

Determination of the Safety of Monsanto's
Canola RT73 (Glyphosate- Herbicide Tolerant Canola)
for Direct Use as Food, Feed and Processing

Food and Feed Safety

The product dossier on Canola RT73 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 Canola RT73 is as safe as the conventional corn taking into account dietary impact of any changes in nutritional content or value.

A biosafety permit for Canola RT73 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 October 22, 2003. The permit is valid for five years and shall expire on October 21, 2008 subject to the terms and conditions set forth in DA Administrative Order No. 8, Series of 2002. The said Canola event was included in the Lists of Approval Registry (Delisting) 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 Canola RT73 in the Philippines. Food and Feed use of Canola RT73 and its by-products is therefore authorized as of October 22, 2003. The Biosafety Permit (No. 03-009) stated that "Glyphosate Herbicide-Tolerant Canola RT73 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:	Canola RT73
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:	Canola (<i>Brassica napus</i> L.)
Parent Material:	Westar Canola Variety
Center of Origin:	Central Asia-Himalayas region

Toxic Factors/Allergen(s):	Erucic acid and its constituents such as tocopherols, sterols, sinapine and phytic acid are potential toxicants but are negligible if present in low amount
Trait Description:	Glyphosate - herbicide tolerant canola
Trait Introduction Method:	<i>Agrobacterium tumefaciens</i> mediated transformation
Donor Organism:	<i>Agrobacterium</i> sp. CP4 strain, a source of <i>epsps</i> gene and <i>Ochrobactrum anthropi</i> strain LBAA, a source of <i>gox</i> gene that confer together to herbicide, Roundup.
Pathogenicity:	Both the CP4 EPSPS from <i>Agrobacterium</i> sp and GOX protein from <i>Ochrobactrum anthropi</i> are non-pathogenic to humans, animals and other non-target organisms (although <i>Agrobacterium</i> is known to be a phytopathogen). Plants and microorganisms produce EPSP because they drive the shikimate pathway in the biosynthesis of aromatic acid such as phenylalanine, tyrosine and tryptophan. Humans and animals do not have the capacity to produce EPSP so they derive their sources of aromatic amino acids from plants and animals. GOX is an enzyme similar to those involved in the basic metabolism of mammalian systems. Both proteins are also non-toxic and non-allergenic based on comparative analysis of their amino acid sequences to known protein toxins and allergens using specific bioinformatics tools.
Proposed Use:	For direct use as food, feed and for processing

II. Background Information

Using modern biotechnology, Monsanto Company has developed Roundup Ready® canola plants (*Brassica napus* L.) that are tolerant to glyphosate. The genetically modified canola plant was produced by the introduction of: the *cp4 epsps* gene derived from the common soil bacterium *Agrobacterium* strain CP4 which encodes for the production of the CP4 EPSPS enzyme and the *gox* gene from *Ochrobactrum anthropi* strain LBAA which encodes for the production of the enzyme glyphosate oxidase (GOX). Both gene products are responsible for conferring tolerance to glyphosate.

On May 19, 2003 Monsanto Philippines, Inc. submitted an application to the Bureau of Plant Industry requesting for Biosafety Permit under AO#8 Part 5 for Canola RT73 which has been genetically modified for herbicide resistance.

Monsanto Philippines, Inc. has provided data on the identity of line Bt 176, a detailed description of the transformation method, data and information on the gene insertion sites, copy number and levels of expression in the plant, the role of the inserted genes and regulatory sequences in donor organisms and full nucleotide sequences. The novel proteins were identified, characterized and compared to the original bacterial proteins, including an evaluation of their potential toxicity to livestock and non-target organisms. Relevant scientific publications were supplied.

Canola RT73 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 canola.

The petitioner/applicant published the said application on two widely circulated newspapers (Malaya and Daily Tribune) on June 5, 2003 for public comment/review. During the 30-day comment period BPI had not received comments on the application.

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

Round up ready canola plants produce the CP4 5-enolpyruvylshikimate-3-phosphate synthase protein (CP4 EPSPS) derived from *Agrobacterium* strain CP4. The CP4 EPSPS is naturally less sensitive to inhibition by glyphosate and has been shown to impart tolerance to glyphosate in several crops. Round up ready canola produces the glyphosate oxidoreductase (GOX) protein, derived from the bacteria *Ochrobactrum anthropi* strain LBAA, as a second mechanism to impart tolerance to glyphosate. The GOX protein breaks glyphosate down into the non-toxic compounds aminomethylphosphonic acid (AMPA), the primary metabolite of glyphosate in plants, and glyoxycyclic acid. Together, CP4 EPSPS and GOX confer glyphosate tolerance to canola plants containing these proteins.

Safety of Expressed Proteins

The CP4 EPSPS protein is from *Agrobacterium* sp. CP4 strain, a common soil bacterium, and the GOX v247 coding sequence from *Ochrobactrum anthropi* strain LBAA, also a common soil bacterium. Both bacteria do not encode for any known pathogenic or allergenic proteins.

The CP4EPSPS proteins are functionally similar to a diverse family of EPSPS proteins typically present in food and feeds derived from plant microbial sources. EPSPS proteins are found ubiquitously in all plant-derived foods. The amino acid sequence of CP4EPSPS and other EPSPS proteins found in food are comparable. The CP4 EPSPS proteins have no known similarity with known protein toxins; CP4 EPSPS are not stable to heat or processing. The CP4 EPSPS is rapidly degraded by proteolytic enzymes (digestibility in vitro), limiting the exposure of the GIT and less likelihood that the protein can exert pharmacological, toxic or allergic effects.

GOX is an enzyme involved in the oxidation of a synthetic compound known as glyphosate and is not directly involved in the basic metabolism of mammalian systems.

Both proteins are non-toxic and non-allergenic based on comparative analysis of their amino acid sequences to known protein toxins and allergens using specific bioinformatics tools.

Glyoxylate is a compound naturally present in plant cells involved in carbohydrate and amino acid metabolism. It is of no safety concern.

AMPA is of no toxicological concern. It can be non-selective bound to natural plant constituents, further degraded to one carbon fragment that are incorporated into natural products, or conjugated with naturally occurring organic acids. Both substances are not prevalent in canola event RT73 grains. They are not stable to digestion and processing, and have no similarity to known allergens.

IV. Nutritional Composition (Compositional Analysis)

Under the same agronomic condition as conventional counterpart canola, the oils derived from canola event RT73 + grains did not significantly (statistically and biologically) differ in terms of quantity and quality of the key nutrients, the fatty acids-palmitic, gadoleic, palmitoleic, eicosadienoic, stearic, behenic, oleic, erucic, linoleic, lignoceric and linolenic. CP4EPSPS and GOXv247 proteins have no effects on the key nutrients. Values were well within the range.

The compositional analyses and established studies on rats and rainbow trout performances demonstrate that the composition and feeding value of herbicide-tolerant Canola RT73 is also equivalent to conventional canola.

V. Anti-Nutritional Factors

The levels of anti-nutrients (glucosinolates, sinapine, phytic acid and erucic acid prepared from Roundup Ready Canola seed are at or below levels currently found in commercial canola.

Erucic acid, glucosinolate and sinapine contents of oil derived from canola event RT73 and all its progenies were not significantly different (statistically and biologically) in terms of quality and quantity from conventional canola. The values were within the range.

VI. Regulatory Decision

After reviewing the scientific data and information relevant to the application of Monsanto Philippines Inc., it is concluded that Canola event RT73 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 and for processing 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.