

**Determination of the Safety of Monsanto's
Corn MON 87460
For Direct use as Food, Feed, and for Processing**

Food and Feed Safety

The product dossier on Monsanto's Corn event: MON 87460 was 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 MON 87460 is as safe as the conventional corn taking into account the safety and nutritional quality of MON 87460.

A biosafety permit for Drought tolerant Corn event MON 87460, 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 and for processing was issued to Monsanto Philippines Inc. on November 15, 2012. The biosafety permit notification is valid for five years and shall expire on November 14, 2017 subject to the terms and conditions set forth in DA Administrative Order No. 8, Series of 2002, as amended by DA Administrative Order No. 22, Series of 2007. The said Corn MON 87460 was included in the Lists of Approval Registry prepared by the Department of Agriculture- Bureau of Plant Industry.

This approval is for use as food, feed and for processing only. This does not include cultivation of Corn MON 87460 in the Philippines. Food and feed use of Corn MON 87460 and its by-products is therefore authorized as of November 15, 2012. The biosafety permit (No. 12-060) stated that "Corn MON 87460 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:	Drought tolerant
Applicant:	MONSANTO PHILIPPINES, INC. 23 rd Floor Tower II Insular Life Corporate Centre Insular Life Drive, Filinvest Corporate City Alabang, Muntinlupa City Philippines 1781
Plant Species:	
Name:	Corn (<i>Zea mays</i>)
Parent Material:	LH59 (a non-transgenic conventional corn variety)
Center of Origin:	Corn originated in the highlands of Mexico 7,000 to 10,000 years ago.
Toxic Factors/Allergen(s):	Corn is not a common allergenic food. Allergies to corn are rare (less than six in over one hundred patients referred to a pediatric allergy specialty center for grain allergy). Anti-nutrients including trypsin inhibitor, phytic acid, and secondary metabolites such as raffinose, ferulic acid and p-coumaric acid are present in low amount in corn. 2-4 dihydroxy-7-methoxy-2H-1, 4 benzoxazin- 3(4H)- one (DIMBOA) is a potential toxicant but declines rapidly as the plant grows
Trait Description:	Drought tolerant
Trait Introduction Method:	<i>Agrobacterium</i> -mediated transformation
Donor Organisms:	<i>Bacillus subtilis</i> - source of <i>cspB</i> which confers tolerance to water-limited conditions <i>Escherichia coli</i> - source of <i>nptII</i> gene which acts as a selectable marker that confers tolerance to certain antibiotics such as neomycin and paromomycin and facilitates selection of plants containing <i>cspB</i> during early product development
Pathogenicity:	The safety of <i>Bacillus subtilis</i> and products derived from <i>B. subtilis</i> for use in food has been confirmed consistently by numerous studies. It is non-pathogenic and safe for human

consumption. It is present in many fermented foods, and has a history of safe consumption.

Escherichia coli is a non-pathogenic bacteria and has a history of safe use as antibiotic resistance markers in commercially grown genetically-modified crops.

Proposed Use: For direct use as food, feed and for processing

II. Background Information

Monsanto company has developed Drought tolerant maize event, MON 87460.

On August 28, 2009, Monsanto Philippines submitted an application to the Bureau of Plant Industry requesting for biosafety permit under Administrative Order (AO) No. 8 for Corn MON 87460 which has been genetically modified for drought tolerance.

Monsanto Philippines Inc. has provided data and/or information on the identity of corn MON 87460 including a detailed description of the modification method, the safety of donor organism, the role of the inserted genes and regulatory sequences, the insertion sites, copy numbers and genetic stability of the insert(s), and the levels of protein expression in the plant. The introduced proteins were identified, characterized, and evaluated for their potential toxicity and allergenicity to human and livestock. Relevant scientific publications were also supplied.

Corn MON 87460 has been evaluated according to BPI's safety assessment by concerned agencies [Bureau of Animal Industry (BAI), Bureau of Agriculture and Fisheries Standards (BAFS) and a Scientific and Technical Review Panel (STRP)]. The process involved an extensive safety evaluation of the nature of the genetic modification with a consideration of general safety issues, toxicological and nutritional issues associated with the corn products.

The petitioner/applicant published the said application on two widely circulated newspapers: The Malaya Business Insight and Tribune Publishing on August 23, 2012 for public comment/review. During the 30-day comment period, BPI had not received comment on the said application.

Review of results of evaluation by the BPI Biotech Core Team completed the approval process.

III. Description of Novel (Introduced) Traits

MON 87460 was developed through *Agrobacterium*-mediated transformation of corn using the binary plasmid vector, PV-ZMAP595. This plasmid contains two expression cassettes. The first expression cassette produces *Bacillus subtilis* cold shock protein B (CSPB) and the second expression cassette produces neomycin phosphotransferase II (NPTII) from *Escherichia coli* strain K12, a selectable marker that confers tolerance to certain antibiotics such as neomycin and paromomycin. The insertion of the *cspB* gene in MON 87460 confers tolerance to water-limited conditions that would otherwise negatively impact yield. The *nptII* gene was inserted to facilitate selection of plants containing *cspB* during early product development.

Safety of the Expressed Proteins

A history of safe use has been established for MON 87460 CSPB protein. Its donor organism, *B. subtilis*, is ubiquitous in the environment, is used to manufacture food and is an ingredient in certain probiotic formulations. CSPB shares homology with a variety of proteins that are present in commonly used foods and have a history of safe use. CSPB is not homologous to known toxic or bioactive proteins. Also CSPB protein was shown to be rapidly degraded in simulated gastric fluid (SGF) and simulated intestinal fluid (SIF) indicating that it is highly unlikely that the CSPB protein and its fragment will reach absorptive cells of the intestinal mucosa. Finally CSPB did not exhibit any signs of toxicity when administered to mice via oral gavage. This weight of evidence supports the conclusion that CSPB is unlikely to exhibit toxic effects when consumed in food and feeds prepared from MON87460.

Further, NPTII has an established record of safety. Its source organism, *E. coli*, is also ubiquitous in the environment and is present in the digestive tracts of vertebrate species. Enzyme preparations derived from *E. coli* have GRAS status (Flamm, 1991). NPTII has GRAS status when used in biotechnology-derived crops (Bradford et. Al., 2005). Additionally, no structurally relevant similarity exists between the NPTII protein and any known toxic or other biologically active proteins that would be harmful to human or animal health. Finally an acute toxicity study with adult mice found no adverse effects when NPTII was administered at dose far exceeding those that would be experienced consuming grain produced by MON87460.

IV. Nutritional Composition (Compositional Analysis)

Detailed compositional analyses in accordance with OECD guidelines were conducted to determine whether levels of key nutrients, anti nutrients and secondary metabolites in MON 87460 were comparable to levels present in the near isogenic conventional control and several commercial reference corn hybrids. Forage and grain samples of MON 87460 and its conventional control were harvested from plants grown in Chile during 2006-2007. The experiment was arranged with irrigation treatment (well-watered or water-limited).

Compositional analyses of the forage samples included measurement of proximates (moisture, fat, protein, ash), carbohydrates by calculation, acid detergent fiber (ADF), neutral detergent fiber (NDF), calcium, and phosphorus. Compositional analyses of the grain samples included measurement of proximates (moisture, fat, protein, ash), carbohydrates by calculation, ADF, NDF, total dietary fiber (TDF), total amino acid composition, fatty acid composition (C8-C22), minerals (calcium, copper, iron, magnesium, manganese, phosphorus, potassium, sodium, zinc), vitamins (vitamin B1 [thiamine], vitamin B2 [riboflavin], vitamin B6 [pyridoxine], vitamin E, niacin, folic acid), furfural, raffinose, phytic acid, *p*-coumaric acid, and ferulic acid.

Based on the data and information presented, it was concluded that corn grain and forage derived from MON 87460 are compositionally and nutritionally equivalent to those of conventional corn under well-watered condition and water-limited condition. The few statistical differences between MON 87460 and control corn likely reflect the natural variability of the components since the mean levels of analytes for MON 87460 are well within the 99% tolerance intervals for conventional corn, and/or within the ranges in the ILSI database and the scientific literature.

V. Anti-Nutritional Factors

The antinutrients assessed included phytic acid and raffinose. Phytic acid is widely distributed in plants and can limit the uptake of minerals such as calcium in higher animals. Raffinose is a non-digestible oligosaccharide that is considered to be an antinutrient due to gas production and the resulting flatulence caused by its consumption. The secondary metabolites included ferulic acid, *p*-coumaric acid and furfural. Ferulic acid and *p*-coumaric acid are derived from the aromatic amino acids, phenylalanine and tyrosine, and serve as precursors for a large group of phenylpropanoid compounds.

The statistical analysis highlighted no differences within or across sites in the levels of antinutrient components and secondary metabolites in MON 87460 and the control, grown in well watered condition. Under water limited condition, statistical analysis highlighted no consistent differences across sites in the levels of antinutrient components and secondary metabolites in MON 87460 and the conventional control.

Thus, a comprehensive evaluation of anti-nutrient components and key secondary metabolites supported the compositional equivalence of MON 87460 and conventional corn.

VI. Regulatory Decision

After reviewing the scientific data and information relevant to the application of Monsanto Philippines Inc., it is concluded that Corn MON 87460 and all progenies derived from crosses of this product with any conventionally-bred corn except when such cross involves another transformation event is as safe and substantially equivalent to its unmodified counterpart, and is therefore approved for direct use as food, feed and for processing.

Monsanto Philippines, Inc. 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, and that imports of this product are covered by conditions for approval as provided in Department of Agriculture Memorandum Circular No. 8, Series of 2003.