

US EPA ARCHIVE DOCUMENT

V. *Bt* Corn Confirmatory Data and Terms and Conditions of the Amendment

A. *Bt* Corn Confirmatory Data

The Agency has considered the database available on Cry1Ab and Cry1F PIP expressed in corn in light of our scientific review, the Scientific Advisory Panel (SAP) report of March 2001, and the public comments received. The Agency has made the determination that some additional data are needed to better characterize certain potential impacts from the continued use of this product. The following describes the data needed and the time frame for submission of these data. Requests for timeline extensions will be considered if there are EPA delays in reviewing protocols or other circumstances beyond the control of the registrant(s).

1. Residue Analytical Methods

Analytical methods and method validation are not typically required for active ingredients where a tolerance exemption has been granted. However, these data are useful for determining whether or not the protein is expressed in the corn plant and international bodies such as the Codex Alimentarius Commission (Codex) are gathering the validated methods for products of biotechnology that can be found in food. The Agency and the Federal Food and Drug Administration have also recently found value in having validated analytical methods for Plant-incorporated Protectants. EPA has guidelines for producing and validating analytical methods (under OPPTS Guidelines OPPTS 860.1340). These guidelines call for development of the method, validation by an independent laboratory, and validation by EPA before being accepted. For each registered Cry1Ab and Cry 1F active ingredient, an analytical method for detection of the protein in corn grain and a thorough characterization of the antisera used in the method(s) is required. The analytical method for each registered Cry1Ab protein and for the Cry 1F protein expressed in corn and independent laboratory validations for each active ingredient must be submitted to EPA by June 1, 2002. EPA intends to complete its validation within one year of the registrant submission.

2. Protein Expression Data

EPA requested guidance from the SAP in December 1999 on the appropriate method to test for and report the amount of pesticidal protein in PIPs. Their recommendation to EPA was that the amount of pesticidal protein in a tissue be provided as either total protein or dry weight of the plant tissue and indicating the value of each type of data. The Panel went on to explain the value of collecting these data at different plant growth states in order to do appropriate toxicological testing. (SAP Report No. 99-06. February 4, 2000.) [Characterization and Non-Target Organism Data Requirements for Protein Plant-Pesticides. SAP Report No. 99-06. February 4, 2000. 49 pp.]

The Agency has received protein expression data for Cry1Ab and Cry1F and found it acceptable

for the initial registration. However, data are not available for all types of tissues and the Agency agrees with the SAP that all of the expression data should be in a consistent format for all of the *Bt* crop products. These supplementary data must be determined and presented, in terms of dry weight, as the amount of protein present in the given tissue. Tissues for which expression data must be provided include: leaf, root, pollen, seed, and whole plant. In addition, data for each of these tissues should be provided for young plants in rapid growth, during flowering, and mature plants before harvest when that part of the plant is present. Data are due on or before March 15, 2003.

3. Amino Acid Sequence Data

Amino acid sequence bioinformatics data have been submitted for *Bt*11 and Mon810. These data were found acceptable, but since the time of initial registration, the value of comparing the amino acid sequence to known toxins and allergens has been highlighted and generally supported by the Scientific Advisory Panel. Data for *Bt*11 Cry1Ab protein which compares the amino acid sequence of the Cry1Ab protein expressed in field corn and sweet corn with known toxins and allergens must be submitted to the Agency for evaluation. For allergens, these data must also include a stepwise 8 amino acid analysis of the subject protein against available allergen sequence databases. These additional data are required to augment the health effects database for Cry1Ab expressed in corn. These data must be submitted on or before March 15, 2003.

For Mon810 Cry1Ab protein expressed in field corn, an additional amino acid sequencing analysis using required are for a stepwise 8 amino acid analysis of the subject protein against newly available known allergen sequence databases must be submitted to EPA for evaluation. In addition, a processing and/or heat stability study must also be conducted. These additional data are required to augment the health effects database for Cry1Ab expressed in corn. These data must be submitted on or before March 15, 2003. In addition, for Mon810, a processing and/or heat stability study is required and must also be submitted on or before March 15, 2003.

Finally, the registrants are encouraged to use new methods (e.g. MALDI-TOFF), as they are validated to confirm amino acid sequence of the expressed proteins more precisely.

4. Determination of Cry Protein Levels in Soils Following Several Years of *Bt* PIPs

In the March 12, 2001 SAP Report No. 2000-07 on *Bt* Plant-Pesticides Risk and Benefit Assessment, the October 2000 Scientific Advisory Panel (SAP) concluded that published data at that time did not adequately address the persistence of Cry proteins from *Bt* crops in the soil. Since it is difficult to correlate the relevance of the published laboratory studies to field situations, the SAP recommended field studies be conducted in established *Bt* fields in a variety of soil types and climatic conditions. The SAP suggested the determination of the amount, concentration, and persistence of biological activity of Cry proteins in the soil are areas that should be investigated. The EPA agrees with the SAP that actual field data on Cry protein levels in soil will yield

relevant data on persistence and natural variation of plant-produced *Bt* proteins in soil. If high levels of Cry proteins are found in field soils, reevaluation of the risks to certain non-target organisms might be required. Therefore, EPA is requiring additional supplementary studies regarding Cry protein in soil.

The Agency is requiring testing of Cry1Ab and Cry1F protein under a range of conditions typical of *Bt* corn cultivation. EPA requires each registrant or the registrants in cooperation to submit test protocols before the studies are actually conducted. In general, the Agency anticipates that soils would be sampled from fields where *Bt* corn has been grown continuously for at least 3 years compared with fields where no *Bt* crop has been grown. These paired fields would include several locations throughout the corn growing area of the US representing different soil and climatic variations. The Agency anticipates that samples would need to be taken 2 or 3 times during the growing season. Each registrant is required to submit a protocol on or before March 15, 2002. For Cry1Ab, an interim report is due 12 months after the protocol is approved and a final report is due 24 months after the final protocol is approved. For Cry1F, due dates for any interim reports will be determined at the time the protocol is approved. The final data for Cry1F will be submitted no later than March 15, 2008, but may be due earlier depending upon the final approved protocol.

5. Non-target Insects

In the February 7, 2000 report from the Scientific Advisory Panel meeting of December 8, 1999, the SAP responded to a question from EPA on field scouting to supplement acute testing of a few indicator insect species. The SAP stated:

Field scouting is an important tool to risk assessment, but should not replace Tier 1 testing. Only a limited number of species can be tested in laboratory bioassays, but field studies can be used to detail the impacts on species appropriate for the [PIP] being tested and in a manner that is relevant to determining ecological impacts. It is important that the conclusions drawn from the field studies be scientifically sound and not just correlative and that it reflect actual exposure to the [PIP]. . . Since ecological effects are critical to safety issues addressed by the Agency proposed rules, it would appear that field studies be included in the decision packet.

Ecological field studies were not required by EPA for the original registration decision for Cry1Ab in 1995 and Cry1F in 2001. EPA is now requiring confirmatory field data for possible impacts on non-target insects. Either existing studies must be submitted or the registrants must submit a protocol for field survey studies on or before March 15, 2002 with an interim report submitted 12 months after approval of the protocol and a final report submitted 36 months after approval of the protocol.

6. Monarch Butterflies

Based upon research recently published in the Proceedings of the National Academy of Sciences and upon the response of the Agricultural Biotechnology Stewardship Technical Committee to the December 1999 *Bt* corn Data Call-in Notice, EPA has concluded that the weight of scientific data indicate that *Bt* corn poses no unreasonable adverse impact on monarch butterfly populations. However, it has been identified in one of these papers, (Stanley-Horne, et al, 2001) that the published data only cover acute exposure and longer term exposure to *Bt* corn pollen should be considered. EPA is aware that studies are underway to assess the potential for longer-term exposure to *Bt* corn pollen to adversely impact monarch populations. The registrants for MON 810 and *Bt*11 must report the results of these studies to EPA as soon as the results are available publicly or the registrants must provide valid scientific studies to address this issue by January 31, 2003. The report must be able to be made available to the public at the time it is submitted to EPA.

7. Chronic Avian Dietary Exposure

Submitted avian toxicity data on Cry1Ab and Cry1F protein containing corn were scientifically sound and no treatment mortality or behavior change was observed between the dosed and control replicates. These data show no adverse effects to avian wildlife from incidental field exposure to Cry1Ab or Cry1F expressed in corn. However, data from repeated exposure(s) to higher doses of *Bt* corn are needed to make a hazard assessment. A supplemental study is required. The study must be of appropriate duration to represent the start and growing periods of the test species such as six weeks in meat-type chickens. Balanced diets should be formulated according to the National Research Council guidelines ("Nutrient Requirements of Poultry," Ninth Revised Edition, 1994) with the energy requirements of the test species being met by the inclusion of corn in the diet to assess hazards from chronic exposure of wild or domesticated fowl. A protocol for poultry studies must be submitted on or before March 15, 2002 with a final report submitted 18 months after approval of the protocol.

8. Insect Resistance Management

a. North/South Movement of *Helicoverpa zea*

Helicoverpa zea is known as cotton bollworm when attacking cotton and corn earworm when attacking corn. It has other common names for some of its other host plants. *Helicoverpa zea* can have several generations per year and frequently the insect moves from corn to cotton. There is not a high dose of the Cry proteins for *Helicoverpa zea* in either *Bt* corn or *Bt* cotton. If *Helicoverpa zea* survives exposure to *Bt* corn and then moves to *Bt* cotton, the chances of resistance development are increased through the added exposure.

The October 2000 SAP indicated there was more evidence of corn earworm (*Helicoverpa zea*) migration from the north to the south than evidence against this migration pattern. The Panel went on to discuss how the movement of corn earworm 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%. The registrants are required to evaluate the impacts of north-south movement of *Helicoverpa zea* from corn-growing regions to cotton-growing regions on the resistance management of corn earworm, including field studies, as needed, to determine the adequacy of the current resistance management program. Either existing studies must be submitted or submit a protocol for field studies must be submitted on or before March 15, 2002 with an interim report submitted 12 months after approval of the protocol and a final report submitted 24 months after approval of the protocol.

b. Impact of Insecticidal Sprays of Refuge Effectiveness

Both the USDA NC-205 group and the 2000 Scientific Advisory Panel have indicated that corn-growing areas regularly treated with insecticides (i.e., the High Plains region for southwestern corn borer or spider mites) may pose an additional risk for insect resistance. This is because highly effective insecticides applied to refuges and not to *Bt* corn may significantly reduce the number of susceptible adults emerging from the refuge, possibly reducing the overall refuge efficacy. For example, a 20% refuge treated with an insecticide with high efficacy (>90% kill) might be equivalent to a 2% unsprayed refuge because the insecticide kills susceptible insects and reduces the goal of 500 susceptible insects for every 1 resistant insect. Along these lines, the NC-205 has initiated a research project to determine the implications for IRM.

Research on the impacts of insecticidal sprays on the effectiveness of the refuge are required. EPA understands that the NC-205 group is about to begin such research. Each registrant must submit either a copy of the NC-205 protocol or a protocol of its own to the Agency by March 15, 2002. An interim report is due in 12 months after submitting the NC-205 protocol or approval of the registrant's protocol and a final report is due 24 months after submitting the NC-205 protocol or approval of the registrant's protocol.

c. Development of a Discriminating Concentration for Cry1F

The registrants of Cry1F protein expressed in corn must develop a discriminating concentration (diagnostic concentration) assay for field resistance (field screening) for European corn borer, corn earworm, and southwestern corn borer. Studies must be submitted on or before March 15, 2003.

B. *Bt* Corn Terms and Conditions of the Amended Registrations

1. Expiration Date

The Cry1Ab registrations for Bt11 and MON 810 and the Cry1F registrations will automatically

expire on midnight October 15, 2008.

2. Required Data

The protocols and data described in section V. A. above must be submitted to the Agency as part of the terms and conditions of the amendment to the Cry1Ab protein and Cry1F protein product registrations. The following table outlines the protocols and data as well as the due dates for these.

Data	Description	Due Date
Residue Analytical Methods	Analytical method including characterization of the antisera and independent laboratory validation required	June 1, 2002
Protein Expression	Expression data provided for initial registration; confirmatory data required to provide consistency across <i>Bt</i> crops	March 15, 2003
For <i>Bt</i> 11: Amino Acid Sequencing	Comparison of AA sequence to known toxins and allergens Stepwise 8 amino acid analysis	March 15, 2003
For MON810: Amino Acid Sequencing and heat stability	Stepwise 8 amino acid analysis and processing and/or heat stability study	March 15, 2003
Cry1Ab Protein Levels in Soil	Supplemental studies; protocol to be submitted before studies are initiated	Protocol by March 15, 2002; interim report 12 months after protocol approved; final report 24 months after protocol approved
Cry1F Protein Levels in Soil	Supplemental studies; protocol to be submitted before studies are initiated	Protocol by March 15, 2002; final report due no later than March 15, 2008

Non-target Insects	Either existing studies or protocol and studies	Existing studies or protocol by March 15, 2002; interim report 12 months after protocol approved; final report 36 months after protocol approved
Monarch Long-Term Exposure for Cry1Ab	Examine fitness and reproductive costs to monarchs from subchronic exposure to <i>Bt</i> corn	January 31, 2003 or earlier.
Chronic Avian Study	Test a diet for chronic exposure to high levels of <i>Bt</i> corn that may occur in the field	Existing studies or protocol by March 15, 2003; final report 18 months after approval of protocol.
IRM–North/South Movement of Corn Earworm	Potential for north to south movement of corn earworm	Protocol by March 15 2002; interim report 12 months after protocol approved; final report 24 months after protocol approved
IRM–Insecticide Impact on Effectiveness of Refuge	Studies in areas where the refuge is commonly treated with insecticides	Protocol March 15, 2002; interim report in 12 months; final report in 24 months after protocol submitted or approved
IRM–Discriminating Concentration for Cry1F	Development of discriminating concentration for ECB, CEW, SWCB	Studies must be submitted on or before March 15, 2003

3. Insect Resistance Management (IRM) Program

The Agency has determined that the unrestricted use of Cry1Ab and/or Cry1F in corn is likely to lead to the emergence of resistance in one or more of the target insect pests unless measures are used to delay or halt the development of resistant insects. Because some corn pests also attack other crops, not only would the emergence of resistance affect the benefits of *Bt* corn, such insect resistance could also affect the efficacy of *Bt* cotton products and microbial formulations of *Bt*. The loss of *Bt* as an effective pest management tool – in field corn, sweet corn, or other crops – could potentially have serious adverse consequences for the environment to the extent that growers might shift to the use of more toxic pesticides and a valuable tool for organic farmers

might be lost. The emergence of resistance in corn pests could also have significant economic consequences for corn growers. Therefore, EPA continues to require the registrants to implement an Insect Resistance Management (IRM) program to mitigate the possibility that pest resistance will occur.

The required IRM program for *Bt* corn has the following elements:

- 1] Requirements relating to creation of a non-*Bt* corn refuge in conjunction with the planting of any acreage of *Bt* field corn;
- 2] Requirements for the registrants to prepare and require *Bt* corn users to sign “grower agreements” which impose binding contractual obligations on the grower to comply with the refuge requirements;
- 3] Requirements for the registrants to develop, implement, and report to EPA on programs to educate growers about IRM requirements;
- 4] Requirements for the registrants to develop, implement, and report to EPA on programs to evaluate and promote growers’ compliance with IRM requirements;
- 5] Requirements for the registrants to develop, implement, and report to EPA on programs to evaluate whether there are statistically significant and biologically relevant changes in target insect susceptibility to Cry1Ab protein and/or Cry1F in the target insects;
- 6] Requirements for the registrants to develop, and if triggered, to implement a “remedial action plan” which would contain measures the registrants would take in the event that any insect resistance was detected as well as to report on activity under the plan to EPA;
- 7] Submit annual reports on sales, IRM grower agreements results, compliance, and educational program on or before January 31st each year.

a. Refuge Requirements

1) Field Corn

a) Corn-Belt Refuge Requirements

For Cry1Ab and Cry1F *Bt* field corn grown outside cotton-growing areas (e.g., the Corn Belt), grower agreements (also known as stewardship agreements) will specify that growers must adhere to the refuge requirements as described in the grower guide/product use guide and/or in supplements to the grower guide/product use guide.

- Specifically, growers must plant a structured refuge of at least 20% non-*Bt* corn that may be treated with insecticides as needed to control lepidopteran stalk-boring and other pests.
- Refuge planting options include: separate fields, blocks within fields (e.g., along the edges or headlands), and strips across the field.
- External refuges must be planted within ½ mile (1/4 mile or closer preferred).
- When planting the refuge in strips across the field, refuges must be at least 4 rows wide, preferably 6 rows wide.
- Insecticide treatments for control of ECB, CEW and Southwestern corn borer (SWCB) [Cry1Ab or Cry1F corn hybrids] and/or fall armyworm (FAW) and black cutworm (BCW) [Cry1F corn hybrids only] may be applied only if economic thresholds are reached for one or more of these target pests. Economic thresholds will be determined using methods recommended by local or regional professionals (e.g., Extension Service agents, crop consultants). Instructions to growers will specify that microbial *Bt* insecticides must not be applied to non-*Bt* corn refuges.

b) Cotton-Growing Area Refuge Requirements for *Bt* Corn

For Cry 1Ab and Cry1F *Bt* field corn grown in cotton-growing areas, grower agreements (also known as stewardship agreements) will specify that growers must adhere to the refuge requirements as described in the grower guide/product use guide and/or in supplements to the grower guide/product use guide.

- Specifically, growers in these areas must plant a structured refuge of at least 50% non-*Bt* corn that may be treated with insecticides applied as needed to control lepidopteran stalk-boring and other pests.
- Refuge planting options include: separate fields, blocks within fields (e.g., along the edges or headlands), and strips across the field.
- External refuges must be planted within ½ mile (1/4 mile or closer preferred).
- When planting the refuge in strips across the field, refuges must be at least 4 rows wide, preferably 6 rows wide.
- Insecticide treatments for control of ECB, CEW and Southwestern corn borer (SWCB) [Cry1Ab or Cry1F corn hybrids] and/or fall armyworm (FAW) and black cutworm (BCW) [Cry1F corn hybrids only] may be applied only if economic thresholds are reached for one or more of these target pests. Economic thresholds will be determined using methods

recommended by local or regional professionals (e.g., Extension Service agents, crop consultants). Instructions to growers will specify that microbial *Bt* insecticides must not be applied to non-*Bt* corn refuges.

- Cotton-growing areas¹ include the following states: Alabama, Arkansas, Georgia, Florida, Louisiana, North Carolina, Mississippi, South Carolina, Oklahoma (only the counties of Beckham, Caddo, Comanche, Custer, Greer, Harmon, Jackson, Kay, Kiowa, Tillman, Washita), Tennessee (only the counties of Carroll, Chester, Crockett, Dyer, Fayette, Franklin, Gibson, Hardeman, Hardin, Haywood, Lake, Lauderdale, Lincoln, Madison, Obion, Rutherford, Shelby, and Tipton), Texas (except the counties of Carson, Dallam, Hansford, Hartley, Hutchinson, Lipscomb, Moore, Ochiltree, Roberts, and Sherman), Virginia (only the counties of Dinwiddie, Franklin City, Greensville, Isle of Wight, Northampton, Southampton, Suffolk City, Surrey, Sussex) and Missouri (only the counties of Dunkin, New Madrid, Pemiscot, Scott, Stoddard). The correct list of counties must be in the 2003 grower guide and may be provided as a supplement for the 2002 growing season.

b. Sweet Corn Post-Harvest Requirements

Sweet corn is harvested long before field corn. Therefore, if the sweet corn stalks remaining in the field and any insects remaining in the stalks are destroyed shortly after harvest, a refuge is not needed as a part of the IRM program for sweet corn. Growers must adhere to the following types of crop destruction requirements as described in the grower guide/product use guide and/or in supplements to the grower guide/product use guide.

- Crop destruction must occur no later than 30 days following harvest, but preferably within 14 days.
- The allowed crop destruction methods are: rotary mowing, discing, or plow-down. Crop destruction methods should destroy any surviving resistant insects.

c. Grower Agreements

In addition to describing the standards for an effective IRM program, EPA believes it is important that there be a system to ensure a high level of compliance with such standards. The first element of such a system is a mechanism to create a legally enforceable obligation on *Bt* corn growers to comply with the refuge program. This is accomplished through “grower agreements.” While the registrants will have flexibility to design programs to fit their own business practices, the

¹Counties selected based on approximately 1000 A *Bt* cotton/5000 A total cotton using 1999-2001 cotton acreage reports from Monsanto and USDA/NASS.

registrations are specifically conditioned on meeting the following requirements.

1] Persons purchasing the *Bt* corn product 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] The registrant must establish by the 2003 growing season, a system which is reasonably likely to assure that persons purchasing the *Bt* corn product will affirm annually that they are contractually bound to comply with the requirements of the IRM program. The proposed system will be submitted to EPA on or before March 15, 2002.

4] Each registrant must continue to use their current grower agreement and submit to EPA by November 1, 2001 a copy of that agreement and any specific stewardship documents referenced in the grower agreement. If a registrant wishes 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, thirty days prior to implementing a proposed change, the registrant must submit to EPA the text of such changes to ensure that it is consistent with the terms and conditions of the amendment.

5] Each registrant must establish a system which is reasonably likely to assure that persons purchasing the *Bt* corn sign grower agreement(s), and must provide by January 31, 2002 a written description of that system.

6] Each registrant shall maintain records of all *Bt* corn grower agreements for a period of three years from December 31 of the year in which the agreement was signed.

7] Beginning on January 31, 2003 and annually thereafter, each registrant shall provide EPA with a report showing the number of units of its *Bt* corn seeds sold or 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 the twelve-month period covering the prior August through July. Note: the first report shall contain the specified information for the time frame starting with the date of registration and ending July 31, 2002.

8] Each registrant 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.

EPA believes that this set of requirements collectively will enable the Agency to determine whether the registrants are satisfying the fundamental condition on their registration that growers, who purchase the *Bt* corn product sign a legally enforceable grower agreement which imposes on them a legal obligation to comply with the current IRM program.

d. IRM Education and IRM Compliance Monitoring Programs

Grower knowledge is critical for effective IRM plans. Ensuring compliance with the IRM program involves both educating growers about their obligations and monitoring the extent to which growers comply. The *Bt* corn product registration contains conditions designed to make sure that the registrant carries out effective IRM education and compliance monitoring programs, specifically:

1] The registrants must design and implement a comprehensive, ongoing IRM education program designed to convey to *Bt* corn users the importance of complying with the IRM program. The program shall include information encouraging *Bt* corn users to pursue optional elements of the IRM program relating to refuge configuration and proximity to *Bt* corn fields. 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 its records. The program shall involve at least one written communication annually to each corn user separate from the grower technical guide. The communication shall inform the user of the current IRM requirements. Each registrant shall coordinate its education programs with educational efforts of other registrants and other organizations, such as the National Corn Grower Association and state extension programs.

2] Annually, the registrant shall revise, and expand as necessary, its education program to take into account the information collected through the compliance survey required under paragraphs 6a] or 6b] and from other sources. The changes shall address aspects of grower compliance that are not sufficiently high.

3] Beginning January 31, 2002 and annually thereafter, the registrants must provide a report to EPA summarizing the activities carried out under the education program for the prior year and the plans for their education program during the current year. Each registrant must either submit a separate report or contribute to the report from the industry working group (ABSTC).

4a] Field Corn: Each registrant must design and implement an ongoing IRM compliance assurance program designed to evaluate the extent to which growers purchasing its *Bt* corn product are complying with the IRM program and that takes such actions as are reasonably needed to assure that growers who have not complied with the program either do so in the future or lose their access to the *Bt* corn product. Each registrant shall coordinate with other registrants

in designing and implementing its compliance assurance program. The registrant must prepare and submit by January 31, 2002 a written description of their compliance assurance program including a summary of the program implemented in the 2001 growing season. Other required features of the program are described in paragraphs 5a] - 15] below.

4b] Sweet Corn: The registrant must design and implement an ongoing IRM compliance assurance program designed to evaluate the extent to which customers purchasing its *Bt* corn product are complying with the IRM program and that takes such actions as are reasonably needed to assure that customers who have not complied with the program either do so in the future or lose their access to the *Bt* corn product. The registrant must prepare and submit by January 31, 2002 a written description of their compliance assurance program. Other required features of the program are described in paragraphs 5b] - 15] below.

5a] Field Corn: Each registrant must establish and publicize a “phased compliance approach,” i.e., a guidance document that indicates how the registrant will address instances of non-compliance with the terms of the IRM program and general criteria for choosing among options for responding to any non-compliant growers. While recognizing that for reasons of difference in business practices there are needs for flexibility between different companies, all *Bt* corn registrants must use a consistent set of standards for responding to non-compliance. The options shall include withdrawal of the right to purchase *Bt* corn for an individual grower or for all growers in a specific region. An individual grower found to be significantly out of compliance two years in a row would be denied sales of the product the next year. Similarly, seed dealers who are not fulfilling their obligations to inform/educate growers of their IRM obligations will lose their opportunity to sell *Bt* corn.

5b] Sweet Corn: The registrant must establish and publicize a “phased compliance approach,” i.e., a guidance document that indicates how the registrant will address instances of non-compliance with the terms of the IRM program and general criteria for choosing among options for responding to any non-compliant users. The options shall include withdrawal of the right to purchase *Bt* corn for an individual customer. An individual customer found to be significantly out of compliance two years in a row would be denied sales of the product the next year. Similarly, seed dealers who are not fulfilling their obligations to inform/educate customers of their IRM obligations will lose their opportunity to sell *Bt* sweet corn.

6a] Field Corn: The IRM compliance assurance program shall include an annual survey of a statistically representative sample of *Bt* corn growers conducted by an independent third party. The survey shall measure the degree of compliance with the IRM program by growers in different regions of the country and consider the potential impact of non-response. The sample size and geographical resolution may be adjusted annually, based upon input from the independent marketing research firm and academic scientists, to allow analysis of compliance behavior within the four ABSTC regions or between regions. The sample size must provide a reasonable sensitivity for comparing results across the U.S.

6b] Sweet Corn: The IRM compliance assurance program shall include an annual survey of all *Bt* sweet corn customers who purchase 5 or more bags of *Bt*11 sweet corn. The survey shall measure the degree of compliance with the IRM program, identify the response rate (e.g., the percent of *Bt* sweet corn acres covered by the responses), and consider the potential impact of non-response. An independent third party will participate in the design and implementation of the survey. Data and information derived from the annual survey will be audited by an independent third party.

7a] Field Corn: The survey shall be designed to provide an understanding of any difficulties growers encounter in implementing IRM requirements. An analysis of the survey results must include the reasons, extent, and potential biological significance of any implementation deviations.

7b] Sweet Corn: The survey shall be designed to provide an understanding of any difficulties growers encounter in implementing IRM requirements.

8] The survey shall be designed to obtain grower feedback on the usefulness of specific educational tools and initiatives.

9a] Field Corn: The registrants shall provide a preliminary summary of their findings by November 15 and a final written summary of the results of the prior year's survey (together with a description of the regions, the methodology used, and the supporting data) to EPA by January 31 of each year. Each registrant shall confer with other registrants and EPA on the design and content of the survey prior to its implementation.

9b] Sweet Corn: The registrant shall provide a written summary of the results of the prior year's survey (together with a description of the methodology used, and the supporting data) to EPA by January 31 of each year. The registrant shall confer with EPA on changes to the design and content of the survey prior to its implementation.

10] Annually, each registrant shall revise and expand, as necessary, its compliance assurance program to take into account the information collected through the compliance survey required under paragraphs 6] through 8] and from other sources. The changes shall address aspects of grower compliance that are not sufficiently high. The registrants must confer with the Agency prior to adopting any changes.

11] Each registrant shall train its representatives who make on-farm visits with *Bt* corn growers to perform assessments of compliance with IRM requirements. In the event that any of these visits result in the identification of a grower who is not in compliance with the IRM program, the registrant shall take appropriate action, consistent with its "phased compliance approach," to promote compliance.

12] Each registrant shall carry out a program for investigating legitimate “tips and complaints” that its growers are not in compliance with the IRM program. Whenever an investigation results in the identification of a grower who is not in compliance with the IRM program, the registrant shall take appropriate action, consistent with its “phased compliance approach.”

13] If a grower, who purchases *Bt* corn for planting, was specifically identified as not being in compliance during the previous year, the registrant shall visit with the grower and evaluate whether that the grower is in compliance with the IRM program for the current year.

14] Beginning January 31, 2003 and annually thereafter, each registrant shall provide a report to EPA summarizing the activities carried out under their compliance assurance program for the prior year and the plans for the compliance assurance program during the current year. The report will include information regarding grower interactions (including, but not limited to on-farm visits, verified tips and complaints, grower meetings and letters), the extent of non-compliance, corrective measures to address the non-compliance, and any follow-up actions taken. The registrants may elect to coordinate information and report collectively the results of their compliance assurance programs.

15] Each registrant and the seed corn dealers for the registrant must allow a review of the compliance records by EPA or by a State pesticide regulatory agency if the State agency can demonstrate that confidential business information, including the names, personal information, and grower license number of the growers will be protected.

e. Insect Resistance Monitoring

The registrations of Cry1Ab protein products and Cry1F protein products expressed in corn are conditioned on the registrants carrying out appropriate programs to detect the emergence of insect resistance as early as possible. The goal of resistance monitoring is to detect resistance at a low enough resistance allele frequency so that changes to the insect resistance management plan can be made to increase the longevity of the product and prevent field failure. A resistance monitoring plan should be designed so that there is a high level of confidence in detecting resistance. This goal can be achieved by a number of measures, such as increasing the number of insects collected per site, increasing the number of collection sites, sampling in *Bt* corn fields, and/or use of the F₂ screen. Resistance monitoring programs include: surveying insects for potential resistance and collection of information from growers about events that may indicate resistance.

1) *Bt* Field Corn and/or Sweet Corn

The Agency is imposing the following conditions for all *Bt* corn products:

- a) The registrants will monitor for resistance and/or trends in increased tolerance for *Ostrinia*

nubilalis (European corn borer), *Diatraea grandiosella* (Southwestern corn borer), and/or *Helicoverpa zea* (corn earworm). Sampling should be focused in those areas in which there is the highest risk of resistance development. The ABSTC has identified four regions for its compliance and monitoring programs. Sampling target for each insect pest will be at least 200 insects in any region where adoption of *Bt* corn exceeds 50% and the insect is a pest species in that region. Sampling target for each insect pest will be at least 100 insects in all other regions where the insect is a pest species in that region.

b) The ABSTC will convene an advisory panel of academic experts from NC-205, USDA, and EPA to examine the current monitoring program and methodology and to consider enhancements to the current monitoring program for implementation in 2002. Consensus changes recommended by the joint panel will be implemented as soon as possible, beginning in 2002, including modification in the number of insects collected per site, number of sites, number of regions sampled, and/or modifications in methodology, such as field screening or F₂ screening.

c) The registrant shall provide to EPA a description of its resistance monitoring plan by January 31, 2003. The description shall include: sampling (number of locations and samples per locations), sampling methodology, bioassay methodology, standardization procedures, detection technique and sensitivity, and the statistical analysis of the probability of detecting resistance.

d) The registrants must follow up on grower, extension specialist or consultant reports of less than expected results or control failures for the target lepidopteran pests *Ostrinia nubilalis* (ECB), *Diatraea grandiosella* (SWCB), and *Helicoverpa zea* (CEW/CBW) *Spodoptera frugiperda* (FAW) [for Cry1Ab sweet corn and Cry1F corn hybrids only] and *Agrotis ipsilon* (BCW) [for Cry1F corn hybrids only]. Each registrant will instruct its customers (growers and seed distributors) to contact them (e.g., via a toll-free customer service number) if incidents of unexpected levels of damage occurs from these target pests. Each registrant will investigate all damage reports submitted to the company or the company's representatives. See Remedial Action Plans section below.

e) A report on results of resistance monitoring and investigations of damage reports must be submitted to the Agency annually by April 30th each year for the duration of the conditional registration.

2) Bt Sweet Corn Only

The registrant will develop and ensure the implementation of a plan for resistance monitoring for *Spodoptera frugiperda* (fall armyworm or FAW) in counties in which Cry1Ab sweet corn acreage exceeds 5,000 acres and the pest is capable of overwintering in that county. The registrant should consult with academic and USDA experts in developing the monitoring plan and will provide EPA with a copy of its proposed resistance monitoring plan for EPA's approval prior to implementation. This proposed FAW monitoring plan must be submitted to EPA by January 31

of the year following that in which Cry1Ab sweet corn acreage exceeds the trigger specified in this requirement (i.e., greater than 5,000 acres in any county in which FAW overwinters). The proposed plan must be implemented the season following the acreage trigger being met. The proposed plan will remain in place until an EPA approved plan can be implemented.

f. Remedial Action Plans

Specific remedial action plans are required for *Bt* corn for the purpose of containing resistance and perhaps eliminating resistance if it develops. There are two types of situations, first suspected resistance and second confirmed resistance.

1) Suspected Resistance

EPA defines “suspected” resistance to mean, in the case of reported product failure, that:

- the corn in question has been confirmed to be *Bt* corn
- the seed used had the proper percentage of corn expressing *Bt* protein;
- the relevant plant tissues are expressing the expected level of *Bt* protein; and
- it has been ruled out that species not susceptible to the protein could be responsible for the damage, that no climatic or cultural reasons could be responsible for the damage, and that other reasonable causes for the observed product failure have been ruled out.

The Agency does not interpret “suspected resistance” to mean grower reports of possible control failures, nor does the Agency intend that extensive field studies and testing to confirm scientifically insect resistance be completed before responsive measures are undertaken.

If resistance is “suspected,” the registrant must instruct growers to do the following:

- Use alternate control measures to control the pest suspected of resistance to *Bt* corn in the affected region.
- Destroy crop residues in the affected region immediately after harvest (i.e. within one month) with a technique appropriate for local production practices to minimize the possibility of resistant insects overwintering and contributing to the next season’s pest population.

2) Confirmed Resistance

The registrant assumes responsibility for the implementation of resistance mitigation actions undertaken in response to the occurrence of resistance during the growing season. When resistance has been confirmed, the registrant must immediately stop sale and distribution of *Bt* corn in the remedial action zone (may be less than a single county, single county, or multiple counties) where the resistance has been shown until an effective local mitigation plan approved by EPA has been implemented.

A resistance event becomes confirmed if the progeny of the sampled ECB, CEW, or SWCB population would exhibit all of the following characteristics in bioassays initiated with neonates:

- i) if there is > 30% survival and > 25% leaf area damaged in a 5-day bioassay using Cry1Ab-positive or Cry1F-positive leaf tissue under controlled laboratory conditions.
- ii) if standardized laboratory bioassays using diagnostic doses for ECB (Marçon et al. 2000), SWCB (Trisyono and Chippendale 1999), CEW/CBW (USDA/ARS/SIMRU, unpublished) demonstrate resistance has a genetic basis and survivorship in excess of 1% (gene frequency of population ≤ 0.1).
- iii) if an LC_{50} in a standard Cry1Ab or Cry1F diet bioassay that exceeds the upper limit of the 95% confidence interval of the standard unselected laboratory population LC_{50} for susceptible ECB, SWCB, or CEW populations, as established by the ongoing baseline monitoring program.

3) Remedial Action Plan for Field Corn

A Remedial Action Plan covering both suspected and confirmed resistance for European corn borer, corn earworm, and southwestern corn borer is provided in Appendix 3. If resistance involves any of these three target pests, the registrants collectively must implement the Remedial Action Plan contained in Appendix 3. The registrant must obtain approval from EPA before modifying the Remedial Action Plan for Corn.

4) Remedial Action Plan for Sweet Corn

The registrant will abide by the Remedial Action Plan for Field Corn as an interim Remedial Action Plan for Sweet Corn until a plan specific for sweet corn can be approved by EPA. After consultation with sweet corn growers and academic experts, the registrant will submit a revised Remedial Action Plan by May 15, 2002 for EPA's review and approval. The registrant must obtain approval from EPA before modifying the Remedial Action Plan for Sweet Corn once the Plan has been approved by EPA.

4. Annual Reports

Each registrant will provide an annual report to EPA on its Cry1Ab or Cry1F PIP expressed in corn report on or before January 31st each year.

Report	Description	Due Date
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Annual Sales	Reported by county and state; summed by state	January 31 st each year
Grower Agreement	Number of units of <i>Bt</i> corn seeds shipped or sold and not returned, and the number of such units that were sold to persons who have signed grower agreements	January 31 st each year beginning in 2003
Grower Education	Education program completed previous year and plan for next year	January 31 st each year
Proposed Compliance Plan	Written description of Compliance Assurance Program	January 31, 2002
Compliance Assurance Plan	Compliance Assurance Program Results	January 31 st each year starting in 2003
Compliance	To include annual survey results and plans for the next year	Preliminary survey report November 15 th each year and full report January 31 st each year thereafter
Insect Resistance Monitoring	Description of the program including sampling (number of locations and samples per locations), sampling methodology, bioassay methodology, standardization procedures, detection technique and sensitivity, and the statistical analysis of the probability of detecting resistance.	January 31, 2003

Certain additional reports excluding confirmatory data for specific studies described in V. A. and summarized in V. B. 2.

IRM Grower Agreements	Proposed system for growers sign grower agreements	January 31, 2002
IRM Affirmation Plan	System to assure annual affirmation by growers of their IRM obligations	March 15, 2002
Changes to Grower Agreement and/or IRM documents	Current grower agreement(s) and any specific stewardship documents	November 1, 2001 and at least 30 days before any changes related to IRM are expected to be imposed.

Insect Resistance Monitoring Results	Results of monitoring and investigations of damage reports	April 30 th each year
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VI. Regulatory Position on *Bt* Corn

A. Overview

Currently registered *Bt* corn products were conditionally approved for commercial use in August 1996 (Bt11 Cry1Ab field corn amendment), December 1996 (MON810 Cry1Ab field corn registration), February 1998 (Bt11 Cry1Ab sweet corn registration), May 2001 (Cry1F field corn registration) under FIFRA Section 3(c)(7)(B). The data reviewed for the initial commercial approvals as well as new data and reports received, results of public meeting, hearings, workshops, forums, and Scientific Advisory Panel meetings, and public comments received regarding the *Bt* crops reassessment have been taken into consideration. The scientific assessment has included product characterization, human health effects, gene flow, effects on non-target organisms, ecological exposure, insect resistance management, and benefits. Over the last five years, new data and information have been provided to the Agency in each of these areas and these data have been incorporated into the science assessment and has been taken into account in making regulatory decisions.

Tests have shown no toxicity to mammals from the Cry1Ab and Cry1F proteins; the proteins are readily digestible in gastric fluids and are non-glycosylated, the proteins are inactivated by typical food processing, and anticipated exposure of farm workers to the proteins is negligible. The Cry1Ab protein acute oral toxicity data submitted demonstrated no effects at the relatively high dose level of 4,000 mg/kg. The Cry1F protein acute oral toxicity data submitted demonstrated no effects at the relatively high dose level of 5,050 mg/kg. The Cry1Ab and Cry1F proteins were readily degraded in gastric fluid *in vitro*. Exposure via the skin or inhalation is not likely since the Cry1Ab and Cry1F proteins are contained within corn plant cells which essentially eliminates or reduces exposure routes to negligible. Oral exposure, at very low levels, may occur from ingestion of processed products and drinking water. Worker exposure to the Cry protein via seed dust is also expected to be negligible because of the low amount of protein expressed in seeds of the transformed plants. Taken in total, these data allow the Agency to make a determination that for human health, there is a reasonable certainty that no harm will result from aggregate exposure to the U.S. population, including infants and children, to the Cry1Ab and Cry1F proteins and the genetic material necessary for their production. Thus, EPA concludes that there are no adverse effects on human health from the use of Cry1Ab or Cry1F proteins expressed in corn.

EPA has also reviewed the original data base and the new data, information, and comments regarding ecological effects. EPA has reviewed the potential for gene capture and expression of the Cry1Ab/Cry1F endotoxin in corn by wild or weedy relatives of corn in the United States, its possessions or territories. The Agency has determined that there is no significant risk of gene capture and expression of any *B.t.* endotoxin by wild or weedy relatives of corn product registrations in the U.S., its possessions or territories. In addition, the USDA/APHIS has made this same determination under its statutory authority under the Plant Pest Act.

The Agency has concluded that based on the weight of evidence there are no unreasonable adverse effects of Cry1Ab or Cry1F protein expressed in corn to non-target wildlife or beneficial invertebrates. However, EPA is requiring insect census estimates from representative fields to determine if there are long-term adverse impacts from the use of *Bt* corn, field tests of Cry1Ab and Cry1F protein accumulation and/or persistence in soil under a range of conditions typical of *Bt* crop cultivation as confirmatory data, and chronic avian data.

In the Cry1Ab ecological effects testing done, no treatment related effects were observed in Bobwhite quail or catfish fed Cry1Ab corn as part of their diet. No measurable deleterious effects from the Cry1Ab protein on honey bee larvae, honey bee adults, parasitic wasps, Ladybird beetles, green lacewings, Collembola (springtails), and Daphnia were observed in submitted studies.

In the Cry1F ecological effects testing done, no treatment related effects were observed in Bobwhite quail fed Cry1Ab corn as part of their diet. No measurable deleterious effects from the Cry1F protein on honey bees, parasitic wasps, Ladybird beetles, green lacewings, Collembola (springtails), earthworms, Daphnia, and Monarch butterflies were observed in submitted studies.

MON 810 and Bt11 show relatively low toxicity to monarch larvae and the Cry1F protein has no detectable impact on monarch larvae. Overall, the available information indicates a very low probability of risk to monarchs in areas beyond the near edge of corn fields. Inside corn fields and at the near edge of corn fields there is low probability of monarch larvae encountering a toxic level of pollen for the *Bt* corn products covered by this risk assessment.

Limited data do not indicate that Cry proteins have any measurable effect on microbial populations in the soil. Horizontal transfer from transgenic plants to soil bacteria has not been demonstrated. Cry1Ab protein bioactivity from Cry1Ab corn tissue added to the soil decreased with an estimated DT_{50} (Degradation Time) of 1.6 days and an estimated DT_{90} of 15 days. The bioactivity of purified Cry1Ab protein in soil decreased with an estimated DT_{50} of 8.3 days and an estimated DT_{90} of 32.5 days. The bioactivity of purified Cry1F protein in soil decreased with an estimated DT_{50} of 3.13 days.

The issue of insect resistance management has generated more data, meetings, and public comments than all of the other sections covered in this BRAD. Insect resistance management (IRM) is the set of practices aimed at reducing the potential for insect pests to become resistant to a pesticide. *Bt* IRM is of great importance because of the threat insect resistance poses to the future use of *Bt* plant-pesticides and *Bt* technology as a whole. EPA considers protection of insect (pest) susceptibility of *Bt* to be in the "public good." EPA has determined that development of resistant insects would constitute an adverse environmental effect. In order to delay the development of insect resistance to *Bt* field corn by maintaining insect susceptibility, growers must choose at least one of structured refuge (a portion of the total acreage using non-*Bt* seed) options listed in Section V.B.4.a. above.

For *Bt* sweet corn, no specific refuge requirements are necessary because sweet corn is typically harvested much earlier than field corn, 18-21 days after silking, and before most lepidopteran larvae complete development. However, to mitigate the development of resistance, EPA has determined that crop residue destruction is necessary within 30 days. This practice will likely destroy any live larvae left in *Bt* sweet corn stalks and prevent overwintering of any resistant insects.

The IRM program for *Bt* field and sweet corn also require: 1) anyone purchasing *Bt* corn to sign a grower agreement which contractually binds the grower to comply with the IRM program and that there will be a mechanism by the year 2003 by which every grower affirms, annually, their contractual obligations to comply with the IRM program, 2) an IRM education program, 3) an IRM compliance monitoring program including a third party compliance survey and mechanisms to address non-compliance, 4) an insect resistance monitoring program for each target insect pest, 5) remedial action plans to be implemented if resistance does develop, and 6) annual reporting of the IRM (and other) activities. No other pesticide products than the *Bt* crop products have such extensive IRM requirements.

In addition to assessing the risks from the use of Cry1Ab and Cry1F expressed in corn, EPA has evaluated the benefits from the use of these products. Direct grower benefits include improved yield and profitability, improved crop management effectiveness, reduction in farming risk, and improved opportunity to grow field corn in case of severe pest infestation. Total annual monetary grower benefits from the use of *Bt* field corn are less than \$219 million annually. The magnitude of benefits for any year is largely a function of the level of lepidopteran insect pressure in that year. That is, other things being equal, the higher the insect pressure, the higher the benefits. The major environmental benefit is potential reduction in mycotoxins. EPA believes that use of *Bt* sweet corn would result in significant reductions in the use of chemical pesticides. However, the current use of *Bt* sweet corn is very low.

Pursuant to FIFRA Section 3(c)(7)(A), EPA may conditionally amend the registration of a pesticide if the Agency determines (i) that the pesticide and proposed use are identical or substantially similar to a currently registered pesticide and use thereof, or differs only in ways that would not significantly increase the risk of unreasonable adverse effects on the environment, and (ii) approving the amendment in the manner proposed by the applicant would not significantly increase the risk of unreasonable adverse effect on the environment. FIFRA defines “unreasonable adverse effects on the environment” in pertinent part as: “any unreasonable risk to man or the environment, taking into account the economic, social, and environmental costs and benefits of the use of any pesticide” Thus, the FIFRA unreasonable adverse effects standard requires EPA to balance the risks and benefits of using the pesticide in reaching its regulatory decision.

EPA finds that the use of Cry1Ab or Cry1F expressed in corn will not significantly increase the risk of unreasonable adverse effects on the environment. This finding, however, applies only to

the use of Cry 1Ab or Cry1F protein expressed corn under the terms and conditions of registration specified below, and only for the limited time period of 7 additional years (to October 15, 2008). The following sections set forth the basis for EPA's finding in general, and the basis for the decision to approve the registration subject to the specific terms and conditions identified below.

B. General Finding

EPA's finding that Cry1Ab or Cry1F protein as expressed in corn will not significantly increase the risk of unreasonable adverse effects on the environment is based on the analysis contained in the preceding sections of this BRAD and the specific terms and conditions that are imposed upon this registration, as set forth in Section V. In general terms, EPA concludes that use of Cry1Ab or Cry1F expressed in corn is effective at controlling significant lepidopteran pests of corn including European corn borer, corn earworm, and southwestern corn borer. Therefore, these products have clear benefits for users. Beyond these economic benefits, EPA determines that Cry1Ab and Cry1F corn hybrids, to the extent they are an alternative to the use of other corn insecticides, will provide benefits in that use of Cry1Ab or Cry1F protein expressed in corn results in less human and environmental risk than chemical alternatives. In addition, EPA finds that the use of these products, subject to the specific terms and conditions set forth below, would not pose risks to human health or to non-target species. EPA also concludes that the use of Cry1Ab or Cry1F corn hybrids expressed in corn raises concerns with respect to insect resistance management. As discussed below, the registrations for Cry1Ab and Cry1F proteins expressed in corn is subject to specific terms and conditions that effectively restrict the use of the product in ways that EPA determines will adequately mitigate these concerns. Therefore, EPA determines that the allowed use will not significantly increase the risk of unreasonable adverse effects on the environment. Finally, EPA has identified the need for certain confirmatory data on potential accumulation of Cry1Ab and Cry1F proteins in soil and field impacts of Cry1Ab and Cry1F proteins on non-target species. The registration of these products is specifically conditioned on submission of these data.

By this reassessment, EPA has completed its tolerance reassessment for Cry1Ab (180.1173) under 408(q) of the FFDCFA. The tolerance exemption for Cry1F (180.1217) does not require reassessment at this time.

C. Insect Resistance Management (IRM) Program

Rationale for IRM Requirements:

In deciding on the size, proximity, configuration, and management of the non-*Bt* corn refuge, EPA has taken into account empirical data on the pest biology and ecology of the three primary target pests, European corn borer (*Ostrinia nubilalis* (Huebner)), corn earworm (*Helicoverpa zea* (Boddie)), and southwestern corn borer (*Diatraea grandiosella* (Dyar)), models that predict the estimated time that resistance would develop to compare the effectiveness of various IRM

strategies, economics, sustainability, and grower feasibility.

Beginning with the first *Bt* plant-incorporated pesticide registration, the Agency has taken steps to manage insect resistance to *Bt* with IRM plans being an important part of the regulatory decision. The Agency identified (later confirmed by the 1995 SAP) seven elements that should be addressed in a *Bt* plant-incorporated protectant resistance management plan: 1) knowledge of pest biology and ecology; 2) appropriate dose expression strategy; 3) appropriate refuge; 4) resistance monitoring and a remedial action plan should resistance occur; 5) employment of integrated pest management (IPM); 6) communication and education strategies on use of the product; and 7) development of alternative modes of action. IRM plans also include grower education and measurement of the level of compliance.

The Agency has determined that the 20% non-*Bt* field corn refuge requirements for *Bt* corn grown in the Corn-Belt and the 50% non-*Bt* corn refuge requirements for *Bt* corn grown in cotton-growing areas are scientifically-sound, protective, feasible, sustainable, and practical to growers. Models have been developed by scientists in academia to predict the estimated time that insect resistance would develop to compare IRM strategies for *Bt* field corn. For example, if a high dose is achieved to control ECB (as it is for the currently registered *Bt* corn products), then these models predict that ECB will not evolve resistance for at least 99 years if a 20% refuge is implemented in the Corn Belt. Models are also used to predict the evolution of CEW resistance have also been used. These models indicate that 50% non-*Bt* field corn refuge in cotton-growing areas is sufficient to delay CEW resistance for at least the time frame of the registrations. A 20% non-*Bt* field corn refuge in the Corn Belt is sufficient to delay CEW resistance because CEW do not overwinter in the Corn Belt. EPA believes that the use of these models provides confidence that resistance will not evolve under the time frame of the registrations.

However, it should be noted that these predictive models cannot be validated without actual field resistance. They have limitations and the information gained from the use of such models can only be used as a part of the weight of evidence determination conducted EPA to assess the risks of resistance developing in target pest populations. EPA agrees with the October 2000 SAP that models are an important tool in determining appropriate *Bt* crop IRM strategies and that model design should be peer reviewed and parameters validated. In the absence of field resistance, EPA agrees with the October 2000 SAP that models are “the only scientifically rigorous way to integrate all of the biological information available, and that without these models, the Agency would have little scientific basis for choosing among alternative resistance management options.” While the absolute number of years to resistance is not precisely determined from the models, the relative difference in effectiveness between refuge options can be determined. Thus, the utility of the models is not that they make accurate quantitative predictions, rather, it is that they enable the Agency to make informed judgments of the potential effects of using various refuge options.

In addition to assessing the likelihood of resistance, EPA has mandated specific requirements for annual resistance monitoring to determine, in a pro-active fashion, whether insect susceptibility

has changed or whether resistance is likely to occur (or is occurring). After five years of analyzing resistance monitoring data (1996-2000), there is no evidence of European corn borer, corn earworm, or southwestern corn borer resistance developing in the field to the Cry1Ab delta-endotoxins produced by current registered *Bt* corn products. There are no resistance monitoring reports yet available for Cry1F field corn products because they were just registered in 2001. Therefore, EPA believes that resistance is not occurring in the field based on the available data. The Agency is mandating enhancements to the resistance management programs that will improve the certainty of detection of resistance. If insect resistance occurs, EPA has also mandated a specific remedial action plan that will contain (and perhaps eradicate) resistance prior to the occurrence of any widespread, endemic resistance.

In addition, to the use of biological data, predictive models, and resistance monitoring information, EPA also weighed practical considerations in deciding which refuge options to allow. Grower education and compliance with refuge options are essential to the success of any IRM strategy. Growers must be able to implement the refuge options within the constraints of their farming operations. Based upon the currently available scientific data and information and understanding of farming operations, EPA believes that the 20% non-*Bt* field corn refuge options in the Corn-Belt and the 50% non-*Bt* field corn refuge options in the cotton-growing areas provide an adequate time-to-resistance for *Bt* field corn and are practical, sustainable, and feasible to growers. If the 20% non-*Bt* field corn refuge options in the Corn-Belt and the 50% non-*Bt* field corn refuge options are deployed correctly then, there is a very limited chance of insect resistance evolving over the next seven years of the registration of these products.

EPA has determined that a mandatory refuge strategy was not necessary for *Bt* sweet corn products to reduce the likelihood of resistance for the following reasons: 1) sweet corn is typically harvested earlier than field corn (18-21 days after silking (before most lepidopteran larvae complete development); and 2) all *Bt* sweet corn residues are mandated by the terms and conditions of the registration to be destroyed within one month of harvest (a practice that presumably would destroy any live larvae left in corn stalks). The 2000 SAP agreed that destruction of *Bt* sweet corn residues would be sufficient to mitigate pest resistance to *Bt* sweet corn.

To strengthen the IRM strategies for *Bt* field and sweet corn, EPA has mandated that the registrants have grower agreements that contractually bind the grower to the IRM requirements, ongoing grower education programs, ongoing research programs, ongoing resistance monitoring programs, and a multi-faceted compliance monitoring program (including an annual third-party compliance survey) to ensure that IRM strategies are deployed correctly. EPA will be obtaining annual reports on grower agreements, grower education programs, resistance monitoring programs, research programs, and compliance monitoring programs. EPA has asked for additional data on the effect of insecticides on refuge effectiveness for *Bt* field corn and north-south movement of CEW to further enhance the IRM strategies. Part of the compliance monitoring program (to be developed as part of the terms and conditions of registration) includes

specific actions for growers or growers in a region who are found to be non-compliant with IRM requirements. As noted above, if resistance were to occur, EPA has mandated refinements to specific remedial action plans for the *Bt* corn products to contain (and perhaps eradicate) resistance.

Appendix 3

Remedial Action Plan for Responding to Resistance in European Corn Borer Corn Earworm and/or Southwestern Corn Borer (October 15, 2001)

I. Definitions

Suspected resistance

EPA defines “suspected” resistance to mean, in the case of reported product failure, that:

- the corn in question has been confirmed to be *Bt* corn
- the seed used had the proper percentage of corn expressing *Bt* protein;
- the relevant plant tissues are expressing the expected level of *Bt* protein; and
- it has been ruled out that species not susceptible to the protein could be responsible for the damage, that no climatic or cultural reasons could be responsible for the damage, and that other reasonable causes for the observed product failure have been ruled out.

The Agency does not interpret “suspected resistance” to mean grower reports of possible control failures, nor does the Agency intend that extensive field studies and testing to confirm scientifically insect resistance be completed before responsive measures are undertaken.

If resistance is “suspected,” the registrant must instruct growers to do the following:

- Use alternate control measures to control the pest suspected of resistance to *Bt* corn in the affected region.
- Destroy crop residues in the affected region immediately after harvest (i.e. within one month) with a technique appropriate for local production practices to minimize the possibility of resistant insects overwintering and contributing to the next season’s pest population.

Confirmed Resistance

The registrant assumes responsibility for the implementation of resistance mitigation actions undertaken in response to the occurrence of resistance during the growing season. When resistance has been confirmed, the registrant must immediately stop sale and distribution of *Bt* corn in the remedial action zone (may be less than a single county, single county, or multiple counties) where the resistance has been shown until an effective local mitigation plan approved by EPA has been implemented.

A resistance event becomes confirmed if the progeny of the sampled ECB, CEW, or SWCB population would exhibit all of the following characteristics in bioassays initiated with neonates:

1. If there is > 30% survival and > 25% leaf area damaged in a 5-day bioassay using Cry1Ab-positive or Cry1F-positive leaf tissue under controlled laboratory conditions.
2. If standardized laboratory bioassays using diagnostic doses for ECB (Marçon et al. 2000), SWCB (Trisyono and Chippendale 1999), or CEW/CBW (USDA/ARS/SIMRU, unpublished) demonstrate resistance has a genetic basis and survivorship in excess of 1% (gene frequency of population ≥ 0.1).
3. If an LC_{50} in a standard Cry1Ab or Cry1F diet bioassay exceeds the upper limit of the 95% confidence interval of the standard unselected laboratory population LC_{50} for susceptible ECB, SWCB, or CEW populations, as established by the ongoing baseline monitoring program.

II. Remedial Action

The registrant assumes responsibility for the implementation of resistance mitigation actions undertaken in response to the occurrence of resistance during the growing season. In cases of “confirmed” resistance, the following strategy for Cry1Ab and/or Cry1F *Bt* corn hybrids:

The registrant will report all instances of confirmed pest resistance, as defined above, to the Agency within 30 days. Upon identification of a confirmed instance of resistance, registrants will take the following immediate mitigation measures:

1. Notify customers and extension agents in the affected area,
2. Require to customers and extension agents in the affected area the use of alternative control measures to reduce or control the local target pest population,
3. Where appropriate, require to customers and extension agents in the affected area that crop residues be incorporated into the soil following harvest, to minimize the possibility of overwintering insects.
4. Immediately stop sale and distribution of *Bt* corn in the remedial action zone (may be a single or multiple counties) where the resistance has been shown until an effective local mitigation plan approved by EPA has been implemented.

Within 90 days of a confirmed instance of pest resistance, as defined above, registrants will:

1. Notify the Agency of the immediate mitigation measures that were implemented,

2. Submit to the Agency a proposed long-term resistance management action plan for the affected area,
3. Work closely with the Agency in assuring that an appropriate long-term resistance management action plan for the affected area is implemented, and
4. Implement an action plan that is approved by EPA and that consists of some or all the following elements, as warranted:
 - a. Informing customers and extension agents in the affected area of pest resistance,
 - b. Increasing monitoring in the affected area, and ensuring that local target pest populations are sampled on an annual basis,
 - c. Recommending alternative measures to reduce or control target pest populations in the affected area,
 - d. Implementing intensified local IRM measures in the affected area based on the latest research results. The implementation of such measures will be coordinated by the Agency with other registrants; and
 - e. The implementation of the remedial action strategy will be coordinated by the Agency with other registrants and stakeholders.

For mitigation of resistance in the growing season(s) following a confirmed resistance incident(s), use of the following procedures:

1. Maintenance of the sales suspension of all *Bt* corn hybrids (with the same protein or similar *Bt* proteins as the *Bt* corn hybrids with the resistant population) in the affected region would remain in place until an EPA-approved local resistance management plan is in place to mitigate resistance in the affected region(s).
2. The development and recommendation of alternative resistance management strategies for controlling the resistant pest(s) on corn in the affected region.
3. Notification of all relevant personnel (e.g., growers, consultants, extension agents, seed distributors, processors, university cooperators, and state/federal authorities) in the affected region of the resistance situation.