



## NOVEL FOOD INFORMATION - FOOD BIOTECHNOLOGY

### INSECT-PROTECTED ROUNDUP READY™ CORN LINE MON 802

Health Canada has notified Monsanto Canada Inc. that it has no objection to the food use of grain from the genetically modified Corn line MON 802, which is tolerant to glyphosate herbicide and resistant to insect pests. The Department conducted a comprehensive assessment of Corn line MON 802 according to its *Guidelines for the Safety Assessment of Novel Foods* (Sept. 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**

Corn line MON802 was developed through genetic modification to be tolerant to glyphosate and protect the plant from the European corn borer (*Ostrinia nubilalis*). The modified corn line permits farmers to use the herbicide for weed control and prevents the loss in crop production due to the damaging corn borer insect pest.

#### **2. Development and Production of the Modified Plant**

A commercial corn line was transformed by particle gun acceleration technology using a DNA solution containing two plasmids, PV-ZMBK15 and PV-ZMGT03. Molecular analysis of the resultant corn line, identified as MON 802, established that the line contains the *cryIA(b)*, CP4 EPSPS, and *gox* genes. Segregation and stability data were consistent with a single active site of insertion into the genomic DNA of line MON 802.

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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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The *cryIA(b)* gene was derived from the common soil bacterium *Bacillus thuringiensis* subspecies *kurstaki* (*B.t.k.*). This gene encodes for the production of the CryIA(b) protein which imparts protection from European corn borer (*Ostrinia nubilalis*), a damaging lepidopteran insect pest in Canadian corn production. The CryIA(b) protein encoded by the vector used to produce corn line MON 802 is identical to the protein found in nature and in commercially registered microbial formulations.

The CP4 EPSPS gene was derived from the soil bacterium *Agrobacterium* sp. Strain CP4. The CP4 EPSPS protein produced by this gene is highly tolerant to inhibition by glyphosate, and allows the modified corn plant to be treated with levels of the glyphosate herbicide that control competing weed species.

The *gox* gene was cloned from *Achromobacter* sp. strain LBAA and was also inserted to provide glyphosate tolerance. The GOX enzyme accelerates the normal degradation of glyphosate into aminomethylphosphonic acid (AMPA) and glyoxylate. This provides an additional mechanism for the modified corn's tolerance to applications of the glyphosate herbicide.

### 3. Product Information

Corn is a cultivated species with a long history of safe food and feed use. Animal feeding is by far the largest use of corn with the majority of annual production fed to cattle, poultry, and swine. Corn is readily consumed by livestock and because of its high starch-low fibre content. Corn does not normally contain toxins or antinutritional factors. A significant quantity of corn is fed to livestock directly or in formulated feeds. In addition to corn grown for grain, a portion of annual corn acreage is utilized as whole plant corn silage with consumption confined almost entirely to ruminants. The low price and ready availability of corn has also resulted in the development of large volume food and industrial uses.

Insect-protected Roundup Ready corn line MON 802 differs from its parental counterpart in the insertion of the aforementioned genes, *cryIA(b)*, CP4 and *gox*. The proteins encoded by these genes are expressed throughout the plant tissue and throughout the life of the plant. Average levels of the expressed protein from field trials are as follows:

COMPONENT	LEVEL OF PROTEIN (Fg/g fresh wt.)		
	CryIA(b)	CP4 EPSPS	GOX
Leaf	9.55	26.99	10.18
Whole Plant	1.35	1.85	1.68
Grain	3.20	2.27	ND

ND = not detected



#### **4. Dietary Exposure**

Corn grain is composed of approximately 61% starch, 19.2% protein and fibre, 3.8% oil, and 16% water (U.S. National Corn Growers Association, 1997). Although an ideal source of energy, little whole kernel or processed corn is consumed by humans worldwide when compared to corn-based food ingredients. Corn is an excellent raw material for the manufacture of starch, not only because of price and availability, but also because the starch is easily recovered in high yield and purity. A portion of corn starch is sold as starch products while the majority of the starch is converted to a variety of sweetener and fermentation products including high fructose corn syrup and ethanol. Additionally, corn oil is commercially processed from the germ. Each of these materials is a component of many foods including bakery and dairy goods, beverages, confections, and meat products. By-products of the wet and dry milling process for corn, primarily corn gluten meal and feed, are fed to livestock.

#### **5. Nutrition**

The major components of corn grain and forage were analysed on plant material harvested from field trials. Compositional data for protein, fat, ash, carbohydrates, calories, moisture, amino acids, and fatty acids for line MON 802 grain were comparable to the data from the control line and within published ranges for commercial hybrids. Similarly, proximates (protein, fat, ash, carbohydrates, calories, and moisture), acid detergent fibre (ADF) and neutral detergent fibre (NDF) analyses were performed on forage for line MON 802 and an appropriate control. Based on these compositional data, it was concluded that the forage from line MON 802 and the control line were substantially equivalent.

#### **6. Toxicology Data**

The safety assessments of the CryIA(b), CP4 EPSPS and GOX proteins were confirmed in experiments which included protein characterization, digestive fate studies in simulated gastric and intestinal fluids and acute oral toxicity in mice. Data were generated that demonstrated that the active CryIA(b) protein product of the inserted *cryIA(b)* gene was equivalent to that produced in the naturally occurring bacterium *Bacillus thuringiensis*, and that the CP4 and GOX proteins were equivalent to those produced in *E. coli* that had been transformed with the same genetic traits. The CryIA(b) protein is rapidly degraded and its insecticidal activity lost under conditions that simulate mammalian digestion. Similarly, the enzymatic activity of CP4 and GOX protein disappeared rapidly as these proteins were rapidly degraded under these same conditions. There were no indications of toxicity as measured by the absence of treatment related adverse effects in mice administered CryIA(b), CP4 EPSPS or GOX proteins by oral gavage. Using sophisticated computerized search capabilities, the evidence showed that the CryIA(b) protein did not show meaningful amino acid sequence homology when compared to known allergens or protein toxins, with exception of other *B.t.* proteins. Similarly, the CP4 and GOX proteins did not show meaningful amino acid sequence homology when compared to known allergens or protein toxins. These studies support the safety of the proteins and are consistent with the history of safe use of *B.t.* and CryIA(b), and the ubiquitous distribution of *Agrobacterium* and *Achromobacter* spp. in the soil.

#### **CONCLUSION:**



Based on the data and information submitted by Monsanto Canada, and a thorough comparison of insect-protected Roundup Ready corn line MON 802 with an appropriate control line and published ranges for other corn varieties, Health Canada has concluded that corn line MON 802 is as safe and nutritious as current commercial corn varieties.

Health Canada's opinion deals only with the food use of grain from the genetically modified corn line MON 802. Issues related to growing corn line MON 802 in Canada and its use as animal feed are addressed separately through existing regulatory processes in the Canadian Food Inspection Agency