

524-595

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

OFFICE OF CHEMICAL SAFETY
AND POLLUTION PREVENTION

MAY 01 2012

Dr. Diane M. Ruezinsky
Regulatory Affairs Manager
Monsanto Company
800 North Lindbergh Blvd.
St. Louis, MO 63137

Subject: MON 89034 x TC1507 x MON 88017 x DAS-59122-7 and MON 89034 x TC1507 x MON 88017 x DAS-59122-7 RIB Complete™ April 30, 2012 Applications to Amend the Terms and Conditions for Monsanto SmartStax Products and Response to April 19, 2012 Insect Resistance Management Review of MRID No. 487490-01 EPA Registration Nos. 524-581 and 524-595

Dear Dr. Ruezinsky:

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

The definitions of "unexpected damage", "suspected resistance", and "confirmed resistance" will be periodically evaluated by EPA and the registrants as additional information becomes available. Modified definitions from those at the date of this letter will be considered and may be implemented for the 2013 field season and no later than May 1, 2013, provided they are found acceptable to BPPD.

We note that the enhanced rootworm resistance monitoring plan and enhanced remedial action plan have been submitted and are acceptable subject to the following changes and clarifications.

1. "Unexpected Damage" Conclusions

- a. The assessment of lodged plants which may lead to a finding of "unexpected damage" is 25% of plants within a 1-acre or greater area within a field, with the assessment being focused on the area of greatest damage within the field. This is intended to be more sensitive than would be 25% of plants across an entire field because corn rootworm damage and lodging is often localized. The assessment will be made by visually surveying the area of lodged plants, and therefore incidents of lodging that are approximately 25% of an acre may be classified as "unexpected damage" if the other criteria of the definition are also met.
- b. SmartStax plants adjacent to refuge plants in an interspersed refuge setting are not to be ignored when assessing root damage. Feeding injury (e.g. root rating > 0.5) to such plants may be indicative of "unexpected damage" if rootworm populations are sufficiently low that larval movement off refuge plants is not expected to be an important factor. However, under higher rootworm pressure, feeding injury to SmartStax plants adjacent to refuge plants is expected and known to occur and therefore may not be indicative of "unexpected damage".
- c. The registrants will include the names of the laboratories used for bioassays in their annual reports. Consistency in the bioassays, including the laboratories where they are conducted and the protein source, is important when looking for trends in bioassay results over time.
- d. The registrants agreed to continue to explore improvements to bioassay approaches, including use of plant-based assays in addition to diet bioassays.
- e. The descriptor "not yet confirmed cases of "suspected resistance" is hereby replaced with "unexpected damage"

2. "Suspected Resistance" Conclusions

- a. The registrants agreed to continue to explore improvements to bioassay approaches, including use of plant-based assays in addition to diet bioassays.
- b. The registrants will continue to explore the most appropriate (i.e. sensitive) statistical analyses of concentration-response data from diet bioassays.
- c. The registrants agreed that remedial action efforts for "suspected resistance" will be applied to the entire farm in which the "suspected resistance was identified". Where appropriate, the registrants also will attempt to work with other nearby customers.

3. "Confirmed Resistance" Conclusions

- a. The registrants clarified that the definition of "confirmed resistance" must necessarily include economic injury to SmartStax plants in order for the definition to be field-

relevant. The registrants are revising the definition to read "... and (5) is field-relevant, resulting in economic root injury as defined in local extension recommendations."

- b. The registrants agree to report "confirmed resistance" to EPA within 30 days, as required in other registrations. In any case, EPA regularly will be kept informed of investigations into unexpected damage and suspected resistance as described in the monitoring and remedial action plans.

Revised Definitions and Remedial Action Plans

The revised definitions for 2012 are as follows:

Unexpected Damage

Definition

During the initial investigation of a performance inquiry described above, damage will be defined as **Unexpected Damage** if: (1) the affected plants are confirmed to be SmartStax plants (and, in the case of the blended refuge products and high rootworm pressure, not to be adjacent to a refuge plant); (2) there is approximately 25% or more plant lodging over any area of at least one acre within a field; and (3) corn rootworm feeding caused root damage NIS > ≈ 0.5 to 0.75 on at least 6 of 10 SmartStax plants sampled. NIS values in the 0.5 to 0.75 range can be expected for SmartStax under conditions that favor corn rootworm feeding, therefore the lower end of this range will be used as the cut-off for unexpected damage in conditions that lead to lower expected damage and the higher end will be used in conditions that lead to higher expected feeding damage. It is well known that extremely high populations of susceptible corn rootworm and other insects can occasionally result in unexpected damage so this is just the initial trigger for further investigation.

Investigative steps

During the same visit that results in a finding of "unexpected damage", the additional investigative steps below will be taken immediately to support an assessment of potential Suspected Resistance:

1. If suitable green tissue is available, leaf samples will be taken and shipped to the registrant's laboratories. If depressed *Bt* protein expression is suspected as a possible cause of the rootworm damage, quantitative ELISA assays using validated protocols will be conducted on the leaf material to determine whether levels of the corn rootworm-active proteins are within the normal range. Comparisons will be made to historical data on the relevant hybrid/s.
2. If corn rootworm adults are present and are believed to have not yet laid their eggs, beetle collections will be made consisting of at least 250 (ideally 500 or more) individuals. If sufficient corn rootworm adults are not available in the target field, collections can be extended to a contiguous corn field (if available and accessible), which ideally will also contain SmartStax corn. Collections will be sent to an appropriate laboratory for oviposition and storage of the resulting eggs. After a period of egg diapause, the progeny will be

bioassayed against both Cry3Bb1 and Cry34/35Ab1 following established protocols for each protein using artificial diets. The LC_{50} and EC_{50} values, or other appropriate measures of sensitivity, of the population for each protein will be compared with historical baseline data and the results from annual monitoring studies and, if available, with the LC_{50} and EC_{50} values of a laboratory susceptible population bioassayed at the same time. Methods and laboratories involved will be described in reports to the Agency.

In addition to these collections made during the initial investigation, a further visit to the affected field or farm will be made the following year (assuming the grower purchases SmartStax corn from the registrant for the following season). During this visit, if suitable corn rootworm adults were not available in the target field or in a contiguous accessible corn field at the time of the initial investigation, an attempt will be made to collect corn rootworm adults from the same or a contiguous corn field. This collection will be attempted regardless of the level of corn rootworm damage but, if remedial actions were implemented and effective, this collection may not be successful. In such a situation, on-going communication with the grower about SmartStax product performance and best practices for corn rootworm management is warranted.

Remedial actions

Because the investigation following a finding of unexpected damage may take a year or more, the registrant will review with the grower their corn rootworm management practices. This review may also involve local corn rootworm experts, such as consultants or extension entomologists. As part of this review, additional corn rootworm management practices will be recommended according to the situation and the factors that have been identified as contributing to the unexpected damage. Growers are expected to follow such recommendations in their affected fields to improve their ability to manage the pest in an economically and environmentally favorable manner. The implementation and effectiveness of those rootworm management recommendations will be examined the following year during the follow-up visit.

If the investigation shows that Unexpected Damage to SmartStax was not related to Suspected Resistance, then the registrant will work with the grower to understand the SmartStax performance and advise the grower on best practices for corn rootworm management, and the investigation will be considered complete.

Suspected Resistance

Suspected Resistance is defined as (1) an initial performance inquiry investigation resulting in a finding of Unexpected Damage, (2) protein levels in green plant tissue of affected plants found to be within the documented range for that hybrid (if data are available), and (3) bioassays of insect collections from the affected fields showing statistically significantly lower sensitivity (e.g. elevation of the LC_{50} or EC_{50}) compared with the historical baseline and laboratory susceptible populations for either or both of the rootworm-active proteins in SmartStax.

Investigative steps

Following a finding of suspected resistance, as defined above, the insect population will be characterized further to confirm whether or not the corn rootworm population is resistant. This characterization is intended to identify whether the reduced sensitivity in the bioassay is heritable, whether it is sufficient to cause an increase in survival to adult when feeding on SmartStax, and whether it is sufficiently high to cause economic root injury in circumstances where a normally susceptible population would not. Specific experiments to ascertain these characteristics currently are under development and may consist of additional diet-based bioassays, bioassays in growth chambers using SmartStax, MON 88017 and DAS-59122-7 corn seedlings, or greenhouse bioassays using potted SmartStax, MON 88017 and DAS-59122-7 corn. Additionally, it is important to determine whether the suspected resistant population actually persists in the field. Methods and laboratories involved will be described in reports to the Agency.

If the investigation shows that Suspected Resistance to SmartStax does not meet the definition of Confirmed Resistance, then the registrant will work with the grower to understand the SmartStax performance and advise the grower on best practices for corn rootworm management, and the investigation will be considered complete. On-going communication with the grower about performance of SmartStax and corn rootworm management may be warranted.

Remedial actions

The remedial actions in the case of Suspected Resistance are intended to reduce the corn rootworm population in the affected fields and farms. Options available to growers may include crop rotation to a non-host crop (this is the most preferred approach in situations where crops other than corn are commonly raised and economically justified). Alternatively, the use of additional corn rootworm control tools in combination with or in place of SmartStax may be recommended. For example, soil insecticides, seed-applied insecticides or chemigation in combination with SmartStax are expected to reduce the corn rootworm larval population. Insecticides applied to control corn rootworm adults during the period of adult emergence, but before oviposition, should reduce the subsequent corn rootworm egg population. Use of an alternative corn rootworm-active plant-incorporated protectant may also reduce the local surviving population.

The success of remedial actions in the case of Suspected Resistance will be monitored in the affected fields the following year and may include examination of SmartStax product performance, local corn rootworm population density, and/or additional corn rootworm adult collections for bioassay.

Confirmed Resistance

Confirmed Resistance is defined as: (1) Unexpected Damage in SmartStax corn fields resulting from (2) a heritable, significant reduction in sensitivity to one or both SmartStax proteins for a corn rootworm population that (3) persists in the field, resulting in (4) increased survival of adults on SmartStax corn and (5) is field-relevant, resulting in economic root injury as defined in local extension recommendations.

Confirmed Resistance may affect a single field, multiple fields in a localized area, or affect fields across larger areas. The geographic extent of confirmed resistance will be determined based upon SmartStax product performance in surrounding areas, using information available from follow-up investigations of other performance inquiries in the area, Unexpected Damage situations, and cases of Suspected or Confirmed Resistance. 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 SmartStax 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.

Remedial actions

In situations of Confirmed Resistance, SmartStax 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, 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 SmartStax, such as crop rotation, 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 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, SmartStax may or may not fit within the resistant rootworm management program. For example, if the level of corn rootworm survival on SmartStax that is conferred by resistance is low (e.g., if resistant insects still show reduced fitness on SmartStax corn, or if resistance is to one but not both of the rootworm-active components of SmartStax), then continued use of SmartStax in combination with other pest management tools may be the most effective approach for reducing the local population. In such cases, the appropriate refuge size for SmartStax will be evaluated. On the other hand, if the level of corn rootworm survival on SmartStax that is conferred by resistance is high, SmartStax 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.

For cases of Confirmed Resistance, the registrants individually will report to the EPA within 30 days of confirming the resistance. Registrants will also inform relevant state extension entomologists, crop consultants, and other registrants as appropriate so that remedial measures can be coordinated. These reports will include a description of the known affected areas (Remedial Action Zone) and the recommended resistant rootworm management program. EPA and the registrant(s) must agree upon the specific remedial action plan to be implemented in cases of confirmed resistance.

On-going Research and Monitoring

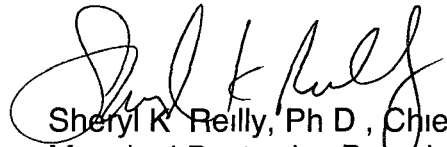
The goal of the remedial action plan is to manage the resistant corn rootworm population. For a corn rootworm population found to be resistant to SmartStax, research will be conducted to

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understand the resistance, with the intention of using information generated to refine the management program. Such research may include characterization of 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 SmartStax, 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 SmartStax 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 SmartStax as a primary tool for corn rootworm management.

Sincerely,



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