Product Safety Assessment

WideStrike™3 Insect Protection

Select a Topic:

- Names
- Product Overview
- Manufacture of Product: Plant Transformation Process
- Product Description
- Product Uses
- Exposure Potential
- Health Information
- Environmental Information
- Regulatory Information
- Additional Information

Names

- Cry1F
- Cry1Ac
- Vip3A
- Bacillus thuringiensis proteins
- Cry1F x Cry1Ac x Vip3A
- DAS-24236-5 X DAS-21023-5 X SYN-IR102-7

- Bt proteins
- 281-24-236
- DAS-21023-5
- DAS-24236-5
- SYN-IR102-7
- DAS-24236-5 X DAS-21023-5
- COT102

- Vip3Aa19
- WideStrike™3 Insect Protection
- WideStrike 3
- WideStrike

Product Overview

- WideStrike™3 Insect Protection cotton is a combined trait product consisting of three traits to provide insect protection in cotton. WideStrike 3 Insect Protection was developed by Dow AgroSciences LLC and utilizes Dow AgroSciences’ WideStrike cotton conventionally bred with cotton containing Syngenta’s event COT102.

- WideStrike 3 contains genes that express the insecticidal proteins Cry1F, Cry1Ac, and Vip3A, providing three modes of action. The genes originate from different strains of a naturally occurring soil microorganism, Bacillus thuringiensis (Bt). For more information on Bt, Cry1F, Cry1Ac, and Vip3A, see Product Description. WideStrike 3 Insect Protection offers a high level of protection against several economically significant insect pests including tobacco budworm, bollworm, pink bollworm, fall armyworm, beet armyworm, loopers, and several other species listed in the Product Description.

- WideStrike 3 also expresses the selectable markers phosphinothricin acetyltransferase (PAT) and hygromycin B phosphotransferase (APH4).

- WideStrike 3 Insect Protection provides season-long, whole-plant protection against feeding damage by certain lepidopteran insect species throughout the growing season. Full-season protection against insect damage facilitates cotton varieties reaching their full genetic growing and yield potential. WideStrike 3 Insect Protection also can increase farmers’ productivity by reducing various inputs (e.g., labor, fuel, equipment, insecticides) typically required for conventional insect control programs. For further details, see Product Uses & Regulatory Information.

- The presence of three insecticidal proteins that differ in their modes of action reduces the potential for target insect populations to evolve resistance to WideStrike 3 compared with single- and dual-mode of action Bt cotton.

- On the basis of rigorous testing and analysis of data on agronomic performance, disease and insect susceptibility, and compositional profiles of the seeds and fiber, regulatory agencies concluded that cotton with WideStrike Insect Protection is similar to conventional, non-transgenic cotton. The primary route of potential exposure occurs through ingestion. The proteins in

© Trademark of The Dow Chemical Company (“Dow”) or an affiliated Company of Dow

Created: March 4, 2015
The Dow Chemical Company
Page 1 of 7
WideStrike™ 3 Insect Protection are present in common soil organisms, so exposure can also occur naturally but at much lower levels. The insecticidal proteins have no known effects on microorganisms, plants or animals (other than lepidopteran insects), including humans and livestock. For further details, see Exposure Potential and Health Information.

- Extensive safety data were provided to the U.S. Department of Agriculture (USDA), Environmental Protection Agency (EPA), and the Food and Drug Administration (FDA) before cotton with WideStrike™ 3 Insect Protection was granted non-regulated status for cultivation in the USA. For further details, see Environmental Information and Health Information.

**Back to top**

**Manufacture of Product**

Plant biotechnology can be defined as a precise process in which scientific techniques (e.g., genetic modifications) are used to develop useful and beneficial plants with desirable “traits.” A trait refers to characteristics that are associated with the plant, including agronomic qualities and resistance to insects, herbicides, and disease. Plant biotechnology first identifies the genes responsible for the desired trait and then inserts them into the plant genome. The trait may come from the plant itself or from a very specific gene of another organism, such as a bacterium.

DNA is the “genetic backbone” found in all microorganisms, plants, animals, and humans. Sequences of nucleotides (bases) in DNA encode the organisms’ genes. Organisms that carry DNA sequences introduced via genetic modification are referred to as transgenic, and the introduced DNA sequence is termed a transgene. The first step in creating WideStrike™ 3 cotton was the isolation and replication of gene sequences from different strains of *Bacillus thuringiensis* that were responsible for the expression of the desired insecticidal proteins (Cry1F, Cry1Ac, and Vip3A). The isolated gene sequences were then chemically re-synthesized to create the final transgenes, including plant-preferred DNA sequences that optimize expression of the insecticidal proteins in the plant.

**WideStrike™ 3 Cotton** – WideStrike 3 Cotton was produced through conventional breeding by first crossing Cry1F cotton with Cry1Ac cotton to produce WideStrike cotton, and subsequently crossing WideStrike cotton with COT102 cotton.

**WideStrike™ Cotton** – Details on the plant transformation process used to produce WideStrike Cotton are found in the WideStrike Product Safety Assessment. WideStrike cotton contains the combined events DAS-21023-5 (which produces Cry1Ac) and DAS-24236-5 (which produces Cry1F).

**COT102 Cotton** – Event COT102 cotton was produced by *Agrobacterium tumefaciens*-mediated transformation of hypocotyls of *Gossypium hirsutum* L. cultivar Coker 312 with plasmid pNOV3001 (referred to as pCOT1). Through the genetic transformation, COT102 cotton contains an insecticidal Vip3A(a) gene derived from *Bacillus thuringiensis* (Bt) strain AB88 under the control of the actin-2 promoter derived from Arabidopsis thaliana, which confers expression of the VIP3A(a) protein throughout the plant with the exception of the fiber and nectar. Event COT102 cotton also contains the selectable marker gene aph4 derived from *Escherichia coli*. The aph4 gene encodes the enzyme hygromycin B phosphotransferase and its expression is controlled by the ubiquitin-3 promoter from A. thaliana.

Numerous tests and checks are in place to ensure quality of the genetically modified seed and, ultimately, the generations of seed formed afterward. Both WideStrike™ and COT102 cotton have been extensively tested for the stability of the trait through several growing cycles, for safety to animals, humans, and the environment, and for retention of nutritional value. The individual traits have been granted non-regulated status by the USDA, FDA, and EPA, as well as other regulatory agencies globally.

**WideStrike 3 Insect Protection** cotton, produced by conventional breeding of WideStrike with COT102 cotton, has been registered by the US EPA, and approved by other regulatory agencies globally. WideStrike 3 is sold to farmers to grow for production of fiber, cottonseed meal and hulls for livestock.

™ Trademark of The Dow Chemical Company (“Dow”) or an affiliated Company of Dow
consumption, and cottonseed oil for human consumption. Successful development of genetically modified crops requires a deep understanding of the food chain, biology, regulatory requirements, and more.

Back to top

Product Description

The product purchased by growers is seed cotton with WideStrike™3 Insect Protection. Protection against insect pests is achieved by conventionally breeding WideStrike cotton with Event COT102 cotton, rendering the cotton plants resistant to certain insect pests. The expression of the proteins (Cry1F, Cry1Ac, and Vip3A) by the introduced genes (cry1F, cry1Ac, and COT102) allows the plants to produce proteins similar to naturally occurring soil bacterium from which the genes were isolated. Following is background information about each protein and its effects.

Cry1F – The cry1F gene, isolated from the common soil bacterium Bacillus thuringiensis var. aizawai (often referred to as Bt), produces the Cry1F protein.

Cry1Ac – The cry1Ac gene (which produces the Cry1Ac protein) was isolated from a different strain of Bacillus thuringiensis (subsp. kurstaki).

Vip3A – The COT102 gene (which produces the Vip3A protein) produces a variant of the naturally occurring Vip3Aa1 protein isolated from Bacillus thuringiensis strain AB88. Vip3A is a vegetative (i.e., produced during the vegetative stage of bacterial growth) insecticidal protein from Bacillus thuringiensis.

Bt – Bacillus thuringiensis (Bt) was first discovered in 1901 by the Japanese biologist S. Ishiwatari as the source of disease that was killing large populations of silkworms. Bt was first used as an insecticide in 1920, and spray formulations containing either Bt bacteria or Bt proteins have been used for more than 40 years for crop protection, including Bt-based insecticides for organic farming operations. The development and use of EPA-approved Bt insecticides as an alternative to synthetic chemical insecticides expanded in the 1980s.

Beginning in the 1980s, the genes responsible for making Bt proteins were isolated and transferred into crop plants. In the United States, Bt was commercially approved first in transgenic cotton seed in 1995. Compared with conventional Bt spray formulations, transgenic plants expressing Bt proteins provide much more effective insect protection throughout the growing season. In addition to the Bt proteins Cry1F, Cry1Ac, Vip3A other Bt proteins have been used to genetically modify commercial crops including potatoes, corn, and cotton.

Bt proteins must be ingested to kill the insect. A susceptible immature insect (larva) eats the protein, which then binds to specific receptors in the larva’s gut. Binding initiates a cascade of effects in the larva that ultimately leads to death.

Bt proteins are highly selective against certain groups and/or species of insects. The Cry1F, Cry1Ac and Vip3A proteins affect larvae of damaging lepidopteran (moth) species on cotton, including tobacco budworm (Heliothis virescens), bollworm (Helicoverpa zea), fall armyworm (Spodoptera frugiperda), southern armyworm (Spodoptera eridania), beet armyworm (Spodoptera exigua), pink bollworm (Pectinophora gossypiella), cabbage looper (Trichoplistia ni), soybean looper (Chrysodeix includens), saltmarsh caterpillar (Estigmene acrea), European corn borer (Ostrinia nubilalis), cotton leaf perforator (Bucculatrix thurburiella), omnivorous leafroller (Platynota sulatana), and citrus peelminer (Marmar gulos) in the United States.

Cry1F, Cry1Ac, and Vip3Aa proteins are expressed at effective concentrations throughout the growing season of WideStrike 3 cotton. Targeted insect larvae are exposed to the insecticidal proteins when...
feeding on WideStrike™3 plants at all stages in their life cycle. Thus, WideStrike 3 cotton provides season-long protection against targeted pests.

Cry1F, Cry1Ac, and Vip3Aa proteins do not adversely affect beneficial insects or other organisms, including honey bees, earthworms, lady beetles, springtails, green lacewings, predatory ants, and parasitic wasps. For more information, see Environmental Information.

**APH4** – Hygromycin B phosphotransferase (APH4) is a selectable marker used during initial selection of transformed cells. This enzyme catalyzes the phosphorylation of hygromycin and some related aminoglycosides.

**PAT** – Phosphinothricin-N-acetyltransferase (PAT) is an enzyme isolated from the common soil bacterium Streptomyces viridochromogenes. Used as the “marker gene,” PAT imparts transgenic plants with a certain amount of tolerance to the herbicide glufosinate-ammonium and facilitates the selection of plants expressing Cry1F and Cry1Ac. Glufosinate-ammonium was developed from the same bacterium as PAT and causes ammonia to build up in the plant tissues. Excess ammonia disrupts cell membranes and stops photosynthesis, which eventually kills the plants (either non-transformed cotton or certain species of weeds). PAT essentially is the antidote to glufosinate-ammonium, allowing the plant to detoxify the chemical. However, because the tolerance to glufosinate-ammonium herbicides provided by the pat gene in WideStrike™3 Insect Protection cotton is not equivalent to the glufosinate-ammonium herbicide tolerance of LibertyLink® cotton, the use of glufosinate-ammonium herbicides on WideStrike 3 Cotton is not labeled.

**Product Uses**

**Product Uses & Regulatory Information**

When a stacked combination of traits (e.g., WideStrike™ cotton crossed with COT102 cotton) is created, field and laboratory testing are conducted to verify that the crop performs as expected and that the introduced genes continue to function as they did in the varieties. The safety assessment for the breeding stacks (e.g., WideStrike 3 cotton) relies on the safety assessment of the individual varieties.

Cotton seed with WideStrike 3 Insect Protection is used to produce high-quality cotton with greater efficiency by ensuring higher yields and less loss due to insect damage to the cotton plants. WideStrike 3 Insect Protection also greatly reduces the number of pesticide applications usually required for common lepidopteran insect pests. WideStrike 3 cotton may be used for production of fiber, cottonseed meal and hulls for livestock consumption, and cottonseed oil for human consumption. Regulations may exist that govern the manufacture, sale, transportation, use, and/or disposal of cotton with the WideStrike 3 traits, especially if the seed is treated with an insecticide or fungicide. These regulations may vary by city, state, country or geographic region. Please review the product information for the specific product being used.

**Exposure Potential**

The Cry1F, Cry1Ac, and Vip3A insecticidal proteins are present in common, non-pathogenic soil bacteria, so exposure occurs naturally and without concern. WideStrike™3 cotton may be used for production of fiber, cottonseed meal and hulls for livestock consumption, and cottonseed oil for human consumption. Thus, consumers may wear or eat processed cotton products from cotton containing WideStrike 3 traits. Moreover, none of the expressed proteins are detectable in the oil, meal, and hulls of WideStrike 3 cotton. Processed linters are composed of pure (>99%) cellulose and are treated with
heat and solvent that remove and destroy residual protein. A number of studies have been conducted to demonstrate the human and animal safety of proteins present in WideStrike™3 cotton. None of the proteins are associated with toxicity or allergenicity. See Health Information.

Farmers and cotton-gin workers may be exposed to harvested cotton products. Standard workplace procedures and precautions used when handling other cultivars of G. hirsutum should be followed when handling WideStrike 3 Insect Protection cotton. See Health Information.

Health Information

On the basis of rigorous testing, WideStrike™3 Insect Protection has received full food, feed, and environmental registration from regulatory agencies in the United States. The US EPA found that there is reasonable certainty that no harm will result from exposure to the proteins in WideStrike 3 Insect Protection cotton. Analysis of compositional profiles of the WideStrike seeds and fiber indicate that the profiles are similar to their non-transgenic parent counterparts and other cultivars of G. hirsutum. None of the expressed proteins in WideStrike 3 Insect Protection have biochemical characteristics or homology (relevant similarities) with known food allergens or toxins, indicating that WideStrike 3 Insect Protection is highly unlikely to pose any risk of allergic reaction.

Acute mouse oral toxicity studies concluded that the proteins expressed in WideStrike 3 cotton do not pose any toxicological risk to human and animals. There are no differences in the nutrient composition of respective oil, meal, or hull products between WideStrike 3 and conventional cotton. Poultry feeding studies have demonstrated no difference in body weight gains between chickens fed with WideStrike 3 cottonseed meal and conventional cottonseed meal.

Seed Treatments—Agricultural seeds, including cotton with WideStrike™3 traits, may be treated with insecticides and/or fungicides, and these seed treatments can present certain risks. These potential risks are associated with the seed treatments and not the WideStrike 3 traits. Consult the appropriate Safety Data Sheet and/or product label or tag for seed treatment hazard information, follow all directions for use, and wear all recommended personal protective equipment.

Herbicide-tolerant traits—Many cottonseed products with the WideStrike™3 traits also have a trait that provides tolerance to herbicides such as glyphosate. Consult the appropriate product information sheets for the safety profile and precautions associated with such traits.

Environmental Information

Before a stacked trait product can be introduced to the market, review by appropriate governmental agencies is required. Using the criteria established by these agencies, extensive, validated studies are conducted for these new products.

Cotton with the WideStrike™3 traits produces minute quantities of the Cry1F, Cry1Ac, and Vip3A proteins, contained in the plant and plant parts such as leaves, squares, flowers, and cottonseed. All three proteins degrade rapidly in the soil, minimizing the potential for run-off or exposure to soil-dwelling non-target organisms.

A number of non-target organisms were tested as part of the registration processes for WideStrike Insect Protection cotton and COT102 cotton, and no adverse effects were observed. Some of the organisms tested were honey bees, earthworms, lady beetles, springtails, green lacewings, and beneficial predatory ants, beetles, and parasitic wasps. No adverse effects were observed in birds or fish. In addition, there is very low risk for impact on Monarch butterflies, and none were observed in endangered species.

™ Trademark of The Dow Chemical Company (“Dow”) or an affiliated Company of Dow
Another important environmental consideration with biotech product is how cross-pollination will affect the environment. Cotton (Gossypium hirsutum) is mainly a self-pollinating plant, and the chance for gene exchange between WideStrike™3 cotton and other cotton varieties, although possible, is minimal due to its physiological characteristics and various environmental/biological factors. In countries where cultivated, the risk of gene flow to plant species related to cotton (either under cultivation or wild) is very unlikely. There is no selective advantage for cotton varieties with WideStrike 3 Insect Protection in the natural environment.

There is a potential long-term risk of target pest adaptation to the Cry1F, Cry1Ac, and Vip3A proteins, which would lead to the possibility of reduced efficacy. The presence of three insecticidal proteins that differ in their modes of action reduces this potential for WideStrike 3 insect protection compared with single- and dual-mode of action Bt cotton. Additional insect resistance management measures are employed by WideStrike 3 cotton growers to help further mitigate this risk.

**Back to top**

**Additional Information**

- Biotechnology Industry Organization “Commercial Status of Certain Agricultural Biotechnology Products” ([www.biotradestatus.com](http://www.biotradestatus.com))
- US EPA, 2008. Biostatistics Registration Action Document. *Bacillus thuringiensis* modified Cry1Ab (SYN-IR67B-1) and Vip3Aa19 (SYN-IR102-7) insecticidal proteins and the genetic material necessary for their production in COT102 X Cot67B Cotton.
- Expanded technical summary and additional references that support the information summarized here on WideStrike 3 traits can be found in the GM Crop Database at the International Life Sciences Institute’s Center for Environmental Risk Assessment web site ([http://cera-gmc.org/index.php?action=gmc_crop_database](http://cera-gmc.org/index.php?action=gmc_crop_database))
- FDA Consultation Note to File ([http://www.cfsan.fda.gov/~lrd/biocon.html](http://www.cfsan.fda.gov/~lrd/biocon.html))

For more business information about WideStrike™3 Insect Protection, visit the website for Dow AgroSciences.

**Back to top**
NOTICES

As part of its 2015 Sustainability Goals, Dow has committed to make publicly available safety assessments for its products globally. This product safety assessment is intended to give general information about the chemical (or categories of chemicals) addressed. It is not intended to provide an in-depth discussion of health and safety information. Additional information is available through the relevant Safety Data Sheet, which should be consulted before use of the chemical. This product safety assessment does not replace required communication documents such as the Safety Data Sheet.

The information herein is supplied upon the condition that the persons receiving same will make their own determination as to its suitability for their purposes prior to use. In no event will Dow be responsible for damages of any nature whatsoever resulting from the use of or reliance upon the information herein or the product to which that information refers.

Nothing contained herein is to be construed as a recommendation to use any product, process, equipment or formulation in conflict with any patent, and Dow makes no representation or warranty, express or implied, that the use thereof will not infringe any patent.

NO REPRESENTATIONS OR WARRANTIES, EITHER EXPRESS OR IMPLIED, OF MERCHANTABILITY, FITNESS FOR A PARTICULAR PURPOSE OR OF ANY OTHER NATURE ARE MADE HEREUNDER WITH RESPECT TO INFORMATION OR THE PRODUCT TO WHICH INFORMATION REFERS.

Dow makes no commitment to update or correct any information that appears on the Internet or on its World-Wide Web server. The information contained in this document is supplemental to the Internet Disclaimer, www.dow.com/homepage/term.asp.

Back to top

Form No. 233-01185-NN-0315