United States
Environmental Protection
Agency

Office of Prevention,
Pesticides
and Toxic Substances
(7501P)

Pesticide Fact Sheet

Name of Plant-Incorported Protectant(s):

Bacillus thuringiensis Cry 1A.l05 protein and the genetic material necessary (vector PV-ZMIR245) for its production in corn event MON 89034

Bacillus thuringiensis Cry2Ab2 protein and the genetic material necessary (vector PV-ZMIR245) for its production in corn event MON 89034

Bacillus thuringiensis Cry1F protein and the genetic material necessary (vector PHP8999) for its production in corn event TCI507

Bacillus thuringiensis Cry3Bbl protein and the genetic material necessary (vector PV-ZMIR39) for its production in com event MON 88017

Bacillus thuringiensis Cry34Ab1 protein and the genetic material necessary (vector PHP17662) for its production in corn event DAS-59122-7

Bacillus thuringiensis Cry35Ab1 protein and the genetic material necessary (vector PHP I7662) for its production in corn event DAS-59122-7

OECD Unique Identifier: MON-89Ø34-3 x DAS- Ø15Ø7-1 x MON-88Ø17-3 x DAS-59122-7)

Reason for Issuance: Updated Expiration Date and Additional Terms and Conditions

Date Issued: November 29, 2011

I. Description of the Plant-Incorporated Protectant

- **Pesticide Name:** MON 89034 x TC1507 x MON 88017 x DAS-59122-7
- **Date Registered:** July 20, 2009
- **Registration Numbers:** 524-581 & 68467-7

- **Trade and Other Names:** MON 89034 x TC1507 x MON 88017 x DAS-59122-7 Insect Protected, Herbicide-Tolerant Corn, Genuity™SmartStax™, SmartStax™

- **OPP Chemical Codes: 006490, 006481, 006502, 006515, 006514**

- **Basic Manufacturers:** Monsanto Company
  800 North Lindbergh Blvd
  St. Louis, MO 63167

  Mycogen Seeds c/o Dow AgroSciences LLC
  9330 Zionsville Road
  Indianapolis, Indiana 46268-1054

- **Type of Pesticide: Plant-Incorporated Protectant (PIP)**

- **Uses: Field Corn**

- **Target Pest(s):** European corn borer (ECB)
  Southwestern corn borer (SWCB)
  Southern cornstalk borer (SCSB)
  Corn earworm (CEW)
  Fall armyworm (FAW)
  Stalk borer
  Lesser corn stalk borer
  Sugarcane borer (SCB)
  Western bean cutworm (WBC)
  Black cutworm
  Western com rootworm (WCRW)
  Northern corn rootworm (NCRW)
  Mexican corn rootworm (MCRW)

II. Summary

EPA has conditionally registered MON 89034 x TC1507 x MON 88017 x DAS-59122-7, "SmartStax,", a new bioengineered corn seed product containing genes for two Bt PIPs active against corn rootworm (CRW and three Bt PIPs to control different corn borer pests.. After reviewing all pertinent data, the Agency has concluded that a lower CRW refuge of 5% is scientifically justified for SmartStax corn and will further reduce the use of conventional insecticides.

EPA has approved bioengineered "Bt corn" to control corn rootworm (CRW) since 2003. The use of such Bt corn in the U.S. has reduced conventional insecticide use for CRW by more than 75%.

Bt corn products for CRW could lose their effectiveness due to the development of insect resistance. To mitigate this risk, EPA currently requires the use of an external structured 20%

refuge of non-Bt corn. Refuges produce Bt susceptible insects to dilute any resistance genes in the pest population.

Monsanto and Dow have developed a new Bt corn product (SmartStax) with two Bt toxins (Cry34Ab1/Cry35Ab1 and Cry3Bb1) active against CRW. The use of multiple toxins against the same pest is termed a "pyramid."

SmartStax also contains three Bt PIPs to control different corn borer pests. (Corn borers have separate refuge requirements.)

EPA has previously approved a 5% refuge for corn borer pests where the corn earworm is not a significant pest and a 20% combined refuge in cotton growing regions where the corn earworm is a significant pest. The reduced CRW refuge could result in further reduction in conventional insecticide use, increased crop yields for growers, and increased grower compliance with refuge requirements.

EPA has approved a combined 5% refuge for corn rootworm and lepidopteran pests where the corn earworm is not a significant pest and a 20% combined refuge in cotton growing regions where the corn earworm is a significant pest.

III. Science Assessment

Product Characterization and Human Health Assessment

Current tolerance exemptions in 40 CFR Part 174 applicable to MON 89034 × TC1507 × MON 88017 × DAS-59122-7.

§ 174.502 Bacillus thuringiensisCry1A.105 protein; exemption from the requirement of a tolerance.

(a) Residues of *Bacillus thuringiensis* Cry1A.105 protein in or on the food and feed commodities of corn; corn, field, flour; corn, field, forage; corn, field, grain; corn, field, grits; corn, field, meal; corn, field, refined oil; corn, field, stover; corn, sweet, forage; corn, sweet, kernel plus cob with husk removed; corn, sweet, stover; corn, pop, grain and corn, pop, stover are exempt from the requirement of a tolerance when the *Bacillus thuringiensis* Cry1A.105 protein is used as a plant-incorporated protectant in these food and feed corn commodities.

§ 174.506 Bacillus thuringiensis Cry34Ab1 and Cry35Ab1 proteins in corn; exemption from the requirement of a tolerance.

Residues of *Bacillus thuringiensis* Cry34Ab1 and Cry35Ab1 proteins in corn are exempted from the requirement of a tolerance when used as plant-incorporated protectants in the food and feed commodities of corn; corn, field; corn, sweet; and corn, pop.

§ 174.507 Nucleic acids that are part of a plant-incorporated protectant; exemption from the requirement of a tolerance.

Residues of nucleic acids that are part of a plant-incorporated protectant are exempt from the requirement of a tolerance.

§ 174.518 Bacillus thuringiensis Cry3Bb1 protein in corn; exemption from the requirement of a tolerance.

Residues of *Bacillus thuringiensis* Cry3Bb1 protein in corn are exempt from the requirement of a tolerance when used as plant-incorporated protectants in the food and feed commodities of corn; corn, field; corn, sweet; and corn, pop.

§ 174.519 Bacillus thuringiensis Cry2Ab2 protein in corn and cotton; exemption from the requirement of a tolerance.

Residues of *Bacillus thuringiensis* Cry2Ab2 protein in or on corn or cotton are exempt from the requirement of a tolerance when used as a plant–incorporated protectant in the food and feed commodities of corn; corn, field; corn, sweet; corn, pop; and cotton seed, cotton oil, cotton meal, cotton hay, cotton hulls, cotton forage, and cotton gin byproducts.

§ 174.520 Bacillus thuringiensis Cry1F protein in corn; exemption from the requirement of a tolerance.

Residues of *Bacillus thuringiensis* Cry1F protein in corn are exempt from the requirement of a tolerance when used as plant-incorporated protectants in the food and feed commodities of corn; corn, field; corn, sweet; and corn, pop.

§ 174.523 CP4 Enolpyruvylshikimate-3-phosphate (CP4 EPSPS) synthase in all plants; exemption from the requirement of a tolerance.

Residues of the CP4 Enolpyruvylshikimate-3-phosphate (CP4 EPSPS) synthase enzyme in all plants are exempt from the requirement of a tolerance when used as plant-incorporated protectant inert ingredients in all food commodities.

§ 174.522 Phosphinothricin Acetyltransferase (PAT); exemption from the requirement of a tolerance.

Residues of the Phosphinothricin Acetyltransferase (PAT) enzyme are exempt from the requirement of a tolerance when used as plant-incorporated protectant inert ingredients in all food commodities.

Southern Blot Analysis

Southern blot analysis confirmed in the combined trait corn product MON 89034 × TC1507 × MON 88017 × DAS-59122-7 the presence of sequences identical to sequences derived from MON 89034 and MON 88017.Hybridization patterns for the combined trait product were identical to those of the parental lines with *cry*1F, *cry*34Ab1, *cry*35Ab1, and the *pat* gene probes indicating that the TC1507 and DAS-59122-7 insertions were unaffected by combining with MON 89034 and MON 88017 through conventional breeding.

Expression Levels

MON 89034 x TC1507 x MON 88017 x DAS-59122-7 is a combined trait corn that produces lepidopteran-active and coleopteran-active *Bacillus thuringiensis* (*Bt*) proteins, as well as the 5-enolpyruvylshikimate-3-phosphate synthase protein from *Agrobacterium* sp. strain CP4 (CP4 EPSPS) to confer tolerance to glyphosate herbicides and PAT to confer tolerance to glufosinate herbicides. The levels of the lepidopteran-active Cry1A.105, Cry2Ab2, Cry3Bb1 proteins and the CP4 EPSPS protein were determined in tissues from MON 89034 x TC1507 x MON 88017 x DAS-59122-7 plants grown at five US field sites in 2006. The test also included a conventional corn as a negative control and MON 89034 and MON 88017 corns as positive controls. Leaf, root, and whole plant samples were collected over the growing season, as well as pollen and grain samples at the appropriate times. The samples were extracted and analyzed using enzyme-linked immunosorbent assays. The levels of the Cry1A.105, Cry2Ab2, Cry3Bb1, and CP4 EPSPS proteins in MON 89034 x TC1507 x MON 88017 x DAS-59122-7 corn were comparable to those in the appropriate MON 88017 or MON 89034 positive control.

The levels of the coleopteran-active *Bacillus thuringiensis* (*Bt*) proteins Cry34Ab1, Cry35Ab1, and Cry1F, and the PAT protein were determined in tissues from MON 89034 x TC1507 x MON 88017 x DAS-59122-7 plants grown at five US field sites in 2006. The test also included a conventional corn as a negative control and TC1507 and DAS-59122-7 parental event corn as positive controls. Leaf, root, and whole plant samples were collected over the growing season, as well as pollen and grain samples at the appropriate times. The samples were extracted and analyzed using enzyme-linked immunosorbent assays (ELISA). The results indicate that the levels of Cry34Ab1, Cry35Ab1, and Cry1F in MON 89034 x TC1507 x MON 88017 x DAS-59122-7 were comparable to the levels produced in the appropriate TC1507 or DAS-59122-7 control corn. The level of PAT in MON 89034 x TC1507 x MON 88017 x DAS-59122-7 was higher in the combined trait products compared to TC1507 and DAS-59122-7, likely due to the presence of multiple copies of the *pat* gene in the stacks (one from each of the DAS parent lines).

Environmental Assessment

At present, the Agency has not identified any significant adverse effects of the Cry1A.105, Cry2Ab2, Cry1F, Cry3Bb1, or Cry34Ab1/35Ab1 proteins on the abundance of non-target organisms in any field population, whether expressed individually or as MON 89034 x TC1507 x

MON 88017 x DAS-59122-7 combined PIP corn product. The potential for synergistic effects has been evaluated and the data that were reviewed for the individual parental events can be bridged to support the Sec. 3 registration of MON 89034 x TC1507 x MON 88017 x DAS-59122-7 combined PIP corn product.

It is unlikely that direct or indirect harmful effects to non-target organisms, including federally-listed threatened or endangered species, would result from the insecticidal proteins Cry1A.105, Cry2Ab2, Cry1F, Cry3Bb1, or Cry34/35Ab as a result of the proposed Sec. 3 registration. The Agency anticipates that for full commercial cultivation, no hazard will result to the environment.

Event MON 89034 produces the Cry1A.105 and Cry2Ab2 Bt proteins, and Event TC1507 produces Cry1F. These proteins are intended to control or suppress several lepidopteran pests of corn, including European corn borer (ECB, *Ostrinia nubilalis*), corn earworm (CEW, *Helicoverpa zea*), fall army worm (FAW, *Spodoptera frugiperda*), and black cutworm (BCW, *Agrotis ipsilon*). MON 88017 produces the Cry3Bb1 protein, and Event DAS-59122-7 produces the Cry34Ab1 and Cry35Ab1 proteins. These two events provide additional control for coleopteran pests, particularly corn rootworm pests (*Diabrotica* spp.).

It has been determined that each individual event has protein expression levels that are comparable to the MON 89034 x TC1507 x MON 88017 x DAS-59122-7 corn hybrid (Kough, 2009). Therefore, the margins of exposure that were previously determined for the insecticidal proteins in the individual events are applicable for the risk assessment of these proteins in the stacked hybrid. Additionally, no synergistic or antagonistic effects were observed in several combinations of the individual events in MON 89034 x TC1507 x MON 88017 x DAS-59122-7, as well as the MON 89034 x TC1507 x MON 88017 x DAS-59122-7 hybrid itself. As a result, the Agency concludes that there is no indication of synergistic effects or increased levels of protein expressed in the combined PIP product, so the environmental risk assessment for the single PIP lines are applicable to the assessment of MON 89034 x TC1507 x MON 88017 x DAS-59122-7.

As a result, the environmental risk assessment of the individual events, as well as an additional study submitted on the toxicity of MON 89034 x TC1507 x MON 88017 x DAS-59122-7 to a non-target insect, the Agency concludes that there will be no unreasonable adverse effects to the environment, including endangered species, by MON 89034 x TC1507 x MON 88017 x DAS-59122-7 combined trait corn.

Insect Resistance Management

1) Overall, Monsanto/Dow have provided sufficient scientific justification to support a reduced corn rootworm (CRW) refuge of 5% for SmartStax Bt corn. Data reviewed by BPPD include studies on dose for CRW, cross resistance between the Cry3Bb1 and Cry34Ab1/35Ab1 toxins, and simulation modeling to predict potential resistance evolution. However, BPPD notes that there is still uncertainty regarding the true CRW dose expressed by SmartStax (and its single trait

components) and worst case simulation modeling (as described in the conclusions below). Therefore, additional data have been required to be generated (as described below) to verify and further buttress the current data supporting lower refuge. BPPD intends to conduct a post-registration assessment of the lower refuge within several years of approval once any new data have been submitted and reviewed.

2) Monsanto has previously provided data to support a 5% refuge for lepidopteran target pests of SmartStax corn.

3) Given that SmartStax will likely have different refuge requirements for Lepidoptera and CRW than other registered Bt corn products, BPPD has required that Monsanto/Dow submit a revised compliance plan. This strategy should be specific for SmartStax and the new refuge requirements. Compliance is an area of ongoing concern -- recent data have shown that refuge compliance for Bt corn has fallen in recent years.

4) Existing programs for resistance monitoring and remedial action that were established for MON 89034 (Cry1A.105 and Cry2Ab2), MON 88017 (Cry3Bb1), and Herculex Xtra (Cry1F and Cry34Ab1/35Ab1) should be applicable to SmartStax corn. In light of lower required structured Bt corn structured refuge for SmartStax, BPPD has required that the CRW resistance monitoring program be expanded (i.e. with additional sampling and collection sites or improved monitoring techniques). Also, a revised definition of "resistance" may be needed for the CRW monitoring and remedial action plans based on recent research and selection experiments (Lefko et al. 2008; Meihls et al. 2008).

Conclusions Regarding Dose, Resistance Allele Frequency, and Modeling Data

5) BPPD agrees with Monsanto/Dow that the methodology used to calculate dose for SmartStax (developed in Storer et al. 2006 and used in Hucakaba and Storer 2008) is a reasonable approach to addressing dose for CRW. There is some conflicting evidence about the effect of density dependent mortality on dose calculations; BPPD agrees with Monsanto/Dow's use of the data from the Huckaba and Storer (2008) study that was not adjusted for density dependent effects. These more conservative dose estimates (96.17 - 99.96% for Cry3Bb1, 94.20 - 99.18% for Cry34/35, and 98.22 - 99.97% for Cry3Bb1 + Cry34/35 pyramid) were used in a revised model simulation.

6) Although Monsanto/Dow have used the best available dose estimates for CRW, BPPD believes that there is still uncertainty on dose in both the methodology and interpretation of available studies. This is largely due to the biology of CRW -- assessing larval response and behavior in a subterranean environment is difficult and confounding factors such as density-dependent (or independent) mortality must be considered. Storer et al. (2006) is probably the best current approach to evaluating dose, but BPPD notes that limited data have been developed using this technique (e.g. only one year with six locations of data were developed for Cry3Bb1).

Other *Diabrotica* spp. may also need to be investigated: data previously submitted for northern corn rootworm revealed mortality as low as 92.8% on Cry34/35 .

7) To address the uncertainty regarding CRW dose and buttress the dose assumptions used in the models, BPPD has required that Monsanto/Dow provide additional dose data (using the methods of Storer et al. 2006) for Cry3Bb1 and Cry34Ab1/35Ab1. Further dose studies could also be conducted with varying egg infestation levels (above and below egg levels expected to trigger density-dependent mortality) to tease out any egg density effects. New techniques to assess CRW dose may need to be pursued as well, if Monsanto/Dow or academic researchers can develop such approaches.

8) Monsanto/Dow conducted modeling simulations to investigate the effect of initial resistance allele frequency (RAF). The results from these simulations with a pyramid showed that the initial RAF was insensitive in the model -- the final RAF did not increase significantly from the initial frequency after 10 generations of selection (regardless of the starting value). Nevertheless, BPPD is still concerned that resistance alleles for CRW-targeted Bt traits may be relatively common in the field based on published CRW selection studies (Lefko et al. 2008; Meihls et al. 2008). Monsanto/Dow's default assumption of an initial RAF of 0.001. This may be suitable for other pests (e.g. Lepidoptera), but BPPD must consider the possibility that actual RAF for CRW is higher (perhaps close to 0.01). To further investigate this issue, BPPD recommends resistance selection experiments to further characterize putative resistance alleles and frequency of occurrence in CRW populations.

9) As with Monsanto/Dow's previous modeling, revised simulation modeling conducted with the lower dose estimates (described in #5 above) showed that resistance did not evolve to a pyramid with a 5% refuge, while single trait PIPs with a 20% refuge developed resistance in < 10 generations. An initial resistance allele frequency of 0.001 was used in the model; as discussed in #8 above, BPPD is concerned that resistance alleles may be more common among CRW in natural populations. However, BPPD notes that all modeling reviewed to date, including models submitted by Monsanto/Dow and published by independent researchers (Roush 1998; Zhao et al. 2003; Gould et al. 2006; Onstad 2009 - draft), strongly suggest that pyramided PIPs are superior to the current single trait CRW products and can justify a lower refuge for the SmartStax pyramid.

10) BPPD has required that new model simulations be conducted to incorporate new data (i.e. from studies conducted under #7 and 8 above) or using possible "worst case" parameters. Although Monsanto/Dow's new model simulations have been more conservative than previous runs, BPPD remains concerned that "worst case" scenarios for SmartStax have not yet been fully investigated. CRW-protected corn is highly adopted in some areas with heavy infestations so that intense selection pressure for resistance can be expected. In light of this, and the large proposed reduction in minimum refuge (from 20% to 5%; a 75% total reduction), BPPD believes that worst case analyses are warranted to help determine the potential for resistance. In

particular, model parameters for dose and initial resistance allele frequency could be adjusted to include more conservative estimates (e.g. dose ranges < 94% and RAF > 0.001).

Gould, F., M. B. Cohen, J. S. Bentur, G. C. Kennedy, and J. Van Duyn. 2006. Impact of small fitness costs on pest adaptation to crop varieties with multiple toxins: a heuristic model. J. Econ. Entomol. 99: 2091-2099.

Lefko, S.A. et al., 2008. Characterizing laboratory colonies of western corn rootworm (Coleoptera: Chrysomelidae) selected for survival on maize containing event DAS 59122-7. J. Appl. Entomol. 132: 189-204.

Meihls, L., M. Hidgon, B. Siegfried, N. Miller, T. Sappington, M. Ellersieck, T. Spencer, and B. Hibbard, 2008. Increased survival of western corn rootworm on transgenic corn within three generations of on-plant greenhouse selection. Proc. Nat. Acad. Sci. 105 (49): 19177-19182.

Onstad, D., 2009 (draft). Modeling Evolution of *Diabrotica virgifera virgifera* (Coleoptera: Chrysomelidae) to Transgenic Corn with Two Insecticidal Traits. J. Econ Entomol. Draft - to be submitted in 2009.

Roush, R.T., 1998. Two toxin strategies for management of insecticidal transgenic crops: pyramiding succeed where pesticide mixtures have not? Phil. Trans. R. Soc. Lond. 353:1777-1786.

Zhao, J., J. Cao, Y. Li, H. Collins, R. Roush, E. Earle, and A. Shelton, 2003. Transgenic plants expressing two *Bacillus thuringiensis* toxins delay insect resistance evolution. Nature Biotechnology. 21: 1493-1497.

IV. Terms and Conditions of the Registration

1) The subject registration will automatically expire on midnight November 30, 2013.

2) The subject registration will be limited to MON 89034 x TC1507 x MON 88017 x DAS-59122-7 in field corn.

3) Submit the following data in the time frames listed:

OPPTS Guideline/ Study Type	Required Data	Due Date
Insect Resistance Management	To address the uncertainty regarding CRW dose and buttress the dose assumptions used in the models, provide additional dose data (using the methods of Storer et al. 2006) for Cry3Bb1 and Cry34Ab1/35Ab1. Further dose studies could also be conducted with varying egg infestation	Report Due 11/30/2010

OPPTS Guideline/ Study Type	Required Data	Due Date
	levels (above and below egg levels expected to trigger density-dependent mortality) to tease out any egg density effects. New techniques to assess CRW dose may need to be pursued as well, if Monsanto/Dow or academic researchers can develop such approaches.	
Insect Resistance Management	Monsanto/Dow conducted modeling simulations to investigate the effect of initial resistance allele frequency (RAF). The results from these simulations with a pyramid showed that the initial RAF was insensitive in the model -- the final RAF did not increase significantly from the initial frequency after 10 generations of selection (regardless of the starting value). Nevertheless, BPPD is still concerned that resistance alleles for CRW-targeted Bt traits may be relatively common in the field based on published CRW selection studies (Lefko et al. 2008; Meihls et al. 2008). Monsanto/Dow's modeling has assumed an initial RAF of 0.001. This may be suitable for other pests (e.g. lepidoptera), but BPPD must consider the possibility that actual RAF for CRW is higher (perhaps close to 0.01). To further investigate this issue, resistance selection experiments must be conducted to further characterize the potential for resistance alleles and frequency of occurrence in CRW populations.	Annually First Report Due 11/30/2010
Insect Resistance Management	New model simulations must be conducted to incorporate new data (i.e. from studies conducted under items above) or using possible "worst case" parameters. Although Monsanto/Dow's new model simulations have been more conservative than previous runs, BPPD remains concerned that "worst case" scenarios for SmartStax have not yet been fully investigated. CRW-protected corn is highly adopted in some areas with heavy infestations so that intense selection pressure for resistance can be expected. In light of this, and the large proposed reduction in refuge (from 20% to 5%; a 75% total reduction), BPPD believes that worst case analyses are warranted to help determine the potential for resistance. In particular, model parameters for dose and initial resistance allele frequency could be adjusted to include more conservative estimates (e.g. dose ranges < 94% and RAF > 0.001).	Annually First Report Due 11/30/2010

4) Submit or cite all data required to support the Herculex Xtra and the MON 89034 x MON 88017 stacked plant-incorporated protectant products within the timeframes required by the terms and conditions of EPA Registration Numbers 68467-6 and 524-576.

5) Do the following Insect Resistance Management Program for MON 89034 x TC1507 x MON 88017 x DAS-59122-7.

The required IRM program for MON 89034 x TC1507 x MON 88017 x DAS-59122-7 corn must have the following elements:

Requirements relating to creation of a non-*Bt* corn refuge in conjunction with the planting of any acreage of MON 89034 x TC1507 x MON 88017 x DAS-59122-7corn;
Requirements for Monsanto/Dow to prepare and require MON 89034 x TC1507 x MON 88017 x DAS-59122-7 corn users to sign "grower agreements," which impose binding contractual obligations on the grower 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 target insect susceptibility to Cry1A.105, Cry2Ab2, Cry3Bb1, Cry1F and Cry34Ab1/Cry35Ab1 proteins in the target insects;
Requirements regarding a "remedial action plan," which contains measures Monsanto/Dow 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;

Annual reports on units sold by state (units sold by county level will be made available to the Agency upon request), IRM grower agreements results, and the compliance assurance program including the educational program on or before January 31st each year, beginning in 2011.

a) Refuge Requirements for MON 89034 x TC1507 x MON 88017 x DAS-59122-7

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.

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 MON 89034 x TC1507 x MON 88017 x DAS-59122-7 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 MON 89034 x TC1507 x MON88017 x DAS-59122-7 corn must also be planted on rotated ground. If the combined refuge is planted on continuous corn, the MON 89034 x TC1507 x MON88017 x DAS-59122-7field 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 MON 89034 x TC1507 x MON 88017 x DAS-59122-7 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 MON 89034 x TC1507 x MON 88017 x DAS-59122-7 planted) or 5% in non-cotton growing regions (5 acres of non-Bt corn for every 95 acres of MON 89034 x TC1507 x MON 88017 x DAS-59122-7 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 MON 89034 x TC1507 x MON 88017 x DAS-59122-7, 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 MON 89034 x TC1507 x MON 88017 x DAS-59122-7 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 MON 89034 x TC1507 x MON 88017 x DAS-59122-7. 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 MON 89034 x TCl507 x MON 88017 x DAS-59122-7 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,	20% non-Bt corn	Yes	Yes

Region	Refuge size	In-field or adjacent refuge is allowed	Refuge separated by up to 1/2 mile is allowed
Madison, Obion, Rutherford, Shelby, and Tipton) AL, MS, LA, VA (only the counties of Dinwiddie, Franklin City, Greensville, 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-Bt 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-Bt 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, Greensville, 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-Bt corn	Yes	Yes
Non-cotton growing where WCRW, NCRW and/or MCRW are significant: KS, NE, SD, ND, MN, IA, MO (except	5% non-Bt corn	Yes	No

Region	Refuge size	In-field or adjacent refuge is allowed	Refuge separated by up to 1/2 mile is allowed
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)			

b) Grower Agreement for *MON 89034 x TC1507 x MON 88017 x DAS-59122-7* Corn

1) Persons purchasing MON 89034 x TC1507 x MON 88017 x DAS-59122-7 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) Monsanto and Dow must implement a system (equivalent to what is already approved for previously registered Monsanto and Dow *Bt* corn products), which is reasonably likely to assure that persons purchasing *MON* 89034 x TC1507 x MON 88017 x DAS-59122-7 corn will affirm annually that they are contractually bound to comply with the requirements of the IRM program. A description of the system must be submitted to EPA within 90 days from the date of registration.

4) Monsanto and Dow must use a grower agreement and must submit to EPA, within 90 days from the date of registration, a copy of that agreement and any specific stewardship documents referenced in the grower agreement. If Monsanto and Dow wishe 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, 30 days prior to implementing a proposed change, Monsanto and Dow must submit to EPA the text of such changes to ensure that it is consistent with the terms and conditions of this registration.

5) Monsanto and Dow must implement a system (equivalent to what is already approved for previously registered Monsanto and Dow *Bt* corn products), which is reasonably likely to assure

that persons purchasing MON 89034 x TC1507 x MON 88017 x DAS-59122-7 corn sign grower agreement(s). A description of the system must be submitted to EPA within 90 days from the date of registration.

6) Monsanto and Dow shall maintain records of all MON 89034 x TC1507x MON 88017 x DAS-59122-7 corn grower agreements for a period of three years from December 31st of the year in which the agreement was signed.

7) Beginning on January 31, 2011 and annually thereafter, Monsanto and Dow shall provide EPA with a report on the number of units of MON 89034 x TC1507 x MON 88017 x DAS-59122-7 corn seed shipped and not returned, and the number of such units that were sold to persons who have signed grower agreements. The report shall cover the time frame of a twelve-month period. Note: The first report shall contain the specified information from the time frame starting with the date of registration and extending through the 2010 growing season.

8) Monsanto and Dow must allow a review of the grower agreements and grower agreement records by EPA or by a State pesticide regulatory agency if the State agency can demonstrate that confidential business information, including names, personal information, and grower license number, will be protected.

c) IRM Education and IRM Compliance Monitoring Program for *MON 89034 x TC1507 x MON 88017 x DAS-59122-7*Corn

1) Monsanto and Dow must design and implement a comprehensive, ongoing IRM education program designed to convey to MON 89034 x TC1507 x MON 88017 x DAS-59122-7 corn users the importance of complying with the IRM program. 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 their records. The program shall involve at least one written communication annually to each MON 89034 x TC1507 x MON 88017 x DAS-59122-7 corn user separate from the grower technical guide. The communication shall inform the user of the current IRM requirements. Monsanto and Dow shall coordinate its education program with the educational efforts of other registrants and other organizations, such as the National Corn Growers Association and state extension programs.

2) Annually, Monsanto/Dow shall revise, and expand as necessary, its education program to take into account the information collected through the compliance survey and from other sources. The changes shall address aspects of grower compliance that are not sufficiently high.

3) Beginning January 31, 2011, Monsanto and Dow must provide a report to EPA summarizing the activities it carried out under its education program for the prior year. Annually thereafter, Monsanto and Dow must provide EPA any substantive changes to its grower education activities

as part of the overall IRM compliance assurance program report. Monsanto/Dow must either submit a separate report or contribute to the report from the industry working group, Agricultural Biotechnology Stewardship Technical Committee (ABSTC).

4) Given that MON 89034 x TC1507 x MON 88017 x DAS-59122-7 will likely have different refuge strategies for lepidoptera and CRW than other registered Bt corn products, Monsanto/Dow must submit a revised compliance assurance program (CAP) within 90 days of the date of registration. This revised CAP must be found acceptable by BPPD by April 1, 2010. This strategy should be specific for MON 89034 x TC1507 x MON 88017 x DAS-59122-7 and the new refuge requirements. Availability of non-Bt corn refuge seeds in desirable varieties must be addressed. Compliance is an area of ongoing concern -- recent data have shown that refuge compliance for Bt corn has fallen in recent years.

d) Insect Resistance Monitoring and Remedial Action Plans for *MON 89034 x TC1507 x MON 88017 x DAS-59122-7* Corn

Existing programs for resistance monitoring and remedial action that were established for MON 89034 (Cry1A.105 and Cry2Ab2), MON 88017 (Cry3Bb1), and Herculex Xtra (Cry1F and Cry34Ab1/35Ab1) should be applicable to MON 89034 x TC1507 x MON 88017 x DAS-59122-7 corn. In light of potentially lower overall structured Bt corn structured refuge, the CRW resistance monitoring program must be expanded (i.e. with additional sampling and collection sites or improved monitoring techniques). Also, a revised definition of "resistance" may be needed for the CRW monitoring and remedial action plans based on recent research and selection experiments (Lefko et al. 2008; Meihls et al. 2008). Monsanto/Dow must submit a revised resistance monitoring and remedial action plan within 90 days of the date of registration that must be found acceptable to BPPD by April 1, 2010.

A report on results of resistance monitoring and investigations of damage reports must be submitted to the Agency annually by August 31st each year, beginning in 2011, for the duration of the conditional registration.

e) Annual Reporting Requirements for *MON 89034 x TC1507 x MON 88017 x DAS-59122-7* Corn

1) Annual Sales: reported and summed by state (county level data available by request) January 31st each year, beginning in 2011;

2) Grower Agreements: number of units of MON 89034 x TC1507 x MON 88017 x DAS-59122-7corn seed shipped or sold and not returned, and the number of such units that were sold to persons who have signed grower agreements, January 31st each year, beginning in 2011;

3) Grower Education: substantive changes to education program completed previous year, January 31st each year, beginning in 2011;

4) Compliance Assurance Program: compliance assurance program activities and results for the prior year and plans for the compliance assurance program for the current year, January 31st each year, beginning in 2011;

5) Compliance Survey Results: results of annual surveys for the prior year and survey plans for the current year; full report January 31st each year, beginning in 2011;

6) Insect Resistance Monitoring Results: results of monitoring and investigations of damage reports, August 31st each year, beginning in 2011.

Additional Terms and Conditions as of November 22, 2011

1) 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 SmartStax field is > 0.5 on the nodal injury scale (NIS) and the frequency of SmartStax with > 0.5 nodes destroyed exceeds 50% of the sampled plants.

2) Within 90 days of this amendment, you must submit an enhanced rootworm resistance monitoring plan for SmartStax 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 SmartStax must be found acceptable to BPPD by May 1, 2012 and utilized by The registrant beginning in the 2012 season. This enhanced monitoring program should:

    - o Be practical and adaptable, and provide information on relevant changes in corn rootworm population sensitivity to SmartStax;

    - o Be focused on areas where the potential for resistance is greatest for SmartStax and for the corn rootworm active single event components of SmartStax (Cry3Bb1and 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, other registrants of SmartStax, 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 SmartStax.

3) Within 90 days of this amendment, you must submit an enhanced remedial action plan for SmartStax 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 SmartStax corn that could indicate potential suspected resistance. The enhanced remedial action plan must be found acceptable to BPPD by May 1, 2012.

4) The Grower Guide or its supplements must include language directing the user to contact a company representative if they observe unexpected insect feeding damage to their SmartStax corn. As part of its follow up on reports of unexpected damage to SmartStax corn, the registrant must determine the nodal injury scale (NIS) of affected corn. If the NIS results fall within the definition of suspected resistance for SmartStax, then until such time as the Agency accepts a modified remedial action plan, the registrant must provide specific guidance to affected growers in managing corn rootworms in the affected fields. This will include 1) providing specific grower guidance to control the adult stage of corn rootworms, where adult beetles are still present and laying eggs during the season that unexpected damage meets the suspected resistance definition; and 2) where the grower continues to be an existing customer of the registrant or seed company licensee into the following season, providing specific grower guidance and assistance to use an additional or alternative pest control method during the season following the initial finding that unexpected damage meets the suspected resistance definition.

5) The registrant will submit additional modeling, scientific literature, and other scientific information addressing the impact of pyramid PIP use in areas of confirmed resistance to one of the rootworm-active components of the pyramid by August 30, 2012.

6) Should resistance to any of the constituent toxins of SmartStax be confirmed (from target pest populations collected in 2012 or prior growing seasons) in accordance with the existing definition of "confirmed resistance" for the appropriate toxin, EPA will reassess and, if EPA concludes it is necessary, The registrant will revise the refuge/seed blend requirements for SmartStax. The registrants may independently submit updated definitions of confirmed resistance for their respective SmartStax active proteins for EPA's consideration in order to harmonize and/or keep definitions current with scientific standards; any such submission must be found acceptable to BPPD by May 1, 2012. EPA will incorporate all relevant scientific information (including the data required above) in its reassessment of the refuge/seed blend requirements. The revised refuge/seed blend requirements will be effective for the following growing season (after resistance confirmation) in the geographic areas in which resistance was confirmed. The geographic area of confirmed resistance could be less than a single county, a single county, or multiple counties, depending on EPA's analysis of the collected data.

7) For the SmartStax block refuge products, submit a revised Compliance Assurance plan by February 28, 2012.

V. Contact Person at EPA

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

Office location and telephone number:

8th Floor
One Potomac Yard
2777 S, Crystal Drive
Arlington, VA 22202
(703) 308-8715
Email: mendelsohn.mike@epa.gov

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