

29964-22

8/29/2013

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U.S. ENVIRONMENTAL PROTECTION AGENCY

Office of Pesticide Programs
Biopesticides and Pollution
Prevention Division (7511P)
Ariel Rios Building
1200 Pennsylvania Ave., NW
Washington, D.C. 20460

EPA Reg. Number:

Date of Issuance:

29964-22

AUG 29 2013

Term of Issuance: Conditional

Name of Pesticide Product:

4114 x MON810 x MIR604

NOTICE OF PESTICIDE:

- x Registration
Reregistration
(under FIFRA, as amended)

Name and Address of Registrant (include ZIP Code):

Pioneer Hi-Bred International, Inc.
7100 N.W. 62nd Avenue
P.O. Box 1000
Johnston, Iowa 50131-1000

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

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

This product is conditionally registered in accordance with FIFRA Section 3(c)(7)(A) of the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), as amended, provided that you do the following terms and conditions.

- 1] The subject registration will automatically expire on midnight September 30, 2021.
2] The subject registration will be limited Cry1F [Bacillus thuringiensis Cry1F protein and the genetic material (PHP27118 T-DNA) necessary for its production in corn event DP- 004114-3] x Cry 34Ab1 [Bacillus thuringiensis Cry 34Ab1 protein and the genetic material (PHP27118 T-DNA) necessary for its production in corn event DP-004114-3] x Cry35Ab1 [Bacillus thuringiensis Cry 35Ab1 protein and the genetic material (PHP27118 T-DNA) necessary for its production in corn event DP- 004114-3] x Cry1Ab [Bacillus thuringiensis Cry1Ab protein and the genetic material (vector PV-ZMBK07) necessary for its production in corn event MON- 00810-6] x mCry3A [Bacillus thuringiensis mCry3A protein and the genetic material (via elements of pZM26) necessary for its production in corn event SYN-IR604-5] for use in field corn.

Signature of Approving Official:

Date:

[Handwritten signature]

AUG 29 2013

Robert McNally, Director
Biopesticides and Pollution Prevention Division (7511P)

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 4114 (Cry1F x Cry34Ab1/Cry35Ab1), MON810 (Cry1Ab), and MIR604 (mCry3A), within the time frames required by the terms and conditions of EPA Registration Numbers 29964-17 and 29964-18 respectively.

5] This plant-incorporated protectant (PIP) 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 do the following Insect Resistance Management (IRM) Program, consisting of the following elements:

- Requirements relating to creation of a refuge for the Cry1F, Cry1Ab, Cry34/35Ab1 and mCry3A components. The refuge for these 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 Cry1F and Cry1Ab components, and lepidopteran-resistant *Bt* corn may be planted in the corn rootworm refuge for the mCry3A and Cry34/35Ab1 components.
- Requirements for Pioneer Hi-Bred International, Incorporated (Pioneer) to prepare and require 4114 x MON810 x MIR604 corn users to sign grower agreements that impose binding contractual obligations on growers to comply with the refuge requirements.
- Requirements regarding programs to educate growers about IRM requirements.
- Requirements regarding programs to evaluate and promote growers' compliance with IRM requirements.
- Requirements regarding programs to evaluate whether there are statistically significant and biologically relevant changes in susceptibility to the Cry1F, Cry1Ab, Cry34/35Ab1 and mCry3A proteins in the target insects.
- Requirements regarding a "remedial action plan" that would contain measures Pioneer 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 Pioneer 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. Pioneer is required to submit reports within three months of the Agency's request.
- Requirements for Pioneer, on or before August 31st of each year, to submit reports on resistance monitoring.

a) **Refuge Requirements for 4114 x MON810 x MIR604 corn**

These refuge requirements do not apply to seed propagation of inbred and hybrid corn seed 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. Grower agreements (also known as stewardship agreements) will specify that growers must adhere to the following refuge requirements as described in the grower guide/product use guide and/or in supplements to the grower guide/product use guide.

The following information must be included on the product bag or bag-tag as sold per respective region and in the Grower Guide:

A common refuge must be planted for both corn borers and corn rootworms. The refuge must be planted with corn hybrids that do not contain *Bt* technologies for the control of corn rootworms or corn borers. The refuge and 4114 x MON810 x MIR604 corn should be sown on the same day, or with the shortest window possible between planting dates to ensure that corn root development is similar among varieties. If the refuge is planted on rotated ground, then the 4114 x MON810 x MIR604 corn must also be planted on rotated ground. If the combined refuge is planted on continuous corn, the 4114 x MON810 x MIR604 field may be planted on either continuous or rotated land (option encouraged where WCRW rotation resistant biotype may be present). Refuge options are based on the planting of 4114 x MON810 x MIR604 corn in cotton or non-cotton growing regions and the insect pressure present in those locations. The refuge sizes for these regions are either 20% in cotton growing regions (i.e. 20 acres of non-*Bt* corn for every 80 acres 4114 x MON810 x MIR604 corn planted) or 5% in non-cotton growing regions (5 acres of non-*Bt* corn for every 95 acres of 4114 x MON810 x MIR604 corn planted). If corn rootworms are significant within a region, the structured refuge must be planted as an in-field or adjacent refuge using corn hybrids that do not contain *Bt* technologies for the control of corn borers or corn rootworms. It can be planted as a block within or adjacent (e.g., across the road) to the 4114 x MON810 x MIR604 corn 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 refuge can be protected from lepidopteran damage by use of non-*Bt* insecticides if the population of one or more target lepidopteran pests of 4114 x MON810 x MIR604 corn in the refuge exceeds economic thresholds. In addition, the refuge can be protected from CRW damage by an appropriate seed treatment or soil insecticide; however, insecticides labeled for adult CRW control must be avoided in the refuge during the period of CRW adult emergence. If insecticides are applied to the refuge for control of CRW adults, the same treatment must also be applied in the same timeframe to 4114 x MON810 x MIR604 corn fields. Economic thresholds will be determined using methods recommended by local or regional professionals (e.g., Extension Service agents, crop consultants). If corn rootworms are not significant within a region, the structured refuge may be planted as an in-field or adjacent refuge or as a separate block that is within 1/2 mile of the 4114 x MON810 x MIR604 corn field. The structured refuge must be planted with corn hybrids that do not contain *Bt* technologies for the control of corn borers or corn rootworms. Economic thresholds will be determined using methods recommended by local or regional professionals (e.g., Extension Service agents, crop consultants).

Region	Refuge size	In-field or adjacent refuge is allowed	Refuge separated by up to 1/2 mile is allowed
Cotton growing where CEW is a significant pest and WCRW, NCRW and MCRW are not significant: AR, NC, SC, GA, FL, TN (only the counties of Carroll, Chester, Crockett, Dyer, Fayette, Franklin, Gibson, Hardeman, Hardin, Haywood, Lake, Lauderdale, Lincoln, Madison, Obion, Rutherford, Shelby, and Tipton) AL, MS, LA, VA (only the counties of	20% non- <i>Bt</i> corn	Yes	Yes

Region	Refuge size	In-field or adjacent refuge is allowed	Refuge separated by up to 1/2 mile is allowed
Dinwiddie, Franklin City, Greenville, Isle of Wight, Northampton, Southampton, Suffolk City, Surrey, and Sussex)			
Cotton growing where CEW is a significant pest and WCRW, NCRW, and/or MCRW are significant: TX (except the counties of Carson, Dallam, Hansford, Hartley, Hutchinson, Lipscomb, Moore, Ochiltree, Roberts, and Sherman), OK (only the counties of Beckham, Caddo, Comanche, Custer, Greer, Harmon, Jackson, Kay, Kiowa, Tillman, and Washita), MO (only the counties of Dunkin, New Madrid, Pemiscot, Scott, and Stoddard).	20% non- <i>Bt</i> corn	Yes	No
Cotton growing where CEW is not a significant pest and WCRW, NCRW and MCRW are not significant: NM, AZ, CA, NV	5% non- <i>Bt</i> corn	Yes	Yes
Non-cotton growing where WCRW, NCRW and MCRW are not significant OR, WA, ID, MT, WY, UT, VA (except the counties of Dinwiddie, Franklin City, Greenville, Isle of Wight, Northampton, Southampton, Suffolk City, Surrey, and Sussex), WV, PA, MD, DE, CT, RI, NJ, NY, ME, MA, NH, VT, HI, AK, TN(except the counties of Carroll, Chester, Crockett, Dyer, Fayette, Franklin, Gibson, Hardeman, Hardin, Haywood, Lake, Lauderdale, Lincoln, Madison, Obion, Rutherford, Shelby, and Tipton)	5% non- <i>Bt</i> corn	Yes	Yes
Non-cotton growing where WCRW, NCRW and/or MCRW are significant: KS, NE, SD, ND, MN, IA, MO (except the counties of Dunkin, New Madrid, Pemiscot, Scott, and Stoddard), IL, WI, MI, IN, OH, KY, CO, OK (except the counties of Beckham, Caddo, Comanche, Custer, Greer, Harmon, Jackson, Kay, Kiowa, Tillman, and Washita), TX (only the counties of Carson, Dallam, Hansford, Hartley, Hutchinson, Lipscomb, Moore, Ochiltree, Roberts, and Sherman)	5% non- <i>Bt</i> corn	Yes	No

b) Grower Agreements for 4114 x MON810 x MIR604

1] Persons purchasing 4114 x MON810 x MIR604 corn 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] Pioneer must integrate this registration into the current system used for previously registered Pioneer *Bt* corn plant-incorporated protectants, which is reasonably likely to assure that persons purchasing 4114 x MON810 x MIR604 corn will affirm annually that they are contractually bound to comply with the requirements of the IRM program.
- 4] If Pioneer 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, Pioneer must submit to EPA the text of such changes to ensure that it is consistent with the terms and conditions of this registration.
- 5] Pioneer must integrate this registration into the current system used for its other *Bt* corn plant-incorporated protectants, which is reasonably likely to assure that persons purchasing 4114 x MON810 x MIR604 corn sign grower agreement(s).
- 6] Pioneer shall maintain records of all 4114 x MON810 x MIR604 corn grower agreements for a period of three (3) years from December 31st of the year in which the agreement was signed.
- 7] Pioneer shall maintain and make available to the Agency upon request records of the number of units of 4114 x MON810 x MIR604 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. Pioneer is required to submit reports within three months of the Agency's request.
- 8] Pioneer 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 Compliance Monitoring Programs for 4114 x MON810 x MIR604 corn

- 1] Pioneer 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 4114 x MON810 x MIR604 corn users the importance of complying with the IRM program. The program shall include information encouraging 4114 x MON810 x MIR604 corn users to pursue optional elements of the IRM program relating to refuge configuration and proximity to 4114 x MON810 x MIR604 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 4114 x MON810 x MIR604 corn user separate from the grower technical guide. The communication shall inform the user of the current IRM requirements. Pioneer shall coordinate its education programs with educational efforts of other registrants and organizations, such as the National Corn Growers Association and state extension programs.

Pioneer must design and immediately implement a "bag tag" that will be attached to all bags of 4114 x MON810 x MIR604 corn seed sold and delivered for the 2013 growing season and annually thereafter. The

purpose of this bag tag is to remind growers that 4114 x MON810 x MIR604 corn products require a separate 20% lepidopteran refuge in cotton-growing areas. The PIP product label accepted by EPA must include how this information will be conveyed to growers via text and graphics. A revised PIP product label must be submitted by January 31, 2014.

2] Annually, Pioneer 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, Pioneer 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 the industry working group Agricultural Biotechnology Stewardship Technical Committee (ABSTC). The required features of the compliance assurance program are described in paragraphs 4–22 of this section.

4] Pioneer must continue to implement and improve an ongoing IRM compliance assurance program designed to evaluate the extent to which growers purchasing 4114 x MON810 x MIR604 corn 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 Pioneer's *Bt* corn products. Pioneer shall coordinate with other *Bt* corn registrants in improving its compliance assurance program and integrate this 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 5–22 of this section.

5] Pioneer 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 noncompliant 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, Pioneer must use a consistent set of standards for responding to non-compliance. A grower found with a second incident of significant non-compliance with refuge requirements for the *Bt* corn product within a five-year period will be denied access to Pioneer Hi-Bred's *Bt* corn products 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 *Bt* corn.

6) The IRM compliance assurance program shall include an annual survey, conducted by an independent third party, of a statistically representative sample of growers of 4114 x MON810 x MIR604 corn 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.

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

- 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] Pioneer 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. Pioneer shall confer with other registrants and EPA on the design and content of the survey prior to its implementation.
- 10] Annually, Pioneer 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. Pioneer must confer with EPA prior to adopting any changes.
- 11] Pioneer shall conduct an annual on-farm assessment program. Pioneer shall train its representatives who make on-farm visits with 4114 x MON810 x MIR604 corn 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 identification of a grower who is not in compliance with the IRM program, Pioneer shall take appropriate action, consistent with its phased compliance approach, to promote compliance.
- 12] Pioneer shall carry out a program for investigating legitimate tips and complaints that 4114 x MON810 x MIR604 corn 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, Pioneer shall take appropriate action, consistent with its phased compliance approach.
- 13] If a grower, who purchases 4114 x MON810 x MIR604 corn for planting, was specifically identified as not being in compliance during the previous year, Pioneer shall visit with the grower and evaluate whether that the grower is in compliance with the IRM program for the current year.
- 14] Annually, Pioneer 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, Pioneer 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. Pioneer may elect to coordinate information with other registrants and report collectively the results of compliance assurance programs.
- 15] Pioneer and the seed corn dealers for Pioneer 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] Pioneer shall revise and expand its existing compliance assurance program to include the following elements. Pioneer must prepare and submit, on or before January 31, 2013, a written description of its revised compliance assurance program. Pioneer may coordinate with other registrants in designing and implementing its compliance assurance program.

17] Pioneer will enhance the refuge education program throughout the seed delivery channel:

- i. Ensure sales representatives, licensees, seed dealers, and growers recognize the importance of correct refuge implementation and potential consequences of failure to plant the required refuge.
- ii. Include the refuge size requirement on all 4114 x MON810 x MIR604 corn seed bags or bag tags. Pioneer must submit a revised 4114 x MON810 x MIR604 corn label by January 31, 2014, that includes how this information will be conveyed to growers via text and graphics. Insect Protection corn seed bags or bag tags must occur by the 2014 growing season.

18] Pioneer will focus the majority of on-farm assessments on regions with the greatest risk for resistance:

- i. Use *Bt* corn adoption, pest pressure information, and other available information to identify regions where the risk of resistance is greatest.
- ii. Focus approximately two-thirds of on-farm assessments on these regions, with the remaining assessments conducted across other regions where 4114 x MON810 x MIR604 corn is used.

19] Pioneer will use its available 4114 x MON810 x MIR604 corn sales records and other information to refine grower lists for on-farm assessments of their compliance with refuge requirements:

- i. Identify for potential on-farm assessment growers whose sales information indicates they have purchased 4114 x MON810 x MIR604 corn but may have purchased little or no refuge seed from the registrant, licensees, or affiliated companies.

20] Pioneer 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, Pioneer will refine the on-farm assessment program for 4114 x MON810 x MIR604 corn to reflect the adoption rate and level of refuge compliance for 4114 x MON810 x MIR604 corn.

22] Pioneer 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 two (2) years by Pioneer, a seed supplier, or a third party assessor, after completing the assessment process.
- ii. Pioneer will conduct follow-up checks on growers found to be significantly out of compliance within three (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 4114 x MON810 x MIR604 corn within a 5-year period will be denied access to Pioneer's *Bt* corn products the next year.

d. Insect Resistance Monitoring and Remedial Action Plan for 4114 x MON810 x MIR604 corn

1) EPA is imposing the following conditions for the Cry1F and Cry1Ab toxins expressed in 4114 x MON810 x MIR604 corn:

Pioneer will monitor for resistance to Cry1F and Cry1Ab toxins expressed in 4114 x MON810 x MIR604 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.

Focused Population Sampling

Pioneer 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 4114 x MON810 x MIR604 corn and/or changes in resistance allele frequency in response to the use of 4114 x MON810 x MIR604 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 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 4114 x MON810 x MIR604 corn. EPA shall be consulted prior to the implementation of such modifications.

Pioneer 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 Cry1F and Cry1Ab proteins 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 4114 x MON810 x MIR604 corn 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;
 - 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, Pioneer will consult with EPA to develop and implement a case-specific resistance management action plan.

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

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

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- 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 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 4114 x MON810 x MIR604 corn in commercial production fields before responsive measures are undertaken.

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

- Use alternative control measures in 4114 x MON810 x MIR604 corn fields in the affected region to control the target pest during the immediate growing season.
- Destroy 4114 x MON810 x MIR604 corn 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, Pioneer 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.

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 Pioneer:

- 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;
- Pioneer will develop a case-specific resistance management action plan within 90 days according to the characteristics of the resistance event and local agronomic needs. Pioneer 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 mCry3A, Cry34Ab1 and Cry35Ab1 toxins expressed in 4114 x MON810 x MIR604 corn:

- i. Pioneer must monitor for mCry3A and Cry34/35Ab1 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. Pioneer must develop and utilize a functional “on-plant” diagnostic assay¹ for corn rootworm resistance monitoring to detect potentially resistant individuals and incorporate this assay into the annual resistance monitoring program.
- iv. Pioneer must submit an enhanced corn rootworm resistance monitoring plan for 4114 x MON810 x MIR604 corn that accounts for reports of suspected and/or confirmed resistance. The rootworm resistance monitoring plan and the revised definitions for suspected and confirmed resistance for 4114 x MON810 x MIR604 corn must be found acceptable to BPPD and utilized by Pioneer beginning in the 2014 season. This enhanced monitoring program should:
- o Be practical and adaptable and provide information on relevant changes in corn rootworm population sensitivity to 4114 x MON810 x MIR604 corn;
 - o Be focused on areas where the potential for resistance is greatest for 4114 x MON810 x MIR604 corn and for the corn rootworm active single event components of 4114 x MON810 x MIR604 corn (mCry3A and Cry34Ab1/Cry35Ab1), based on available information on historical pest pressure, unexpected performance issues, historical suspected and/or confirmed resistance incidents as currently defined or as modified in EPA accepted enhanced monitoring programs, prevailing agronomic practices (e.g., crop rotation versus continuous corn), and academic and extension publications on *Bt* corn field performance;
 - o Involve coordination to the extent possible with other stakeholders, such as academic and extension experts in the states where corn rootworm is a major pest, and other registrants of similar products, as appropriate;
 - o Be responsive to incidents of suspected or confirmed resistance to the registrant’s other products containing the same active ingredient(s), as well as to publicly available reports of suspected or confirmed resistance to other *Bt* protein toxins in 4114 x MON810 x MIR604 corn.
- v. Pioneer must develop a proactive resistance monitoring program for northern corn rootworm (*Diabrotica barberi*) by the 2014 season, with reporting in 2014. This program should include a proposal for annual sampling and testing of northern corn rootworm susceptibility to mCry3A and Cry34/35Ab1. As part of the effort, Pioneer may need to investigate novel techniques for rearing and conducting bioassays with northern corn rootworm. A report on Pioneer’s progress towards this requirement must be submitted within one (1) month from the date of this registration (This information has been submitted and is being evaluated by the Agency).
- vi. Pioneer must follow-up on grower, extension specialist, or consultant reports of unexpected damage or control failures for corn rootworm.

¹ 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.

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

viii. Remedial Action Plan for Corn Rootworm and 4114 x MON810 x MIR604 corn.

Within one year of this registration, you must submit an enhanced remedial action plan for 4114 x MON810 x MIR604 corn that includes actions to be taken in response to both suspected and confirmed resistance. This remedial action plan must include a description of steps to be taken in response to customer product performance inquiries and annual reporting to the agency on the outcomes of investigations into any such inquiries that might indicate potential resistance. The program must include revised definitions of unexpected damage to 4114 x MON810 x MIR604 corn that could indicate potential suspected resistance. The enhanced remedial action plan must be found acceptable to BPPD and implemented by Pioneer in the 2014 growing season.

The remedial action plan is designed as a tiered approach for mitigating western and northern corn rootworm resistance development specifically due to the commercialization of 4114 x MON810 x MIR604 corn. The following program summary describes, in order of events, the steps that must be taken to implement a remedial action plan if resistance to target pests is confirmed.

1. Suspected Resistance from Population Monitoring

Definition of Suspected Resistance - Resistance will be suspected if investigations of target pest injury potential to 4114 x MON810 x MIR604 corn from the Sublethal Seedling Assay show that:

- Injury potential of a target pest population obtained as part of the annual insect monitoring program has increased to a level representative of product failure in field conditions;
- The seeds used in the investigation of this population's injury potential contain Cry34/Cry35Ab1 and mCry3A at levels representative of (and in the same genetic background as) the benchmark study; and
- The change in injury potential has been documented as a heritable characteristic of the target pest population and not a result of experimental error.

If resistance is "suspected", Pioneer will inform growers in the area of the potential benefit of augmenting CRW control such as adulticide treatment and/or crop rotation or use of soil or seed-applied insecticides at rates providing corn rootworm control the following year. These measures are intended to educate growers of the potential for change in efficacy, reduce the possibility of grower loss from change in efficacy and reduce potentially resistant insects contributing to the following year's pest population.

2. Confirmed Resistance from Population Monitoring

Definition of Confirmed Resistance - Resistance will be confirmed if all of the following criteria are met by progeny from a subsequent rootworm population collected from the area of "suspected resistance" the following year:

- Injury potential of the subsequent field-collected rootworm population feeding on plants containing Cry34/Cry35Ab1 and mCry3A remains at a level likely to produce repeated product failure in field conditions;
- The change in injury potential has been documented as a heritable characteristic of the target pest population;
- Greenhouse node-injury evaluation confirms product failure;
- Subsequent populations collected from the area and assayed show that the results are repeatable; and
- Continued monitoring of the area suggests that the change is spreading.

3. Suspected Resistance – Investigation of Field Reports

The registrant will follow up on grower, extension specialist or consultant reports of unexpected product performance due to corn rootworm species listed on the label. The registrants will instruct its customers to contact them if such incidents occur. The registrants will investigate all such reports submitted to the company or the company's representatives to:

- Confirm the corn in question is rootworm-active *Bt* corn;
- Confirm the field in question contains the correct blend rate of refuge corn;
- Confirm that species not susceptible to the protein are not responsible for the damage, that no climatic or cultural reasons could be responsible for the damage, and that all other reasonable causes based on historical experience for the observed root damage have been ruled out;
- If not due to other reasons, the registrant will conduct a thorough investigation of the factors known to affect the manifestation of corn rootworm feeding damage.

The Agency recognizes that large corn rootworm populations, environmental conditions, and protein expression levels can influence corn root damage and may affect the definition of suspected CRW resistance. The Agency plans to work with the registrants to refine the definition of suspected resistance based on these factors. Until such time that the Agency accepts a modified definition of suspected resistance to corn rootworm, resistance will be suspected in cases where the average root damage in the 4114 x MON810 x MIR604 corn field is > 0.5 on the nodal injury scale (NIS) and the frequency of 4114 x MON810 x MIR604 corn with > 0.5 nodes destroyed exceeds 50% of the sampled plants.

If resistance is "suspected", Pioneer will inform growers in the area of the potential benefit of augmenting CRW control such as adulticide treatment, crop rotation the following year or use of soil or seed insecticides the following year. These measures are intended to educate growers of the potential for change in efficacy, reduce the possibility of grower loss from change in efficacy and reduce potentially resistant insects contributing to the following year's pest population.

Pioneer will collect insects as soon as possible from the area for laboratory studies to test for resistance by comparing with benchmark susceptibility data. These studies will be performed following the same laboratory protocols as used for the benchmark determination and monitoring programs.

4. Confirmed Resistance – Investigation of Field Reports

- Injury potential of the field-collected rootworm population feeding on plants containing Cry34/Cry35Ab1 and mCry3A remains at a level likely to produce repeated product failure in field conditions;
- Subsequent populations collected from the area and assayed show that the results are repeatable;
- The change in injury potential has been documented as a heritable characteristic of the target pest population;
- Greenhouse node-injury evaluation confirms product failure; and
- Continued monitoring of the area suggests that the change is spreading.

5. Remedial Action

When resistance is "confirmed", the following steps will be taken:

- The EPA will receive notification within 30 days of confirmed resistance;
- Affected customers and Extension specialists will be immediately notified about confirmed resistance;
- Affected customers and Extension specialists will be strongly encouraged to implement alternative CRW control measures such as adulticide treatment, crop rotation the following year, or use of soil or seed insecticides the following year;
- Sale and distribution of 4114 x MON810 x MIR604 corn in the affected area will cease immediately until an effective mitigation plan has been approved by EPA.

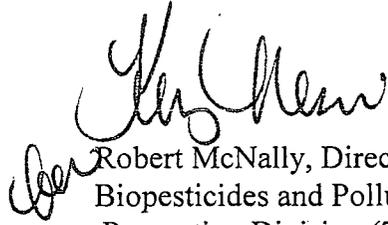
e. Annual Reporting Requirements for 4114 x MON810 x MIR604 corn

1. Compliance Assurance Program: compliance assurance program activities, including IRM Grower Survey and on-farm assessment results for the prior year and plans for the compliance assurance program for the current year, on or before January 31st each year beginning in 2014;
2. Insect Resistance Monitoring Results: results of monitoring and investigations of damage reports, on or before August 31st each year.

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

The basic confidential statement of formula (CSF) dated 8/13/13 is acceptable and supersedes all prior basic CSFs. A copy has been placed in the file jacket for this registration.

Sincerely,


Robert McNally, Director
Biopesticides and Pollution
Prevention Division (7511P)

Enclosure

4114xMON810xMIR604

(OECD Unique Identifier: DAS-ØØ4114-3xMON-ØØ81Ø-6xSYN-IR6Ø4-5)

Active Ingredients:

Bacillus thuringiensis Cry1F protein and the genetic material (PHP27118 T-DNA) necessary for its production in corn event DP-ØØ4114-3 ≤0.0012%*

Bacillus thuringiensis Cry34Ab1 protein and the genetic material (PHP27118 T-DNA) necessary for its production in corn event DP-ØØ4114-3 ≤0.0096%*

Bacillus thuringiensis Cry35Ab1 protein and the genetic material (PHP27118 T-DNA) necessary for its production in corn event DP-ØØ4114-3 ≤0.0042%*

Bacillus thuringiensis Cry1Ab protein and the genetic material (vector PV-ZMBK07) necessary for its production in corn event MON-ØØ81Ø-6 ≤0.0011%*

Bacillus thuringiensis mCry3A protein and the genetic material (via elements of pZM26) necessary for its production in corn event SYN-IR6Ø4-5 ≤0.0008%*

Inert Ingredients:

Phosphinothricin acetyltransferase (PAT) protein and the genetic material (PHP27118 T-DNA) necessary for its production in corn event DP-ØØ4114-3 ≤0.00088%*

Phosphomannose isomerase (PMI) protein and the genetic material (via elements of pZM26) necessary for its production in corn event SYN-IR6Ø4-5 ≤0.00076%*

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

KEEP OUT OF REACH OF CHILDREN

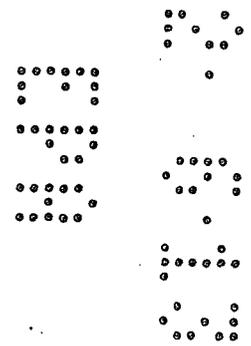
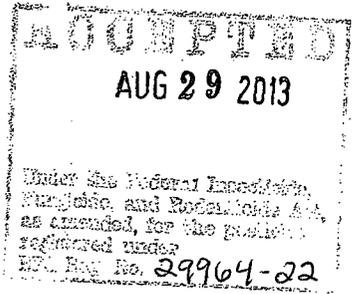
CAUTION

NET CONTENTS _____

EPA REGISTRATION NUMBER: 29964-xx

EPA ESTABLISHMENT NUMBER: 029964-IA-001

Pioneer Hi-Bred International, Inc.
7300 NW 62nd Avenue
Johnston, IA 50131



DIRECTIONS FOR USE

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

This plant-incorporated protectant (PIP) 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.

The plant-incorporated protectant must be used as specified in the terms and conditions of the registration.

4114xMON810xMIR604 corn combines the insect protection features of 4114, MON810 and MIR604 in the same corn hybrid (inbred). 4114xMON810xMIR604 corn hybrids protect corn crops from leaf, stalk and ear damage caused by lepidopteran corn pests such as the European corn borer and root damage caused by corn rootworm larvae. In order to minimize the risk of the corn pests developing resistance to 4114xMON810xMIR604 corn, an insect resistance management plan must be implemented.

INSECT RESISTANCE MANAGEMENT

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 active ingredient per registrant per year.

Corn seed bags or bag tags for products containing 4114xMON810xMIR604 must include the refuge size requirement in text and graphical format.

Growers are instructed to read information on insect resistance management. The following information regarding refuge placement for commercial production must be included in the Grower Guide:

The use of 4114xMON810xMIR604 corn requires accompanying refuge corn for the Cry1F, Cry34/35Ab1, Cry1Ab and mCry3A components as described in the table below.

Region	Refuge size	In-field or adjacent refuge allowed*	Refuge separated by up to ½ mile allowed
Non-cotton growing where WCR, NCR and MCR are not significant: AK, OR, WA, ID, MT, WY, UT, VA (except the counties of Dinwiddie, Franklin City, Greensville, Isle of Wight, Northampton, Southampton, Suffolk City, Surrey, and Sussex), WV, PA, MD, DE, CT, RI, NJ, NY, ME, MA, NH, VT, HI, TN (except the counties of Carroll, Chester, Crockett, Dyer, Fayette, Franklin, Gibson, Hardeman, Hardin, Haywood, Lake, Lauderdale, Lincoln, Madison, Obion, Rutherford, Shelby, and Tipton)	5% non-Bt maize	Yes	Yes

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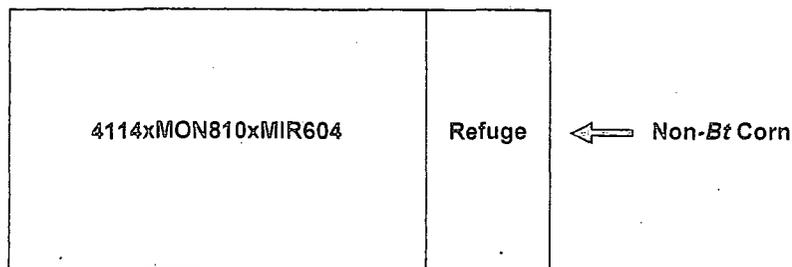
Region	Refuge size	In-field or adjacent refuge allowed*	Refuge separated by up to ½ mile allowed
Non-cotton-growing where WCR, NCR and/or MCR are significant: KS, NE, SD, ND, MN, IA, MO (except the counties of Dunkin, New Madrid, Pemiscot, Scott, and Stoddard), IL, WI, MI, IN, OH, KY, CO, OK (except the counties of Beckham, Caddo, Comanche, Custer, Greer, Harmon, Jackson, Kay, Kiowa, Tillman, and Washita), TX (only the counties of Carson, Dallam, Hansford, Hartley, Hutchinson, Lipscomb, Moore, Ochiltree, Roberts, and Sherman)	5% non-Bt maize	Yes	No
Cotton growing where CEW is not a significant pest and WCR, NCR and MCR are not significant: NM, AZ, CA, NV	5% non-Bt maize	Yes	Yes
Cotton growing where CEW is a significant pest and WCR, NCR, and MCR are not significant: NC, SC, GA, FL, TN (only the counties of Carroll, Chester, Crockett, Dyer, Fayette, Franklin, Gibson, Hardeman, Hardin, Haywood, Lake, Lauderdale, Lincoln, Madison, Obion, Rutherford, Shelby, and Tipton), AL, MS, LA, AR, VA (only the counties of Dinwiddie, Franklin City, Greensville, Isle of Wight, Northampton, Southampton, Suffolk City, Surrey, and Sussex)	20% non-Bt maize	Yes	Yes
Cotton growing where CEW is a significant pest and WCR, NCR, and/or MCR are significant: TX (except the counties of Carson, Dallam, Hansford, Hartley, Hutchinson, Lipscomb, Moore, Ochiltree, Roberts, and Sherman), OK (only the counties of Beckham, Caddo, Comanche, Custer, Greer, Harmon, Jackson, Kay, Kiowa, Tillman, and Washita), MO (only the counties of Dunkin, New Madrid, Pemiscot, Scott, and Stoddard)	20% non-Bt maize	Yes	No

* The common refuge can be separated by a ditch or a road but not by another field. The refuge must be owned or managed by the same grower. A neighbor's field cannot be used as the refuge.

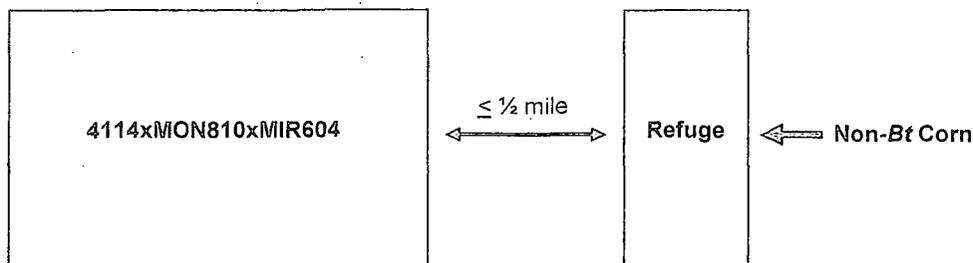
If corn rootworms are significant within a region, the block/strip refuge must be planted as an in-field or adjacent refuge using non-Bt corn hybrids. It can be planted as block within or adjacent (e.g. across the road) to the 4114xMON810xMIR604 field, perimeter strips (i.e. strips around the field), or in-field strips that are at least one (1) row wide. The refuge can be protected from lepidopteran damage use of non-Bt insecticides if the population of one or more target lepidopteran pests of 4114xMON810xMIR604 in the refuge exceeds economic thresholds. In addition, the refuge can be protection from CRW damage by an appropriate seed treatment or soil insecticide; however, insecticides labels for adult CRW control must be avoided in the refuge during the period of CRW adult emergence. Economic threshold will be determined using method recommended by local or

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regional professionals (e.g. Extension Service agents, crop consultants). A schematic of one common refuge deployment option is shown below:



If corn rootworms are not significant within a region, the block/strip refuge may be planted as an in-field or adjacent refuge, or as a separate block that is within a 1/2 mile of the 4114xMON810xMIR604 field. The block/strip refuge must be planted using non-Bt corn hybrids. Economic threshold will be determined using method recommended by local or regional professionals (e.g. Extension Service agents, crop consultants). A schematic of one refuge deployment option with the refuge planted within a 1/2 mile of the 4114xMON810xMIR604 field is shown below:



Use Pattern

Crop	Pests
Field corn	black cutworm corn earworm European corn borer fall armyworm lesser corn stalk borer southern corn stalk borer southwestern corn borer sugarcane borer stalk borer western bean cutworm western corn rootworm northern corn rootworm Mexican corn rootworm