EPA and USDA Position Paper on Insect Resistance Management in Bt Crops

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Purpose

The United States Environmental Protection Agency (EPA) and United States Department of Agriculture (USDA) have co-authored this position paper to provide all stakeholders with a central focal point for discussion of insect resistance management (IRM) for toxin genes from *Bacillus thuringiensis* (Bt) that have been genetically engineered into crop plants (Bt crops). The following five areas will be discussed in more detail: 1) best management principles for IRM for Bt crops, 2) current IRM strategies for 1999, 3) IRM recommendations and implementation for the future, 4) development of regional pest management centers in the future, and 5) workshops on IRM for Bt crops.

Introduction

EPA believes that Bt insect resistance management is important because of the threat insect resistance poses to the high benefits and low risk of using Bt toxins in transgenic crops and in microbial spray formulations. Insect resistance management for Bt crops was one of the first issues brought to the newly formed Office of Pesticide Program's Dialogue Committee (PPDC) in July 1996. The PPDC indicated that EPA should play a role in pest resistance management and should not make resistance management mandatory in all cases for all pesticides. However, the PPDC indicated that EPA should act in the "public good" to protect the efficacy of certain pesticide products that are safer or provide unique public health or other societal benefits. The PPDC agreed that genes from Bt were a special case ("in the public good") and worthy of extra protection. Bt microbial sprays have long been safely used by organic, agronomic, vegetable, fruit farmers and foresters to control pests as part of an integrated pest management (IPM) program in support of sustainable agriculture, organic farming, and forestry. Bt toxins expressed in transgenic plants can and have reduced the use of more hazardous insecticides such as organophosphates and synthetic pyrethroids. For example, since the commercialization of Bt cotton in 1996, industry information has shown that cotton insecticide use has been reduced by approximately 1 million gallons of formulated product per year. In Mississippi, chemical insecticide sprays for tobacco budworm and cotton bollworm control have been reduced from 6-12 sprays annually to an average of 1.4 annually. The insecticide use for Bt sweet corn has been reduced by approximately 90% annually, a savings of >700,000 pounds of insecticide annually. Projected estimates are that $2.7 billion of the $8.1 billion spent annually on insecticides worldwide could be replaced by Bt crops alone (Krattiger, 1997). However, unique to Bt crops is season long expression of the Bt toxins that will likely increase the risk of Bt resistance development. Therefore, IRM is considered a key to the sustainable use of Bt toxins in both transgenic crops and Bt microbial spray formulations.

Because of the public importance of protecting "Bt genes," EPA has requested that all registrants provide the Agency with IRM strategies. The Agency has required or recommended the development of certain research data, annual resistance monitoring, remedial action plans, the development and implementation of structured refuges, grower education, and annual sales and research reporting for certain Bt crops as part of the development and implementation of long-term IRM strategies.

In 1995 when the first Bt plant-pesticide was registered, resistance management for Bt crops was already an issue being discussed by EPA, USDA, registrants, academia, and public interest groups at Scientific Advisory Panel (SAP) meetings. In addition, registrants had been conducting or sponsoring research on the biology and ecology of affected insects and crops (e.g., adult and larval movement, ovipositional and mating behavior, population dynamics, cross-resistance potential, potential resistance mechanisms, refuge strategies, susceptibility etc.) to better understand long-term resistance management of Bt crops to slow or halt the development of insect resistance. Good resistance management is dependent on multiple tactics to decrease the selection pressure on the target pest(s) and employment of different mortality sources. The 1995 SAP subpanel on plant-pesticides agreed with EPA on the essential elements of an IRM plan: (1) knowledge of pest biology and ecology, (2) appropriate dose expression strategy, (3) appropriate refuges (primarily for insecticides), (4) monitoring and reporting of incidents of pesticide resistance development, (5) employment of IPM, (6) communication and educational strategies on use of the product and (7) development of alternative modes of action.

Subsequent to registration of the first Bt crops in 1995, a great deal of scientific information has been developed that has enhanced understanding the need for, and refining of, IRM plans. In order to discuss these issues more openly, EPA convened three SAP subpanels in 1992, 1995, 1998; two public hearings in March and May 1997; and two PPDC meetings in July 1996 and January 1999 to address, in part, IRM for Bt crops. The USDA sponsored a Bt crop insect resistance management forum in April 1996. As part of its scientific basis for developing IRM recommendations and requirements for Bt crops, EPA relied on other scientific expert group reports including: the USDA North Central Regional Research Committee NC-205 (USDA NC-205) refuge recommendations (Ostlie et al, 1997, USDA NC-205 supplement 1998), the International Life Sciences Institute/Health and Environmental Sciences Institute (ILSI/HESI) report entitled *"An Evaluation of Insect Resistance Management in Bt Field Corn: A Science-Based Framework For Risk Assessment And Risk Management"* (ILSI, 1999), and the Union of Concerned Scientists' publication entitled *"Now or Never: Serious New Plans to Save a Natural Pest Control"* (Mellon and Rissler, 1998). EPA also published its own analysis of Bt plant-pesticide resistance management in January 1998 "White Paper on Bt Plant-pesticide Resistance Management"(EPA 739-S-98-001) (*300kb PDF*). The White Paper was the focal point of discussion for the February 1998 SAP subpanel meeting on IRM for Bt crops. The 1998 SAP subpanel agreed with EPA that the widespread use of crops that express Bt toxins is in the public good by providing safer pest control options to producers and by reducing the use of conventional pesticides. In addition, the subpanel recognized that steps to mitigate resistance risks are also in the public interest. Additional scientific knowledge on Bt insect resistance has been garnered from annual research reports submitted to EPA by registrants of Bt crops, Agency hearings and participation in regional and national workshops, and extensive literature review on Bt resistance conducted by EPA scientists.

In these cited reports and the published literature, there is a consensus that a high dose/structured refuge strategy is necessary for mitigating insect resistance to Bt toxins expressed in transgenic crops. The 1998 SAP subpanel recommended that the EPA require the use of structured refuges in all registrations of Bt crops unless it can be shown conclusively that such refuges would harm, rather than aid, durability of the resistance management plan. The subpanel indicated that acceptable refuge configurations may vary among regions. A structured refuge should provide sufficient susceptible adult insects to mate with potential Bt-resistant adult insects to dilute the frequency of resistance genes. The major sources of controversy have been on the size, structure, and deployment of non-Bt crop refuges and how they should be implemented on a regional basis. These issues and grower education and compliance are keys to the success of IRM for Bt crops.

A significantly higher rate of adoption of Bt field corn than originally anticipated based on industry information provided in 1995 has increased the awareness regarding the potential development of resistance. The percent of total acreage in 1996 (the first year of commercialization) planted to these Bt crops was <1% for Bt potato (approximately 10,000 acres), <1% for Bt corn (approximately 400,000 acres), and 14% for Bt cotton (approximately 1.8 million acres). The percent of total acreage planted in 1998 to these Bt crops was approximately 18% for Bt corn (approximately 14.4 million acres), 17% for Bt cotton (approximately 2.3 million acres), and 4% for Bt potato (approximately 50,000 acres). It is anticipated that the Bt corn acreage will continue to increase to 20-25% of the total corn acreage in 1999. Only a slight increase in Bt cotton and Bt potato acreage is expected.

Position on High Dose/Refuge Strategy

Based on current information, EPA and USDA generally support the following strategy to manage the development of pest resistance to Bt toxins expressed in crops. That is, a structured refuge/high dose strategy should be employed for susceptible pests within the current understanding of the technology. The presence of an effective structured refuge, in combination with a high dose expression level of the Bt toxin, has the potential to delay the development of resistance in pests. Refuges are non-Bt host plants that are managed to provide sufficient susceptible adult insects to mate with potential Bt-resistant adult insects to dilute the frequency of resistance genes. The 1998 SAP subpanel on Bt crop resistance management suggested that production of 500 susceptible adults in the refuge should be available for mating with every potentially resistant adult in a Bt field (assuming a resistance allele frequency of 5×10^{-2}) (Final Report of the Subpanel on Bacillus thuringiensis (Bt) Plant-Pesticides and Resistance Management, February, 1998 (*186 kb, PDF*)

SAP, 1998). Refuge options should be developed and managed to achieve this goal. The placement and size of the structured refuge employed should be based on the existing target pest biology data (e.g., larval and adult movement, mating and ovipositional behavior, fecundity). The refuge should be planted with an agronomically similar hybrid and as close as possible to, and at the same time as, the Bt crop. Refuge size should be adjusted or alternative control measures proposed if there is a lack of a high dose for a particular target pest.

In the development of refuge options, the following considerations should be made. First, the applicability of an in-field versus external refuge for each target (susceptible) pest should be evaluated based on larval and adult movement, ovipositional and mating behavior. The proximity of an external refuge must be within the normal adult flight range to mating/ovipositional habitats. In many cases, this information is unknown or more data are needed. If there are multiple pests, the structured refuge options should be inclusive of all potential target (susceptible) pests. If there are regional pest considerations, the structured refuge options should reflect these considerations. Therefore, structured refuge options should be designed within the feasibility and current understanding of the technology to address all of the target pest species including the pest with the greatest susceptibility to the Bt toxin.

Structured refuge options should be designed with a high degree of grower adoption in mind. Consideration should be made if there is a single dominant pest for a particular region or locality and whether there is a high dose. In addition, refuge strategies should consider whether there are stacked genes versus single genes to control the same target pests or different target pests. If alternative crop hosts are to be used as a refuge, justification needs to be provided as to the applicability of these alternative hosts as effective refuges for each target pest. Current data do not support the use of alternative hosts as refuges in conjunction with Bt potato, Bt corn, or Bt cotton. Resistance management strategies, including structured refuge options, should be flexible to accommodate rapidly changing technology (e.g., gene stacking or adding additional Bt proteins), current research data, and improved understanding of resistance management.

Best Management Principles for IRM for Bt Crops

EPA and USDA currently believe the following best management principles should be used as guidance in developing IRM strategies for Bt crops.

(1) A specific IRM plan is necessary to ensure long-term resistance management. Included elements of the IRM plan are: high dose, structured refuge, susceptible pest biology and ecology data, impact on secondary pests, impact on pests affecting multiple Bt crops, cross-resistance potential, resistance mechanisms, monitoring/surveillance, and remedial action.

(2) A high dose/structured refuge strategy is necessary to ensure long-term resistance management.

(3) Grower education, adoption, and compliance are essential to the implementation and success of a long-term resistance management strategy.

(4) Bt crops are to be used as part of an integrated pest management program to enhance pest management goals.

(5) Coordinated annual performance monitoring and surveillance is necessary to detect or follow resistance development.

(6) Immediate and coordinated remedial action for suspected and confirmed incidents of resistance is necessary.

(7) IRM strategies should be tailored to address specific regional resistance management concerns, as appropriate.

(8) Deployment of IPM tactics with different modes of action, including conventional pesticides, Bt toxins expressed in crops with different modes of action, biological control methods, and other control methods, is essential for sustainable pest management goals.

(9) Continued resistance management research should be conducted to evaluate the effectiveness of, and be used to modify, as necessary, IRM strategies for Bt crops.

Current IRM strategies for Bt crops

There are currently nine separate registered Bt toxins (plant-pesticides) for use in potato, corn, and cotton. There is one registration each for Bt potato, Bt cotton, and Bt sweet corn. There are six separate registrations for Bt field corn and one is also registered for popcorn use. The table below provides a summary of the registered Bt toxins in potato, corn, and cotton.

Table 1. Registered Bt Plant-Pesticides

Events/Products	***Year Registered***	***Expiration Date***	***Toxin***	***Crop***	***Company(s)***
NewLeaf	May 1995	None	Cry3A	Potato	Monsanto / NatureMark
NewLeaf Plus	Dec. 1998	None	Cry3A + Potato Leaf Roll Virus Resistance Gene	Potato	Monsanto / NatureMark
Bollgard	Oct. 1995	Jan. 2001	Cry1Ac	Cotton	Monsanto
Event 176 (Knock*Out)*	Aug. 1995/March 1998	April 2001	Cry1Ab	Field Corn/Popcorn (amendment)	Novartis Seeds
Event 176 (NatureGard NGBt1)	Aug. 1995	April 2001	Cry1Ab	Field Corn	Mycogen
BT11 (YieldGard)	Oct. 1996	April 2001	Cry1Ab	Field Corn	Novartis Seeds
BT11 (Attribute)	March 1998	April 2001	Cry1Ab	Sweet Corn	Novartis Seeds
MON810 (YieldGard)	Dec. 1996	April 2001	Cry1Ab	Field Corn	Monsanto
DBT-418 (Bt-Xtra)	March 1997	April 2001	Cry1Ac	Field Corn	DeKalb Genetics Corp. (now part of Monsanto)
CBH-351(StarLink)	May 1998	May 2000	Cry9C	Field Corn	AgrEvo/PGS

Even though EPA has not formally published a policy or data requirements for IRM, general guidance has been provided to the registrants as to the essential elements necessary for an IRM plan. To date, IRM strategies have been submitted to EPA by all of the current registrants: Novartis, Mycogen, Monsanto, DeKalb, and AgrEvo. These strategies were reviewed by the Agency, and in certain cases, IRM requirements were established.

EPA issued conditional registrations that expire in 2001 for Bt cotton and for Bt Cry1Ab and Cry1Ac field corn, popcorn, and sweet corn products to allow, in part, generation of data to support the continuing development of appropriate long-term IRM strategies. EPA issued a registration for Cry9C (CBH-351) field corn (feed and industrial uses only) that expires May 2000. EPA imposed refuge requirements for Bt cotton, Cry9C field corn, and some Cry1Ab field corn and popcorn. EPA also required development of refuge options and implementation of an appropriate EPA- approved long-term refuge strategy for all Cry1Ab and Cry1Ac corn by April 1, 2001. In addition, EPA imposed requirements for monitoring, remedial action, grower education, sales reporting, and development, collection, and reporting of IRM research data for Bt corn and Bt cotton registrations. As part of the registration requirements, EPA will evaluate the effectiveness of each registrant=s IRM strategy before the 2001 expiration date and decide on whether additional requirements will be necessary. The Cry3A Bt potato registration has no expiration date. Initially, a voluntary 20% refuge requirement were agreed to by EPA and Monsanto that followed the recommendations of the March 1995 SAP subpanel. However in May 1999, following the advice of the February 1998 SAP subpanel, EPA amended the Bt potato registration to mandate a 20% refuge be implemented. Below is a brief summary of the current IRM recommendations and requirements for Bt crops.

Bt potatoes (Cry3A)

In 1995, based on the advice of the SAP subpanel on plant-pesticides, EPA established voluntary rather than mandatory IRM requirements. In May 1999, following the advice of the 1998 SAP subpanel on Bt plant-pesticide resistance management, Monsanto and EPA have agreed to a mandatory 20% structured refuge of non-Bt potatoes that is planted in close proximity to the Bt potato field. This made the previous voluntary 20% refuge a mandatory part of the registration. Since 1997, Monsanto/NatureMark has required that growers plant this refuge as part of the terms of a grower contract. In addition, Monsanto/NatureMark conducts annual monitoring/surveillance for Colorado potato beetle (CPB) resistance development. Monsanto/NatureMark surveys all Bt potato growers annually for compliance with and understanding of the 20% refuge. Results of annual surveys provided by Monsanto/NatureMark indicate an extremely high level (approximately 99%) of grower compliance.

Bt cotton (Cry1Ac)

In 1995, two structured refuge options were mandated by EPA for Bt cotton to mitigate the development of tobacco budworm (TBW), cotton bollworm (CBW), and pink bollworm (PBW) resistance. These options were: (1) 20% non-Bt cotton, treated as needed with non-Bt pesticides to control TBW, CBW, and PBW; or, (2) 4% untreated non Bt-cotton, planted. However, subsequent to Bt cotton exceeding 75% of cotton acreage in any county or parish, the 4% untreated refuge must be planted within one mile of the Bt cotton field. Monsanto will notify growers who are in an affected county or parish. Monsanto requires that growers sign a grower contract. Growers must plant at least one of these two structured refuges on their farm according to the terms of the contract.

Bt corn (Cry1Ab, Cry1Ac, Cry9C)

Beginning in 1995, when the first Cry1Ab (Event 176) field corn registration was issued, no scientific consensus existed to establish EPA-mandated structured refuge requirements for managing two primary target pests, European corn borer (ECB) and corn earworm (CEW) resistance. Because of this lack of scientific consensus, among other issues, the Agency required the development of draft refuge strategies to be submitted to EPA by August 1998 for review, finalized in 1999, and implemented by April 1, 2001. Draft refuge strategies for all Cry1Ab and Cry1Ac field corn and popcorn products were submitted to EPA and have been reviewed. The Agency has received the final refuge strategies for Cry1Ab and Cry1Ac field corn products developed by industry in association with the National Corn Growers Association (NCGA) (see http://www.ncga.com/, April 19, 1999). These strategies focus on the implementation of a 20% refuge that may be treated if the level of pest pressure meets or exceeds economic thresholds. In their plan, growers will be encouraged to plant their non-Bt corn refuge within one-quarter mile of their Bt corn acreage where feasible, and required to plant the refuge within one-half mile of their Bt corn acreage. If treatment of the refuge is expected, growers will be required to plant the refuge acreage within one-quarter mile of their Bt corn plantings. The industry/NCGA insect resistance management plan for Cry1A field corn products is under review by EPA.

In December 1997, the USDA NC-205 regional research committee on ecology and management of European corn borer and other stalk-boring Lepidoptera (supported by the Land-Grant University System, USDA-CSREES, and USDA-ARS) published their IRM recommendations in the NCR 602 publication entitled *"Bt corn & European Corn Borer: Long-Term Success Through Resistance Management"* and followed in October 1998 with a supplement (Ostlie et. al, 1997; NC-205 Supplement, 1998). NC-205 currently recommends at least a 20-30% untreated refuge or 40% treated refuge planted within close proximity (<320 acre section) of Bt corn (NC-205 Supplement, 1998). NC-205 has reviewed the April 1999 industry/NCGA insect resistance management plan for Cry1A field corn products. They have concluded that a 20% sprayed refuge may be adequate in most corn growing areas where economic thresholds for ECB are not regularly exceeded. This would apply to most of the Corn Belt east of the High Plains region. However, NC-205 indicated that further research regarding the efficacy of a 20% sprayed refuge was needed, especially in higher risk areas such as the High Plains region, in which insecticide use has been historically high. NC-205 also noted that all Bt corn should be placed within one half mile of the non-Bt corn refuge, but that refuge plantings within one quarter mile would be even better.

EPA mandated specific structured refuge options for Novartis's Event 176 (Cry1Ab) popcorn and AgrEvo's CBH351 (Cry9C) field corn registration in March and May 1998, respectively, following the findings and recommendations of the February 1998 FIFRA SAP subpanel on Bt plant-pesticide resistance management and the USDA NC-205 regional research committee.

The specific Bt field corn and popcorn structured refuge requirements for 1999 are as follows. For CBH351 (Cry9C) field corn (registered 1998), growers are instructed via grower contract to plant at least a 20-30% unsprayed refuge or, if treated with non-Bt insecticides, a 40% refuge planted within 1500-2000 feet of Bt corn fields. For Event 176 (Cry1Ab) popcorn (registered 1998) growers are instructed via grower contract to plant a 20-30% unsprayed refuge, or, if treated with non-Bt insecticides, a 40% refuge planted within 0.5 miles of Bt corn fields. For MON810 (Cry1Ab) and DBT418 (Cry1Ac) Bt field corn (registered 1996 and 1997, respectively), growers are instructed via grower contract to plant a 10% unsprayed or 20% sprayed refuge within close proximity of Bt corn fields. For Event 176 (Cry1Ab) and BT11 (Cry1Ab) field corn (registered 1995 and 1996, respectively), the Novartis 1999 grower guide instructs growers to plant a 20% non-Bt corn refuge that may be treated with non-Bt insecticides. Mycogen's 1999 grower materials for Event 176 (Cry1Ab) (registered 1995) field corn instruct growers to plant a 20% untreated non-Bt corn refuge or if treated with non-Bt insecticides, a 40% non-Bt corn refuge. Both Novartis's and Mycogen's refuge recommendations are based on the NC-205 publication NCR-602 *"Bt Corn & European Corn Borer- Long-Term Success Through Resistance Management."*

The Agency registered BT11 (Cry1Ab) in sweet corn (Bt sweet corn) in March 1998. Specific monitoring and sales reporting were made requirements of the Bt sweet corn registration. No specific refuge requirements were mandated for Bt sweet corn because harvesting occurs before insects mature, approximately 21 days after silking. Growers are instructed in all labeling and technical material to destroy any Cry1Ab sweet corn stalks that remain in the fields following harvest or within a short period of time (a maximum of one month) later in accordance with local production practices. Stalk destruction should help reduce the possibility of larvae surviving to the next generation.

An additional concern for both Bt corn and Bt cotton relates to insects that are pests of more than one Bt crop; for example the corn earworm (CEW)/cotton bollworm (CBW). CEW is a pest of both corn and cotton and is known to funnel through corn to cotton during the growing season. Up to six generations of CEW can be exposed to the same or related Bt toxins expressed in Bt corn and Bt cotton; thus, increasing the likelihood for the development of resistance. There is also an increased potential for resistant CEW/CBW to move to other host crops that may be treated with Bt foliar sprays and rendering them ineffective. Therefore, EPA originally restricted the sale or distribution of some of Bt corn products (i.e., MON810, BT11, and DBT418) in certain southern U.S. counties and states where most cotton is grown. These sales restrictions were necessary to mitigate the development of resistance to Bt toxins in CEW/CBW populations feeding on both corn and cotton. EPA also requested data to develop appropriate refuge options for areas in which corn and cotton are grown.

Based on recent models, EPA has developed the following regulatory requirements to mitigate the development of CEW resistance in corn and cotton growing areas for the 1999 growing season. Event DBT418 corn expressing the Cry1Ac toxin is not allowed to be sold in the areas in which cotton is grown because the risk of CEW/CBW resistance development is considered to be much higher because of the presence of Bollgard7 cotton which also contains the Cry1Ac toxin. A 50% non-Bt corn refuge planted in close proximity (0.25 miles when feasible and must be within 0.5 miles) must be employed for MON 810 corn and BT 11 corn (both express Cry1Ab toxins) planted in all cotton growing areas. No specific southern restrictions or refuge requirements are made for Event 176 (Cry1Ab) corn and CBH351 (Cry9C) corn. Cry9C is not toxic to CEW and therefore does not select for resistance. Event 176 Bt corn hybrids do not produce the Bt toxins in silks and kernels and therefore silk-feeding CEW (post silk-feeding CEW move from corn to cotton) are not substantially exposed to the Bt toxin.

Proposed IRM Strategies for Future

In coming years, EPA seeks to continue to improve upon existing IRM recommendations and requirements for Bt crops based on the most current understanding of the science and technology while providing flexibility to the growers. EPA and USDA seek to provide a consistent set of IRM recommendations and requirements for similar Bt products, such as Bt field corn products, as appropriate.

EPA and USDA have decided to re-examine current IRM strategies for the following reasons: 1) IRM plans should reflect the current state of the science; 2) IRM plans should be consistent for similar Bt crop registrations where appropriate, such as for different Bt field corn products; 3) IRM plans should be correctly implemented by users and mechanisms should be developed to ensure compliance; 4) IRM plans should reflect regional characteristics for a given pest/Bt crop situation; and 5) IRM plans should reflect the significantly higher rate of adoption of Bt field corn than originally anticipated in 1995.

In general, EPA is actively considering changes to existing registrations, especially for Bt potato and Bt field corn registrations, to stipulate appropriate structured refuges for these crops. EPA is also seeking a unified approach to address IRM for Bt corn. In addition, EPA is working to support development and implementation of regional IRM plans that are reflective of the regional differences in pest/crop combinations, pest biology, and climate. In this vein, EPA is considering the need for regional IRM plans for control of the PBW in Arizona, northwestern New Mexico, and California in Bt cotton and control of the ECB, CEW, and other lepidopteran pests in Bt corn grown in cotton-growing regions. EPA is also investigating modifications to the current structured refuge requirements for control of TBW and CBW in Bt cotton.

Short-Term Approach

For all Bt crops, EPA and USDA believe that structured refuges are appropriate. Based on the current understanding of the science, EPA and USDA propose the following examples of how the existing IRM recommendations and requirements could be modified for Bt potato, Bt corn, and Bt cotton. These refuge options address regional pest/crop concerns. Some existing registrations have already incorporated the IRM modifications described below. The Agency is working with the remaining registrants to update their IRM strategies.

Bt potato

The following structured refuge option to mitigate the development of CPB resistance to the Cry3A delta-endotoxin expressed in Bt potatoes is based on the 1995 and 1998 SAP subpanel reports, the chapter by Whalon and Ferro entitled "Bt-potato Resistance Management" appearing in the Feb. 1998 publication "Now or Never: Serious New Plans to Save a Natural Pest Control," and the published literature. The 1998 SAP indicated that there was no scientific evidence that indicated that the current 20% structured refuge is an inadequate refuge size for CPB resistance management in the long-term. Therefore, EPA amended the existing Bt potato registrations to mandate the current 20% structured refuge. Under the terms of the label amendment, growers are instructed in the product grower guides on the location and management of the 20% non-Bt potato refuge. The refuge may be treated with non-Bt insecticides based on economic thresholds according to local/state IPM recommendations. While, the product grower guide indicates that the non-Bt potato refuge should be planted as close as possible to Bt potato fields, EPA believes that the proximity description should be refined. For example, a proposed description of the proximity of the refuge is that the non-Bt potato refuge should be planted within close proximity, preferably adjacent to, but must be within 0.5 miles, of the farthest Bt potato in a field to provide Bt-susceptible adult beetles. To minimize CPB movement into Bt potato fields planted that following year, Monsanto/NatureMark indicates in the product grower guide that Bt potatoes should be planted as far as possible from the previous year's Bt potato fields. EPA believes that this description should be refined. For example, Bt potatoes should be planted as far as possible, preferably >0.5 miles, from the previous year's Bt potato fields. Therefore, the short-term IRM proposal for Bt potatoes would be to focus on refining the proximity and management of the refuge. In addition, EPA considers it important to require annual monitoring/surveillance, research, sales, and compliance data be submitted.

Bt cotton

The following two structured refuge options to mitigate tobacco budworm and cotton bollworm resistance to Bt toxins expressed in cotton are based on the expert recommendations from a group of southern cotton entomologists led by Dr. Dick Hardee (USDA-ARS-SIMRU) and Dr. John Van Duyn (North Carolina State University).

(1) An external refuge of at least 30% non-Bt cotton should be implemented. The placement of the structured refuge should planted within 0.5 miles of the farthest Bt cotton in a field to provide Bt-susceptible moths. The

external refuges of non-Bt cotton can be treated with any other registered non-Bt insecticides or other insect control measures.

(2) In-field refuges of at least 10% non-Bt cotton refuge should be implemented. In-field refuges should be planted entirely within the field as blocks, minimum size to be determined based on planter size, to provide Bt-susceptible moths. Cotton fields may be treated with any registered non-Bt insecticide or other control measures, as long as the entire field is treated in the same manner. This means that Bt cotton rows cannot be treated independently from non-Bt cotton rows with insecticides or other insect control measures.

In both options, (1) and (2), agronomic practices used for farming the non-Bt cotton must ensure adequate production of susceptible TBW and CBW adults to mate with resistant adults emerging from Bt cotton. In particular, termination of growth of non-Bt cotton should not be done until termination of growth of Bt cotton has begun. In general, agronomic practices for non-Bt cotton should be as similar, as practical, to those of the Bt cotton grown in the same management unit, especially regarding crop nutrition, irrigation, and termination.

The following are two structured refuge options to mitigate PBW resistance to Bt toxins in cotton. These options are based on the recent (May 21, 1999) recommendations of the Arizona Bt Cotton Working Group convened by Arizona Bt cotton resistance management workgroup led by Dr. Tim Dennehy (U. of Arizona):

(1) An external refuge of at least 20% non-Bt cotton should be implemented. The placement of refuges should be based on management units on each farm of no more than 160 acres (quarter sections). Within each quarter section, at least 20% of the cotton grown will be non-Bt cotton. The external refuges of non-Bt cotton can be treated with any registered non-Bt insecticides or other insect control measures including pheromones, sterile pink bollworm, or natural enemies.

(2) In-field refuges of at least 10% non-Bt cotton should be implemented. For example, within every six to ten rows of cotton, at least one row will be non-Bt cotton. This range is chosen so that growers using six-, eight-, or ten-row planters can readily implement this option by putting non-Bt cotton seed in at least one hopper per planter. Cotton fields may be treated with any registered non-Bt insecticide or other control measures, as long as the entire field is treated in the same manner. This means that Bt cotton rows cannot be treated independently from non-Bt cotton rows with insecticides or other insect control measures.

In both options, (1) and (2), agronomic practices used for farming the non-Bt cotton must ensure adequate production of susceptible PBW adults to mate with resistant adults emerging from Bt cotton. In particular, termination of growth of non-Bt cotton should not be done until termination of growth of Bt cotton has begun. In general, agronomic practices for non-Bt cotton should be as similar, as practical, to those of the Bt cotton grown in the same management unit, especially regarding crop nutrition, irrigation, and termination.

Additional research on other resistance management tactics for PBW, including temporal refuges, random mixtures of Bt and non-Bt cotton seed (prepackaged seed mixtures), and rotation among varieties of Bt cotton that each produce different toxins should be conducted.

Bt field corn and popcorn

The scientific experts of the USDA NC-205 committee, ILSI expert panel (majority opinion), and Union of Concern Scientist's experts (report "Now or Never") recommend planting at least a 20% (UCS recommends 25%) untreated non-Bt corn refuge or at least a 40% (UCS recommends 50%) refuge if a grower anticipates treating with insecticides in the major corn growing areas (Ostlie *et al*., 1997, NC-205 Supplement, Oct. 1998; ILSI, 1999; and Andow and Alstad, 1998). Based on the ILSI report, if Bt corn is planted in Bt cotton areas in which there is expected to be >30% Bt cotton then a 50% non-Bt corn refuge is recommended (ILSI, 1999). The industry/NCGA insect resistance management plan calls for a 20% refuge in the major corn growing areas that may treated if pest pressure exceeds economic thresholds. In cotton growing areas, the industry/NCGA insect resistance plan calls for either a 20% refuge or 50% refuge depending on Bt corn and Bt cotton acreage and CEW overwintering data.

The following refuge recommendations are based on the consensus of these scientific expert groups to mitigate European corn borer, corn earworm, southwestern corn borer, and other susceptible lepidopteran pests for Bt field corn and Bt popcorn. These recommendations are applicable for the high dose events: MON810, BT11, and CBH351. CBH351 Bt corn hybrids express the Cry9C toxin which is not toxic to CEW/CBW; therefore, no special refuge requirements are necessary for cotton-growing areas.

In corn growing areas (no cotton), growers should plant a minimum of 20% non-Bt corn to serve as a refuge. In areas where European corn borer (ECB), southwestern corn borer (SWCB), corn earworm (CEW), or other target lepidopteran pests have historically been high and insecticide treatment of the refuge is anticipated, the refuge size should be increased beyond 20%. Where a 20% refuge is used, but ECB (or other target lepidopteran pests) populations occur in the refuge at levels exceeding economic thresholds for the pests, conventional (non-Bt) insecticides may be used to salvage the crop. Refuges should be treated to control target lepidopteran pests only as needed with non-Bt insecticides or other appropriate IPM practices. Insecticide use should be based on scouting using adjusted economic thresholds as part of an IPM program. Untreated refuges should not be treated with any insecticides targeting susceptible lepidopteran pests. Non-Bt corn refuges should be planted preferably within 0.25 miles, but no further than 0.50 miles, from the farthest Bt corn in a field to provide a refuge where Bt-susceptible moths may exist. Non-Bt corn hybrids for use as refuges in a field should be selected for growth, maturity, fertility, irrigation, weed management, planting date, and yield traits similar to the Bt corn hybrid used in the remainder of the field. Refuge areas may be planted either as external blocks on the edges or headlands of fields or in strips across the entire field. When refuge corn is planted in strips across a field, a minimum of six rows should be planted with non-Bt corn alternating with a Bt corn hybrid across the entire field. Refuge created by mixing seed in the hopper should not be used as this method is ineffective and may, in fact, hasten the development of resistance if employed.

In cotton growing areas, growers should plant a minimum of a 50% non-Bt corn refuge to minimize the development of corn earworm/cotton bollworm resistance in cotton growing regions especially those regions growing Bt cotton. Refuges should be treated to control lepidopteran insects with conventional insecticides only as needed with non-Bt insecticides or other appropriate IPM practices. Insecticide use should be based on scouting using economic thresholds as part of an IPM program. Non-Bt corn should be planted preferably within 0.25 miles, but no further than 0.50 miles, from the farthest Bt corn in a field to provide a refuge where Bt-susceptible moths may exist.

Additional information is needed to address whether Event 176 and DBT418 express a high dose of Bt toxin throughout the growing season. Evidence suggests that these two events do not produce a high dose of Bt toxin for second or later generations of ECB or SWCB. For non-high events, EPA and USDA currently believe that larger refuges may be necessary. For example, the ILSI report recommends at least a 40% unsprayed refuge in non-cotton growing regions (Corn Belt) and a 60% unsprayed refuge in cotton growing regions (ILSI, 1999). The non-Bt corn refuge should be planted preferably within 0.25 miles, but no further than 0.50 miles, from the farthest Bt corn in a field to provide a refuge where Bt-susceptible moths may exist.

Bt sweet corn

A structured refuge for Bt sweet corn is not anticipated for the following reasons: 1) sweet corn is typically harvested earlier than field corn (within 18-21 days after silking), a practice that should remove any developing and potentially resistant larvae in corn ears; and 2) all Bt sweet corn post-harvest crop residues are required by EPA to be destroyed within one month of harvest, a practice that should destroy any live larvae occurring in corn stalks. However, if successive planting of Bt sweet corn are routinely planted, then a structured refuge would be necessary. EPA will reevaluate the need for a required structured refuge for Bt sweet corn as additional information or concerns are brought to light.

Long-term approach

EPA will continue to use a science-based risk assessment and risk management process to evaluate and determine IRM requirements for Bt crops. EPA will use all information available including the literature, registrant submissions, and expert research groups. EPA will use the science-based risk assessment and risk management decision tree matrices developed by the ILSI expert group on IRM to help evaluate the resistance risk and possible risk management decisions for regulating new Bt toxins or new pesticidal active ingredients expressed in plants as stacked gene situations (ILSI, 1999). Stacked genes with dissimilar modes of action, high dose, common pest spectrum will likely need smaller structured refuges to mitigate the development of resistance. When new data, (e.g., measurements of resistance gene frequency and gene expression) show that smaller refuges are adequate, the size of existing structured refuges would be reduced. Similarly if new data (e.g. larval and adult movement, ovipositional and mating behavior) suggest the location (or size) of a structured refuge should be changed, the proximity (and/or size) requirements for certain refuge options would be changed. In addition, EPA believes the Regional Pest Management Centers, once they are operational, may provide information on the region specific implementation of IRM plans including structured refuges (see below).

Regional Pest Management Centers

The 1998 SAP subpanel encouraged the EPA to provide a flexible process for modifying IRM strategies to address regional specific pest/crop situations. Because crops, pests, and weather patterns differ from region to region within the United States, a single, national approach to pest management across all the agricultural regions is not always the optimal way to handle these issues. It is also not economically efficient to have redundant pest management program efforts in states with similar production regions. This sentiment has also been provided to EPA and USDA by industry, seed companies, and grower associations as part of their concerns that there will be inflexible, national IRM requirements for Bt toxins expressed in crops. The subpanel recommended that EPA establish regional working groups for each of the major Bt crop producing regions, and that these working groups include representatives from all stakeholders. The subpanel suggested that these working groups would meet annually to develop and recommend implementable Bt resistance management programs for their region that are based on the best available field data and model predictions. In addition, these working groups would identify regional research needs and coordinate remedial action plans.

Recently, the USDA proposed the development of Regional Pest Management Centers based on similarity of cropping patterns, pest problems and environmental conditions. The regional centers would provide a forum for a discussion of pest management issues for pesticides as part of the implementation of the more stringent, food safety standards mandated by the Food Quality Protection Act of 1996. These regional centers could also assist in the development and establishment of appropriate regional resistance management strategies for Bt crops.

USDA's current proposal is that these Regional Pest Management Centers would be organized in twelve different agricultural regions of the country. These centers would be located at existing land-grant universities or other appropriate facilities such that no new infrastructure would be required. Some of the activities of these Regional Pest Management Centers would be to address Bt crop resistance management. Activities of the centers would be to:

1) Develop and evaluate new agricultural pest management technologies, such as Bt toxins expressed in crops;

2) Identify and organize pest management expertise within the regions to ensure rapid response capability for pest problems or public information needs;

3) Organize and deliver pest management education programs for agricultural producers as well as consumers;

4) Provide science-based, region-specific input for public policy and regulatory issues; and

5) Manage and report on pest management research projects within the region.

When the Regional Pest Management Centers are established, EPA believes these Centers may provide EPA with additional scientific information regarding appropriate resistance management standards including refuge sizes, planting distances, treatment (IPM practices, adjusted economic thresholds etc.) for a region. This process is likely to take some time, but as regional centers are established, the centers would serve as a stakeholder body to provide regional IRM recommendations. The whole system would not have to be in place for some regional centers to begin operations. One possible example of a regional pest management center that could begin operations for the North-Central corn belt would be the USDA-NC-205 regional research working committee on "Ecology and Management of ECB and other Stalk Boring Lepidoptera" which is currently supported by the land-grant university systems, and the USDA-CSREES and USDA-ARS. The NC-205's existing role would be expanded to examine implementation issues.

EPA and USDA Workshops

EPA and USDA will conduct stakeholder workshops in 1999 and beyond to explore ways of designing and implementing sustainable resistance management programs that are flexible and can accommodate rapidly changing technology (e.g., stacking genes, novel Bt genes, or other novel genes). The stakeholder workshops will provide a forum for discussion and consensus-building on what should be implemented as sustainable IRM programs for the future. A major focus of these workshops will be on grower education and implementation of refuge strategies to minimize the risk of insect resistance development to Bt toxins expressed in transgenic crops. Implementation will focus on the size, structure, and deployment of non-Bt crop refuges on a national versus regional level. Grower education will focus on how to achieve the implementation of refuge strategies within the context of integrated pest management programs. In addition, the two Agencies would like to discuss sales incentives, grower contracts, crop insurance, grower surveys/audits, and other mechanisms to ensure grower implementation and compliance with specific refuge requirements. The Agencies would also like to discuss potential actions if growers or counties/regions are found to be routinely out of compliance with refuge requirements such as fines, limited access to the technology, and state/county/regional sales caps. Both Agencies are seeking input on the issues of annual monitoring/surveillance for resistance and remedial action in cases of substantiated resistance. In addition, USDA and EPA seek input on the development and implementation of the proposed Regional Pest Management Centers with the focus on IRM strategies for Bt crops.

Information gathered at these workshops will aid EPA in developing future IRM recommendations and requirements for Bt crops.

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