

October, 2002

## **NOVEL FOOD INFORMATION– FOOD BIOTECHNOLOGY Cry1F INSECT-RESISTANT/GLUFOSINATE-TOLERANT MAIZE LINE 1507**

Health Canada has notified Dow AgroSciences Canada Inc. (DAS) and Pioneer Hi-Bred International Inc. (PHI) that it has no objection to the food use of Cry 1F insect resistant/glufosinate-tolerant corn line 1507 derived through particle mediated transformation introducing a DNA construct into corn plant cells rendering it resistant to insect pests and tolerant to glufosinate-ammonium herbicides. The Department conducted a comprehensive assessment of this corn according to its Guidelines for the Safety Assessment of Novel Foods. These Guidelines are based upon internationally accepted principles for establishing the safety of foods with novel traits.

### **BACKGROUND:**

The following provides a summary regarding DAS and PHI's notification to Health Canada and contains no confidential business information.

#### **1. Introduction**

Dow Agrosciences Canada Inc. developed Maize line 1507 through genetic modification to be tolerant to glufosinate-ammonium herbicides and protect the plant from certain lepidopteran larvae (including European corn borer, southwestern corn borer, fall armyworm, and black cutworm). The modified corn line permits farmers to use the herbicide for weed control and prevents loss in crop production due to the damaging insect pests.

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

Corn line 1507 was a result of using particle mediated transformation which introduced a DNA construct into corn plant cells. The construct consisted of a linear portion of DNA containing the cry 1F and pat coding sequences and the regulatory components necessary for expression.

Molecular analysis indicates that line 1507 contains a full length construct containing both the truncated cry1F and pat genes at one insertion site in the genome. Sequencing of the flanking regions of the insert indicate that in addition to the full length copies of cry1F and pat, there are small fragments of cry1F and pat in the 5' border and a second fragment of pat in the 3' border of the insert. This information was determined by Southern blot and Polymerase Chain Reaction (PCR) analysis. Northern and Western blot analysis demonstrates that only the full length truncated cry1F and pat expression products are

produced in line 1507.

The truncated version of the cry1F gene expressed in line 1507 is derived from *Bacillus thuringiensis* var. *aizawai*. B.t. based biopesticidal products have been used for insect control for more than 30 years. The protein encoded by the truncated cry1F gene is nearly identical to the first 605 amino acids of the Cry1F protein protoxin produced by *B. thuringiensis* var. *aizawai*. This truncated protein corresponds to the insecticidally active portion of the delta endotoxin that remains following cleavage in the gut of lepidopteran larvae. The pat gene is derived from *Streptomyces viridochromogenes* which is a common soil bacterium. The gene encodes for the enzyme phosphinothricin-N-acetyltransferase (PAT) which inactivates the herbicide glufosinate ammonium. PAT was used as a selectable marker in the development process of line 1507. The gene sequences for both pat and cry1F were optimized for improved expression in plants without altering function or activity.

### **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.

Cry 1F Insect-Resistant/Glufosinate-tolerant Maize Line 1507 differs from its parental counterpart in the insertion of the aforementioned genes, cry1F and pat. The proteins encoded by these genes are expressed throughout the plant tissue and throughout the life of the plant.

### **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 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.

Products derived from corn line 1507 are intended for use in human food and animal feed. It is expected to be used in similar applications as traditional corn varieties by the food

industry.

## **5. Nutrition**

A significant amount of nutrient data was provided to Food Directorate for the evaluation of corn line 1507. The petitioner analyzed over 40 nutrients and other biochemical components in the line, finding that all were within the range of results reported for conventional corn lines. It can be concluded that the genetic modification of line 1507 did not result in substantial changes in the levels of nutrients analyzed and was very unlikely to have caused any other changes that would significantly impact the nutritional quality of the corn line.

## **6. Toxicology**

B.t. Cry proteins have a long history of safe and widespread use. The PAT protein is expressed in a number of genetically modified foods previously approved by Health Canada. The Cry1F and PAT proteins were subjected to an acute oral toxicology evaluation in addition to in vitro digestive fate studies and sequence homology searches with known allergens and toxins. The LD50s of these proteins (576 mg/kg bw and 5040 mg/kg bw, respectively) were orders of magnitude above expected human exposure levels. Human exposure to these proteins would be extremely low, based on expression levels in the grain and the rapid digestion of these proteins in simulated gastric fluid. The novel proteins were not homologous to known food allergens, established on sequence comparisons of computerized databases. The rapid digestibility of both proteins indicates that they are not similar to known food allergens and that exposure to intact protein would be minimal. Therefore, based on this data, the Cry1F and PAT proteins expressed by insect-resistant/glufosinate tolerant corn line 1507 are unlikely to be toxins or allergens.

## **CONCLUSION:**

Information on the parent plant, the modification process, and the modified plant was reviewed. On the basis of that review, it was concluded that: the novel phenotype incorporated into corn line 1507 is stable, and is expressed as expected. Also, that the genetic modification results in the addition of the cry1F and pat genes in the corn genome of line 1507 and the expression of two protein products (Cry1F and PAT). The additional sequence fragments of cry1F and pat genes found in the border regions of the insert are non-functional. As well, the genetic modification process used in the development of line 1507 does not raise any specific concerns.

The safety assessment conducted by Food Directorate scientific evaluators determined that Cry 1F insect resistant/glufosinate-tolerant corn line 1507 is as safe and nutritious as traditional corn varieties currently sold on the Canadian marketplace.

Health Canada's opinion deals with the food use of grain from the genetically modified Cry 1F insect resistant/glufosinate-tolerant corn line 1507. Issues related to growing corn line 1507 in Canada and its use as an animal feed are addressed separately through existing

regulatory processes in the Canadian Food Inspection Agency.

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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 Products and Food 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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