

iii. A grower found with a second incident of significant non-compliance with refuge requirements for *Bt* corn within a 5-year period will be denied access the next year to Monsanto's *Bt* corn products for which the grower is required to plant a separate structured refuge.

23) Monsanto will continue to conduct and support grower education (e.g. corn clinics, certified crop advisor training, etc.) that demonstrates the economic and technology – preserving value of crop rotation as a best agronomic practice. Monsanto will submit to EPA a report with evidence of the 2012 grower education program (specifically including the number of education sessions/trainings held, locations, number of attendees, examples of presentation materials and grower survey results if available) by July 31st 2013. For the following seasons, Monsanto will submit a similar report upon the request of the agency within three months of the request.

d. Insect Resistance Monitoring and Remedial Action Plans for MON 88017 x MON 810

1) EPA is imposing the following conditions for the Cry1Ab toxin expressed in MON 88017 x MON 810:

Monsanto will monitor for resistance to Cry1Ab expressed in MON 88017 x MON 810. 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.

Focused Population Sampling

Monsanto shall annually sample and bioassay populations of the key target pests: *Ostrinia nubilalis* (European corn borer; ECB), *Diatraea grandiosella* (southwestern corn borer; SWCB), 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 MON 88017 x MON 810 and/or changes in resistance allele frequency in response to the use of MON 88017 x MON 810 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 twelve (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 (6) populations. For CEW, the target will be a minimum of ten (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 MON 88017 x MON 810. EPA shall be consulted prior to the implementation of such modifications.

Monsanto will report to EPA, on or before August 31st of each year, the results of the population sampling and bioassay monitoring program.

Any incidence of unusually low sensitivity to the Cry1Ab 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 EPA annually on or before August 31st. The investigative steps will include the following:

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 MON 88017 x MON 810 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 the following:

    - 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, Monsanto will consult with EPA to develop and implement a case-specific resistance management action plan.

Investigation of Reports of Unexpected Levels of Damage by Target Lepidopteran Pests

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

EPA does not interpret ***suspected resistance*** to mean grower reports of possible control failures or suspicious results from annual insect monitoring assays, nor does EPA intend that extensive field studies and testing be undertaken to confirm scientifically the presence of insects resistant to MON 88017 x MON 810 in commercial production fields before responsive measures are undertaken.

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

- Use alternative control measures in MON 88017 x MON 810 fields in the affected region to control the target pest during the immediate growing season.

- Destroy MON 88017 x MON 810 crop residues in the affected region within one (1) 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 residues, Monsanto 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 of 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.

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 Monsanto:

- 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;

- Monsanto will develop a case-specific resistance management action plan within 90 days according to the characteristics of the resistance event and local agronomic needs. Monsanto 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 EPA, on or before August 31st of each year, for the duration of the registration.

2) EPA is imposing the following conditions for the Cry3Bb1 toxin expressed in MON 88017 x MON 810:

i. Monsanto must monitor for Cry3Bb1 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.

ii. The resistance monitoring plan must include the following: baseline sensitivity data, sampling (number of locations, samples per locations), sampling methodology and life stage sampled, bioassay methodology, standardization procedures (including quality assurance/quality control provisions), detection technique and sensitivity, statistical analysis of the probability of detecting resistance, and a revised description of rootworm damage guidelines.

iii. Monsanto must develop and utilize a functional "on-plant" diagnostic assay[2] for corn rootworm resistance monitoring to detect potentially resistant individuals and incorporate this assay into the annual resistance monitoring program.

iv. Monsanto must work to develop a proactive resistance monitoring program for northern corn rootworm (*Diabrotica barberi*). This program should include a proposal for annual sampling and testing of northern corn rootworm susceptibility to Cry3Bb1. As part of the effort, Monsanto may need to investigate novel techniques for rearing and conducting bioassays with northern corn rootworm. A report on progress towards this requirement must be included in the annual resistance monitoring report to EPA.

v. Monsanto must follow-up on grower, extension specialist, or consultant reports of unexpected damage or control failures for corn rootworm (as described in section ***(a)*** below.

vi. Monsanto must provide EPA with a resistance monitoring report on or before August 31st of each year, reporting on populations collected the previous year.

---

[2] Examples of on-plant bioassays include:
Nowatzki T, Lefko SA, Binning RR, Thompson SD, Spencer TA, Siegfried BD. 2008. Validation of a novel resistance monitoring technique for corn rootworm (Coleoptera: Chrysomelidae) and event DAS-59122-7 maize. *J. Appl. Entomol.* 132:177–188 and Gassmann A.J., J.L. Petzold-Maxwell, R.S. Keweshan, and M.W. Dunbar, 2011. Field-evolved resistance to *Bt* maize by western corn rootworm. *PLOS one*, Vol. 6 (7): 1-7.

(a) Investigation of Reports of Unexpected Levels of Damage by the Corn Rootworm (CRW). Performance Inquiries

a) Investigation. Monsanto is required to investigate "performance inquiries" (i.e., reports of unexpected corn rootworm damage to MON 88017 x MON 810 corn) from growers. Fields with unexpected damage that meet both of the criteria below must be subjected to the follow-up actions described in part b) below:

1. The affected plants are confirmed to be MON 88017 x MON 810 plants; **and**

2. Corn rootworm feeding caused root damage with a Node Injury Score (NIS) > 1.0 on at least 50% of plants sampled.

b) Follow-up actions (performance inquiries). For MON 88017 x MON 810 fields meeting the criteria in part a) above, Monsanto must take the following actions:

- Take leaf samples to determine the presence of the *Bt* protein.
- Collect at least 250 (ideally 500 or more) CRW adult individuals from field in question. Collections may be extended to any bordering corn fields, if necessary to obtain sufficient CRW adult individuals. Collected populations must be subjected to the steps described for "investigation of populations of concern" (part ***(b)*** below).
- Visit affected farm or field the following year (assuming repurchase) and attempt to collect corn rootworm adults, if collections are unsuccessful.
- Review with the grower their CRW management practices and provide CRW management recommendations. Options include, but are not limited to the following:
    - Rotation to non-host crop
    - Use of pyramided products
    - Use of additional corn rootworm control tools (e.g., soil insecticides, seed-applied insecticides, chemigation)
    - Use of an alternative corn rootworm-active plant incorporated protectant
- Include information on unexpected damage reports in its annual CRW monitoring submission to EPA.

(b) Investigation of Populations of Concern

Monsanto must conduct investigations of all CRW populations collected as part of the performance inquiry process (part ***(a)*** b) above). A CRW population will be considered resistant to Cry3Bb1 if the following criteria are met and additional collections and testing are not deemed to be necessary (see below):

1. An initial performance inquiry investigation results in a finding of Unexpected Damage; **and**

2. Where green tissues are available and plants are unusually stressed, *Bt* protein levels in affected plants are found to be within the documented range for that hybrid (if data are available); **and**

3. Single, on-plant bioassays of insect collections from the affected fields show the following:

    - A statistically significant difference in measures of either lethality/mortality or sublethal effects (growth/development) between the field population and the control population on *Bt* corn **and**

    - A lack of a statistically significant difference in the same measures of the field population raised on *Bt* corn and non-*Bt* corn plants.

Mitigation, as detailed in part *(c)* below, is required for any CRW population/ MON 88017 x MON 810 field that meets the above resistance criteria, unless the circumstances described below are applicable.

To minimize the potential for incorrectly reaching a conclusion of resistance, another year of CRW adult collections and additional testing would be needed to determine resistance if:

- The results of the single, on-plant bioassays are inconclusive (e.g., the results of the statistical analysis are unclear because of low sample sizes) or

- Another reasonable explanation for the unexpected damage exists (e.g., high pest pressure and/or high plant stress).

In these cases, Monsanto and EPA will discuss and align on next steps before any resistance conclusion is reached.

If CRW collections are not possible in the current year or subsequent years due to successful management practices, then no further investigation is needed. The population would be considered "mitigated" meaning, in this case, that the population is suppressed or extirpated in this location. However, EPA recommends that Monsanto continue to be vigilant in areas where CRW populations were successfully mitigated.

(c) Mitigation of Resistant CRW Populations

For any CRW population found to be resistant under the criteria described in part *(b)* above, Monsanto must take the following steps:

- Monsanto must inform EPA of the results of the on-plant bioassays as soon as possible, but at least within 30 days if measures appear to be triggered

- Resistance may affect a single field, multiple fields in a localized area, or affect fields across larger areas. The geographic extent of resistance will be determined based upon product performance in surrounding areas, using information available from follow-up investigations of other performance inquiries in the area. Additional rootworm population collections and bioassays may be conducted to establish the geographic scope of confirmed resistance. These investigations will determine the Remedial Action Zone. Because this enhanced resistance monitoring program is designed to be highly responsive to changes in product performance and to implement protective measures even in the absence

of confirmed resistance, it is expected that resistant populations will be limited in geographic scope and size at the time of confirmation.

- In situations where Resistance is confirmed, the product is expected to no longer reliably provide economic levels of control of corn rootworm populations. Upon confirmation of resistance, stakeholders in the Remedial Action Zone, including customers, extension agents and crop consultants and other registrants, as appropriate, will be informed so that best management practices can be followed. Management of resistant populations in the Remedial Action Zone will involve the integration of multiple pest management practices (i.e. "IPM") that are already used in the absence of the product, such as:
  - crop rotation,
  - pyramided products,
  - pest population monitoring,
  - soil-applied and seed-applied insecticides,
  - insecticides to control corn rootworm adults, and
  - alternative corn rootworm-active traits.

The goal of the resistant corn rootworm management program will be to manage the rootworm population economically while reducing the probability or rate that the resistant population spreads to surrounding areas. Depending on the characteristics of the resistant population, the product may or may not fit within the management program. For example, if the level of rootworm survival on the product conferred by resistance is low (e.g., if resistant insects still show reduced fitness on the product), then continued use of the product in combination with other pest management tools may be an effective approach for reducing the local population. On the other hand, if the level of corn rootworm survival on the product that is conferred by resistance is high, the product would not be expected to contribute significantly to population reduction and ceasing its use in the Remedial Action Zone may allow the population to return to susceptibility.

Research will be conducted to understand the resistance, with the intention of using information generated to refine the management program. Such research may include characterizing the genetics of resistance (e.g., number of genes, functional dominance, mechanism of resistance, and cross-resistance) and the biology of resistant insects (e.g., fitness in the presence and absence of the product, and other control tactics).

The corn rootworm population in the Remedial Action Zone will continue to be monitored annually for reversion to susceptibility. This monitoring may include continued investigation into product performance as well as sampling and bioassays of the local corn rootworm population. If population susceptibility returns to baseline levels, the remedial actions can be lifted and growers can resume the use of the product as a primary tool for corn rootworm management.

e. Annual Reporting Requirements for MON 88017 x MON 810

1) Compliance Assurance Plan: Compliance Assurance Program activities, including IRM Grower Survey and on-farm assessment results, for the previous year and plans for the compliance assurance program during the current year, on or before January 31st of each year.

2) Insect Resistance Monitoring Results: results of monitoring and investigations of damage reports, on or before August 31st each year.

If these conditions are not complied with, the registration will be subject to cancellation in accordance with FIFRA section 6(e).

Sincerely,

Kimberly Nesci
Chief, Microbial Pesticides Branch
Biopesticides and Pollution
Prevention Division (7511P)