GM Crop Database

Database Product Description

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MON-ØØ863-5 (MON863)

Host Organism / Variety	*Zea mays L.* L. (Maize)
Trait	Resistance to corn root worm (Coleopteran, *Diabrotica sp.*)
Trait Introduction	Microparticle bombardment of plant cells or tissue
Proposed Use	Production of *Z. mays* for human consumption (wet mill or dry mill or seed oil), and meal and silage for livestock feed. These materials will not be grown outside the normal production area for corn.
Company Information	Monsanto Company Chesterfield Village Research Center (MO) 700 Chesterfield Parkway North St. Louis MO USA

Summary of Regulatory Approvals

Country	Environment	Food and/or Feed	Food	Feed	Marketing
Australia			2003		
Canada	2003		2003	2003	
China		2004			
European Union			2006	2005	
Japan			2002	2002	2001
Korea			2003	2004	
Mexico		2003			
Philippines			2003	2003	
Taiwan			2003		
United States	2003	2001			

Click on the country name for country-specific contact and regulatory information.

Notes

European Union: Import and use as feed were approved by decision of the EU commission on August 8th, 2005. Use as food was approved by decision of the EU commission on January 13th, 2006.

Introduction

Maize line MON 863 was produced using recombinant-DNA techniques to express the *cry3Bb1* gene encoding a Coleopteran-specific insecticidal protein from *Bacillus thuringiensis* (subsp. *kumamotoensis*) in order to control infestation with corn root worm (CRW; *Diabrotica sp.*). This gene was introduced into the publicly available inbred line, A634, by particle acceleration (biolistic) transformation.

The *cry3Bb1* gene encodes the insect control protein Cry3Bb1, a delta-endotoxin. Cry proteins, of which Cry3Bb1 is only one, act by selectively binding to specific sites localized on the lining of the midgut of susceptible insect species. Following binding, pores are formed that disrupt midgut ion flow, causing gut paralysis and eventual death due to bacterial sepsis. Cry3Bb1 is lethal only when eaten by Coleopteran species, including corn root worm, and its specificity of action is directly attributable to the presence of specific binding sites in the target insects. There are no binding sites for the delta-endotoxins of *B. thuringiensis* on the surface of mammalian intestinal cells, therefore, livestock animals and humans are not susceptible to these proteins.

An antibiotic resistance marker gene (*neo*; synonym *nptII*) encoding the enzyme neomycin phosphotransferase II (NPTII), which inactivates aminoglycoside antibiotics such as kanamycin and neomycin, was also introduced into the genome of this transgenic maize. This gene was derived from a bacterial transposon (Tn5 transposable element from *Escherichia coli*) and was included as a selectable marker to identify transformed plants during tissue culture regeneration and multiplication. The expression of the *nptII* gene in these plants has no agronomic significance and the safety of the NPTII enzyme as a food additive was evaluated by the United States Food and Drug Administration in 1994 (US FDA, 1994).

Summary of Introduced Genetic Elements

Code	Name	Type	Promoter, other	Terminator	Copies	Form
cry3Bb1	cry3Bb1 delta-endotoxin *(Bacillus thuringiensis subsp. kumamotoensis)*	IR	4-AS1 (single CaMV 35S plus four repeats of activating sequence) 5' untranslated leader sequence from wheat chlorphyll a/b binding protein, and rice actin intron	3' untranslated sequence of wheat heat shock protein 17.3 (*tahsp17*)	1	Addition of alanine residue at position 2 of protein
nptII	neomycin phosphotransferase II *(Escherichia coli)*	SM	CaMV 35S	*A. tumefaciens* nopaline synthase (*nos*) 3'-untranslated region	1	The *nptII* cassette also contains 153 bp portion of bleomycin binding protein gene

Characteristics of *Zea mays* L. (Maize)

Center of Origin	Reproduction	Toxins	Allergenicity
Mesoamerican region, now Mexico and Central America	Cross-pollination via wind-borne pollen is limited, pollen viability is about 30 minutes. Hybridization reported with teosinte species and rarely with members of the genus Tripsacum.	No endogenous toxins or significant levels of antinutritional factors.	Although some reported cases of maize allergy, protein(s) responsible have not been identified.

Donor Organism Characteristics

Latin Name	Gene	Pathogenicity
Bacillus thuringiensis	*cry3Bb1*	While coleopterans are susceptible to oral doses of Cry3Bb1 protein, there is no evidence of toxic effects in laboratory mammals or birds. There are no

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Product Related Info

Documents

1. Product summary prepared by Monsanto
2. 90-Day subchronic rat study
3. Key food and feed nutrients and antinutrients of maize

Detection

1. EU CRL validated method
2. CRL validation report

Synopsis

› Overview of all products in database

subsp. *kumamotoensis*		significant mammalian toxins or allergens associated with the host organism.

Modification Method

Maize line MON 863 was produced by biolistic transformation of the inbred line A634 (reportedly one of the most popular publicly available inbred lines used in hybrid maize production in the United States) using linearized plasmid PV-ZMIR13 DNA purified following *Mlu I* restriction endonuclease digestion. The introduced DNA contained the modified *cry3Bb1* gene from *B. thuringiensis* subsp. *kumamotoensis* under the control of the 4-AS1 promoter (CaMV 35S promoter with 4 repeats of an activating sequence), plus the 5' untranslated leader sequence of the wheat chlorophyll a/b binding protein (wt CAB leader) and the rice actin intron. The transcription termination sequence was provided from the 3' untranslated region of the wheat 17.3 kD heat shock protein (*tahsp17*). The modified *cry3Bb1* gene encodes a protein of 653 amino acids whose amino acid sequence differs from that of the wild-type protein by the addition of an alanine residue at position 2 and by seven amino acid changes.

The introduced DNA also contained a copy of the neomycin phosphotransferase II (NPTII) encoding gene (*neo*; synonym *nptII*) derived from the Tn5 transposon of *Escherichia coli*. This gene was introduced as a selectable marker under the control of the CaMV 35S promoter and the 3' untranslated termination sequence (NOS 3') from the *Agrobacterium tumefaciens* nopaline synthase gene. The *nptII* cassette also contained a 153 base pair portion of the bleomycin binding protein gene (*ble*; 378 bp total size).

Characteristics of the Modification

The Introduced DNA

Southern blot analyses of genomic DNA from MON 863 demonstrated that there was a single site of integration containing one functional copy each of the modified *cry3Bb1* and *nptII* genes and their associated regulated regulatory sequences. No deletions, truncations, or rearrangements were reported, nor were any additional plasmid-derived sequences detected.

Genetic Stability of the Introduced Trait

Segregation and stability of the introduced trait were examined by Southern blot analyses performed on genomic DNA extracted from plants spanning three generations, and by enzyme linked immunosorbent assay (ELISA) to detect expression of the Cry3Bb1 protein over five generations of progeny plants. These results demonstrated that the introduced trait continued to segregate as a single locus, and that protein expression remained stable over multiple generations.

Expressed Material

The levels of expression of Cry3Bb1 protein in various plant tissues, including young leaf, grain, mature root, forage, silk, and pollen, were measured by ELISA and were found to vary between 10 to 81 micrograms/g fresh weight of plant tissue, depending on the tissue type and the time of harvest. Expression of the NPTII protein was also confirmed in young leaf, forage, and grain, obtained from MON 863, with levels ranging from undetectable to 1.4 micrograms/g when measured by ELISA (limit of detection: <=0.076 micrograms/g).

Environmental Safety Considerations

Outcrossing

The genetic insertion which resulted in MON 863 did not change its physiological characteristics of pollen production and pollen viability nor were there any changes in the plant's sexual compatibility with other maize varieties. Pollen dispersal and outcropping frequency should be equivalent to that of untransformed maize lines, therefore gene exchange between MON 863 maize and other maize varieties will be similar to that which occurs between non-transformed lines. There are no wild relatives to maize in Canada or the United States, making gene flow to wild species extremely remote.

Maize (*Zea mays* ssp. *mays*) freely hybridizes with annual teosinte (*Zea mays* ssp. *mexicana*) when in close proximity. These wild maize relatives are native to Central America but are not present in Canada and the United States, except for special plantings. Tripsacum, another genus related to Zea, contains sixteen species, of which twelve are native to Mexico and Guatemala. *Tripsacum floridanum* (Florida gamagrass) is native to the southern tip of Florida. Outcrossing with Tripsacum species is not known to occur in the wild and it is only with extreme difficulty that maize can be crossed with Tripsacum. The lack of compatible wild relatives in Canada and the maize –growing regions in the United States makes the possibility of gene flow into wild species in these areas very remote.

Weediness potential

The flowering period, vegetative vigour, time to maturity and seed production of MON 863 were within the normal range currently found in commercial maize hybrids. Maize does not possess the potential to become weedy due to traits such as a lack of seed dormancy, the non-shattering nature of maize cobs and the poor competitive ability of seedlings. Resistance to maize rootworm does not, in itself, render maize weedy or invasive of natural habitats as none of the reproductive or growth characteristics were modified. It was determined that it is very unlikely that MON863 would become a weedy pest of agriculture.

Secondary and Non-Target Adverse Effects

The *Bt* protein expressed in maize MON 863 (Cry3Bb1) was shown to be equivalent to microbial *Bt* used in sprays for over thirty years. The history of use and literature suggest that the bacterial *Bt* protein is not toxic to humans, other vertebrates and non-coleopteran invertebrates. This protein is active only against specific coleopteran insects. There are no coleopteran species listed as threatened or endangered in Canada or the United States.

Field studies indicated that MON863 did not have a negative effect on the abundance of non-target organisms compared to a non-*Bt* hybrid. Species studied included arthropods, earthworms and soil microbes. Coleopteran families including Carabidae, Staphylinidae and Coccinellidae were observed. Consideration was also given to the exposure of fireflies (family Lampyridae) to MON 863 since fireflies are coleopterans. It was concluded that the possibility of firefly exposure to Cry3Bb1 protein from MON 863 would be very unlikely as these insects generally do not occur sub-surface and do not feed on maize.

Feeding trials on non-target invertebrates, including honeybees, ladybird beetles, daphnia, collembola and earthworms, were also conducted. In addition, feeding trials were conducted on the non-target vertebrates such catfish and quail. MON 863 was demonstrated to be safe to these indicator species. MON 863 also did not demonstrate an increased level of anti-nutritional factors such as trypsin inhibitor and phytic acid when compared to unmodified control lines.

When compared with currently commercialized maize lines, MON 863 did not present an elevated risk to or impact on interacting organisms, including humans, with the exception of certain target coleopterans.

Potential Impact on Biodiversity

MON 863 has no novel characteristics that would extend its use beyond the current geographic range of maize production. Since the risk of outcrossing in the United States and Canada is remote, it was determined that the risk of transfer of novel traits to unmanaged environments was insignificant. The potential impact on biodiversity of MON 863 was judged to be equivalent to its unmodified counterparts.

Other Considerations

In Canada, the authorization for unconfined release into the environment and livestock feed

use of MON 863 was limited to one year initially. Renewal of the one year authorization was conditional upon the submission of additional information requested by the CFIA. This additional information included a new beneficial insect study as the original study protocol for toxicity of the Cry3Bb1 protein to green lacewing larvae (Neuroptera: Chrysopidae) was not of an optimal design. The renewal of the permit was granted in 2004.

In addition, the use of MON 863 in unconfined releases is contingent upon the implementation of specific insect resistance management (IRM) plans in Canada and the United States. IRM strategies are required to prolong the effectiveness of plant-expressed *Bt* toxins and the microbial spray formulations of these toxins. These programs are mandatory for all transgenic *Bt*-expressing plants, including MON 863 maize, and require that growers plant a minimum of 20 percent of their acreage to non-transgenic varieties in order to reduce the potential for selecting *Bt*-resistant insect populations. The refuge acres must be planted adjacent to or within the *Bt* crop. Details on the specific design and requirements of individual IRM programs are published by the relevant regulatory authority.

Food and/or Feed Safety Considerations

Dietary Exposure
In the United States and Canada, the primary form of consumption for field maize is as maize-based food ingredients with little whole kernel or processed field maize directly consumed by comparison. Field maize is used as a raw material for the manufacture of starch, which is in turn converted to a variety of sweeteners (such as high fructose maize syrup) and fermentation products (ethanol). The germ of the maize kernel is also used for the production of maize oil. These materials are commonly found in many foods, resulting in wide population dietary exposure to all maize products. The human food uses of grain from MON 863 are not expected to be different from the uses of non-transgenic field maize varieties and therefore the dietary exposure of the general population to MON 863 grain should not be different from that of other field maize varieties.

Nutritional Data
Compositional analyses were conducted on plant material (forage and grain) obtained from MON 863 and non-transgenic parental control plants grown at four replicated field trial sites in the United States. As a further comparison, similar analyses were conducted on plant material derived from nine different non-transgenic commercial maize hybrids grown under field conditions at two replicated sites.

Grain samples were analyzed for levels of protein, fat, ash, moisture, carbohydrates, acid detergent fibre (ADF), neutral detergent fibre (NDF), amino acids, fatty acids, vitamin E, minerals [calcium, copper, iron, magnesium (Mg), manganese (Mn), phosphorus (P), potassium, sodium, and zinc (Zn)], phytic acid, and trypsin inhibitor. Other than for the exceptions noted below, there were no statistical difference in the measured values for each of these parameters between MON 863 and the non-transgenic control line, and in each case the values obtained from both were within the range of values for the nine control varieties and those reported in the literature. The exceptions noted were:

1. Carbohydrate levels and levels of the non-essential amino acids cysteine, aspartic acid, and glycine were higher in MON 863 than in the non-transgenic parental control, but were within the range of values measured for the nine commercial varieties.

2. Levels of protein, the essential amino acids leucine and phenylalanine, and the non-essential amino acid glutamic acid, were lower in MON 863 than in the non-transgenic parental control, yet were within the range of values measured for the nine commercial varieties.

3. The levels of P, Mg, Zn, Mn, and vitamin E were lower in MON 863 than in the non-transgenic parental control, but were within the range measured for the nine commercial varieties and those reported in the scientific literature.

4. The level of phytic acid (a phosphorus-binding dietary antinutrient) was lower in MON 863 than in the non-transgenic parental control, but within the range of values measured for the nine commercial varieties.

Data on levels of protein, fat, ash, moisture, carbohydrates, ADF, and NDF, obtained from forage samples did not reveal any significant differences between MON 863 and the non-transgenic parental control, and all values fell within the range measured for the nine commercial varieties

Toxicity
Cry3Bb1 protein extracted and purified from a heterologous *E. coli* fermentation system was used as the test material for an acute oral toxicity study with mice. The identical *cry3Bb1* coding sequence used in the transformation of event MON 863 was used in the transformation of *E. coli*. The protein expressed by *E. coli* was assessed and found to be physicochemically and functionally equivalent to that expressed in plant tissue. The bacteria expression platform was used since a sufficient amount of the protein could not be purified from plant tissue. In the acute gavage study, the No Observed Adverse Effect Level (NOAEL) was found to exceed 3200 mg/kg the maximum dose achievable. At that level, no mortality or grossly observable adverse effects were noted.

The NOAEL was considered to be four orders of magnitude (5.8 X 104) times greater than the expected human intake of Cry3Bb1 protein from MON 863 maize. The NOAEL was 1000 times greater than the expected livestock dietary intake of Cry3Bb1 protein from MON 863 maize.

The sequence of amino acids making Cry3Bb1 protein was compared to that of known toxins. There was no sequence homology noted with toxins. As well, there were no structural similarities noted between Cry3Bb1 and known toxins.

These factors indicated that Cry3Bb1 had a low probability to exhibit toxicity to humans or livestock consuming MON 863 maize or products derived from it.

Allergenicity
Current scientific knowledge indicates that many food allergens tend to be abundant proteins within the food product, resistant to proteolytic digestion and heat inactivation and are often glycosylated. The Cry3b1 protein was assessed for allergenicity by examining its digestibility; amino acid sequence homology to known allergens; its glycosylation profile; and history of safe use of microbial sprays.

The results of an *in vitro* digestive fate study using simulated gastric fluid (SGF) indicated that Cry3Bb1 protein degraded to nondetectable levels in 15 seconds. The protein is also quickly deactivated upon exposure to heat. The protein was compared to known allergens and did not exhibit amino acid sequence homology. The Cry3Bb1 protein is not glycosylated. As well, the protein is present only at very low levels in edible portions of maize.

The long history of use of *Bt* toxins in microbial sprays has produced numerous safety studies which have demonstrated its low mammalian toxicity. As well, there have been no confirmed cases of allergic reactions to Cry proteins in scientific literature.

From these collective data it was judged that Cry3Bb1 protein in MON 863 maize was unlikely to be a human allergen.

Links to Further Information

Canadian Food Inspection Agency, Plant Biosafety Office [PDF Size: 202640 bytes]
Decision Document DD2003-43: Determination of the Safety of Monsanto Canada Inc.'s Insect Resistant Corn (Zea mays L.) Line MON 863.

European Commission [PDF Size: 47170 bytes]
COMMISSION DECISION of 13 January 2006 authorising the placing on the market of foods and food ingredients derived from genetically modified maize line MON 863 as novel foods or novel food ingredients under Regulation (EC) No 258/97 of the European Parliament and of the Council.

European Commission [PDF Size: 50624 bytes]
COMMISSION DECISION of 8 August 2005 concerning the placing on the market, in accordance with Directive 2001/18/EC of the European Parliament and of the Council, of a maize product (Zea mays L., line MON 863) genetically modified for resistance to corn rootworm.

European Commission: Community Register of GM Food and Feed [PDF Size: 18968 bytes]
Notification of the placing on the Community Register of MON-ØØ863-5.

European Food Safety Authority [PDF Size: 271505 bytes]
Opinion of the Scientific Panel on Genetically Modified Organisms on a request from the Commission related to the safety of foods and food ingredients from insect-protected genetically modified maize MON 863 and MON863 x MON 810, for which a request for placing on the market was submitted under Article 4 of the Novel Food Regulation (EC) No 258/97 by Monsanto. The EFSA Journal (2004) 50, 1-25.

Food Standards Australia New Zealand [PDF Size: 475220 bytes]
Final assessment report: Application A484, food from insect-protected MON863 corn.

Japanese Biosafety Clearing House, Ministry of Environment [PDF Size: 139807 bytes]
Outline of the biological diversity risk assessment report: Type 1 use approval for MON863

Monsanto Company [PDF Size: 380448 bytes]
Safety assessment of YieldGard Rootworm corn.

Monsanto Company [PDF Size: 5849612 bytes]
13-Week dietary subchronic comparison study with MON 863 corn in rats preceded by a 1-week baseline food consumption determination with PMI certified rodent diet #5002.

Office of Food Biotechnology, Health Canada [PDF Size: 98944 bytes]
Novel Food Information: Insect-protected corn Cry2Bb1event MON863

Philippines Department of Agriculture, Bureau of Plant Industry [PDF Size: 25239 bytes]
Determination of the Safety of Monsanto's Corn MON 863 (Insect-Resistant Corn) for Direct Use as Food, Feed and for Processing

U.S. Department of Agriculture, Animal and Plant Health Inspection Service [PDF Size: 85635 bytes]
Monsanto Co.; Availability of Determination of Nonregulated Status for Corn Genetically Engineered for Insect Resistance.

U.S. Department of Agriculture, Animal and Plant Health Inspection Service [PDF Size: 1696342 bytes]
Petition for the Determination of Non-Regulated Status: Corn Rootworm Protected Corn Event MON 863 (CBI-deleted)

U.S. Environmental Protection Agency, Office of Pesticide Programs [PDF Size: 609555 bytes]
Biopesticides Registration Action Document: Event MON863 Bacillus thuringiensis Cry3Bb1 Corn

US Food and Drug Administration [PDF Size: 98322 bytes]
Memorandum to file concerning corn rootworm protected maize, MON 863.

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Compositional Analysis

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Digestive Fate

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Environmental Fate

Icoz, I. and Stotzky, G. (2008). Cry3Bb1 protein from *Bacillus thuringiensis* in root exudates and biomass of transgenic corn does not persist in soil. *Transgenic Research* **17**(4): 609-620.

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Herbicide Residues

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Nutritional Equivalence

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Potential Non-Target Organism Effects

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Mattila, H., Sears, M. and Duan, J. (2005). Response of *Danaus plexippus* to pollen of two new Bt corn events via laboratory bioassay. *Entomologia Experimentalis et Applicata* **116**: 31-41.

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