# Bacillus thuringiensis var. aizawai Cry1F and the genetic material (from the insert of plasmid pGMA281) necessary for its production in cotton and Bacillus thuringiensis var. kurstaki Cry1Ac and the genetic material (from the insert of plasmid pMYC3006) necessary for its production in cotton Fact sheet

## I. Description of the Plant-Incorporated Protectant

Pesticide Active Ingredient: Bacillus thuringiensis var. aizawai Cry1F and the genetic material (from the insert of plasmid pGMA281) necessary for its production in cotton and Bacillus thuringiensis var. kurstaki Cry1Ac and the genetic material (from the insert of plasmid pMYC3006) necessary for its production in cotton

- **EPA Registration Number:** 68467-3
- **Date Registered**: September 30, 2004
- **Trade and Other Names:**

  Mycogen Brand Cry1F (synpro)/Cry1Ac (synpro) Construct 281/3006 Cotton;
  WideStrike7 cotton

- **OPP Chemical Codes:** 006512 and 006513
- Basic Manufacturer

  Mycogen Seeds c/o Dow AgroSciences LLC
  9330 Zionsville Road
  Indianapolis, IN 46268

- **Type of Pesticide:** Plant-Incorporated Protectant
- **Uses:** Cotton
- **Target Pest(s):** Cotton bollworm, tobacco budworm, pink bollworm, soybean looper, cabbage looper, beet armyworm, fall armyworm, southern armyworm, black cutworm, citrus peelminer, cotton leafperforator, European corn borer, ominivorous leafroller, and saltmarsh caterpillar.

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## II. Background

Dow AgroSciences submitted an application for a full commercial use under Section 3 of the Federal Insecticide, Fungicide, and Rodenticide Act, as amended (FIFRA) for WideStrike7 cotton [Mycogen Brand Cry1F (synpro)/Cry1Ac (synpro) Construct 281/3006 Cotton] on November 13, 2002. WideStrike7 expresses both the Cry1F and Cry1Ac synthetic insecticidal crystalline proteins (ICPs). Previously, Dow AgroSciences

submitted an application on November 5, 2001 for an Experimental Use Permit (EUP) under Section 5 of the Federal Insecticide, Fungicide, and Rodenticide Act, as amended, (FIFRA) for WideStrike7 cotton to be planted on 407.2 acres. This EUP was subsequently amended to increase the acreage to 2826 acres on November 6, 2002. The EUP was granted on April 11, 2003.

An existing tolerance exemption, CFR 40 Section 180.l155, exists for Bacillus thuringiensis subsp. kurstaki Cry1Ac and the genetic material necessary for its production in all plants. An existing tolerance exemption, CFR 40 Section 180.1151, exists for phosphinothricin acetyltransferase (PAT) and the genetic material necessary for its production in all plants. The PAT in Mycogen Brand Cry1F (synpro)/Cry1Ac (synpro) Construct 281/3006 Cotton is covered by the existing tolerance exemption, CFR 40 Section 180.1151. Similarly, data provided by Dow AgroSciences are adequate to support the existing tolerance exemption for Cry1Ac.

In the Federal Register of August 11, 2004 (69 FR 48870; FRL-2), EPA issued a notice pursuant to section 408(c)(3) of the FFDC, U.S.C. 346a(d)(3), announcing the filing of a pesticide tolerance petition (PP 3F6785) by Dow AgroSciences. The petition requested that 40 CFR 174 be amended by establishing a tolerance exemption from the requirement of a tolerance for residues of Bacillus thuringiensis subsp aizawai.strain PS811 (Cry1F insecticidal control protein) and the genetic material necessary for its production in cotton when used as a plant-incorporated protectant. This notice included a summary of the petition prepared by the petitioner Dow AgroSciences.

The only comments received in response to the notice of filing were from the National Cotton Council supporting this petition. A tolerance exemption was issued on September 30, 2004 (69 FR 58280 under 40 CFR 174.455 for the Bacillus thuringiensis Cry1F protein and the genetic material necessary for its production in or on cotton. Originally, a temporary tolerance exemption for the Cry1F protein (and the genetic material necessary for its production in or on cotton) was issued by the Agency on April 30, 2003 (40 CFR 180.1227). This temporary tolerance exemption, 40 CFR 180.1227, was extended by the Agency on March 31, 2004 (68 FR 16819) to May 1, 2005. The temporary tolerance exemption was replaced by the permanent tolerance exemption for the Bacillus thuringiensis Cry1F protein and the genetic material necessary for its production in or on cotton on September 30, 2004 (40 CFR 174.455).

The only comments received in response to the notice of filing were from the National Cotton Council supporting this petition. A tolerance exemption was issued on September 30, 2004 (69 FR 58280 under 40 CFR 174.455 for the Bacillus thuringiensis Cry1F protein and the genetic material necessary for its production in or on cotton. Originally, a temporary tolerance exemption for the Cry1F protein (and the genetic material necessary for its production in or on cotton) was issued by the Agency on April 30, 2003 (40 CFR 180.1227). This temporary tolerance exemption, 40 CFR 180.1227, was extended by the Agency on March 31, 2004 (68 FR 16819) to May 1, 2005. The temporary tolerance exemption was replaced by the permanent tolerance exemption for the Bacillus thuringiensis Cry1F protein and the genetic material necessary for its production in or on cotton on September 30, 2004 (40 CFR 174.455).

Prior to registration of this new two toxin product, WideStrike7 cotton, a Science Advisory Panel (SAP) was convened June 8-10, 2004 to discuss the Agency’s review of the product characterization, ecological toxicity, and insect resistance management data submitted by Dow AgroSciences. The Agency considered those recommendations from the SAP Report, dated August 19, 2004, that were directly responsive to the specific questions that the Agency presented to the SAP. EPA conditionally registered this product under FIFRA 3(c)(7)(C) on September 30, 2004. This registration expires on September 30, 2009.

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## III. Science Assessment

### Product Characterization

Dow AgroSciences transformed Acala cotton line GC510 with plasmids pAGM281 and pMYC3006. Cotton

event 281-24-236 (Cry1F) resulted from an insertion from pAGM281 of one intact copy of cry1F and one intact copy of the pat gene (plant selectable marker gene, phosphinothricin acetyltransferase, PAT). Cotton event 3006-210-23 (Cry1Ac) resulted from an insertion from pMYC3006 of one intact copy of cry1Ac and one intact copy of the pat gene. These two Acala cotton lines, Event 281-24-236 (Cry1F) and Event 3006-210-23 (Cry1Ac) were separately backcrossed three times with cotton line PSC355 followed by one generation of self-pollination to yield the BC3F1generation. The two BC3F1 events were then intercrossed and self-pollinated to the F3 generation, forming cottonseed designated 281-24-236/3006-210-23, which contains the genes for expression of Cry1F, Cry1Ac, and PAT proteins designated as WideStrike7 (MXB-13).

The characterization data submitted by the registrant provides adequate product information to guide the risk assessment. These data indicate that plant-produced and bacterially-produced Cry1F, Cry1Ac, and PAT proteins are biologically, biochemically, and immunologically equivalent. Southern blot data of restriction enzyme digests suggest that the Cry1Ac event, Cry1F event, and the pyramided Cry1F/Cry1Ac cotton event all contain a single, unique, insertion of the transgenic DNA from the appropriate plasmids. An additional hybridizing fragment of pat gene was integrated into the cotton genome from pAGM281.

The field expression data for Cry1F (synpro), Cry1Ac (synpro) and phosphinothricin acetyltransferase (PAT) proteins in transgenic cotton plants, cottonseed and cottonseed processed products provides quantitative data on the expression of Cry1F and Cry1Ac proteins in different cotton plant tissues which are: young leaves, squares,, flowers, boll, whole plant, pollen, nectar, root, seed, and cottonseed process fractions consisting of kernel, hulls, meal and oil. The Cry1Ac and Cry1F proteins were detected in all matrices except nectar, meal and oil, Cry1Ac was also not detected in hulls. Mean Cry1Ac expression was approximately three- to twenty-times lower than Cry1F expression in leaves, squares, flowers, whole plant, boll, and seed tissue, depending on the tissue. Pollen was the only tissue in which Cry1Ac expression was higher than Cry1F expression. Expression levels of individual Cry1F and Cry1Ac proteins were similar for the single event and two-protein cotton lines. PAT proteins were detected in the cotton samples from the Cry1F event and the Cry1F/Cry1Ac event, but generally not detected in the Cry1Ac event samples.

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**Human Health Assessment**

The health effects assessment concludes that there is a reasonable certainty that no harm will result from exposure to Cry1F and Cry1Ac proteins. For purposes of the dietary risk assessment, the maximum levels of expression in cottonseed (cotton processed fraction) were 0.46 and 3.1 ng protein/mg tissue fresh weight for Cry1Ac and Cry1F proteins in the Cry1F/Cry1Ac cotton lines, respectively, based on the expression data.

Based upon the human health data provided, there does not appear to be a significant risk of toxic effects and/or allergenic effects to humans or animals due to exposure to the Cry1F (synpro) and Cry1Ac (synpro) proteins. Adequate information was submitted to show that the Cry1F and Cry1Ac test material derived from microbial cultures were biochemically and functionally similar to the proteins produced as the plant-incorporated protectant ingredients.

The Cry1F and Cry1Ac proteins are classified as Toxicity Category III: LD50> 700 mg/kg body weight for Cry1Ac, LD50> 600 mg/kg body weight for Cry1F and LD50> 375 mg Cry1F/kg body weight and LD50>350 Cry1Ac mg/kg body weight for the pyramided Cry1F/Cry1Ac proteins. The Cry1Ac and Cry1F proteins are not stable to digestion in simulated gastric fluid (<1 min), nor do they share any significant sequence similarity to known toxins or allergens using an eight amino acid step-wise comparison. In addition, Cry1F and Cry1Ac proteins have not been implicated in toxic and/or allergenic reactions in humans or animals.

An existing tolerance exemption, 40 CFR Section 180.l155, exists for Bacillus thuringiensis subsp. kurstaki Cry1Ac and the genetic material necessary for its production in all plants. Similarly, an existing tolerance exemption, 40 CFR Section 180.1151, exists for the PAT protein and the genetic material necessary for its production in all plants. The PAT in Mycogen Brand Cry1F (synpro)/Cry1Ac (synpro) Construct 281/3006 Cotton is covered by the existing tolerance exemption, 40 CFR Section 180.1151. Data provided by Dow

AgroSciences support issuance of a tolerance exemption for the Bacillus thuringiensis aizawai Cry1F protein and the genetic material necessary for its production in or on cotton. The analytical methods for the Cry1Ac and Cry1F proteins are acceptable.

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**Environmental Assessment**

From all of the required and voluntarily developed indicator and host range species test data on WideStrike7 cotton, including the supplementary field data, the Agency concludes that the levels of Cry1F and Cry1Ac protein in cotton will not pose unreasonable adverse effects to cotton agroecosystem flora and fauna. Available data also indicate that there should be minimal short term accumulation of Cry1F and Cry1Ac protein in agricultural soil. In addition, no adverse effects on endangered and threatened species listed by the US Fish and Wildlife Service are expected from the proposed WideStrike7 cotton registration.

Incidental exposure to sensitive larval stages of a non-target butterfly or moth to Cry1F or Cry1Ac may occur if MXB-13 pollen is present on host plants and is consumed; however, the likelihood of such exposure is remote due to the insignificant outflow of pollen from cotton and the presence of other food sources which occur near cotton fields; thus, there is negligible risk from cropping of MXB-13. In excess of 300 different species of beneficial insects are known to inhabit cotton fields. Common arthropod predators and parasites of cotton fields represent orders that are insensitive to the Cry1 proteins. Additionally, these beneficial organisms are predominately predators and parasites and only in a few instances are plant product consumers. Therefore, direct risks to beneficial insects from exposure to Cry1F and Cry1Ac expressed in MXB-13 are negligible. Risk from indirect exposure through tritrophic feeding on insect host/prey is also negligible due to the low levels of exposure anticipated in comparison to effect levels shown in testing of surrogates.

Analysis of effect levels (selectivity and activity on non-targets) and exposure (exposure routes, concentrations and habitat for taxa of concern) indicates negligible ecological risks are posed by cropping of MXB-13 cotton expressing Cry1F and Cry1Ac PIPs.

At present, the Agency is aware of no identified significant adverse effects of Cry1F and Cry1Ac proteins on the abundance of non-target beneficial organisms in any population in the field, whether they are pest parasites, pest predators, or pollinators. Field census data submitted to the Agency show minimal to undetectable changes in the beneficial insect abundance or diversity. In cotton fields densities of predatory and non-target insects are generally higher on Bt crops than non-Bt crops primarily because the Bt crops are not subjected to the same number of applications of nonspecific pesticides. In genera invertebrate abundance studies in Bt crop fields do not show a shift in biodiversity, except in cases where the predators are dependent on the pest insect as prey. In contrast, treatment with chemical pesticides, when studied, had significant effects on the total numbers of insects and on the numbers within the specific groups. To date the available field test data show that compared to crops treated with conventional chemical pesticides, the transgenic crops have no detrimental effect on the abundance of non-target insect populations. Additional field studies were not recommended by the 2004 SAP.

The Agency believes that cultivation of WideStrike7 cotton may result in fewer adverse impacts to non-target organisms than result from the use of chemical pesticides. Under normal circumstances, WideStrike7 cotton requires substantially fewer applications of chemical pesticides. This should result in fewer adverse impacts to non-target organisms because application of nonspecific conventional chemical pesticides is known to have an adverse effect on non-target beneficial organisms found living in the complex environment of an agricultural field. Many of these beneficial organisms are important integrated pest management controls (IPM) for secondary pests such as aphids and leafhoppers. The overall result of cultivation of cotton expressing Cry proteins is that the number of chemical insecticide applications for non-target pest control is reduced for management of multiple pest problems.

The Agency has reviewed the potential for gene capture and expression of the Cry proteins in cotton by wild or weedy relatives of cotton in the United States, its possessions or territories. There is a possibility for gene

transfer in locations where wild or feral cotton relatives exist. There are only three areas in the United States and its territories wherein cultivated cotton has the opportunity to outcross to wild or feral species which are genetically compatible: (1) southern Arizona, (2) Hawaiian islands, and (3) southern Florida. Therefore, EPA requires stringent sales and distribution restrictions on Bt cotton within these areas to preclude outcrossing or hybridization from the crop to sexually compatible relatives (see Section IV. Terms and Conditions of Registration).

The fate of Cry1F and Cry1Ac proteins in soils and indirect effects on soil biota has also been evaluated. Test data show that most of the Cry protein deposited into soil is quickly degraded, although a residual amount may persist in biologically active form for a longer period of time. It is also reported that detectable Bt Cry protein persistence exists in soils that have been exposed to repeat Bt spray applications. Limited data do not indicate that Cry proteins have any measurable effect on microbial populations in the soil. Horizontal transfer of genes or toxins from transgenic plants to soil bacteria has not been demonstrated. Published studies of Bt Cry protein in soil show no effect on bacteria, actinomyces, fungi, protozoa, algae, nematodes, springtails or earthworms. In addition, a new crop planted in Bt Cry protein containing soil does not take up the Bt protein.

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**Insect Resistance Management**

Dow AgroSciences has provided an Aacceptable IRM plan for WideStrike7-protected cotton. They have provided a detailed analysis of the scientific basis for the product durability plan (insect resistance management strategy) and the practical implementation of the durability plan.

The complex of Bt proteins involved in WideStrike® and other Bt cotton products reduces the selection pressure for TBW or CBW resistance to any one Bt protein, especially given the complexity of binding receptors. TBW and CBW binding studies involving Cry1F and Cry1Ac indicate that there are at least two, and probably at least six binding sites for these two proteins and thus, incomplete cross-resistance is likely.

WideStrike7 expresses Cry1Ac and Cry1F at a high dose against tobacco budworm. The addition of a second protein, makes the 20% refuge even more durable than for a single protein expressed at a high dose and reduces the refuge size (as compared to a single protein, high dose product needed for the same level of protection as predicted by Peck et al. (1999) across the same time horizon. Neither Cry1F nor Cry1Ac is expressed at a high dose in WideStrike7 against cotton bollworm; although Cry1Ac mortality is much higher in WideStrike7 than for Bollgard7 cotton and Cry1F efficacy is moderate. This pest has numerous alternate hosts and is highly migratory. Dow AgroScience’s modeling efforts indicate that refuge size is not very important to management of CBW resistance since WideStrike7 is a pyramid of two proteins with limited cross-resistance and is inherently durable when coupled with the natural refugia from alternative hosts. Thus, a 20% sprayable refuge is likely to be more than adequate for prolonging durability against CBW.

For PBW, WideStrike7 is a high dose for Cry1Ac. Cry1F has no apparent control of PBW based on field efficacy data and high dose data and thus, WideStrike7 effectively expresses a single protein (Cry1Ac) to control PBW. A small structured refuge in combination with the high dose, planted as close as practicable to the Bt cotton, would increase the WideStrike7 durability.

The specific IRM requirements that were mandated by EPA are specified in Section IV. “Terms and Conditions of the Registration.”

**Benefits**

EPA concludes that use of WideStrike7-protected cotton is in the public interest and supports the conditional registration of this pesticide under FIFRA section 3(c)(7)(C). This product will likely result in reductions of chemical insecticide use of higher risk insecticides (organophosphates, organochlorines, pyrethroids, and carbamates), and in direct and indirect human health and environmental benefits and provide the grower with additional control options that will likely reduce the selection pressure resistance to the other technologies

(chemical insecticides and Bt cottons), and thus contribute to the sustainability of all of these technologies.

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## IV. Terms and Conditions of the Registration

EPA Registration Number 68467-3

Dow AgroSciences is required to do the following as terms and conditions of the registration.

1. This FIFRA Section 3(c)7(C) conditional registration will automatically expire on September 30, 2009.

2. The subject registration will be limited to Bacillus thuringiensis Cry1Ac (synpro) and Cry1F (synpro) proteins and the genetic material necessary for their production in or on cotton.

3. Submit/cite all required data required for registration of your product under FIFRA Section 3(c)5 when the Agency requires registrants of similar products to submit such data.

4. Submit production information for this product to Mr. Owen Beeder of the Office of Pesticide Programs, Registration Division (mail code 7505C) for the fiscal year in which this product is conditionally registered., in accordance with FIRA Section 29. The fiscal year begins October 1 and ends September 30. Production information will be submitted to the Agency no later than December 15, following the end of the preceding fiscal year.

5. By July 31, 2005, Dow AgroSciences must provide the Agency with additional empirical data or published literature (other than Gould et al., 2002) that supports the use of CBW alternate hosts as natural refugia. Data would include larval and adult production of CBW on each alternate host for each generation relative to cotton and WideStrike7 cotton and the spatial scale and source of moth production.

6. Should Dow AgroSciences wish to use their CBW resistance management model to support changes to the insect resistance management strategy, then this model must be revised per the recommendations of the June 8-10, 2004 SAP report dated August 19, 2004 and submitted to the Agency for review.

7. Dow AgroSciences must submit an avian chronic exposure study by September 30, 2008.

8. Dow AgroSciences must submit a non-target insect more appropriate for cotton fields, i.e., a maximum hazard dose laboratory toxicity study using the organism, Orius insidiosus (minute pirate bug) by September 30, 2008.

9. Dow AgroSciences must submit soil fate/terrestrial expression studies for long range soil persistence by September 30, 2008.

10. Gene Flow: The following information regarding commercial production must be included in the grower guide for WideStrike7 Cotton and is a term of this amendment:

    a. No planting of WideStrike7 cotton is permitted south of Route 60 (near Tampa) in Florida.

    b. Commercial culture of WideStrike7 cotton is prohibited in Hawaii, Puerto Rico, and the US Virgin Islands.

       The following information regarding test plots and seed production must occur on bags of WideStrike7 cotton intended for these purposes and is a term of this amendment.

    c. Test plots or breeding nurseries, regardless of the plot size, established in Hawaii must not be

planted within 3 miles of Gossypium tomentosum and must be surrounded by 24 border rows of a suitable pollinator trap crop.

d. Experimental plots and breeding nurseries of Bt.-cotton are prohibited on the U.S. Virgin Islands, and

e. Test plots or breeding nurseries, regardless of the plot size, established on the island of Puerto Rico must not be planted within 3 miles of feral cotton plants and must be surrounded by 24 border rows of a suitable pollinator trap crop.

Upon approval by EPA, test plots and/or breeding nurseries in Hawaii, the U.S. Virgin Islands, and Puerto Rico may be established without restrictions if alternative measures, such as insecticide applications, are shown to effectively mitigate gene flow.

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11. Insect Resistance Management

Requirements relating to creation of a non-Bt cotton refuge in conjunction with the planting of any acreage of Bt cotton;

Requirements for Dow AgroSciences to prepare and require Bt cotton users to sign Agrower agreements@ which impose binding contractual obligations on the grower to comply with the refuge requirements;

Requirements for Dow AgroSciences to develop, implement, and report to EPA on programs to educate growers about IRM requirements;

Requirements for Dow AgroSciences to develop, implement, and report to EPA on programs to evaluate and promote growers= compliance with IRM requirements;

Requirements for Dow AgroSciences to develop, implement, and report to EPA on programs to evaluate whether there are statistically significant and biologically relevant changes in susceptibility to the Cry1Ac and Cry1F proteins in the target insects;

Requirements for Dow AgroSciences to develop, and if triggered, to implement a Aremedial action plan which would contain measures Dow AgroSciences would take in the event that any insect resistance was detected as well as to report on activity under the plan to EPA;

Annual reports on or before January 31st each year.

a. **Refuge Requirements**

All growers of WideStrike7 cotton must employ one of the following structured refuge options:

1. **External, Unsprayed Refuge**

Ensure that at least 5 acres of non-Bt cotton (refuge cotton) is planted for every 95 acres of WideStrike7 cotton. The size of the refuge must be at least 150 feet wide, but preferably 300 feet wide. This refuge may not be treated with sterile insects, pheromone, or any insecticide (except listed below) labeled for the control of tobacco budworm, cotton bollworm, or pink bollworm. At the pre-squaring cotton stage only, the refuge may be treated with any lepidopteran insecticide to control foliage feeding caterpillars. The refuge may be treated with acephate or methyl parathion at rates which will not control tobacco budworm or the cotton bollworm (equal to or less than 0.5 lbs active ingredient per acre). The variety of cotton planted in the refuge must be comparable to WideStrike7 cotton, especially in the maturity

date, and the refuge must be managed (e.g., planting time, use of fertilizer, weed control, irrigation, termination, and management of other pests) similarly to WideStrike7 cotton. Ensure that a non-Bt cotton refuge is maintained within at least 2 linear mile (preferably adjacent to or within 1/4 mile or closer) from the Bt cotton fields.

2. **External Sprayed Refuge**

   Ensure that at least 20 acres of non-Bt cotton are planted as a refuge for every 80 acres of WideStrike7 cotton (total of 100A). The variety of cotton planted in the refuge must be comparable to Bt cotton, especially in the maturity date, and the refuge must be managed (e.g., planting time, use of fertilizer, weed control, irrigation, termination, and management of other pests) similarly to WideStrike7 cotton. The non-Bt cotton may be treated with sterile insects, insecticides (excluding foliar Btk products), or pheromones labeled for control of the tobacco budworm, cotton bollworm, or pink bollworm. Ensure that a non-Bt refuge is maintained within at least 1 linear mile (preferably within 2 mile or closer) from the Bt cotton fields.

3. **Embedded Refuge**

   Plant at least 5 acres of non-Bt cotton (refuge cotton) for every 95 acres of WideStrike7 cotton. The refuge cotton must be embedded as a contiguous block within the Bt cotton field, but not at one edge of the field (i.e., refuge block(s) surrounded by WideStrike7 cotton). For very large fields, multiple blocks across the field may be used. For small or irregularly shaped fields, neighboring fields farmed by the same grower can be grouped into blocks to represent a larger field unit, provided the block exists within one mile squared of the WideStrike7 cotton and the block is at least 150 feet wide, but preferably 300 feet wide. Within the larger field unit, one of the smaller fields planted to non-Bt cotton may be utilized as the embedded refuge. The variety of cotton planted in the refuge must be comparable to WideStrike7 cotton, especially in the maturity date, and the refuge must be managed (e.g., planting time, use of fertilizer, weed control, irrigation, and management of other pests) similarly to WideStrike7 cotton. This refuge may be treated with sterile insects, any insecticide (excluding foliar Btk products), or pheromone labeled for the control of tobacco budworm, cotton bollworm, or pink bollworm whenever the entire field is treated. The refuge may not be treated independently of the surrounding WideStrike7 cotton field in which it is embedded (or fields within a field unit), except only at the pre-squaring cotton stage when the refuge may be treated with any lepidopteran insecticide to control foliage feeding caterpillars.

4. **Embedded Refuge for Pink Bollworm Only**

   Plant the refuge cotton as at least one single non-Bt cotton row for every six to ten rows of WideStrike7 cotton. The refuge may be treated with sterile insects, any insecticide (excluding foliar Btk products), or pheromone labeled for the control of pink bollworm whenever the entire field is treated. The in-field refuge rows may not be treated independently of the surrounding Bt cotton field in which it is embedded. The refuge must be managed (fertilizer, weed control, etc.) identically to the WideStrike7 cotton. There is no field unit option.

5. **Community Refuge**

   This option allows multiple growers to manage refuge for external, unsprayed and external, sprayed refuge options or both. This option is not allowed for the embedded/in-field options. The community refuge for insect resistance management must meet the requirements of either the 5% external unsprayed refuge and/or the 20% sprayed option, or an appropriate combination of the two options. The community refuge pilot must consist of the following:

   There will be a community refuge coordinator for each pilot site. Each community refuge

coordinator must submit a signed community refuge form listing all of the participants at the pilot site to Dow AgroSciences by July 1st annually. Dow AgroSciences must provide EPA, if requested, with a copy of the signed community refuge form. The community refuge coordinator will maintain a copy of the field map (to scale) or suitable scalar representation of the community refuge for review by Dow AgroSciences or EPA as part of the compliance program.

On an annual basis, Dow AgroSciences must conduct at least one telephone audit of a statistically representative sample of community refuge coordinators from communities in all states participating in the community refuge. EPA shall review the questions annually prior to the start of the growing season.

The community refuge program users must be included in the telephone compliance survey and the on-farm visits to be conducted by Dow AgroSciences under section 3.c. below.

On an annual basis, Dow AgroSciences must conduct a review of the community refuge program and submit that review to the Agency as to any proposed changes by January 31st. An appropriate amendment for any proposed changes must be submitted to the Agency.

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b. **Grower Agreements**

While Dow AgroSciences will have flexibility to design its program to fit its own business practices, the registration is specifically conditioned on meeting the following requirements.

1. Persons purchasing the Bt cotton product must sign a grower agreement. The term Agrower 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. Dow AgroSciences must establish by the 2005 growing season, a system which is reasonably likely to assure that persons purchasing the Bt cotton 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 December 1, 2004.

4. Dow AgroSciences must submit a copy of its grower agreement to EPA by December 1, 2004. If Dow AgroSciences wishes to change any part of 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, Dow AgroSciences must submit to EPA the text of such changes to ensure the agreement is consistent with the terms and conditions of this amendment.

5. Dow AgroSciences must establish a system which is reasonably likely to assure that persons purchasing the Bt cotton sign grower agreement(s), and must provide by December 1, 2004 a written description of that system.

6. Dow AgroSciences shall maintain records of all Bt cotton 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, 2006 and annually thereafter, Dow AgroSciences shall provide EPA with a report on the number of units of the Bt cotton seed 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 October through September. Note: the first report shall contain the specified information for the time frame starting with the date of registration and ending September 30, 2005.

8. Dow AgroSciences 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 the names, personal information, and grower license number will be kept as confidential business information.

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c. **IRM Education and IRM Compliance Monitoring Programs**

Dow AgroSciences must implement the following IRM education and compliance monitoring programs:

1. Dow AgroSciences must design and implement a comprehensive, ongoing IRM education program designed to convey to Bt cotton users the importance of complying with the IRM program. The program shall include information encouraging Bt cotton users to pursue optional elements of the IRM program relating to refuge configuration and proximity to Bt cotton fields. The education program shall involve the use of multiple media, e.g. face-to-face meetings, mailing written materials, and electronic communications such as by internet or television commercials. Copies of the materials, including the Grower Guide or other technical bulletins, must be submitted to EPA for their records. The program shall involve at least one written communication annually to each WideStrike7 cotton grower separate from the grower agreement. Dow AgroSciences shall coordinate its education program with educational efforts of other organizations, such as the National Cotton Council and state extension programs.

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

3. Beginning January 31, 2006 and annually thereafter, Dow AgroSciences shall provide a report to EPA summarizing the activities it carried out under its education program for the prior year and its plans for its education program during the current year.

4. Dow AgroSciences shall design and implement an ongoing IRM compliance assurance program designed to evaluate the extent to which growers 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 cotton product. Dow AgroSciences shall prepare and submit by January 31, 2005 a written description of its compliance assurance program. Other required features of the program are described in paragraphs 5 - 12 below.

5. Dow AgroSciences shall establish and publicize a Aphased compliance approach, i.e., a guidance document that indicates how Dow AgroSciences 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. The options shall include withdrawal of

the right to purchase WideStrike7 cotton 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.

6. The IRM compliance assurance program shall include an annual survey of a statistically representative sample of WideStrike7 cotton 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. Dow AgroSciences shall provide a written summary of the results of the prior year's survey to EPA by January 31st of each year. Dow AgroSciences shall confer with EPA on the design and content of the survey prior to its implementation for the 2005 growing season and annually, thereafter.

7. Annually, Dow AgroSciences shall revise, and expand as necessary, its compliance assurance program to take into account the information collected through the compliance survey required under paragraph 6] and from other sources. The changes shall address aspects of grower compliance that are not sufficiently high. Dow AgroSciences will confer with the Agency prior to adopting any changes.

8. Dow AgroSciences shall train its representatives who make on-farm visits with WideStrike7 cotton growers to perform assessments of compliance with IRM requirements. In the event that any of these visits results in the identification of a grower who is not in compliance with the IRM program, Dow AgroSciences shall take appropriate action, consistent with its Aphased compliance approach, to promote compliance.

9. Dow AgroSciences shall carry out a program for investigating Atips and complaints that an individual grower or growers is/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, Dow AgroSciences shall take appropriate action, consistent with its Aphased compliance approach.

10. If a grower, who purchases WideStrike7 cotton for planting, was specifically identified as not being in compliance during the previous year, Dow AgroSciences shall visit the grower and evaluate whether that the grower is in compliance with the IRM program for the current year.

11. Beginning January 31, 2006 and annually thereafter, Dow AgroSciences shall provide a report to EPA summarizing the activities it carried out under its compliance assurance program for the prior year and its plans for its compliance assurance program during the current year. Included in that report will be the percent of growers using each refuge option (or combination of options) by region, the approximate number or percent of growers visited on farm by Dow AgroSciences and the results of these visits the number of tips investigated, the percent of growers not in compliance with each refuge option (both size and distance), and the follow-up actions taken.

12. Dow AgroSciences must allow a review of the compliance records by EPA or by a State pesticide regulatory agency if the State agency can demonstrate that the names, personal information, and grower license number of the growers will be kept as confidential business information.

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d. **Insect Resistance Monitoring.**

The registration of Cry1Ac and Cry 1F PIPs expressed in cotton is conditioned on Dow AgroSciences carrying out appropriate programs to detect the emergence of insect resistance as early as possible. Resistance monitoring programs include: surveying insects for potential resistance and collection of information from growers about events that may indicate resistance. Dow AgroSciences should coordinate its monitoring efforts for WideStrike7 with the current resistance monitoring programs for other Bt ICPs. The Agency is imposing the following conditions:

1. Dow AgroSciences will develop and ensure the implementation of a plan for resistance monitoring for Heliothis virescens (tobacco budworm) and Helicoverpa zea (cotton bollworm). The plan shall include provision for conducting annual studies to evaluate any potential change in susceptibility of tobacco budworm and cotton bollworm population to Cry1Ac and Cry1F proteins. Sites must be focused in areas with high risk of resistance (e.g. where adoption is at least 75% of the cotton planted in that county or parish) while overall being distributed throughout the areas where tobacco budworm and cotton bollworm are important pests. The sampling program should be segregated into different sampling regions rather than sampling within each state in which these insects are economic pests At least 20 specific collection sites will be established in time for the 2005 growing season. Discriminating doses for each toxin must be developed for tobacco budworm and cotton bollworm. Dow AgroSciences must provide EPA with the baseline susceptibility data for the Cry1F and Cry1Ac proteins and establish diagnostic/discriminating dose concentrations for both the Cry1F and Cry1Ac proteins by September 1, 2005.

2. Dow AgroSciences will develop and ensure the implementation of a plan for resistance monitoring for Pectinophora gossypiella (pink bollworm). The plan shall include provision for conducting annual studies to evaluate any potential change in susceptibility of pink bollworm population to Cry1Ac and Cry 1F proteins. Collection sites must be focused in areas of high adoption, with the goal of including all states where pink bollworm is an economic pest. Dow AgroSciences must provide EPA with the baseline susceptibility data for the Cry1Ac protein and establish a diagnostic/discriminating dose concentration for both the Cry1Ac proteins by September 1, 2005.

3. Dow AgroSciences shall provide a detailed description to EPA of its resistance monitoring plan by January 31, 2005. 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.

4. Dow AgroSciences must also follow up on grower, extension specialist or consultant reports of less than expected results or control failures (such as increases in damaged squares or bolls) for the target lepidopteran pests (Heliothis virescens (TBW) and Helicoverpa zea (CBW), Pectinophora gossypiella (PBW)) as well as for cabbage looper, soybean looper, , fall armyworm, southern armyworm, and beet armyworm. Dow AgroSciences 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 tobacco budworm, cotton bollworm, or pink bollworm damage occur. Dow AgroSciences will investigate all damage reports. See Remedial Action Plans section below.

5. A report on results of resistance monitoring and investigations of damage reports must be submitted to the Agency annually by September 1st each year for the duration of the conditional registration.

e. **Remedial Action Plans**

Specific remedial action plans are required for WideStrike7 cotton for the purpose of containing

resistance and perhaps eliminating resistance if it develops. One remedial action plan is for the area where pink bollworm is the predominate pest and the other is for the area where tobacco budworm and cotton bollworm are the predominate pests.

1. Remedial Action Plan for Pink Bollworm

   If resistance involves the pink bollworm (Pectinophora gossypiella), Dow AgroSciences must implement the Arizona Bt Cotton Working Group's Remedial Action Plan. Dow AgroSciences must obtain approval from EPA before modifying the Arizona Bt Cotton Working Group's Remedial Action Strategy.

2. Remedial Action Plan for Tobacco Budworm and Cotton Bollworm

   Based upon the Arizona model, a Remedial Action Plan for cotton bollworm and tobacco budworm must be developed and implemented by Dow AgroSciences if suspected or confirmed resistance is found. Dow AgroSciences must submit a remedial action plan (or plans) for tobacco budworm and cotton bollworm to the Agency by January 31, 2006 for approval prior to its implementation. Dow AgroSciences must obtain approval from EPA before modifying the Remedial Action Plan for Cotton Bollworm and Tobacco Budworm.

**Annual Reports**

Dow AgroSciences will provide an annual report to EPA on its Cry1Ac and Cry1F PIPs expressed in cotton on or before January 31st each year. This report must include, but is not limited to, annual sales (both units sold and estimated acres planted) by county and by state (sales data must be summed individually for each state), research status for any outstanding data requirements as covered above, grower education completed last year and planned for the following year with any changes highlighted, the description of grower agreements in place, grower compliance with IRM requirements including compliance with the community refuge option, and insect resistance monitoring results.

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## V. Additional Contact Information

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