

AGENDA

FIFRA SCIENTIFIC ADVISORY PANEL (SAP)

OPEN MEETING

February 23 – 25, 2009

FIFRA SAP WEB SITE <http://www.epa.gov/scipoly/sap/>

OPP Docket Telephone: (703) 305-5805

Docket Number: EPA-HQ-OPP-2008-0836

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

Scientific Issues Associated with Evaluation of the Resistance Risks from Using a Seed Mix Refuge with Pioneer's Optimum AcreMax1 Corn Rootworm-Protected Corn

Please note that all times are approximate (see note at end of Agenda).

Monday, February 23, 2009

- 1:30 P.M. Opening of Meeting and Administrative Procedures** – Joseph Bailey, Designated Federal Official, Office of Science Coordination and Policy, EPA
- 1:40 P.M. Introduction and Identification of Panel Members** – Steven Heeringa, Ph.D., FIFRA Scientific Advisory Panel Chair
- 1:50 P.M. Welcome and Opening Remarks** – Steven Bradbury, Ph.D., Deputy Office Director for Programs, Office of Pesticide Programs, EPA
- 1:55 P.M. Welcome and Introductions** – Janet Andersen, Director, Biopesticides and Pollution Prevention Division, Office of Pesticide Programs, EPA
- 2:00 P.M. AcreMax Risk Assessment** – Jeannette Martinez, M.S., Biopesticides and Pollution Prevention Division, Office of Pesticide Programs, EPA
- 3:00 P.M. Break**
- 3:15 P.M. Public Comment**
- 5:30 P.M. ADJOURN**

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Tuesday, February 24, 2009

- 8:30 A.M. Opening of Meeting and Administrative Procedures** – Joseph Bailey, Designated Federal Official, Office of Science Coordination and Policy, EPA
- 8:35 A.M. Introduction and Identification of Panel Members** – Steven Heeringa, Ph.D., FIFRA Scientific Advisory Panel Chair
- 8:45 A.M. Charge to Panel** – Alan Reynolds, M.S., Biopesticides and Pollution Prevention Division, Office of Pesticide Programs, EPA

Charge Question 1 - Pioneer suggested based on their host search behavior results (MRID 473567-07) that Cry34/35Ab1 protects against corn rootworm through deterrence and sub-lethal toxicity leading to death by starvation. Pioneer's larval recovery study demonstrated high survival rate of CRW that were exposed to 59122 maize at any stage during their development but allowed to recover on non-Bt corn (MRID 473567-01). Conversely, larval exposure to 59122 maize without a recovery phase resulted in a mortality rate of 0.05 for neonates and 0.01 for 2nd and 3rd instars. BPPD concluded that it cannot be determined whether mortality or survival occurred due deterrence or some other mechanism.

BPPD would like the panel to discuss whether there is evidence that repellency or deterrence by 59122 maize could also be described as a realistic mode of action, specifically for a non-high dose toxin such as Cry34/35Ab1, and any implications for a seed blend refuge strategy.

- 10:00 A.M. BREAK**
- 10:15 A.M. Charge to Panel (continued)**

Charge Question 2 – Lefko et al. (2008) collected WCR individuals from two geographically distinct and susceptible populations and introgressed a non-diapausing trait from a WCR lab strain. The resulting offspring were selected on 59122 maize for 11 generations. A number of measurements were taken during the selection experiment to establish the mean survival rate, fecundity, fertility, and percentage of females produced for all cohorts of the 11 generations. Multiple greenhouse experiments were conducted with 4 generations per selected lines to determine if injury potential changed on 59122 roots. In addition, the realized heritability ($h^2 = R/S$) of the tolerance trait was estimated. Pioneer speculates that CRW tolerance for 59122 and apparent rarity of resistance genes in the CRW population may support Lande's (1983) less popular hypothesis that "pest adaptation via a major resistance gene can be prevented or delayed by a minor resistance gene despite strong selection pressure; rarity of major resistance is an essential condition for this interaction".

The Panel is asked to discuss the concept of major vs. minor gene as hypothesized by Lefko et al. and the implications for selection of resistance to 59122 and implications for a seed blend strategy.

11:15 A.M. Charge to Panel (continued)

Charge Question 3 – In BPPD’s review it was concluded that varying the selection pressure could have identified different resistance genes. In corn fields across the country the selection pressure will likely be different and more variable than in the lab because of, for example, variability in host-pest interactions and environmental conditions.

Please comment on BPPD’s conclusion that different selection intensities could possibly select different genes, maybe a major resistance gene. If different selection intensities could possibly select different genes, maybe a major resistance gene, what does the Panel think are the implications for resistance evolution to 59122 maize in a seed blend environment?

12:00 P.M. LUNCH

1:15 P.M. Charge to Panel (continued)

Charge Question 4 – In their selection experiment (Lefko et al. 2008), Pioneer found that heritability of the tolerance trait first increased and then decreased again. The tolerance trait could not get fixed by generation 11; Lefko et al. hypothesized that this could be due to an interaction between two tolerance genes. Pioneer did not address the potential presence of more than one tolerance gene in the modeling submission. Furthermore, CRW survival rate due to the tolerance trait and off-type seed rate (0.00075) was assumed to be half of the survival rate observed by Nowatzki et al. (2008, MRID 473567-05).

Please comment on whether there is reason to believe that the relative rate of adaptation could be affected by including more than one minor gene in the model and whether the assumption of equal survival of susceptible (AA) individuals with genotype XX (0.0125) and genotypes XY and YY (0.0125) is realistic.

2:15 P.M. Charge to Panel (continued)

Charge Question 5 – After having completed the review of the modeling submission, BPPD has identified several uncertainties and/or weaknesses of the model. Please comment on which of these uncertainties and/or modeling weaknesses are important to explore the risk of resistance evolution to 59122 maize in a seed blend environment.

- A. Initial frequency of major resistance gene (0.005) and dominance (0.05): Pioneer determined initial gene frequency based on the selection results and modeling comparison conducted in Lefko et al. (2008). Major resistance was assumed to be almost completely recessive despite the fact that Cry34/35 does not express a high-dose against CRW.
- B. Lack of inclusion of emergence delays: delays of up to 13 days in initial emergence and eight days in median emergence were observed between adults from 5% seed blends and 59122 maize. Delays of up to 19 days in initial emergence and 12 days in median emergence were observed between adults from 100% refuge fields and 59122 maize (MRID 473567-05).
- C. Lack of inclusion of uneven sex ratios: the field study (MRID 473567-05) showed that the production of female adult CRW was favored over the production of male adults, while in the lab study, the production of males was favored (MRID 473567-01). An inequality in sex ratios results in a special sort of bottleneck in which random genetic drift is enhanced and the effective population size is reduced. For example, if the number of males emerging from Bt plants decreases, then females emerging early from refuge plants could be more likely to mate with refuge males rather than 59122 males, especially when one considers that females have been shown to mate once only.

- D. Lack of inclusion of density-dependent dispersal: Hibbard et al. (2004) reported that in their experiment conducted from 2000-2002, CRW larval movement was dependent upon egg density per plant (independent of Bt plants).
- E. Lack of inclusion of non-random mating: delayed emergence and uneven sex ratios are likely to affect the random mating between adult CRW emerging from refuge maize and adults emerging from 59122 maize.
- F. Lack of exploratory modeling: Pioneer's model did not explore the production of different percentages of males and females and non-random mating and, ultimately, their effects on the relative rate of adaptation to 59122 maize.

3:15 P.M. Break

3:30 P.M. Charge to Panel (continued)

Charge Question 6 – The delay in evolution of resistance in Pioneer's model when the tolerance gene, major resistance gene, and off-type seed rate were included was driven by the rapid increase in frequency of the susceptible genotypes carrying the Y-allele (mostly AAYY). The proportion of susceptible individuals heterozygous for the tolerance trait (AAXY) peaked at 0.62 after generation 2; the proportion of susceptible individuals homozygous for the tolerance trait (AAYY) reached 0.5 by generation 3. The population was 90% homozygous for the Y-allele after generation 7 with an interaction emerging between the Y and B allele around generation 9 when AAYY genotypes declined at a similar rate to its earlier rate of increase. The proportion of population homozygous for both the major resistance gene and the tolerance (BBYY) gene reached 0.5 and 0.9 around generation 17 and 19, respectively.

Please comment on whether it is realistic to assume that the minor tolerance trait, specifically the AAYY genotype, might drive the delay of major resistance to 59122 maize in a seed blend environment.

5:00 P.M. Adjourn

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Wednesday, February 25, 2009

- 8:30 A.M. Opening of Meeting and Administrative Procedures** – Joseph Bailey, Designated Federal Official, Office of Science Coordination and Policy, EPA
- 8:35 A.M. Introduction and Identification of Panel Members** – Steven Heeringa, Ph.D., Scientific Advisory Panel Chair
- 8:45 A.M. Charge to Panel (continued)** - Alan Reynolds, M.S., Biopesticides and Pollution Prevention Division, Office of Pesticide Programs, EPA

Charge Question 7 - BPPD has reviewed Pioneer's request to register a Bt maize seed blend ($\geq 2\%$) for corn rootworm, all the supporting studies, and the model with its general assumptions, parameters and their values, as well as modeling analyses and concludes the following: At this point, BPPD believes that the proposed seed blend of $\geq 2\%$ for Optimum® AcreMax™ 1 Insect Protection has many uncertainties with respect to biological and genetic parameters and lack of exploratory modeling. BPPD believes these uncertainties must be resolved before a seed blend refuge is a viable long-term alternative to a structured refuge for corn rootworm. In the interim, BPPD has concluded that no less than 10% refuge seed blend is appropriate. BPPD bases its conclusion on: 1) the Relative Rate of Adaptation (RRA) at the 10% refuge proportion (value ~ 0.7) compared to the higher RRA values at lower proportions of refuge as estimated in Pioneer's model (MRID 473567-08), 2) root protection results for the 10% seed blend (Nowatzki and Meinke, 2008, MRID 473567-06), 3) efficacy results (Davis and MacIntosh, 2008, MRID 473567-10), 4) CRW emergence curve similarities for the 10% seed blend and 100% refuge maize (Nowatzki *et al.*, 2008, MRID 473567-05), 5) similarity in fitness results between females emerging from the 10% seed blend and the 100% refuge maize, and 6) modeling uncertainties.

Please comment on whether the scientific evidence submitted by Pioneer and available in public literature supports a seed blend strategy for CRW protected maize given the uncertainties and what is currently known about CRW biology, ecology, and genetics.

- 10:00 A.M. Break**
- 10:15 A.M. Charge to Panel (continued as needed)**
- 12:00 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, Joseph Bailey, via telephone: (202) 564-0130; fax: (202) 564-8382; or email: bailey.joseph@epa.gov.