



Decision Document DD2006-57

Determination of the Safety of Monsanto Canada Inc.'s Glyphosate-Tolerant, Corn-Rootworm-Protected Corn (*Zea mays* L.) Event MON 88017

This Decision Document has been prepared to explain the regulatory decision reached under the directive Dir94-08 *Assessment Criteria for Determining Environmental Safety of Plants with Novel Traits* and its companion document BIO1994-11 *The Biology of Zea mays L. (Corn/Maize)* and the directive Dir95-03 *Guidelines for the Assessment of Novel Feeds: Plant Sources*.

The Canadian Food Inspection Agency (CFIA), specifically the Plant Biosafety Office and the Feed Section of the CFIA, have evaluated information submitted by Monsanto Canada Inc. This information is in regard to the glyphosate tolerant, corn rootworm (*Diabrotica spp.*) resistant corn event MON 88017. The CFIA has determined that this plant with novel traits does not present altered environmental interactions, does not present concerns for the safety of livestock consuming feed derived from this plant with novel traits, when compared to currently commercialized corn varieties in Canada.

Unconfined release into the environment and livestock feed use of corn event MON 88017 is authorized as of February 20, 2006 until April 1, 2007. Extension of the authorization is conditional upon the submission of additional research results related to corn rootworm resistance management. All its progeny and sister lines which have been derived from the original transformation event and their respective progenies, are also authorized for unconfined release and livestock feed, provided that: (i) no inter-specific crosses are performed, (ii) the intended uses are similar, (iii) based on characterization, these plants do not display any additional novel traits and are substantially equivalent, in terms of their specific use and safety for the environment and for human and animal health, to plants currently being cultivated, (iv) the novel genes are expressed at a level similar to that of the authorized line and (v) that insect resistance management requirements described in the present document are applied.

The corn event MON 88017 is subject to the same phytosanitary import requirements as its unmodified counterpart.

Please note, that the livestock feed and environmental safety of PNTs and novel feeds are critical steps in the potential commercialization of these plant types. Other requirements, such as the evaluation of food safety by Health Canada, have been addressed separately from this review.

(publié aussi en français)

February 20, 2006

This bulletin is published by the Canadian Food Inspection Agency. For further information, please contact the Plant Biosafety Office or the Feed Section at:

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I. Brief Identification of the Plant with Novel Traits (PNT)

Designation(s) of the PNT:	MON 88017 corn, OECD identifier MON-88Ø17-3
Applicant:	Monsanto Canada Inc.
Plant Species:	Corn (<i>Zea mays</i> L.)
Novel Traits:	Resistance to Western and Northern Corn Rootworms. (<i>Diabrotica virgifera virgifera</i> and <i>Diabrotica barberi</i>); Tolerance to Glyphosate-based herbicides
Trait Introduction Method:	<i>Agrobacterium</i> -mediated transformation
Proposed Use of the PNT:	Production of corn for human consumption (wet mill products, dry mill products and seed oil) and oil, meal, grain, silage and other by-products for livestock feed. These materials are not intended to be grown outside the normal production area for corn in Canada.

II. Background Information

Monsanto Canada Inc. has developed corn lines from event MON 88017 resistant to corn rootworm (*Diabrotica spp.*) and tolerant to glyphosate-based herbicides. The corn event, designated as MON 88017, was developed to provide a method to control yield losses from insect feeding damage caused by rootworm larvae, as well as a method to control weeds in corn production.

Event MON 88017 was developed using recombinant DNA technology, resulting in the introduction of bacterial genes conferring resistance to rootworms and tolerance to glyphosate.

Monsanto Canada Inc. has provided data on the identity of event MON 88017, a detailed description of the transformation method, data on the gene insertion site, gene copy number, levels of gene expression in the plant, the role of the inserted genes and regulatory sequences, and the full nucleotide sequence of the inserted genes. Each novel protein was identified, characterized and compared to the original bacterial protein, including an evaluation of its potential toxicity to livestock and non-target organisms.

Corn event MON 88017 has been field tested in Canada in 2003, and in the United States in 2001, 2002 and 2003.

The CFIA has consulted with the Canadian Corn Pest Coalition on issues related to potential development of rootworm populations resistant to the insecticidal protein produced by MON 88017 corn, and the insect resistance management strategy that would

significantly reduce and delay the development of rootworm resistance to the Cry3Bb1 protein. The Coalition is a group composed of representatives from academia, government, growers and industry.

Agronomic characteristics of corn hybrids derived from MON 88017 corn such as seed dormancy, vegetative vigour, early stand establishment, time to maturity, flowering period, susceptibilities to various corn pests and pathogens, and seed production were compared to those of unmodified corn counterparts.

Nutritional components of MON 88017 corn, such as proximates, amino acids and fatty acids were compared with those of unmodified corn counterparts.

The Plant Biosafety Office, CFIA, has reviewed the above information, in light of the assessment criteria for determining environmental safety of plants with novel traits, as described in the directive Dir94-08. The following have been considered:

- potential of MON 88017 corn to become a weed of agriculture or invasive of natural habitats,
- potential for gene flow from MON 88017 corn to wild relatives whose hybrid progeny may become more weedy or more invasive,
- potential for MON 88017 corn to become a plant pest,
- potential impact of MON 88017 corn on non-target organisms, including humans, and
- potential impact of MON 88017 corn on biodiversity.

The Feed Section of the Animal Health and Production Division, CFIA, has also reviewed the above information with respect to the assessment criteria for determining the safety and efficacy of livestock feed, as described in Dir95-03. The following have been considered:

- potential impact of MON 88017 corn on livestock health and
- potential impact of MON 88017 corn on livestock and workers/by-standers.

III. Description of the Novel Traits

1. Development Method

The corn hybrid A x Hi-II was transformed with a binary plasmid vector carrying the *cry3Bb1* and the *cp4 epsps* genes. The genes were introduced via *Agrobacterium tumefaciens* transformation into corn cells. Transformants were selected based on tolerance to glyphosate. Event MON 88017 was identified as a successfully transformed corn event and was chosen for further development.

2. Resistance to Rootworms (*Diabrotica spp.*)

Foliar insecticides based on *Bacillus thuringiensis* endotoxins (generally known as B.t.) have been registered for over 30 years in Canada and have a long history of safe use. *Bacillus thuringiensis* var. *kumamotoensis* is a common gram-positive soil-borne bacterium. In the spore forming stage, it produces several insecticidal protein crystals, including the δ -endotoxin Cry3Bb1 protein which is active against certain coleopteran insects, such as *Diabrotica spp.* The protein is insecticidal to coleopterans after cleavage in the insect's gut to a bio-active, trypsin resistant core. Insecticidal activity is believed to depend on the binding of the active fragment to specific receptors present in susceptible insects on midgut epithelial cells, forming pores which disrupt osmotic balance and eventually result in cell lysis and insect death. This protein has been shown to be non-toxic to humans, other vertebrates and invertebrates.

MON 88017 corn contains a synthetic *cry3Bb1* gene variant developed to maximize its expression in corn. The gene codes for a protein sharing > 99% sequence identity with the wild type *B. thuringiensis* var. *kumamotoensis* Cry3Bb1 protein. The Cry3Bb1 variant produced in MON 88017 corn differs only by a single amino acid from the Cry3Bb1 variant produced in MON 863 corn, which has been conditionally authorized for unconfined release in Canada since March, 2003. Monsanto has provided a detailed characterization of the Cry3B1 protein expressed in MON 88017 corn.

The *cry3Bb1* gene expressed in corn event MON 88017 is linked to a constitutive promoter. Samples of corn tissues were collected at various growth stages from three representative US field trial sites. Average Cry3Bb1 protein expression in micro-grams protein per gram dry weight tissue ($\mu\text{g/g dwt}$) as evaluated by enzyme-linked immunosorbent assay are as follows: 260-570 $\mu\text{g/g dwt}$ in leaf, 25 $\mu\text{g/g dwt}$ in pollen, 380 $\mu\text{g/g dwt}$ in silk, 100-370 $\mu\text{g/g dwt}$ in root, 95 $\mu\text{g/g dwt}$ in forage and 15 $\mu\text{g/g dwt}$ in grain.

The levels of the Cry3Bb1 protein decline in senescent tissues and the Cry3Bb1 protein was shown to degrade readily in the soil.

No adverse effects were observed when Cry3Bb1 protein was ingested by mice at a dose of 1930 mg/kg body weight. *In vitro* digestive fate studies have shown that the protein is rapidly degraded in simulated gastric fluid unlike protein allergens which are normally resistant to digestion. Furthermore, the protein is not glycosylated in corn and it lacks sequence similarity to known allergens and toxins. When defatted grain of MON 88017 was treated at $\sim 206^\circ\text{C}$ for 20 minutes, the Cry3Bb1 protein level fell below the level of detection (0.1 ng), or decreased by greater than 98% from its original level.

To obtain sufficient quantities of Cry3Bb1 protein for evaluation of environmental and feed safety it was necessary to express the *cry3Bb1* gene in an *E. coli* production system. The equivalency of the plant-produced protein to the *E. coli*- produced protein was evaluated by comparing their molecular weight, immunological reactivity, insecticidal

activity and glycosylation status. Based on the results, both proteins were found to be equivalent.

Monsanto Canada Inc. has provided the CFIA with a method for the detection and identification of corn containing the MON 88017 event.

3. Tolerance to Glyphosate

A gene derived from an *Agrobacterium* sp. strain CP4 (*cp4 epsps*) which imparts field level tolerance to glyphosate, the active ingredient in Roundup brand[®] herbicides, was introduced into corn event MON 88017. A plant-derived coding sequence expressing an optimized chloroplast transit peptide was fused to the *cp4 epsps* coding sequence. This peptide facilitates the import of the newly translated EPSPS enzyme into the chloroplast, the site of amino acid biosynthesis. EPSPS is an enzyme involved in the shikimic acid metabolic pathway which is essential for the production of the aromatic amino acids. The native corn EPSPS enzyme is sensitive to glyphosate. The herbicide disrupts the shikimic acid pathway, leading to growth suppression or death of the plant. The CP4 EPSPS version of this enzyme is expressed in MON 88017 corn, and confers glyphosate tolerance since it continues to catalyze the production of aromatic amino acids in the presence of glyphosate due to a reduction in the binding of glyphosate to the CP4 EPSPS in comparison to the native corn EPSPS.

The CP4 EPSPS protein in MON 88017 corn is structurally and functionally similar to native plant EPSPS enzymes. This protein is the same or shares more than 99% sequence identity with the CP4 EPSPS protein produced in Roundup Ready[®] crops which have already been approved for unconfined release and animal feed uses in Canada. Monsanto Canada Inc. has provided a detailed characterization of the CP4 EPSPS protein expressed in MON 88017 corn.

The *cp4 epsps* gene expressed in corn event MON 88017 is linked to a constitutive promoter. Samples of corn tissues were collected at various growth stages from three representative US field trial sites. Average CP4 EPSPS protein expression in micro-grams protein per gram dry weight tissue ($\mu\text{g/g dwt}$) as evaluated by enzyme-linked immunosorbent assay are as follows: 150-220 $\mu\text{g/g dwt}$ in leaf, 390 $\mu\text{g/g dwt}$ in pollen, 70-150 $\mu\text{g/g dwt}$ in root, 57 $\mu\text{g/g dwt}$ in forage and 5.8 $\mu\text{g/g dwt}$ in grain.

To obtain sufficient quantities of CP4 EPSPS protein for evaluation of environmental and feed safety it was necessary to express the *cp4 epsps* gene in an *E. coli* production system. The equivalency of the MON 88017 corn-produced CP4 EPSPS protein to the *E. coli*-produced CP4 EPSPS was evaluated by comparing their molecular weights, immunoreactivity, glycosylation status and functional activity. Based on the results, both proteins were found to be equivalent.

CP4 EPSPS protein expressed in MON 88017 corn is similar to EPSPS enzymes present in many foods with a long history of safe use in Canada, and therefore would not be expected to be toxic or allergenic. Previous assessments have shown that the CP4 EPSPS protein, unlike many allergens, is readily degraded in simulated mammalian gastric and intestinal fluids and is not glycosylated. In addition, the CP4 EPSPS protein is not homologous to known toxins or allergens. When defatted grain of MON 88017 was

treated at ~ 206°C for 20 minutes, the CP4 EPSPS protein level fell below the level of detection (0.1 ng), or decreased by greater than 98% from its original level.

4. Stable Integration into MON 88017 corn's Genome

Southern blot analysis of MON 88017 corn's genome confirmed that single copies of the *cp4 epsps* and *cry3Bb1* genes are integrated at a single locus in MON 88017 corn's genome with all expression elements intact and no plasmid backbone present. The stability of the insert in MON 88017 corn has been established over 7 breeding generations. Segregation analyses across 10 generations were performed to determine the inheritance of the corn rootworm resistance and glyphosate tolerance traits. The results of the analysis are consistent with the finding of a single active site of insertion that segregates according to the Mendelian laws of genetics.

IV. Criteria for the Environmental Assessment

1. Potential of MON 88017 corn to Become a Weed of Agriculture or be Invasive of Natural Habitats

The biology of corn, described in the CFIA Biology Document BIO1994-11, shows that unmodified plants of this species are not invasive of unmanaged habitats in Canada. Corn does not possess the potential to become weedy due to traits such as lack of seed dormancy, the non-shattering nature of corn cobs, and the poor competitive ability of seedlings. According to the information provided by Monsanto Canada Inc., MON 88017 corn and derived corn hybrids were determined to be similar to their counterparts in this respect.

CFIA evaluated data submitted by Monsanto Canada Inc. on the reproductive and survival biology of corn hybrids derived from MON 88017 corn, and determined that early stand establishment, flowering period, vegetative vigor, time to maturity and seed production were within the normal range of expression of these traits currently displayed by commercial corn hybrids. No competitive advantage was conferred to MON 88017 corn, other than that conferred by resistance to rootworm and tolerance to glyphosate herbicide. These traits were demonstrated not to render corn weedy or invasive of natural habitats since none of the reproductive or growth characteristics were modified.

The above considerations led the CFIA to conclude that MON 88017 corn has no altered weed or invasive potential compared to currently commercialized corn.

2. Potential for Gene Flow from MON 88017 corn to Wild Relatives Whose Hybrid Offspring May Become More Weedy or More Invasive

The biology of corn, as described in BIO1994-11, indicates that there are no wild relatives in Canada that can hybridize with corn. None of the data submitted by Monsanto Canada Inc. on the physiological characteristics of MON 88017 corn indicated any changes in sexual compatibility as a result of the gene insertion.

CFIA therefore concludes that gene flow from MON 88017 corn to wild corn relatives is not possible in Canada.

3. Altered Plant Pest Potential of MON 88017 corn

The intended effects of both novel traits are unrelated to plant pest potential, and corn is not a plant pest in Canada. In addition, agronomic characteristics of MON 88017 corn hybrids were shown to be within the range of values displayed by currently commercialized corn hybrids, and indicate that the growing habit of corn was not inadvertently altered. Field observations did not indicate modifications of disease and pest susceptibilities, other than to rootworm, which is not known to be a principal factor restricting the establishment or distribution of corn in Canada.

Some of the genetic elements introduced into MON 88017 corn were derived from known plant pathogens, but in all cases the genes responsible for the pathogenic qualities of the pathogen were not introduced. Therefore, the introduction of genetic material for *Diabotica* spp. resistance and glyphosate tolerance would not be expected to result in MON 88017 expressing novel pathogenic characteristics.

CFIA has therefore determined that MON 88017 corn does not display any altered pest potential.

4. Potential Impact of MON 88017 corn on Non-Target Organisms

The history of use and literature suggest that the bacterial Cry3Bb1 *B.t.* δ -endotoxins are not toxic to humans, other vertebrates, and non-coleopteran invertebrates. This protein is active only against specific coleopteran insects. There are no coleopteran species currently listed by the Committee on the Status of Endangered Wildlife in Canada as being a threatened or endangered species. (Please refer to <http://www.cosewic.gc.ca/index.htm> for more information)

Monsanto Canada Inc. has submitted data from dietary toxicity and field studies on the effect of the Cry3Bb1 protein on non-target organisms in support of the environmental safety assessment of corn event MON 863 (see DD2003-43). In all cases, MON 863 corn was demonstrated to be safe to non-target organisms. Given that MON 88017 Cry3Bb1 protein differs from the MON 863 CryBb1 protein by a single amino-acid, that both proteins were demonstrated to be equivalent in terms of insecticidal activity against susceptible pest insects and that the levels of Cry3Bb1 expression in both corn lines are similar, MON 88017 corn is expected to be safe to previously assayed non-target

organisms. The Cry3Bb1 protein expressed in MON 88017 corn was also demonstrated to be safe to mammals.

The impact of CP4 EPSPS protein on non-target organisms, including humans, has been thoroughly assessed in previous applications for environmental safety assessments of CP4 EPSPS-expressing crops. The CP4 EPSPS protein expressed in MON 88017 corn tissues is the same or is > 99% identical to CP4 EPSPS proteins produced in glyphosate-tolerant crops with a history of safe use. The environmental and feed safety of the CP4 EPSPS protein in corn has been previously established with the regulatory approval of NK 603 corn by CFIA (see DD2002-35).

Unmodified corn is known to produce low levels of anti-nutrients such as raffinose and phytic acid, and the levels of these compounds in MON 88017 corn were demonstrated to be equivalent to levels found in control lines. Therefore the genetic modification did not alter the expression of endogenous anti-nutritional factors.

Based on the above, CFIA has determined that the unconfined release of MON 88017 corn will not result in altered impacts when compared with currently commercialized corn on interacting organisms, including humans, with the exception of specific coleopteran pest species.

5. Potential Impact of MON 88017 corn on Biodiversity

MON 88017 corn has no novel phenotypic characteristics which would extend its use beyond the current geographic range of corn production in Canada. Since corn does not out-cross to wild relatives in Canada, there will be no transfer of novel traits to unmanaged environments. In addition the novel traits were determined to pose minimal risks to non-target organisms.

MON 88017 corn provides an alternative method to existing methods of control of rootworms, an important agricultural pest of corn in Canada. The control of agricultural pest species is a common practice in Canada that is not restricted to the environmental release of PNTs. Therefore, the reduction in local pest species as a result of the release of MON 88017 corn does not present a significant change from existing agricultural practices. At present, the use of chemical insecticides to control rootworm is permitted in Canada. Currently, crop rotation represents the principal method of rootworm control in Canada.

MON 88017 corn provides an alternative method of weed control in corn production. The use of broad spectrum herbicides has the intended effect of reducing local weed populations within agricultural fields and this may reduce local weed species biodiversity, and possibly other trophic levels which utilize these weed species. It must be noted, however, that reduction in weed biodiversity in agricultural fields is not unique to the use of PNTs, and is a common practice in virtually all modern agricultural systems.

The CFIA has therefore concluded that MON 88017 corn does not present a significantly altered impact on biodiversity in comparison to corn varieties currently being grown in Canada.

6. Potential for Development of Rootworm Resistance to MON 88017 corn

In order to significantly minimize the likelihood of the development of insect pest resistance to PNTs expressing novel insect resistance, the CFIA requires that an insect resistance management (IRM) plan be implemented for these products. Coleopteran insects have a significant ability to develop resistance to conventional chemical insecticides. Therefore it is reasonable to expect that resistance to the insecticidal properties of corn line MON 88017 may develop. The following IRM design is intended to reduce or delay corn root worm (CRW) resistance to the Cry3Bb1 protein. A component of the IRM strategy that will be used with MON 88017 corn is the establishment of a refuge of CRW-susceptible corn within or adjacent to the *B.t.* corn field. Should resistant insects occur, they would then be able to mate with susceptible insects to keep the frequency of resistance genes diluted in the insect population.

CFIA believes that sound management practices and IRM strategies can significantly reduce and delay the development of Cry3Bb1 protein resistant CRW populations. However the CRW populations must be monitored for the development of resistance in a regular and consistent manner.

CFIA understands that Monsanto Canada Inc. has developed and will implement an IRM plan that includes the following key components:

- (i) The use of structured refugia to provide a population of corn rootworms that have not been exposed to the Cry3Bb1 protein and are available to reproduce with potentially resistant rootworms which may emerge from the Bt crop.
- (ii) The early detection of rootworm populations resistant to the corn-expressed insecticidal protein is extremely important. Close monitoring for the presence of such populations, in rootworm-resistant corn fields and surrounding areas, is therefore warranted. Monitoring includes the development of appropriate detection tools such as visual field observations and laboratory bioassays, education of growers, reporting schedules, and mitigation procedures in case of resistance development.
- (iii) Education tools will be developed and provided to all growers, district managers and field managers. These will include information on product performance, resistance management, monitoring procedures and timetables, detection protocols for resistant rootworm individuals, instructions to contact Monsanto Canada Inc. and strategies to be followed if unexpected levels of rootworm damage occur.
- (iv) Monsanto Canada Inc. will have documented procedures in place for responding to these reported instances of unexpected rootworm damage. These procedures will

include, where warranted, the collection of plant tissue and rootworms and use of appropriate bioassays to evaluate suspected Cry3Bb1 resistant individuals, and a protocol for immediate action to control resistant individuals.

(v) Detection of confirmed resistant rootworm populations and mitigation measures will be immediately reported to CFIA.

(vi) Integrated Pest Management practices will be promoted, such as prediction of infestation problems from field histories.

The IRM plan for MON 88017 corn is identical to that of the currently approved corn event MON 863, in that both events have the same potential for development of corn root worm resistance to Cry3Bb1 protein. Research related to the MON 863 IRM plan is ongoing, and as research progresses, the new information will be used to determine if the present IRM plan should be maintained in its present form, or if it will be modified. Therefore, the extension of the present authorization will be contingent upon Monsanto Canada Inc. demonstrating significant progress in research related to IRM for MON 863 corn.

Note: The Plant Biosafety Office periodically audits compliance with the IRM requirements.

7. Potential for the development of multiple herbicide tolerant volunteers and herbicide tolerant weeds

If there is general adoption of several different crop species with novel herbicide tolerances, then the potential exists for the development of crop volunteers with a combination of tolerances to different herbicides. Therefore, this technology should be managed as part of an integrated approach which may include currently available weed control products with alternate modes of action, or alternative methods of weed control. Of additional note is the use several crop species in rotation which all rely on tolerance to the same herbicide. Another potential concern is that the continued use of a specific herbicide may provide significant selective pressure for the potential development of herbicide tolerant weeds. Therefore, agricultural extension personnel in both the private and public sectors should promote careful management practices for growers who use these herbicide-tolerant crops to minimize the development of multiple herbicide tolerant crop volunteers as well as tolerant weed populations. The CFIA understands that Monsanto Canada Inc. has developed and has implemented a Herbicide Management Plan for glyphosate-tolerant corn that adequately addresses these issues.

V. Criteria for the Livestock Feed Assessment

1. Potential Impact of MON 88017 corn on Livestock Nutrition

Nutritional Composition of MON 88017 corn

Composition of grain and whole plant from line MON 88017 corn was compared with a control line with the same genetic background, LH198xLH59. Whole plant analysis included proximates, ADF, NDF, Ca and P, while grain analysis included proximates, major fatty acids, amino acids, vitamin A, tocopherols, B vitamins, minerals, secondary metabolites (raffinose, furfural, P-coumaric acid, ferulic acid) and anti-nutrients (phytic acid and trypsin inhibitor). No significant differences were found for any of the forage analytes when MON 88017 was compared to the control line. Single differences were found for forage analytes when the other comparisons were made. Vitamin B1 was the only grain analyte that was consistently lower in MON 88017 corn relative to the control line at each of the field site. Linoleic acid was more abundant in MON 88017 corn relative to the control line in the statistical analysis of two field sites and in the combined analysis. All the reported values were within the literature ranges, and within Monsanto's calculated 99% tolerance interval with the exception of the vitamin B1 values for the control line. The applicant concluded that forage and grain produced from MON 88017 corn and MON 88017 x MON 810 corn are compositionally equivalent to forage and grain produced from other commercial corn hybrids currently on the market.

Secondary Metabolites and Anti-Nutritional Factors

Concentrations of raffinose, furfural, P-coumaric acid, ferulic acid, phytic acid and trypsin inhibitor were shown to be equivalent in corn grain derived from MON 88017 corn and the control lines.

2. Potential Impacts on Livestock and Workers/By-standers

Corn is not known for the production of endogenous allergens and the transformation event which produced MON 88017 would not be expected to induce their synthesis.

EPSPS is an enzyme present in many foods with a long history of safe use in Canada, and therefore would not be expected to be toxic or allergenic. The CP4 EPSPS enzyme is from *Agrobacterium* strain CP4, a soil bacterium, which is not a known human or animal pathogen. The amino acid sequence of the CP4 EPSPS protein found in line MON 88017 is identical to the CP4 EPSPS protein in Roundup Ready® crops previously approved in Canada. CP4 EPSPS shares no biologically relevant significant homology with known toxins or allergens, it is present in small amounts in the feed, it is heat labile and it is rapidly degraded under the conditions present in the gastrointestinal tract. Additionally, a mouse acute oral toxicity study indicated no adverse effects at 475 mg/kg body weight CP4 EPSPS. Based on the information provided by Monsanto Canada, CP4 EPSPS is unlikely to be a novel toxin or allergen.

The history of use and literature suggest that the bacterial B.t. δ -endotoxin is not toxic to humans and other vertebrates. The B.t. protein produced in corn was shown to be equivalent to the original microbial protein. No receptors for the Cry3Bb1 delta-endotoxin

are present on the surface of mammalian intestinal cells, therefore livestock and workers/by-standers are not expected to be susceptible to these proteins. The Cry3Bb1 protein shares no biologically relevant significant homology with known toxins or allergens, it is present in small amounts in the feed and it is rapidly degraded under the conditions present in the gastrointestinal tract. Additionally, a mouse acute oral toxicity study using Cry3Bb1 was conducted and no adverse effects on growth or survival were observed at 1930 mg/kg body weight. Based on the information provided by Monsanto Canada, Cry3Bb1 is unlikely to be a novel toxin or allergen.

Based on the predicted exposure levels and the results of the above tests, no significant risk to livestock and workers/by-standers is expected from exposure to the CP4 EPSPS or Cry3Bb1 proteins.

VI. New Information Requirements

Where, at any time after providing notification of the proposed unconfined release or receiving authorization for the unconfined release of corn event MON 88017, Monsanto Canada Inc. becomes aware of any new information regarding the environmental safety or animal or human health safety of MON 88017 corn that could result from the release, Monsanto Canada Inc. must immediately provide the CFIA with the new information. On the basis of such new information, the CFIA will re-evaluate the potential risk to environmental, animal or human health that could result from release of MON 88017 corn and will re-evaluate its decision with respect to the livestock feed use and environmental release authorizations of MON 88017 corn. The CFIA may maintain, change, or remove existing conditions respecting the release; impose additional conditions; or refuse or cancel the authorization and require the applicant to stop the release and take any appropriate action necessary to eliminate from, or minimize the risk to, the environment.

VII. Regulatory Decision

Based on the review of data and information submitted by Monsanto Canada Inc., and through comparisons of corn hybrids derived from MON 88017 corn both with unmodified corn counterparts and previously approved corn events NK 603 and MON 863, the Plant Biosafety Office, CFIA, has concluded that the introduced genes and their corresponding traits do not confer to MON 88017 corn any characteristic that would result in intended or unintended environmental effects following unconfined release. Monsanto Canada Inc. has developed and will implement an insect resistance management plan.

Based on the review of submitted data and information by Monsanto Canada Inc., including comparisons of MON 88017 corn with unmodified corn counterparts and

previously approved corn events NK 603 and MON 863, the Feed Section, CFIA, has concluded that the introduced genes and their corresponding traits will not confer to MON 88017 corn any characteristic that would raise any concerns regarding the safety or nutritional composition of MON 88017 corn. Grain corn, its byproducts and corn oil are currently listed in Schedule IV of the *Feeds Regulations* and are therefore approved for use in livestock feeds in Canada. MON 88017 corn has been assessed and found to be as safe as and as nutritious as traditional corn varieties. MON 88017 corn and its products are considered to meet present ingredient definitions and are approved for use as livestock feed ingredients in Canada.

Unconfined release into the environment and livestock feed use of corn line MON 88017 is therefore authorized as of February 20, 2006 until April 1, 2007. Extension of the authorization is conditional upon the submission of additional research results related to corn rootworm resistance management. All its progeny and sister lines which have been derived from the original transformation event and their respective progenies, are also authorized for unconfined release and livestock feed, provided that no inter-specific crosses are performed, provided the intended uses are similar, provided that based on characterization, these plants do not display any additional novel traits and are substantially equivalent, in terms of their specific use and safety for the environment and for human and animal health, to plants currently being cultivated, provided the novel genes are expressed at a level similar to that of the authorized line and provided that insect resistance management requirements described in the present document are applied.

Corn event MON 88017 is subject to the same phytosanitary import requirements as its unmodified counterparts

Please refer to Health Canada's Decisions on Novel Foods for a description of the food safety assessment of MON 88017 corn. The food safety decisions are available at the following Health Canada web site:

http://www.hc-sc.gc.ca/fn-an/gmf-agm/appro/index_e.html