AGENDA
FIFRA SCIENTIFIC ADVISORY PANEL (SAP)
OPEN MEETING

December 8-9, 2010

FIFRA SAP WEB SITE http://www.epa.gov/scipoly/sap/
OPP Docket Telephone: (703) 305-5805
Docket Number: EPA-HQ- OPP-2010-0772

U.S. Environmental Protection Agency
Conference Center - Lobby Level
One Potomac Yard (South Bldg.)
2777 S. Crystal Drive, Arlington, VA 22202

Scientific Issues Related to Insect Resistance Management for SmartStax™ Refuge-in-the-Bag, a Plant-Incorporated Protectant (PIP) Corn Seed Blend

Please note that all times are approximate
(See note at the end of the Agenda)

Wednesday, December 8, 2010

9:00 A.M. **Opening of Meeting and Administrative Procedures –**
Sharlene Matten, Ph.D., Designated Federal Official, Office of Science Coordination and Policy, EPA

9:05 A.M. **Introduction and Identification of Panel Members –**
Steven Heeringa, Ph.D., Chair, FIFRA Scientific Advisory Panel

9:10 A.M. **Welcome and Opening Remarks –**
Steven Bradbury, Ph.D., Director, Office of Pesticide Programs (OPP), EPA

9:15 A.M. **Introduction –**
Keith A. Matthews, M.S., J.D., Director, Biopesticides and Pollution Prevention Division, OPP, EPA

9:20 A.M. **Preliminary Risk Assessment of a 5% SmartStax™ Seed Blend Targeting Lepidopteran and Corn Rootworm Pests –**
Jeannette Martinez, M.S., Biopesticides and Pollution Prevention Division, OPP, EPA

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10:15 A.M. BREAK

10:45 A.M. PUBLIC COMMENTS

12:00 P.M. LUNCH

1:00 P.M. CHARGE QUESTIONS –
Alan Reynolds, M.S., Biopesticides and Pollution Prevention Division, OPP, EPA

Part A: Biology of European Corn Borer, Southwestern Corn Borer, Corn Earworm, and Corn Rootworm

Charge Question 1

European corn borer (ECB) has both local and long distance dispersal capability. Currently, the proportion and frequency of individuals in a population engaging in dispersal before or after mating is unclear. While it has been established that ECB mate in aggregation sits near cornfields, mark-release-recapture studies in the U.S. have typically had a low recapture success (<1%). Recently it was suggested that 1-day old female ECB may engage in obligate pre-mating dispersal (Dorhout *et al.* 2008).

Please comment on the uncertainties regarding ECB movement including mating sites, pre-mating dispersal, and the proportion of the population engaging in long-distance dispersal. How might these aspects of ECB movement affect a potential seed blend strategy?

2:00 P.M. Charge Question 2

Scientific Advisory Panels (1998 and 2000) discouraged the Agency from the use of *Bt* seed mixtures to control lepidopteran target pests because substantial larval movement could be expected between *Bt* and non-*Bt* plants which could lead to more rapid selection of resistance. BPPD has reviewed new data developed by Dow and Monsanto simulating the effects of SmartStax on various instars of potentially mobile lepidoptera. These data provide evidence that SmartStax is highly toxic to 1st, 2nd, and 3rd instars. But, there was greater survivability among 4th and 5th instars. While it has been established that ECB disperse as neonates, there is some uncertainty with respect to lepidopteran propensity for dispersal off non-*Bt* plants as later instars. BPPD notes that simulation models incorporating data on high larval mortality on SmartStax plants have (in some cases) predicted that seed blends may be as durable as structured refuges.

Please comment on ECB larval plant-to-plant movement including uncertainties about late-instar movement and the potential effect on the durability of a seed blend strategy.

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3:00 P.M. BREAK

3:15 P.M. Charge Question 3

It is typically assumed that, since European corn borer (ECB) and southwestern corn borer (SWCB) are similar in many ways, ECB can serve as a surrogate for SWCB to address uncertainties regarding biology and genetics. The applicants' efficacy data, however, suggest that SmartStax is somewhat less toxic to older instars of SWCB. Results of a larval exposure study by Monsanto showed that SWCB survival was higher than ECB on SmartStax. Should some SWCB larvae disperse as older instars, the rate of adaptation to SmartStax could increase in a seed blend deployment. BPPD concluded that simulation models should incorporate such information in their analyses. There is currently a lack of data on the propensity of SWCB larval plant-to plant movement and on how ECB and SWCB differ in this respect, if at all.

Please comment on the assumption that ECB is a suitable biological surrogate for SWCB and BPPD's concerns that a SmartStax seed blend may affect SWCB differently than ECB.

4:00 P.M. Charge Question 4

Corn earworm (CEW) was not considered in the applicants' and EPA/ORD's analyses for a 5% SmartStax seed blend based on the assumption that the insect does not overwinter in the Corn Belt where the blend has been proposed. BPPD is concerned, however, that there could be areas in the southern portion of the Corn Belt where CEW may be able to successfully overwinter, particularly in less severe winters. Such areas may need to be identified because they could contribute to increased selection for CEW resistance to *Bt* corn (including the proposed 5% SmartStax seed blend).

Please comment on the assumption that corn earworm does not successfully overwinter in the Corn Belt and poses less of a risk for resistance. If CEW can potentially overwinter in parts of the Corn Belt, should the insect be considered in the analysis of the proposed 5% SmartStax seed blend?

5:30 P.M. Adjourn

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Thursday, December 9, 2010

9:00 A.M. **Opening of Meeting and Administrative Procedures –**
Sharlene Matten, Ph.D., Designated Federal Official, Office of Science Coordination and Policy, EPA

9:05 A.M. **Introduction and Identification of Panel Members –**
Steven Heeringa, Ph.D., Chair, FIFRA Scientific Advisory Panel

9:10 A.M. **Follow-up from Previous Day's Discussion –**
Jeannette Martinez, M.S., Biopesticides and Pollution Prevention Division, OPP, EPA

9:30 A.M. **Charge Question 5**

To assess dose expression for corn rootworm (CRW) *Bt* toxins, the level of survival (adult emergence) is typically compared between artificially infested *Bt* and non-*Bt* corn plots. However, density-dependent mortality in non-*Bt* plots can potentially confound the comparison by reducing overall survival and adult emergence. (Density-dependent mortality is not expected in *Bt* plots due to effects of the toxin on young larvae.) To account for this effect, the dose calculation can be adjusted by removing density-dependent mortality from the

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control plots. This effectively increases the dose mortality estimate by raising the number of larvae present in non-*Bt* plots relative to the surviving larvae in *Bt* plots.

For the SmartStax toxins, Dow/Monsanto made a density-dependent adjustment to their dose estimates based on density/survival relationships developed by Onstad *et al.* (2006). The resulting dose mortality profile was: Cry34/35Ab1 (99.75%), Cry3Bb1 (99.75%), and Cry34/35Ab1/Cry3Bb1 pyramid (99.95%). On the other hand, BPPD has also considered separate work by Hibbard *et al.* (2010), which suggests that density-dependent mortality occurs at higher egg density levels than those assumed by Dow/Monsanto. In light of this research, BPPD recommended in its 2009 risk assessment of SmartStax that dose should also be evaluated without a density-dependent adjustment. The non-adjusted dose profile for the SmartStax toxin is: Cry34/35Ab1 (94.2%), Cry3Bb1 (97.5%), and Cry34/35Ab1/Cry3Bb1 pyramid (98.2%).

Please comment on dose estimates for the SmartStax toxins (Cry34/35Ab1 and Cry3Bb1) targeting corn rootworm given the different interpretations of density-dependent mortality.

10:15 A.M. BREAK

10:30 A.M. Charge Question 6

Northern and western corn rootworm studies have shown that male emergence in 5% seed blends can be variable and may be up to 60 times lower compared to emergence in non-*Bt* plots (Data submitted by Monsanto). This information was not included in any of the models used in the SmartStax seed blend analysis. The SAP (2009) concluded that a reduction in the number of males from *Bt* seed blends could have a negative impact on the effective refuge. BPPD is concerned with the potentially negative effects a reduction in male emergence might have on product durability.

Please comment on the potential effects of lowered male emergence of Northern and Western corn rootworm on the durability of the seed blend and whether this information should be incorporated into the risk assessment.

Part B: Modeling of Resistance Evolution

11:15 A.M. Charge Question 7

The durability of the proposed 5% SmartStax seed blend strategy was compared to the durability of a 5% structured refuge for lepidoptera and corn rootworm target pests. Monsanto developed a deterministic three locus model for ECB/SWCB and Dow created a stochastic two locus model for CRW. Separate analyses were conducted using EPA/ORD's two locus and three locus deterministic, probabilistic model to estimate the risk of resistance evolution with

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a 5% seed blend and structured refuge. The applicants and EPA/ORD each made conservative assumptions, though of differing degrees, for parameters determined to be sensitive in the models. For example, more conservative initial resistance allele frequencies and fitness assumptions significantly lowered the time to resistance in EPA/ORD's model for ECB and SWCB. In Monsanto's modeling of ECB and SWCB, a greater degree of dispersal between compliant and non-compliant fields significantly affected the estimated time to resistance.

Please comment on the appropriateness of the assumptions and inputs used for the following parameters in the Monsanto, Dow, and EPA/ORD models:

- **Initial resistance allele frequency for single traits Cry1A.105, Cry2Ab2, Cry1F, Cry34/35Ab1, and Cry3Bb1 for all modeled pests;**
- **Survival/fitness for all modeled pests; and**
- **Dispersal for ECB and SWCB as modeled by Monsanto and EPA/ORD.**

12:00 P.M. LUNCH

1:00 P.M. Charge Question 8

EPA/ORD encountered challenges in the lepidopteran modeling with partitioning non-multiplicative interactions that occurred between more than two resistance genes since the mortality caused by each locus was not independent. With two gene pyramids this non-additivity can be assigned to the single two locus interaction, but in a three gene pyramid there are three possible two locus interactions. In the absence of data, this non-additivity was partitioned equally among the three two locus interactions. As more than two *Bt* genes are pyramided, this problem will have to be addressed so that resistance evolution in the target pests to these products can be more accurately simulated.

Does the Panel have any recommendations for distributing non-multiplicative interactions in models to evaluate multi-gene pyramided products?

2:00 P.M. Charge Question 9

Based on a review of the submitted simulation modeling, the preliminary conclusions are:

1) For CRW, a 5% seed mixture and a 5% structured refuge had comparable durability in both the EPA and Dow models;

2) For ECB, a 5% seed mixture was less durable than a 5% structured refuge in

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simulations with EPA's model. However, ECB resistance did not evolve within 158 generations in any of the simulations with the 5% seed mixture, similar to the level of durability predicted by Monsanto's model. There was no difference in durability between the 5% seed mixture and the 5% structured refuge in Monsanto's model. Resistance did not evolve to either refuge option within 100 generations (the extent to which the model was run);

3) For SWCB, a 5% seed mixture was less durable (78 generations) than a 5% structured refuge (118 generations) in EPA's model simulations. Conversely, with Monsanto's model there was no difference in the prediction for durability between the 5% seed mixture and the 5% structured refuge. Resistance did not evolve to either refuge option within 100 generations (the limit of the model simulations).

Please comment on the reliability of the estimates of resistance evolution by each of the three models in light of the biological and parameter uncertainties identified by BPPD.

3:30 P.M. ADJOURN

Please be advised that agenda times are approximate; when the discussion for one topic is completed, discussions for the next topic will begin. For further information, please contact the Designated Federal Official for this meeting, Dr. Sharlene Matten, via telephone: (202)-564-0130; fax: (202) 564-8382; or email: matten.sharlene@epa.gov.