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EPA IRM UPDATE FOR *BT* (*BACILLUS THURINGIENSIS)* COTTON PLANT-INCORPORATED PROTECTANTS

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Abstract

The United States Environmental Protection Agency (EPA) mandates insect resistance management (IRM) programs for Bollgard® (Cry1Ac) cotton (see EPA, 2001; Matten and Reynolds, 2003b) and Bollgard® II cotton (Cry2Ab2 and Cry1Ac) plant-incorporated protectants (PIPs) (Matten and Reynolds, 2003a). There are three structured refuge options with specific deployment requirements:

- **5% external, unsprayed refuge**: >150 ft. wide (>300ft. preferred), <1/2 mile (1/4 mile or adjacent preferred);
- **20% external, sprayed refuge**: <1 mile (1/2 mile or closer preferred);
- **5% embedded refuge**: >150 ft. wide (>300ft. preferred), refuge can only be treated if entire field treated;
- **5% in-field refuge for PBW**: refuge must be at least 1 non-Bt cotton row for every 6-10 rows of Bt cotton; and
- **Community refuge**: use either 5% external, unsprayed and/or 20% external, sprayed refuge.

Other requirements are: annual resistance monitoring program, remedial action plans, grower education, compliance assurance program, research, and annual reporting. The registration for Bollgard® cotton (EPA Registration Number 524-478) expires September 30, 2006, except for the 5% external, unsprayed refuge option which expires September 30, 2004. EPA intends to review the data specified in the data requirements concerning alternate hosts and chemical insecticide sprays on *Bt* cotton, and decide in 2004 whether the new data support continuation of the 5% external, unsprayed refuge. If these data support the continued availability of the 5% external, unsprayed refuge option, EPA may approve an amendment to this registration to maintain the availability of this option.

The registration for Bollgard® II cotton (EPA Reg. No. 524-522) was granted on December 23, 2002 and expires May 1, 2004 due to the expiration of the temporary tolerance exemption for the Cry2Ab2 protein.

Insect Targets

Both Bollgard and Bollgard II cotton target tobacco budworm (*Heliothis virescens,* TBW), pink bollworm (*Pectinophora gossypiella*, PBW), and cotton bollworm (*Helicoverpa zea*, CBW). Bollgard II also controls cabbage looper (*Trichoplusia ni*, CL), saltmarsh caterpillar (*Estigmene acrea,* SC), cotton leaf perforator (*Bucculatrix thurbeiella,* CLP), soybean looper (*Pseudoplusia includens,* SL), beet armyworm (*Spodoptera exigua,* BAW), fall armyworm (*Spodoptera frugiperda*, FAW) and yellowstriped armyworm (*Spodoptera ornithogolli*, YSA).

U.S. PIP Cotton Adoption

Based on the June 30, 2003 United States Department of Agriculture/National Agricultural Statistics Service (USDA/NASS) planting reports there is approximately 41% transgenic cotton acreage. This is divided into acreage planted with stacked trait lines, *Bt* + herbicide-tolerant traits, and *Bt*-only trait lines. In 2003, 76% of the cotton acres planted in Mississippi and Louisiana were to transgenic cotton. Approximately 5.8 million acres of *Bt* cotton were planted in 2001 and 5.0 million acres were planted in 2002 based on sales data submitted by Monsanto to U.S.EPA.

IRM Research Requirements for Bollgard and Bollgard II

Alternate Hosts

While alternate hosts should be considered when attempting to understand pest adaptation and resistance management, empirical evidence regarding their utilization and effective contribution to the production of homozygous susceptible (SS) moths to dilute resistance is not known. As discussed in USEPA's *Bt* Plant-Incorporated Protectants (PIPs) Biopesticide Registration Action Document (EPA, 2001), two Federal Insecticide, Fungicide, and Rodenticide Act Scientific Advisory Panel Subpanels (SAPs) stated explicitly that alternate hosts for TBW and CBW could not be used as a refuge until there were empirical data to support their inclusion (SAP 1998, 2001). To be effective, alternative hosts must produce susceptible, reproductively active insects at

the same time as the *Bt* cotton acreage is producing potentially resistant, reproductively active insects. In addition, the alternative host plants must be close enough for such susceptible insects to mate with the potentially resistant insects on the *Bt* cotton fields. Unfortunately, the available data are not sufficient on the biological equivalence of the insects produced on the various host plants to evaluate the timing issue. Similarly, EPA does not have adequate information on the size and proximity of such potential alternative host acreage to *Bt* cotton fields to evaluate how likely insects from the alternative hosts would be to mate with potentially resistant insects. Without adequate data to address these data deficiencies, there is no basis to rely upon alternate hosts to provide suitable numbers of susceptible TBW or CBW. However, if alternate hosts can be empirically validated to function as a refuge, the models may predict longer time-to-resistance for an IRM approach. Such information does not currently exist; therefore, only non-*Bt* cotton may be used as a refuge.

Hence, EPA required Monsanto to conduct research on alternate host untilization as effective natural CBW refuge. Research topics must include, but are not be limited to: mating and oviposition behavior of *Helicoverpa zea*, fitness of adults, adult population densities coming from the alternate hosts *vs* unsprayed and sprayed *Bt* cotton, synchrony of emergence, proximity of alternate hosts to *Bt* cotton, and refinements to resistance management models to include alternate hosts appropriate for different cotton production regions, e.g., North Carolina *vs* Louisiana. Studies must be conducted across the cotton belt where cotton bollworm is an economic pest. The sites must represent a range of conditions that will affect cotton bollworm biology. Conditions must include such factors as irrigation, soil types, and climatic conditions. Results of the two-year studies must be submitted to the Agency by March 15, 2004.

Supplemental Insecticide Sprays

To study whether *Bt*-resistant cotton bollworm would survive supplemental insecticidal treatments and increase the potential effectiveness of non-*Bt* refuges, research studies must be conducted to determine the IRM value of different insecticide chemistries likely to be used against the cotton bollworm in conventional and transgenic *Bt* cotton (irrigated and non-irrigated, side by side field trials). Any potential effects must be related to survival of putative *Bt*-resistant cotton bollworm and effective refuge size. Usage data must be provided for insecticide use on *Bt* cotton fields from 1997 to 2001. Once this information has been gathered, Monsanto must refine or construct new resistance management models for appropriate cotton producing areas in the US (i.e., areas where *H. zea* typically exceeds economic threshold on *Bt* cotton). Resistance management models must include consideration of supplemental insecticidal treatments for control of cotton bollworm. Results of the two-year studies must be submitted to the Agency by March 15, 2004.

North-South Migration

The October 2000 SAP indicated that there was evidence of north-south migration of *H. zea* (SAP, 2001). Carbon isotope work by Gould et al. (2002) and Gore et al. (2003) indicates that a significant portion of the CBW population in *Bt* cotton areas arose from alternate hosts other than cotton. These findings support the importance of the non- *Bt* corn refuge in the Corn Belt. CBW movement from the north to the south could impact insect resistance management, specifically refuge size. The Panel stated that as long as the amount of *Bt* corn in a (northern) region did not exceed 50%, then the refuge size was adequate. However, there are several areas in the Corn Belt where market penetration of *Bt* corn exceeds 50%. EPA required Monsanto to conduct field experiments on north-south movement of *Helicoverpa zea* from corn-growing regions to cotton-growing regions using radioisotope decay or other suitable methods. These data were submitted to the Agency and are under review.

IRM Questions

Several potential factors must be evaluated to determine a scientifically-based, practical, and implementable IRM plan for a PIP.

- What are the operational, biological, and genetic factors that impact pest adaptation?
  - Operational factors: dose and functional dominance, stacked or single toxins, market share, mode of action, adult *vs* larval effects, expression.
  - Biological factors: adult movement and dispersal, larval movement, alternate hosts, population dynamics, metapopulation dynamics
  - Genetic factors: genetic dominance of R-allele, initial R-frequency, cross-resistance among *Bt* insecticidal control proteins (ICPs), cross-resistance among other control mechanisms
  - In the absence of field resistance, resistance management models are useful tools to compare various resistance management options. Using resistance management models, what is the predicted rate of pest adaptation? What are the assumptions in the model? That is, how conservative are the predictions? Multiple agroecosystems should be evaluated, e.g., North Carolina *vs* Mississippi Delta. Scenarios should include market share impact, refuge size impact and shared-binding impact (if cross-resistance is likely).

  - Several questions are being specifically addressed regarding the utilization of CBW alternate hosts as natural refuge to dilute resistance. This is important because the 5% external, unsprayed refuge option expires September 30, 2004. Metapopulation dynamics of CBW may play a bigger role in diluting resistance than localized non-*Bt* structured refuges. The following issues should be examined: production of moths on each hosts, proximity of each host relative to *Bt* cotton, larval emergence, fitness of moths coming from each hosts, synchrony of insect emergence on alternate hosts and *Bt* cotton, impact of immigrating CBW (long-distance dispersal) on resistance evolution (includes impact of north-south movement on adaptation). Do these data support continuation of the 5% external, unsprayed refuge option?
- What is a scientifically-based, practical, and feasible IRM plan?
- What is an effective resistance monitoring program? What is the sampling plan and is it robust enough? What are the detection methods and are they sensitive enough to detect resistance prior to field failure?
- What is an effective remedial action plan?
- What is an effective grower education and compliance assurance program?

Future Issues

The EPA is planning a SAP meeting in June 2004 to address, in part, IRM issues regarding the utilization of CBW alternate hosts as natural refuge. EPA is currently reviewing the registration applications for Dow AgroSciences' WideStrike (Cry1Ac + Cry1F) cotton PIP and Syngenta's VipCot (VIP3A) cotton PIP.

Disclaimer

References

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