



NOVEL FOOD INFORMATION - FOOD BIOTECHNOLOGY

ROUNDUP READY® CORN LINE 603

Health Canada has notified Monsanto Canada Inc. that it has no objection to the food use of the transgenic corn line 603, which has been developed to be tolerant to glyphosate containing herbicides, specifically Roundup®. The Department conducted a comprehensive assessment of line 603 according to its *Guidelines for the Safety Assessment of Novel Foods* (September 1994). These guidelines are based upon internationally accepted principles for establishing the safety of foods derived from genetically modified organisms.

BACKGROUND:

The following provides a summary regarding the Monsanto Canada Inc. notification to Health Canada and contains no confidential business information.

1. Introduction

The 603 line of corn (*Zea mays* L.) was developed through a specific genetic modification to be tolerant to glyphosate containing herbicides. This novel variety was developed from an inbred dent corn line by insertion of a bacterial 5-enolpyruvylshikimate-3-phosphate synthase (EPSPS) encoding gene which provides enhanced tolerance to glyphosate compared to the native corn EPSPS.

Glyphosate specifically binds to and inactivates EPSPS, which is involved in the biosynthesis of the aromatic amino acids tyrosine, phenylalanine and tryptophan. This enzyme is present in all plants, bacteria and fungi, but not in animals, which do not synthesize their own aromatic amino acids. Thus, EPSPS is normally present in food derived from plant and microbial sources. The modified corn line permits farmers to use glyphosate containing herbicides, such as Roundup®, for weed control in the cultivation of corn.

This Novel Food Information document has been prepared to summarize the opinion regarding the subject product provided by the Food Directorate, Health Protection Branch, Health Canada. This opinion is based upon the comprehensive review of information submitted by the petitioner according to the *Guidelines for the Safety Assessment of Novel Foods*.

(Également disponible en français)

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2. Development of the Modified Plant

Monsanto Canada Inc. has developed a corn line, 603, containing a CP4 EPSPS gene which was derived from the soil bacterium *Agrobacterium* sp. strain CP4. The CP4 EPSPS gene encodes for a version of EPSPS that is highly tolerant to inhibition by glyphosate. This herbicide tolerance trait allows for the control or suppression of economically important weeds in corn production.

The 603 corn line was created through direct DNA transformation by microparticle bombardment of plant cells with DNA-coated gold particles and regeneration of plants by tissue culture on selective medium. The plasmid vector used in the transformation, a gel-isolated linear restriction fragment designated PV-ZMGT32L, contains two adjacent plant gene expression cassettes, each containing a single copy of the CP4 EPSPS encoding gene. In both plant gene expression cassettes, the CP4 EPSPS is fused to a chloroplast transit peptide (CTP) sequence that targets the CP4 EPSPS to the chloroplasts, the site of aromatic amino acid synthesis. Constitutive expression of the CP4 EPSPS encoding gene was controlled by inclusion of sequences from the rice actin promoter (P-act1) or cauliflower mosaic virus promoter (e35S) and the 3'-polyadenylation signal of the nopaline synthase gene (NOS 3') from *Agrobacterium tumefaciens*. The second cassette also contains the maize hsp70 heat shock protein to stabilize the level of gene transcription. The plasmid vector, PV-ZMGT32L, utilized for transformation of line 603, did not contain antibiotic marker genes or a bacterial origin of replication. Segregation and Southern blot analysis across multiple generations was used to demonstrate the stable inheritance of the novel trait.

3. Product Information

The production of CP4 EPSPS in both grain and forage (whole plant minus roots) from transgenic corn line 603 was quantified using ELISA methods and was estimated to range between 6.9-15.6 and 18.0-31.2 mg/g fresh weight tissue, respectively. No significant differences were observed between hybrids derived using original elite lines and the selected 603 line for the agronomic traits of yield, moisture at harvest, ear height, plant height or other phenotypic traits. Other than glyphosate tolerance, the disease, pest and other agronomic characteristics of 603 corn were comparable to non-transgenic lines of corn.

4. Dietary Exposure

The 603 line of transgenic corn is not a sweet corn, but rather, a field corn intended mainly for use in animal feed. However, some human food uses are relevant for field corn. The 603 corn hybrids would typically be either dry- or wet-milled into various processed corn products. The genetic modification of 603 corn will not result in any change in the consumption pattern for this product. Consequently, the dietary exposure of Canadians to this product is anticipated to be the same as for other lines of commercially available field corn.

5. Nutrition

The analysis of nutrients from transgenic 603 corn and non-transgenic corn did not reveal any significant differences in the levels of proximates (protein, fat, fibre, ash, carbohydrates), amino acids, fatty acids, minerals, phytic acid, trypsin inhibitor or vitamin E. In each case the level of each respective component was comparable to the control and within the reported range for conventional corn. The consumption of products from 603 corn will have no significant impact on the nutritional quality of the Canadian food supply.



6. Safety

a) Potential Toxicity:

An analysis of the amino acid sequence of the inserted CP4 EPSPS enzyme did not show homologies with known mammalian protein toxins and it is not judged to have any potential for human toxicity. Safety has also been demonstrated in an acute mouse gavage study by feeding with high doses of the purified protein.

b) Potential Allergenicity:

The CP4 EPSPS enzyme expressed in 603 corn does not possess characteristics typical of known protein allergens. There were no regions of homology when the sequence of this introduced protein was compared to the amino acid sequences of known protein allergens. Unlike known protein allergens, CP4 EPSPS is rapidly degraded by acid and/or enzymatic hydrolysis when exposed to simulated gastric or intestinal fluids ($t_{1/2} < 15$ s in the gastric fluids; $t_{1/2} < 10$ min. in intestinal fluids). The CP4 EPSPS protein is extremely unlikely to be allergenic.

The CP4 EPSPS enzyme also has a history of safe human and animal consumption, as it is also expressed in Roundup Ready® canola and soybean, which have been commercially available and have a history of safe use in Canada for over four years.

CONCLUSION:

Health Canada's review of the information presented in support of the food use of glyphosate tolerant 603 corn concluded that this corn does not raise concerns related to human food safety. Health Canada is of the opinion that products from 603 corn are as safe and nutritious as those available from current commercial field corn varieties. Health Canada's opinion pertains only to the food use of this glyphosate tolerant corn. Issues related to growing glyphosate tolerant corn in Canada and its use as animal feed are addressed separately through existing regulatory processes in the Canadian Food Inspection Agency.