

Determination of the Safety of Monsanto's  
Combined Trait Product Corn: MON 88017 x MON 810  
for Direct Use as Food or Feed or for Processing

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**Food and Feed Safety:**

The product dossiers on Combined Trait Product Corn: MON 88017 x MON 810 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 Combined Trait Product Corn: MON 88017 x MON 810 is as safe as the conventional corn taking into account dietary impact of any changes in nutritional content or value.

A biosafety permit for Combined Trait Product Corn: MON 88017 x MON 810 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 July 3, 2006. The notification is valid for five years and shall expire on July 2, 2011 subject to the terms and conditions set forth in DA Administrative order No. 8, Series of 2002, and Memorandum Circulars Nos. 6 and 8, Series of 2004. The said Combined Trait Product Corn was included in the Lists of Approval Registry (Delisting) being prepared by the Department of Agriculture-Bureau of Plant Industry.

*This approval is for use as Food, Feed and Processing only. This does not include cultivation of Combined Trait Product Corn: MON 88017 x MON 810 in the Philippines. Food and Feed use of Combined Trait Product Corn: MON 88017 x Mon 810 and its by-products is therefore authorized as of July 3, 2006. The biosafety notification (No. 06- 010) stated that combined trait product corn: MON 88017 x MON 810 is as safe for human food, livestock feed and for processing as its conventional counterparts".*

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

<b>Designation:</b>	Combined Trait Product Corn: MON 88017 x MON 810
<b>Applicant:</b>	MONSANTO PHILIPPINES, INC. 7 <sup>th</sup> Floor, Ayala Life-FGU Center Alabang-Zapote Road cor Acacia Avenue Madrigal Business Park Alabang 1770, Muntinlupa City
<b>Plant Species:</b>	
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

<b>Toxic Factors/Allergen(s):</b>	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
<b>Trait Description:</b>	Insect resistance and glyphosate herbicide tolerance
<b>Trait Introduction Method:</b>	Conventional breeding
<b>Donor Organism:</b>	<p><i>Bacillus thuringiensis</i> subs <i>kumamotoensis</i>, is a non-pathogenic spore-forming Gram positive bacterium that is found naturally in soil. It is a source of the <i>cry3Bb1</i> gene which produces a Cry3Bb1 protein with insecticidal activity against the coleopteran pest, corn rootworm.</p> <p><i>Bacillus thuringiensis</i> var <i>kurstaki</i>, strain HD-1 (<i>B.t.k</i>), a widely distributed, non-pathogenic, spore-forming Gram positive bacteria, the source of the <i>cry1Ab</i> gene which produces the Cry1Ab protein with insecticidal activity against Lepidopteran insects.</p> <p><i>Agrobacterium</i> sp. Strain CP4, which encodes only for the naturally occurring, glyphosate-tolerant EPSPS protein.</p>
<b>Pathogenicity:</b>	<p><i>Bacillus thuringiensis</i> subsp. <i>kumamotoensis</i>, the donor for the <i>cry3Bb1</i> coding sequence, is a non-pathogenic spore-forming gram positive bacterium that is found naturally in soil. Bt strains have been used commercially in the US since 1958 to produce microbial-derived products with insecticidal activity. The Cry3Bb1 protein encoded by the <i>cry3Bb1</i> sequence is known to act specifically on the gut of Coleopteran insects. There are no receptors for Cry3Bb1 on mammalian intestinal cell surfaces and humans are not susceptible to this toxin. Additionally, Cry3Bb1 denatures at elevated temperatures during food processing and rapidly degrades in the soil.</p> <p>The <i>cp4</i> gene was derived from the common soil bacterium <i>Agrobacterium</i> sp. Strain CP4 which encodes only for the naturally occurring, glyphosate-tolerant EPSPS protein. No other protein is produced or introduced which may bring about toxicity, allergenicity or may be anti-nutritional in nature. No known pathogenicity in humans and animals because of the absence of the shikimic acid pathway in animals.</p> <p><i>Bacillus thuringiensis</i> var. <i>kurstaki</i>,, the donor for the <i>cry1Ab</i> coding sequence, has been shown to be non-toxic to humans, other vertebrates and beneficial insects. Bt strains have been</p>

used commercially in the US since 1958 to produce microbial-derived products with insecticidal activity. The Cry1Ab protein encoded by the *cry1Ab* sequence is known to act specifically on the gut of lepidopteran insects. There are no receptors for Cry1Ab on mammalian intestinal cell surfaces and humans are not susceptible to this toxin. Additionally, Cry1Ab denatures at elevated temperatures during food processing and rapidly degrades in the soil.

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

## **II. Background Information**

The approach to produce new varieties of corn stacked with insect protection and herbicide tolerance traits follows a typical breeding program. Initial crossing is conducted to introduce each transgene into a corn germplasm containing the desirable trait(s) but lacking the transgene. Once the initial cross is made, multiple generations of backcrosses to the conventional parent, followed by three or more generations of self pollination, result in progeny inbred containing the transgene in the germplasm of the parental line.

Monsanto Philippines has filed an application with attached technical dossiers to the Bureau of Plant Industry on February 22, 2006 for a biosafety notification for direct use as food, feed and for processing under Administrative Order (AO) No. 8 Part 5 for Combined Trait Product Corn: MON 88017 x MON 810 which has been genetically modified for insect resistance and herbicide tolerance.

A safety assessment of combined trait product corn: MON 88017 x MON 810 was conducted by Scientific and Technical Review Panel (STRP) as per Department of Agriculture Administrative Order No. 8 Series of 2002. The focus of risk assessment is the gene interactions between the two transgenes.

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 Cry1Ab protein is an insect control protein and acts through a toxic action in the midgut of specific lepidopteran insects, such as the European corn borer (*Ostrinia nubilalis*). The *cry1Ab* gene was derived from the common soil bacterium, *Bacillus thuringiensis* subsp. *kurstaki* and was introduced into corn to generate MON 810. The Cry3Bb1 protein is an insect control protein and acts through a toxic action in the midgut of corn rootworm larvae, i.e. coleopteran species *Diabrotica virgifera virgifera*, *D. barberi*, and *D. virgifera zea*. The *cry3Bb1* gene was derived from the common soil bacterium *Bacillus thuringiensis* subsp. *kumamotoensis*, and was introduced into corn along with the *cp4 epsps* gene, to generate MON 88017.

A commercial inbred line with the inserted genes of MON 810 is developed by the conventional backcrossing of MON 810 and a non transgenic elite inbred line. The resulting commercial inbred line with the inserted genes of MON 810 is then crossed with another inbred line, which contains the inserted genes of MON 88017. The resulting seeds are stacked traits F1 hybrid variety.

## **Safety of Expressed Proteins**

CP4 EPSPS and the two Bt proteins (Cry1Ab and Cry3Bb) accumulate in different subcellular compartments of the corn plant cells. CP4 EPSPS is a nuclear-encoded, chloroplast-localized enzyme while Cry1Ab and Cry3Bb proteins accumulate in plant cell cytoplasm. Synergistic effects were reported in Cry1 proteins but no interaction was observed in Cry3 class of proteins. Because of the different sites of accumulation and mode of action of the products, unexpected effects of the stacked genes, *cp4 epsps*, *cry1Ab* and *cry3Bb1*, on the metabolism of the plant is less likely to occur.

These novel proteins (*cp4 epsps*, *cry1Ab* and *cry3Bb* gene products) are not proteins that regulate the normal metabolic pathways of plants, therefore, these will not interfere with the plant's normal growth and development. The modes of action of the proteins also differ, hence, interactions of the proteins to produce new allergen or new toxin is very unlikely to occur.

### **IV. Nutritional Composition (Compositional Analysis)**

The World Health Organization (1995) stated that two plants that are substantially equivalent to conventional varieties are crosses by conventional breeding techniques, the combined trait product is expected to be substantially equivalent to the single event products.

### **V. Anti-Nutritional Factors**

No known anti nutritional factors for individual events. Thus, MON 88017 x MON 810 corn has no known anti nutritional factors.

### **VI Regulatory Decision**

After reviewing the scientific data and information relevant to the combined trait corn MON 88017 x MON 810 application of Monsanto Philippines Inc. it is concluded that no interaction found between/among the combined traits, hence this plant product was found to be as safe as its conventional corn and can substitute for its traditional counterpart for direct use as food, feed and for processing. Monsanto is hereby notified that it may proceed with the activities for the above product for direct use as food and feed or for processing following all existing rules and regulations consistent with DA AO #8.