Bacillus thuringiensis Vip3Aa19 (OECD Unique Identifier SYN-IR102-7) and modified Cry1Ab (OECD Unique Identifier SYN-IR67B-1) insecticidal proteins and the genetic material necessary for their production in COT102 X COT67B cotton (006499 and 006529) Fact Sheet

Summary

EPA has conditionally registered a new pesticide product containing Syngenta Seeds Inc.'s new active ingredients, Bacillus thuringiensis Vip3Aa19 (OECD Unique Identifier SYN-IR102-7) and modified Cry1Ab (OECD Unique Identifier SYN-IR67B-1) insecticidal proteins and the genetic material necessary for their production in COT102 X COT67B cotton. Syngenta has trademarked this product as VipCot -- the trademark name of VipCot will be used in this document to describe COT102 X COT67B cotton. The Agency has determined that the use of this pesticide is in the public interest and that it will not cause any unreasonable adverse effects on the environment during the time of conditional registration.

The new cotton plant-incorporated protectant, VipCot, produces its own insecticidal proteins within the cotton plant. These proteins were derived from Bacillus thuringiensis (Bt), a naturally occurring soil bacterium. The modified Cry1Ab and Vip3Aa19 proteins used in this product control lepidopteran pests of cotton.

On June 26, 2008, tolerance exemptions under 40 CFR Part 174 were approved for Bacillus thuringiensis modified Cry1Ab protein as identified under OECD Unique Identifier SYN-IR67B-1 in cotton (40 CFR 174.529) and Vip3Aa proteins in corn and cotton (40 CFR 174.501). The exemption for Vip3Aa is inclusive of the Vip3Aa19 protein and its use in cotton.

I. Target Pests/ Application Sites & Methods

- **Pesticide Name:** Bacillus thuringiensis Vip3Aa19 (OECD Unique Identifier SYN-IR102-7) and modified Cry1Ab (OECD Unique Identifier SYN-IR67B-1) insecticidal proteins and the genetic material necessary for their production in COT102 X COT67B cotton

- **Date Registered:** June 26, 2008

- **Registration Number:** 67979-9

- **Trade and Other Names:** VipCot Cotton; COT102 X COT67B Cotton

- **OPP Chemical Code:** 006499 (Vip3Aa19) and 006529 (modified Cry1Ab)

- **Basic Manufacturers**

  Syngenta Seeds, Inc.
  P.O. Box 12257, 3054 East Cornwallis Road
  Research Triangle Park, NC 27709-2257

- **Type of Pesticide:** Plant-Incorporated Protectant

- **Use Sites:** Cotton

- **Target pests:** Tobacco budworm, Cotton bollworm, Pink bollworm

II. Science Assessment

A. Product Characterization

VipCot (COT102 x COT67B) was developed by conventional breeding of COT102 (Vip3Aa19) plants with COT67B (modified Cry1Ab) plants.

Event COT102 cotton, which was developed by *Agrobacterium*-mediated transformation of cotton using elements of a vector referred to as both pNOV3001 and pCOT1, expresses the insecticidal protein, Vip3Aa19 as well as a selectable marker, hygromycin B phosphotransferase (APH4). The Vip3Aa19 protein is intended to control several lepidopteran pests of cotton including *Heliothis virescens* (tobacco budworm, TBW), *Helicoverpa zea* (cotton bollworm, CBW), *Spodoptera frugiperda* (fall armyworm), *Spodoptera exigua* (beet armyworm), and *Trichoplusia n*i (cabbage looper). Vip3A is a vegetative (i.e., produced during the vegetative stage of bacterial growth) insecticidal protein from *Bacillus thuringiensis* (*Bt*), a gram positive bacterium commonly found in soil.

Event COT67B cotton, which was developed by *Agrobacterium*-mediated transformation of cotton using elements of vectors pNOV4641 and pNOV1914, expresses the insecticidal protein, modified Cry1Ab. This protein contains an additional 26 amino acid sequence at the C-terminus (termed the 'Geiser motif'). The modified Cry1Ab protein is intended to control several lepidopteran pests of cotton including *Heliothis virescens* (tobacco budworm), Helicoverpa zea (cotton bollworm), Pectinophora gossypiella (pink bollworm), *Spodoptera frugiperda* (fall armyworm), *Spodoptera exigua* (beet armyworm), and *Trichoplusia ni* (cabbage looper).

DNA characterization (i.e., Southern blot analysis) was used to confirm the integrity of the COT102 and COT67B inserts in the stacked product COT102 x COT67B. Samples from COT102 x COT67B cotton gave the same results as those observed for the individual events, indicating that the molecular characterization data provided for the individual events are also applicable to COT102 x COT67B.

Protein expression data, together with data indicating that there is no evidence of either a synergistic or antagonistic interaction between Vip3Aa19 and modified Cry1Ab in cotton bollworm or tobacco budworm, demonstrate that data on the individual events and individual proteins can be used to support the safety of the COT102 x COT67B (VipCot) combined product.

B. Human Health Assessment

There is a reasonable certainty that no harm will result from aggregate exposure to the U.S. population, including infants and children, to the modified Cry1Ab and Vip3Aa19 proteins. This includes all anticipated dietary exposures and all other exposures for which there is reliable information. The Agency has arrived at this conclusion because no toxicity to mammals has been observed, nor any indication of allergenicity potential for the plant-incorporated protectant.

Syngenta submitted four acute oral toxicity studies conducted on mice, which all indicated that Vip3Aa is non-toxic to humans. Three of the studies were conducted with microbially-produced Vip3Aa proteins with slight variations in amino acid sequence (1-2 amino acid differences), and one study was conduced with transgenic corn leaf tissue as the test material. No treatment-related adverse effects were observed in any of the studies. The oral LD50 for mice (males, females, and combined) was greater than 3675 mg Vip3Aa/kg body weight (the highest dose tested). For modified Cry1Ab, an acute oral toxicity study in mice indicated that the protein is non-toxic to humans. Groups of five male and five female mice were given 0 or 1830 mg/kg bodyweight microbially-produced modified Cry1Ab by oral gavage

as a single dose. There were no effects on clinical condition, body weight, food consumption, clinical pathology, organ weight, or macroscopic or microscopic pathology that were attributed to the test substance.

Since Vip3Aa and modified Cry1Ab are proteins, allergenic potential was also considered. Currently, no definitive tests for determining the allergenic potential of novel proteins exist. Therefore, EPA uses a weight-of-evidence approach where the following factors are considered: source of the trait; amino acid sequence comparison with known allergens; and biochemical properties of the protein, including in vitro digestibility in simulated gastric fluid (SGF) and glycosylation. This approach is consistent with the approach outlined in the Annex to the Codex Alimentarius "Guideline for the Conduct of Food Safety Assessment of Foods Derived from Recombinant-DNA Plants." The allergenicity assessment for Vip3Aa and modified Cry1Ab is as follows:

1. Source of the trait. Bacillus thuringiensis is not considered to be a source of allergenic proteins.

2. Amino acid sequence. A comparison of the amino acid sequence of Vip3Aa19 and modified Cry1Ab with known allergens showed no significant sequence identity over 80 amino acids or identity at the level of eight contiguous amino acid residues.

3. Digestibility. The Vip3Aa and modified Cry1Ab proteins were digested rapidly in simulated gastric fluid containing pepsin.

4. Glycosylation. Vip3Aa and modified Cry1Ab (expressed in cotton) were shown not to be glycosylated.

5. Conclusion. Considering all of the available information, EPA has concluded that the potential for Vip3Aa and modified Cry1Ab to be food allergens is minimal.

C. Environmental Assessment

The Agency concludes that for the VipCot cotton breeding stack (COT102 x COT67B, containing modified Cry1Ab and Vip3Aa19) no unreasonable adverse effects will result to the environment or any federally-listed threatened or endangered species

from commercial cultivation of COT102 x COT67B cotton. This conclusion is based on prior assessments conducted on Vip3Aa and Cry1Ab proteins individually. Furthermore, the Agency has determined that Events COT102, COT67B, and VipCot cotton will have No Effect (NE) on endangered and/or threatened species listed by the US Fish and Wildlife Service (USFWS) and the National Marine Fisheries Services (NMFS), including mammals, birds, terrestrial and aquatic plants, and invertebrate species. Therefore, no consultation with the USFWS is required under the Endangered Species Act.

The Agency believes that cultivation of VipCot cotton may result in fewer adverse impacts to non-target organisms than result from the use of chemical pesticides. Under normal circumstances, Bt 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. Therefore, the overall result of cultivation of VipCot cotton, expressing Vip3Aa19 and modified Cry1Ab proteins, is that the number of chemical insecticide applications for non-target pest control will be reduced for management of multiple pest problems.

D. Insect Resistance Management

In order to reduce the possibility of the target pests developing resistance to Vip3Aa19 and modified Cry1Ab (as expressed in VipCot cotton), EPA is requiring Syngenta Seeds, Inc. to ensure that a portion of the planted acreage of this product be set aside where non-Bt cotton will be grown to serve as a "refuge." Under the established refuge strategy for Bt cotton, growers can choose from three structured refuge options:

> Option 1: 95:5 external structured, unsprayed refuge; 150 ft wide, within ½ mile of edge of field.
> Option 2: 80:20 external sprayed refuge; within 1 linear mile, preferably ½ mile, of edge of field.
> Option 3: 95:5 embedded refuge; contiguous or within 1 mile2 of field and 150 ft wide.

In addition to the refuge options above, growers of VipCot may participate in a community refuge plan in which multiple growers contribute to the overall required refuge acres by planting 20% external, sprayed or 5% external, unsprayed refuge.

BPPD has concluded that based on the modeling, dose, and efficacy studies, the requested refuge options 1-3 and community refuge plan are acceptable for VipCot cotton. Syngenta will also be required to develop and conduct a resistance monitoring program for Vip3Aa19 and modified Cry1Ab with the major target pests (cotton bollworm, tobacco budworm, and pink bollworm). Additional requirements for remedial action (in the event of resistance), grower education, compliance assurance, and annual reported will also be implemented for VipCot as terms of registration.

E. Benefits

Results of efficacy trials conducted in 2005 and 2006 show that VipCot cotton and its single event cotton isolines provide good protection against three major cotton pests: tobacco budworm (Heliothis virescens), cotton bollworm (Helicoverpa zea), and pink bollworm (Pectinophora gossypiella). The Vip3Aa19 protein expressed in VipCot cotton has not been previously registered and provides a unique mode of action. When coupled with modified Cry1Ab in VipCot, the proteins have the potential to provide benefits for insect resistance management including: high-dose (for both proteins expressed together) against the major target pests, lack of cross-resistance (Vip3Aa19), and the potential to delay development of resistance in other cotton varieties expressing Cry toxins. As an additional registered Bt cotton product, VipCot will likely result in direct and indirect human and environmental health benefits by providing growers with an additional choice of Bt cotton option and the potential to increase grower choice and price competition, resulting in lower seed prices for consumers and higher adoption rates. Registration of VipCot may also result in further reduction of chemical insecticide use by growers.

F. Public Interest Finding

To grant a conditional registration under Section 3(c)(7)(C) of FIFRA, EPA must determine that such conditional registration will, inter alia, be in the public interest. EPA determines whether conditional registration of a pesticide is in the public interest in accordance with the criteria set forth at 51 Fed. Reg. 7628 (Conditional Registration of New Pesticides, March 5 1986). On the basis of analysis utilizing these criteria, EPA concludes that the use of VipCot protected cotton will be in the public interest, because it results in direct and indirect human and environmental health benefits by providing growers with an additional Bt cotton product which has the potential to extend the useful life of Bt cotton technology generally due to a novel mode of action (Vip3Aa19) and low likelihood of cross-resistance with other Bt Cry proteins.

III. Terms and Conditions of the Registration

0. The registration will automatically expire on midnight September 30, 2011.

1. All data required for registration of the product under FIFRA § 3(c)(5) must be submitted when the Agency requires all registrants of similar products to submit such data.

2. The following restrictions regarding gene flow are required:

   The following information regarding commercial production must be included in the grower guide for VipCot Cotton:

   a. No planting of VipCot cotton is permitted south of Route 60 (near Tampa) in Florida.
   b. Commercial culture of VipCot cotton is prohibited in Hawaii, Puerto Rico, and the U.S. Virgin Islands.

   The following information regarding test plots and seed production must be included on bags of VipCot cotton intended for these purposes:

   c. Test plots or breeding nurseries, regardless of the plot size, established in Hawaii must not be planted within 3 miles of Gossypium tomentosum;
   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.

3. The following restrictions regarding Insect Resistance Management are required:

   VipCot Bt cotton is not permitted to be planted in the following counties of the Texas panhandle: Dallam, Sherman, Hansford, Ochiltree, Lipscomb, Hartley, Moore, Hutchinson, Roberts, and Carson.

4. The following data and/or information must be submitted in the time frames listed:

Study Type	Required Data	Due Date
Residue Analytical Method - Plants (Harmonized Test	An independent lab validation of the "SeedChek" analytical method for the detection of Vip3Aa19 and modified Cry1Ab. You must also agree to provide to the EPA laboratory (Ft. Meade, MD) methodology and/or reagents necessary for	May 1, 2009

Guideline 860.1340)	validation of such analytical method within 6 months from the date that the Agency requests them.	
Aquatic Invertebrate Toxicity (Harmonized Test Guideline 885.4240)	A 7-14 day Daphnia study as per the Harmonized Test Guideline 885.4240 guideline must be submitted as a condition of registration. Alternatively, a dietary study of the effects on an aquatic invertebrate, representing the functional group of a leaf shredder in headwater streams, can be performed and submitted in lieu of the 7-14 day Daphnia study. Separate studies for Vip3Aa (COT102) and modified Cry1Ab (COT67B) must be preformed.	May 1, 2009
Insect Resistance Management - Resistance Monitoring	A detailed resistance monitoring plan for the major pests of VipCot cotton: tobacco budworm, cotton bollworm, and pink bollworm.	Within 90 days of the date of registration
Insect Resistance Management - Resistance Monitoring	Baseline susceptibility and diagnostic concentration determinations for tobacco budworm, cotton bollworm, and pink bollworm to Vip3Aa19 and modified Cry1Ab.	January 31, 2009
Insect Resistance Management - Compliance	A compliance assurance program (CAP) for VipCot must be submitted and must include a "phased compliance approach" that outlines instances of non-compliance to the IRM requirements and options of responding to non-compliant growers.	Within 90 days of the date of registration
Insect Resistance Management - Compliance	A copy of the grower agreement/stewardship documents and written description of a system assuring that growers will sign grower agreement must be submitted.	Within 90 days of the date of registration
Insect Resistance Management – Remedial Action Plans	A final remedial action plan for tobacco budworm and cotton bollworm. The remedial action plan must include definitions of "suspected" and "confirmed" resistance and steps to take in the event of confirmed resistance.	Within 90 days of the date of registration

5. The following Insect Resistance Management Program is required for VipCot:

. The required IRM program for VipCot Bt cotton must have the following elements:
   - Requirements relating to creation of a non-Bt cotton refuge in conjunction with the planting of any acreage of VipCot Bt cotton.
   - Requirements for Syngenta Seeds to prepare and require VipCot Bt cotton users to sign "grower agreements" which impose binding contractual obligations on the grower to comply with the refuge requirements;
   - Requirements for Syngenta Seeds to develop, implement, and report to EPA on programs to educate growers about IRM requirements;
   - Requirements for Syngenta Seeds to develop, implement, and report to EPA on programs to evaluate and promote growers' compliance with IRM requirements;
   - Requirements for Syngenta Seeds to develop, implement, and report to EPA on programs to evaluate whether there are statistically significant and biologically relevant changes in susceptibility to the Vip3Aa19 and modified Cry1Ab proteins in the target insects;
   - Requirements for Syngenta Seeds to develop, and if triggered, to implement a "remedial action plan" which would contain measures Syngenta Seeds 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 VipCot cotton must employ one of the following structured refuge options:

1. External, Unsprayed Refuge

nsure that at least 5 acres of non-Bt cotton (refuge cotton) is planted for every 95 acres of VipCot 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 VipCot 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 VipCot cotton. Ensure that a non-Bt cotton refuge is maintained within at least ½ 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 VipCot 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 VipCot cotton. The non-Bt cotton may be treated with sterile insects, insecticides (excluding foliar Bt kurstaki 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 ½ mile or closer) from the Bt cotton fields.

3. Embedded Refuge

Ensure that at least 5 acres of non-Bt cotton (refuge cotton) are planted for every 95 acres of VipCot cotton (total of 100A). The refuge cotton must be embedded as a

contiguous block within the VipCot field, but not at one edge of the field (i.e., refuge block(s) surrounded by Bt cotton). For very large fields, multiple blocks around 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 Bt 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 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 VipCot cotton. The non-Bt cotton may be treated with sterile insects, insecticides (excluding foliar Bt kurstaki products), or pheromones labeled for control of the tobacco budworm, cotton bollworm, or pink bollworm whenever the entire field is treated. The refuge may not be treated independently of the surrounding VipCot field in which it is embedded (or fields within a field unit).

4. Embedded Refuge (for pink bollworm only)

Refuge cotton must be planted as at least one single non-Bt cotton row for every six to ten rows of VipCot cotton. The refuge may be treated with sterile insects, any insecticide (excluding foliar Bt kurstaki 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 VipCot cotton. There is no field unit option.

5. Community Refuge Option

This option allows for 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 refuge options. The community refuge for insect resistance management must meet the requirements of the 5% external, unsprayed and/or 20% sprayed option, or an appropriate combination of the two options. The community refuge program must consist of the following:

There will be a community refuge coordinator for each community. Each community refuge coordinator must submit a signed community refuge form listing all of the participants in the community to Syngenta Seeds by July 1st annually. Syngenta Seeds 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 Syngenta Seeds or EPA as part of the compliance program.

On an annual basis, Syngenta Seeds 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 Syngenta Seeds under section d. below.

Beginning January 31, 2010 and annually each January 31st, Syngenta Seeds must provide a written report to EPA annually on community refuge use and compliance. The community refuge report may be combined in a single report with other compliance activities.

On an annual basis, Syngenta Seeds 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.

b. Grower Agreements

The following provisions regarding grower agreements are required for VipCot:

0. Persons purchasing the VipCot cotton product must sign a grower agreement. The term "grower agreement" refers to any grower purchase contract, license agreement, or similar legal document.

1. 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.

2. Syngenta Seeds must implement 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. A

description of the system must be submitted to EPA within 90 days from the date of registration.

3. Syngenta Seeds must use an approved grower agreement and must submit to EPA within 90 days from the date of registration a copy of that agreement and any specific stewardship documents referenced in the grower agreement. If Syngenta Seeds 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, Syngenta Seeds must submit to EPA the text of such changes to ensure the agreement is consistent with the terms and conditions of this amendment.

4. Syngenta Seeds must implement an approved system which is reasonably likely to assure that persons purchasing VipCot cotton sign grower agreement(s). A description of the system must be submitted to EPA within 90 days from the date of registration.

5. Syngenta Seeds shall maintain records of all VipCot cotton grower agreements for a period of three years from December 31 of the year in which the agreement was signed.

6. Beginning on January 31, 2010 and annually thereafter, Syngenta Seeds shall provide EPA with a report on the number of units of the VipCot 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.

7. Syngenta Seeds 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.

c. IRM Education and IRM Compliance Monitoring Programs

The following IRM education and compliance monitoring programs must be implemented for VipCot:

0. Syngenta Seeds must design and implement a comprehensive, ongoing IRM education program designed to convey to VipCot 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 VipCot cotton grower separate from the grower agreement. Syngenta Seeds shall coordinate its education program with educational efforts of other organizations, such as the National Cotton Council and state extension programs.

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

2. Beginning January 31, 2009 and annually thereafter, Syngenta Seeds 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.

3. Syngenta Seeds shall design and implement an 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 VipCot cotton. Syngenta Seeds must prepare and submit within 90 days of the date of registration a written description of the compliance assurance program. Other required features of the program are described in paragraphs 5 - 12 below.

4. Syngenta Seeds shall establish and publicize a "phased compliance approach," i.e., a guidance document that indicates how Syngenta Seeds 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 VipCot 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.

5. The IRM compliance assurance program shall include an annual survey of a statistically representative sample of VipCot 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. Syngenta Seeds shall provide a written summary of the results of the prior year's survey to EPA by January 31st of each year. Syngenta Seeds shall confer with EPA on the design and content of the survey prior to its implementation.

6. Annually, Syngenta Seeds 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. Syngenta Seeds will confer with EPA prior to adopting any changes.

7. Syngenta Seeds must conduct an annual on-farm assessment program. Syngenta Seeds shall train its representatives who make on-farm visits with VipCot 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, Syngenta Seeds shall take appropriate action, consistent with its "phased compliance approach," to promote compliance.

8. Syngenta Seeds shall carry out a program for investigating "tips 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, Syngenta Seeds shall take appropriate action, consistent with its "phased compliance approach."

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

10. Beginning January 31, 2010 and annually thereafter, Syngenta Seeds 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 Syngenta Seeds 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.

11. Syngenta Seeds 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.

d. Insect Resistance Monitoring.

The registration of Vip3Aa19 and modified Cry1Ab PIPs expressed in VipCot cotton is conditioned on Syngenta Seeds 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. Syngenta Seeds should coordinate its monitoring efforts VipCot with the current resistance monitoring programs for other registered Bt cotton products. The following resistance monitoring terms are required for VipCot:

0. Syngenta Seeds must submit a VipCot cotton (Vip3Aa19 and modified Cry1Ab toxins) resistance monitoring plan for Heliothis virescens (tobacco budworm), Helicoverpa zea (cotton bollworm), and Pectinophora gossypiella (pink bollworm) to EPA within 90 days of the date of registration. The monitoring program description must include sampling (number of locations and samples per location), sampling methodology, bioassay methodology, standardization procedures, detection technique and sensitivity, and the statistical analysis of the probability of detecting resistance. Collection sites must be focused in areas of high adoption of VipCot for tobacco budworm, cotton bollworm, and pink bollworm. Syngenta Seeds shall provide baseline susceptibility and diagnostic concentration determinations for tobacco budworm, cotton bollworm, and pink bollworm to Vip3Aa19 and modified Cry1Ab by January 31, 2009.

1. The following testing scheme for survivors of the diagnostic or discriminating concentrations (or identified survivors of any resistance detection method) must be implemented:
    1. Determine if the observed effect is heritable;
    2. Determine if the increased tolerance can be observed in the field (i.e., survive on VipCot cotton plants);
    3. Determine if the effect is due to resistance,
    4. Determine the nature of resistance (dominant, recessive),
    5. Determine the resistance allele frequency,
    6. Determine, in subsequent years, whether the resistance allele frequency is increasing, and
    7. Determine the geographic extent of the resistance allele (or alleles) distribution.

    Should the resistance allele frequency be increasing and spreading, a specific remedial action plan should be designed to mitigate the extent of Bt resistance. See section f ("Remedial Action Plans") below.

2. Syngenta Seeds 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, saltmarsh caterpillar, black cutworm, fall armyworm, southern armyworm, and European corn borer. Syngenta Seeds 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. Syngenta Seeds will investigate all damage reports. See Remedial Action Plans (section f) below.

3. Syngenta Seeds must provide to EPA for review and approval any revisions to the tobacco budworm, cotton bollworm, and pink bollworm resistance monitoring plans prior to their implementation.

4. Beginning in 2009, 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 VipCot cotton for the purpose of containing resistance and perhaps eliminating resistance if it develops. One remedial action plan is for the areas where pink bollworm is the predominate pest and the other is for the areas where tobacco budworm and cotton bollworm are the predominate pests.

0. Remedial Action Plan for Pink Bollworm

If resistance involves the pink bollworm (Pectinophora gossypiella), Syngenta Seeds must implement the Arizona Bt Cotton Working Group's Remedial Action Plan. Syngenta Seeds must obtain approval from EPA before modifying the Arizona Bt Cotton Working Group's Remedial Action Strategy. The Arizona Bt Cotton Working Group's Remedial Action Plan can be found in Enclosure 1.

1. Remedial Action Plan for Tobacco Budworm and Cotton Bollworm

If resistance involves the tobacco budworm (Heliothis virescens) and/or the cotton bollworm (Helicoverpa zea), Syngenta Seeds must implement a Remedial Action Plan approved by EPA. Once approved, Syngenta Seeds must obtain approval from EPA before modifying the Remedial Action Plan for tobacco budworm and cotton bollworm. A final remedial action plan for tobacco budworm and cotton bollworm must be submitted within 90 days of the date of registration. This remedial action plan must include definitions of "suspected" and "confirmed" resistance and steps to take in the event of confirmed resistance. The plan should be based on the steps described in Syngenta Seed's IRM submission, including:

- Notification to the Agency within 30 days of resistance confirmation;
- Notification to affected customers and extension agents about confirmed resistance;
- Encourage affected customers and extension agents to employ alternative lepidopteran control measures;
- Cease sale and distribution of VipCot cotton in affected area;
- Devise long-term resistance management action plan according to characteristics of resistance event and local agronomic needs.

f. Annual Reporting

The annual reporting requirements for VipCot are as follows:

0. Annual Sales: reported and summed by state (county level data available by request), January 31st each year, beginning in 2010;

1. Grower Agreements: number of units of Bt 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 31st each year, beginning in 2010;

2. Grower Education: substantive changes to education program completed previous year, January 31st each year, beginning in 2009;

3. Compliance Assurance Plan: Compliance Assurance Program activities and results, January 31st each year, beginning in 2010;

4. Compliance Survey Results: to include annual survey results and plans for the next year; full report January 31st each year, beginning in 2010;

5. Insect Resistance Monitoring Results: results of monitoring and investigations of damage reports, September 1 each year, beginning in 2009.

IV. Additional Contact Information

Ombudsman, Biopesticides and Pollution Prevention Division (7511P)
Office of Pesticide Programs
Environmental Protection Agency
1200 Pennsylvania Avenue, NW
Washington, D.C. 20460