

**Determination of the Safety of Monsanto's  
Canola MON 88302  
for Direct use as Food, Feed, or Processing**

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**Food and Feed Safety**

The product dossier of Monsanto's canola event MON 88302 was reviewed for safety and nutritional differences compared to the conventional canola. 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 canola. At the end of the safety assessment, a conclusion was made that herbicide tolerant canola MON 88302 is as safe as the conventional canola taking into account the safety and nutritional quality of MON 88302

A biosafety permit for herbicide tolerant canola MON 88302 and all progenies derived from crosses of the product with any conventionally bred canola and canola containing approved-biotech events for direct use as food, feed or for processing was issued to Monsanto Philippines Inc. on April 24, 2015. The permit is valid for five years and shall expire on April 23, 2020 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 product 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 or Processing only. This does not include cultivation of MON 88302 in the Philippines. Food and Feed use of MON 88302 and its by-products is therefore authorized as of April 24, 2015. The biosafety permit (No. 15-081) stated that MON 88302 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>	MON 88302 Canola
<b>Applicant:</b>	MONSANTO PHILIPPINES, INC. 23 <sup>rd</sup> Floor Tower II Insular Life Corporate Centre Insular Life Drive Filinvest Corporate City Alabang, Muntinlupa City, 1781 Philippines
<b>Plant Species:</b>	
Name:	Canola ( <i>Brassica napus</i> )
Parent Material:	Ebony
Center of Origin:	Central Asia-Himalayas Region

Toxic Factors/Allergen(s): Phytic acid, sinapine, tannins, eruric acid and glucosinolates

**Trait Description:** Herbicide tolerance

**Trait Introduction Method:** *Agrobacterium*-mediated transformation

**Donor Organisms:** *Agrobacterium tumefaciens* strain CP4, source of cp4 epsps (aroA:CP4) which produces the herbicide tolerant form of 5-enolpyruvylshikimate-3-phosphate synthase (EPSPS) enzyme which decreases binding affinity for glyphosate, thereby conferring increased tolerance to glyphosate herbicide.

**Pathogenicity:** *Agrobacterium sp.* strain CP4 the donor organism of cp4 epsps gene is not a food source but is related to microbes commonly present in the soil and in the rhizosphere of plants. All plant, microbial, and fungal food sources contain EPSPS proteins; therefore, this enzyme and its activity are not novel to the food supply.

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

## **II. Background Information**

Monsanto company has developed herbicide tolerant canola event, MON 88302, which was developed by introducing a gene derived from *Agrobacterium sp.* strain CP4 that expresses 5-enolpyruvylshikimate-3-phosphate synthase (CP4 EPSPS) protein which confers tolerance to the herbicide glyphosate.

Monsanto Philippines, Inc. has filed an application with attached technical dossiers to the Bureau of Plant Industry on November 10, 2011 for a biosafety permit for direct use as food, feed or for processing under Administrative Order (AO) No. 8 Part 5 for MON 88302 canola, A safety assessment of MON 88302 was conducted as per Department of Agriculture Administrative Order No. 8 Series of 2002 and Memorandum Circulars Nos. 6 and 8, Series of 2004.

Monsanto has provided data and/or information on the identity of MON 88302 including a detailed description of the transformation method, the safety of donor organism, the role of the inserted genes and regulatory sequences, the insertion sites, copy number and genetic stability of the insert(s), and the levels of expression in the plant, . The introduced protein was identified, characterized and evaluated for their potential toxicity and allergenicity to human and livestock. Relevant scientific publications were supplied.

MON 88302 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 canola product.

The Public Information Sheet (PIS) of the said application was published in two widely circulated newspapers: Malaya Business Insight and Tribune Publishing on July 21, 2014 for public comments/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 completed the approval process.

### III. Description of Novel (Introduced) Traits

Canola MON 88302 contains a gene derived from *Agrobacterium* sp. strain CP4 that expresses 5-enolpyruvylshikimate-3-phosphate synthase (CP4 EPSPS) protein. The CP4 EPSPS protein confers tolerance to the herbicide glyphosate, the active ingredient in the family of Roundup agricultural herbicides.

MON 88302 utilizes a FMV/Tsf1 chimeric promoter sequence to drive CP4 EPSPS expression in different plant tissues. By virtue of CP4 EPSPS expression in pollen, MON 88302 provides tolerance to glyphosate during the sensitive reproductive stages of growth, and enables the application of glyphosate at higher rates up to first flower with no detectable impact to male fertility.

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

A history of safe use has been established for MON 88302 CP4 EPSPS protein. The safety of the cp4 epsps donor organism (*Agrobacterium*) and the ubiquitous presence of homologous EPSPS enzymes in food crops (e.g., soybean and corn) and common microorganisms (e.g., *Saccharomyces cerevisiae*), established that the EPSPS protein, and its enzyme activity pose no novel risks from a food or feed perspective.

The CP4 EPSPS protein in MON 88302 has also been assessed for its potential allergenicity according to safety assessment guidelines and has demonstrated not to be allergenic. The CP4 EPSPS protein showed lack of structural similarity to known toxins, allergens or biologically active or anti-nutritional proteins known to have adverse effects on mammals.

Digestibility studies in SGF and SIF show that CP4 EPSPS is rapidly digestible indicating that it is highly unlikely that these proteins will pose any safety concern to human and animal health.

Finally acute toxicity studies with adult mice found no adverse effects when CP4 EPSPS protein was administered at dose far exceeding those that would be experienced consuming grain produced by MON 88302.

Based on the weight of evidence, it is concluded that the CP4 EPSPS protein expressed in MON 88302 is safe and poses no concerns for humans, animals and the environment.

### IV. Nutritional Composition (Compositional Analysis)

Detailed compositional analyses in accordance with OECD guidelines were conducted to determine whether levels of key nutrients and anti-nutrients in MON 88302 were comparable to levels

present in the conventional canola control and commercially available canola varieties. Canola forage is rarely consumed by animals and is not a source of nutrition for humans. Therefore, the OECD consensus document on compositional considerations for canola does not include analysis of canola forage, so forage samples were not collected.

These compositional comparisons were made by analyzing the seed harvested from five replicated field sites across the United States and Canada during the 2009 field season. The analysis included proximates (ash, carbohydrates by calculation, moisture, protein, and total fat), fibers, amino acids, fatty acids, vitamin E, and minerals, toxicants and anti-nutrients in seed.

The results demonstrated the genetic modification in MON 88302 does not meaningfully impact seed composition and therefore the food and feed safety and nutritional quality of this product is comparable to conventional canola with a history of safe consumption.

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

Oilseed rape contains anti-nutrient components, phytic acid, sinapine and tannins. Phytic acid chelates mineral nutrients, including calcium, magnesium, potassium, iron, and zinc, rendering them biologically unavailable to mono-gastric animals consuming the seed. Sinapine imparts a bitter taste and reduces palatability of the seed for some animal species. Tannins are a third anti-nutrient found in canola seed for some animal species. Although tannins have been shown to have anti-oxidant properties, they also chelate metals such as iron and zinc reducing the absorption of these nutrients. In the combined-site analysis, no significant difference ( $\alpha= 0.05$ ) was observed between MON 88302 and the conventional control for indolylglucosinolates, total glucosinolates, phytic acid, sinapine and tannins. The statistical analyses found a combined-site significant difference in alkyl glucosinolates that was lower than the conventional mean value. The mean alkyl glucosinolates value for MON 88302 was within the natural variability of commercial canola defined by the 99% tolerance interval established from the concurrently grown commercial reference varieties with a history of safe consumption, and the value was within the safety threshold for canola. Total glucosinolate levels in seed from MON 88302 was within the standard for canola. Thus, an evaluation of anti-nutrient components in seed supports the conclusion that MON 88302 is as safe as and compositionally equivalent to conventional canola.

## **VI. Regulatory Decision**

Based on the results of the risk evaluation based on the submitted scientific data and other information relevant to the application of Monsanto Philippines Inc., it is concluded that MON 88302, and all progenies derived from crosses of the product with any conventionally-bred canola, and canola containing approved-biotech events for direct use as food, feed or for processing is as safe and substantially equivalent to its unmodified counterpart, and is therefore approved for direct use as food, feed or 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 that import of this product is covered by conditions for approval as provided in Department of Agriculture Memorandum Circular No. 8, Series of 2003.