

Determination of the Safety of Monsanto's
Corn DBT 418 (Lepidopteran Resistant, Herbicide Tolerant Corn)
for Direct Use as Food, Feed and For Processing

Food and Feed Safety

The product dossiers on corn event DBT 418 were reviewed for safety and nutritional differences compared with the conventional corn. The focus of the review was on any new or altered expression trait and changes in composition and nutritional content or value relative to the conventional corn. At the end of the safety assessment, a conclusion was made that the corn Event DBT 418 is as safe as the conventional corn taking into account dietary impact of any changes in nutritional content or value.

A biosafety permit for corn event DBT 418 and all progenies derived from crosses of the product with any conventionally-bred corn and corn containing approved-biotech events for direct use as food, feed or for processing was issued to Monsanto Philippines, Inc. on June 17, 2003. The permit is valid for five years and shall expire on June 16, 2008 subject to the terms and conditions set forth in DA Administrative Order No. 8, Series of 2002. The said corn event DBT 418 was included in the Lists of Approval Registry (Delisting) prepared by the Department of Agriculture- Bureau of Plant Industry.

This approval is for direct use as Food, Feed and for Processing only. This does not include cultivation of Corn Event DBT 418 in the Philippines. Food and Feed use of Corn Event DBT 418 and its by-products is therefore authorized as of October 22, 2003. The Biosafety Permit (No.03-006) stated that "Corn Event DBT 418 (Lepidopteran Resistant, Phosphinotricin-Tolerant Corn)" is as safe for human food, livestock feed and for processing as its conventional counterparts.

I. Brief Identification of the Genetically Modified Organism (Living Modified Organism)

Designation:	Corn DBT 418
Applicant:	MONSANTO PHILIPPINES, INC. 7 th Floor, Ayala-FGU Center Alabang-Zapote Rd., cor Acacia Avenue Madrigal Business Park Alabang 1770 Muntinlupa City Philippines
Plant Species:	
Name:	Corn (<i>Zea mays</i> L.)
Parent Material:	Inbred corn lines (and/or isolines) developed and produced by Monsanto
Center of Origin:	Mexico, Central America and South America
Toxic Factor/Allergen(s):	Trypsin inhibitor, phytic acid, and secondary metabolites such as raffinose, ferulic acid and p-coumaric acid are present in low amount 2-4 dihydroxy-7-methoxy-2H-1, 4 benzoxazin- 3(4H)- one (DIMBOA) a potential toxicant but declines rapidly as the plant grows
Trait Description:	Lepidopteran Resistance and Herbicide-Tolerance
Trait Introduction Method:	Micro-particle acceleration (biolistic) method
Donor Organism:	<i>Streptomyces hygroscopicus</i> , source of the <i>bar</i> gene produces the PAT protein, responsible for glufosinate tolerance <i>Bacillus thuringiensis</i> subsp. <i>kurstaki</i> , source of <i>cryIA(c)</i> gene responsible for Lepidopteran resistance

Pathogenicity:

Bacillus thuringiensis (subspecies *kurstaki*) is non-pathogenic, spore-forming, gram-positive bacterium found naturally on soil.

Streptomyces hygroscopicus is a common soil microorganism and is not commonly consumed as food or feed.

Proposed Use:

For direct use as food, feed and for processing

II. Background Information

Monsanto Philippines, Inc. has developed a corn line resistant to lepidopteran pests, and at the same time herbicide tolerant. This corn line, designated corn event DBT 418 has been transformed using Particle Gun Method, to produce an insecticidal protein, from *Bacillus thuringiensis* (subspecies *kurstaki*), active against lepidopteran pests. This corn line was developed to provide a method to control yield losses from insect feeding damage caused by lepidopteran pests, without the use of conventional pesticides.

On June 12, 2003, Monsanto Philippines, Inc. submitted an application to the Bureau of Plant Industry requesting for biosafety permit under Department of Agriculture AO#8 Part 5 for corn event DBT 418 which has been genetically modified for lepidopteran resistance and phosphinotricin-tolerance.

Corn DBT418 has been evaluated according to BPI's safety assessment by concerned agencies: [Bureau of Animal Industry(BAI) , Bureau of Agriculture, Fisheries and Product Standards (BAFPS) and a Scientific Technical Review Panel (STRP)]. The process involves an intensive analysis of the nature of the genetic modification together with a consideration of general safety issues, toxicological issues and nutritional issues associated with the modified corn.

The petitioner/applicant published the said application on two widely circulated newspapers: Malaya and Daily Tribune on July 23, 2003 for public comment/review. BPI received no comment on the petition during the 30-day comment period.

Review of results of evaluation by the BPI Biotech Core Team in consultation with DA-Biotechnology Advisory Team (DA-BAT) completed the approval process.

III. Description of Novel (Introduced) Traits

The insect resistance gene that was used to produce transgenic corn line DBT418 encodes a protein that is identical to the first 613 amino acids of the naturally occurring *Bacillus thuringiensis* subsp. *kurstaki* Cry1Ac protein. The *cry1ac* gene in the corn event DBT418 consists of a DNA sequence that have been modified to contain an increased number of codons that are prepared for expression in maize. Also used to produce transgenic corn event DBT418 was the herbicide resistance *bar* gene. The *bar* gene was originally isolated from *Streptomyces hygroscopicus* and encodes phosphinothricin acetyl transferase (PAT). This enzyme is useful as a selectable marker as well as a source of resistance to the herbicide phosphinothricin, also known as glufosinate. Transformants were selected by their ability to survive and grow in the presence of the herbicide bialaphos, which is a tripeptide fermentation product of *Streptomyces hygroscopicus*.

The Cry1Ac and PAT proteins have no similarity to any known allergens or mammalian toxins. Cry1Ac is known to be specifically toxic to lepidopteran insects. PAT is known to specifically catalyze the acetylation of phosphinothricin. Both proteins are present in at low levels in corn seed and whole plants but degraded in vitro digestibility. Only minor differences were observed in the composition of corn grain or silage when comparing corn hybrids containing the DBT418 transformation event and untransformed counterpart hybrids were slightly different.

Safety of the Expressed Proteins

The Cry1Ac protein is insecticidal only to lepidopteran insects. This specificity is directly attributable to the presence of receptors in the target insects. There are no receptors for the protein delta-endotoxin of *Bacillus thuringiensis* subspecies on the surface of mammalian intestinal cells, therefore, humans are not susceptible to these proteins.

Expression of Cry1Ac and PAT proteins in corn is not expected to alter the nutritional value of corn, because the activities of these proteins are highly specific and its expression as protein is less than 0.01% of the total proteins in plant tissues.

Toxicity assay of Cry1Ac protein was tested using the purified cry protein and trypsinized to produce insecticidally active version of the cry protein. The active toxin was administered to mice by gavage feeding for 14 days. No gross internal findings observed at necropsy done on day 14. Only one death was observed to be due to gavage error as confirmed in necropsy. Under the conditions of the test the acute oral LD50 (median lethal dose) of the Bt Cry1Ac protein was estimated to be greater than 5000 mg/kg; the dose administered to the test mice. This indicates non-toxicity of the cry protein under normal conditions of feeding.

Both Cry1Ac and PAT proteins do not pose any significant allergenic risks associated with consumption of products generated from DBT418 since these proteins have shown to rapidly digested in simulated gastric fluid and to lack glycosylation which are the common attributes of protein allergens.

IV. Nutritional Composition (Compositional Analysis)

Corn DBT418 and the non-transgenic corn have no significant difference based on nutritional composition. The Cry1Ac and PAT proteins are not macroconstituents in the human or animal diet, which comprise at most about 0.002% or 0.0175% respectively of the total protein consumed by an animal or human fed exclusively on grain from corn hybrids containing the DBT418 transformation event.

Under the same agronomic condition, corn hybrids containing the DBT418 transformation event is significantly resistance to lepidopteran insects and glufosinate herbicides as compared to the non-transformed counterpart hybrids.

The nutritional equivalence of DBT418 corn to conventional corn was confirmed in numerous feeding studies with broiler chickens and rats which included clinical and histological evaluations. The environmental impact of DBT 418 corn is also comparable to conventional corn.

V. Anti-Nutritional Factors

Both the transgenic and conventional corn contains antinutrients of phytic acid, trypsin and chymotrypsin in trace amounts because these compounds are such minor constituents of corn, they were not specifically analyzed and no safety concerns regarding antinutrients.

VI. Regulatory Decision

After reviewing the scientific data and information relevant to the application of Monsanto Philippines, Inc., it is concluded that Corn DBT418 and all progenies derived from crosses of the product are not significantly different from conventional corn in terms of compositional, nutritional and safety aspect. This transformation event does not decrease nor increase nutrient source for food and feed consumption and is as safe and substantially equivalent to its unmodified counterpart, and is therefore approved for direct use as food, or feed and for processing. Monsanto shall duly inform the public of this approval by way of publishing in any one (1) of the top three (3) leading newspapers in the country that imports of this product is covered by conditions for approval as provided in Department of Agriculture Memorandum Circular No. 8, Series of 2003.