

Determination of the Safety of Monsanto's  
Combined Trait Product Corn: MON810 x MON863  
for Direct use as Food, Feed, and Processing

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**Food and Feed Safety:**

The product dossiers on Monsanto's combined trait product corn: MON 810 x MON 863 were reviewed for safety and nutritional differences compared with the conventional corn. The focus of the food/feed safety assessment is based on three major issues/concerns regarding stacked genes from different sources namely a) gene interaction; b) effect on metabolic pathways and c) differential gene expression due to stacking.

A biosafety notification for combined trait product corn: MON 810 x MON 863 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 were issued to Monsanto Philippines Inc. on November 16, 2004. The notification is valid for five years and shall expire on November 15, 2009 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 will be included in the Lists of Approval Registry (Delisting) being prepared by the Department of Agriculture.

*This approval is for use as Food, Feed and Processing only. This does not include cultivation of combined trait product corn: MON 810 x MON 863 in the Philippines. Food and Feed use of combined trait product corn: MON 810 x MON 863 its by-products is therefore authorized as of November 16, 2004. The biosafety notification (No. 04-003) stated that combined trait product corn: MON810 x MON 863 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)**

**Designation:** Combined trait product corn: MON810 x MON863

**Applicant:** 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

**Plant Species:**

Name: corn (*Zea mays* L.)

Parent Material: Inbred corn lines (and/or isolines) developed and produced by Monsanto

Center of Origin: Mexico, Central America and South America

Toxic Factors/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:** Insect resistance (corn borer & corn rootworm)

**Trait Introduction Method:** Conventionally plant breeding

**Donor Organisms:** *Bacillus thuringiensis* var *kurstaki*, strain HD-1 (*B.t.k*), a widely distributed, non-pathogenic, spore-forming Gram positive bacteria, the source of the *cry1Ab* gene which produces the Cry1Ab protein with insecticidal activity against Lepidopteran insects.

*Bacillus thuringiensis* subs *kumamotoensis*, is a non-pathogenic spore-forming Gram positive bacterium that is found naturally in soil. It is a source of the *cry3Bb1* gene which produces a Cry3Bb1 protein with insecticidal activity against the coleopteran pest, corn rootworm.

**Pathogenicity:** *Bacillus thuringiensis* var. *kurstaki*, the donor for the *cry1Ab* coding sequence, has been shown to be non-toxic to humans, other vertebrates and beneficial insects. Bt strains have been 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.

*Bacillus thuringiensis* subsp. *kumamotoensis*, the donor for the *cry3Bb1* 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 *cry3Bb1* 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.

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

## **II. Background Information**

To produce varieties of Bt lines stacked with the insect resistance traits, process follows a typical backcrossing program. This takes from 5-6 generations to result in the progeny species containing the target gene in the background of the recurrent parent.

Monsanto Philippines, has filed an application with attached technical dossiers to the Bureau of Plant Industry on July 16, 2004 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: MON810 x MON863 which has been genetically modified for insect resistance and herbicide tolerance.

A safety assessment of combined trait product corn: MON 810 x MON 863 was conducted 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**

Corn Event MON 810 (Tradename: Yieldgard®) and all corn lines/hybrids derived from this Event contain the *cry1Ab* coding sequence from *Bacillus thuringiensis* sp *kurstaki* strain. The *cry 1Ab* gene was modified to produce a protein with enhanced insecticidal activity against the lepidopteran pest, ACB.

The novel variety produces a truncated version of the insecticidal protein, Cry1Ab, derived from *Bacillus thuringiensis*. Delta-endotoxins, such as the Cry1Ab protein expressed in MON 810, act by selectively binding to specific sites localized on the brush border midgut epithelium of susceptible insect species. Following binding, cation-specific pores are formed that disrupt midgut ion flow and thereby cause paralysis and death. The insecticidal properties of Cry1Ab is applicable only to lepidopteran insects, and its specificity of action is directly attributed to the presence of specific binding sites in the target insects. There are no binding sites for delta-endotoxins of *B. thuringiensis* on the surface of mammalian intestinal cells, therefore, livestock animals and humans are not susceptible to these proteins.

Corn event MON863 (Trade name: Yieldgard Corn Rootworm) and all corn lines/hybrids derived from this event contain the *cry3Bb1* coding sequence from *Bacillus thuringiensis* sp *kumamotoensis* strain. The *cry3Bb1* gene was modified to produce a protein with enhanced insecticidal activity against the coleopteran pest, CRW, and was codon optimized for expression in monocotyledonous plants.

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 863. The resulting seeds are stacked traits F1 hybrid variety.

#### **Safety of the Expressed Proteins**

It is unlikely that Cry1Ab and Cry Bb1 classes of proteins would interact to produce new allergens or new toxins, given the narrow spectrum of insecticidal activity displayed by Cry1 and Cry3 classes of proteins. There are no possible unexpected effects of the stacked genes on the plant metabolism when safety assessment was conducted and the subsequent approvals were granted.

Selective activities of the Cry1Ab and Cry3Bb1 proteins are not affected by potential interactions with one another in terms of stability and expression. On the gene expression, both proteins express at low levels. This is shown in the efficacy performance of YieldGard® Rootworm and YieldGard® Corn Borer traits on the stacked trait F1 hybrid variety and is confirmed by different bioassays. Therefore, it is concluded that the traits provided by parental insect protection traits are not changed in the stacked trait F1 hybrid.

#### **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 810 x MON 863 corn has no known anti nutritional factors.

#### **VI. Regulatory Decision**

After reviewing the scientific data and information relevant to the combined trait corn MON 810 x MON 863 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 and is therefore approved for direct use as food, or feed or 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.