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Documents

1. Maize biology document
2. Glufosinate facts

Synopsis

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Recent Updates

Canada, US: changes since January 1, 2002.

1. LL Cotton25- Glufosinate Cotton
2. MON863- Insect resistance Maize
3. GT200- Herbicide tolerance Argentine Canola
4. HCN92- Glufosinate Argentine Canola
5. MS1, RF1 => PGS1- Herbicide tolerance + fertility Argentine Canola
6. MS1, RF2 => PGS2- Herbicide tolerance + fertility Argentine Canola
7. 15985- Insect resistance Cotton
8. TC1507- Herbicide tolerance + insect resistance Maize
9. CL121, CL141, CFX51- Herbicide tolerance Rice
10. 55-1/63-1- Virus resistant Papaya

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Essential Information

[Biotech Crop Database](#)

[Principles and Practice of Environmental Safety Assessment of Transgenic Plants](#)

[The Safety of GM Livestock Feeds](#)

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DAS-Ø15Ø7-1 (TC1507)

Host Organism / Variety

Zea mays L. (Maize) Herculex™ I

Trait

Resistance to European corn borer (*Ostrinia nubilalis*); phosphinothricin (PPT) herbicide tolerance, specifically glufosinate ammonium.

Trait Introduction Method

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

Mycogen (c/o Dow AgroSciences); Pioneer (c/o Dupont)



Introduction

Maize line TC1507 was genetically modified to contain two novel genes, *cry1Fa2* and *pat*, for insect resistance and herbicide tolerance respectively. Both genes were introduced into the parental maize hybrid line Hi-II by particle acceleration (biolistic) transformation.

The *cry1Fa2* gene, isolated from the common soil bacterium *Bacillus thuringiensis* (Bt) var. *aizawai*, produces the insect control protein Cry1F, a delta-endotoxin. Cry proteins, of which Cry1F 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. Cry1F is lethal only when eaten by the larvae of lepidopteran insects (moths and butterflies), 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.

The Cry1F protein expressed in TC1507 provides protection against European corn borer (ECB), southwestern corn borer (SWCB), fall armyworm (FAW), black cutworm (BCW), and some control of corn earworm (CEW).

In addition to the *cry1Fa2* gene, TC1507 was developed to allow for the use of glufosinate ammonium, the active ingredient in phosphinothricin herbicides (Basta®, Rely®, Liberty®, and Finale®), as a weed control option, and as a breeding tool for selecting plants that have the insect-tolerant *cry1F* gene. Glufosinate chemically resembles the amino acid glutamate and acts to inhibit an enzyme, called glutamine synthetase, which is involved in the synthesis of glutamine. Essentially, glufosinate acts enough like glutamate, the molecule used by glutamine synthetase to make glutamine, that it blocks the enzyme's usual activity. Glutamine synthetase is also involved in ammonia detoxification. The action of glufosinate results in reduced glutamine levels and a corresponding increase in concentrations of ammonia in plant tissues, leading to cell membrane disruption and cessation of photosynthesis resulting in plant withering and death.

Glufosinate tolerance in TC1507 maize is the result of introducing a gene encoding the enzyme phosphinothricin-N-acetyltransferase (PAT) isolated from the common aerobic soil actinomycete, *Streptomyces viridochromogenes*, the same organism from which glufosinate was originally isolated. The PAT enzyme catalyzes the acetylation of phosphinothricin, detoxifying it into an inactive compound.

Inari Exhibit 1032
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:: Principles and Practice of Novel Food Safety Assessment

:: The Regulation of Agricultural Biotechnology Products

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:: Summary of Introduced Genetic Elements

Code	Name	Type	Promoter, other	Terminator	Copies	Form
<i>pat</i>	phosphinothricin N-acetyltransferase (<i>S. viridochromogenes</i>)	HT	CaMV 35S	CaMV 35S 3' polyadenylation signal	1 functional;	
<i>cry1Fa2</i>	<i>cry1F</i> delta-endotoxin (<i>Bacillus thuringiensis</i> var. <i>aizawai</i>)	IR	ubiquitin (<i>ubi</i>) ZM (<i>Zea mays</i>) promoter and the first exon and intron	3' polyadenylation signal from ORF25 (<i>Agrobacterium tumefaciens</i>)	1 functional; 1-2 partial;	Altered coding sequence for optimal expression in plant cells.

:: 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 <i>Tripsacum</i> .	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
<i>Bacillus thuringiensis</i> var. <i>aizawai</i>	<i>cry1F</i>	While target insects are susceptible to oral doses of <i>Bt</i> proteins, no evidence of toxic effects in laboratory mammals or birds.
<i>Streptomyces viridochromogenes</i>	<i>pat</i>	<i>S. viridochromogenes</i> is ubiquitous in the soil. The spore chains are Spirales and the spore surface is spiny. The spore mass is blue, the reverse is green and its pigments are pH sensitive. It exhibits very slight antimicrobial activity, is inhibited by streptomycin, and there have been no reports of adverse affects on humans, animals, or plants.

:: Modification Method

Transgenic TC1507 maize was produced by biolistic (microprojectile bombardment) transformation of the hybrid maize line Hi-II (Hi-II is a cross between A188 and B73 inbred lines of maize) with plasmid DNA containing sequences corresponding to a modified (synthetic, less than full-length) form of the *cry1Fa2* gene from *Bacillus thuringiensis* var. *aizawai* strain PS811 and the phosphinothricin N-acetyltransferase (PAT) encoding gene from *Streptomyces viridochromogenes*.

In order to optimize expression of the Cry1F protein, the nucleotide sequence of the *cry1Fa2* gene was modified via *in vitro* mutagenesis to contain plant-preferred codons. Transcription of the *cr1Fa2* gene was directed by the promoter and a 5' untranslated region from the maize ubiquitin (*ubi*) gene including the first exon and intron. The 3' termination/polyadenylation sequences were derived from the *Agrobacterium tumefaciens* open reading frame 25 (ORF25 PolyA). The *ubi* exon and intron included in this construct (PHI8999) have no effect on the structure of the Cry1F product, only on the expression of the gene.

Transcriptional regulation of the *pat* gene was via promoter and terminator sequences derived from the 35S transcript of cauliflower mosaic virus (CaMV).

:: Characteristics of the Modification

The Introduced DNA

Southern blot analysis of genomic DNA isolated from seed of different generations of progeny plants demonstrated that the parental transgenic line, TC1507, contained a single copy of an intact fragment containing both the *cry1Fa2* and *pat* gene constructs with their associated noncoding regulatory regions and a second copy of the *cry1Fa2* coding region lacking the majority of the associated ubiquitin regulatory sequences; and (2) these genetic constructs were stably inherited and cosegregated over four generations of backcrossing.

Genetic Stability of the Introduced Trait

The expression of Cry1F protein in hybrid progeny derived from TC1507 was measured using enzyme linked immunosorbent assay (ELISA). Using a chi square analysis with a 95% confidence interval, a Mendelian ratio of 1:1 was observed for first generation progeny. This pattern of segregation was consistent with the integration of a single

functional copy of the *cry1Fa2* gene in the original transformation event.

Expressed Material

Levels of expression of Cry1F protein from TC1507 pollen, grain, and grain-derived feeds were measured using quantitative ELISA or Western immunoblotting, and biological activity was determined using insect bioassays with either tobacco budworm or European corn borer larvae.

Cry1F protein was detectable in whole plants (minus the roots) collected at four weeks prior to pollination and following senescence and in leaves, pollen, silk, stalk, and mature grain; whereas PAT was only detectable in leaf tissue. Levels of Cry1F protein expressed in TC1507 ranged from an average of 32 ng/mg in pollen to an average of 110.9 ng/mg total protein in leaf tissue and 89.8 ng/mg total protein in grain samples. Western immunoblotting of sodium dodecylsulfate (SDS) polyacrylamide gel electrophoresis (PAGE) separated proteins in trypsinized plant extracts prepared from TC1507 leaf tissue revealed the presence of a 65 kDa moiety corresponding to the trypsin-resistant core of the Cry1F delta-endotoxin.

The amounts of detectable PAT protein in TC1507 leaf tissue ranged up to 40.8 ng/mg total protein but were undetectable in other tissues, such as pollen, silk, stalk, and grain.

Based on a bioassay with the tobacco budworm (*Heliothis virescens*), a target species, purified Cry1F proteins incorporated into test soils biodegraded with a half-life of approximately 3.13 days. This half-life is very comparable with the 4-7 days in published reports for other Cry proteins.

:: Environmental Safety Considerations

Outcrossing

Since pollen production and viability were unchanged by the genetic modification resulting in TC1507, pollen dispersal by wind and outcrossing frequency should be no different than for other maize varieties. Gene exchange between TC1507 maize and other cultivated maize varieties will be similar to that which occurs naturally between cultivated maize varieties at the present time. In Canada and the United States, where there are no plant species closely-related to maize in the wild, the risk of gene flow to other species appears remote. Feral species related to corn, as found within Canada or the United States, cannot be pollinated due to differences in chromosome number, phenology (periodicity or timing of events within an organism's life cycle as related to climate, *e.g.*, flowering time) and habitat.

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 and 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. Three species of *Tripsacum* have been reported in the continental United States: *T. dactyloides*, *T. floridanum* and *T. lanceolatum*. Of these, *T. dactyloides*, Eastern Gama Grass, is the only species of widespread occurrence and of any agricultural importance. It is commonly grown as a forage grass and has been the subject of some agronomic improvement (*i.e.*, selection and classical breeding). *T. floridanum* is known from southern Florida and *T. lanceolatum* is present in the Mule Mountains of Arizona and possibly southern New Mexico. Even though some *Tripsacum* species occur in areas where maize is cultivated, gene introgression from maize under natural conditions is highly unlikely, if not impossible. Hybrids of *Tripsacum* species with *Zea mays* are difficult to obtain outside of the controlled conditions of laboratory and greenhouse. Seed obtained from such crosses are often sterile or progeny have greatly reduced fertility.

Weediness Potential

No competitive advantage was conferred to TC1507 that would render maize weedy or invasive of natural habitats, since none of the reproductive or growth characteristics were modified. Cultivated maize is unlikely to establish in non-cropped habitats and there have been no reports of maize surviving as a weed. *Zea mays* is not invasive and is a weak competitor with very limited seed dispersal.

Secondary and Non-Target Adverse Effects

The history of use and literature suggest that *Bt* proteins are not toxic to humans, other vertebrates, and beneficial insects.

Maize inbreds and hybrids expressing the Cry1F protein were compared to their non-transformed counterpart for relative abundance of beneficial arthropods, including: lady beetles (*Cycloneda juncunda* & *Coleomegilla maculata*), predacious Carabids, brown

lacewings (Hemerobiidae), green lacewings (*Chrysoperla plorabunda*), minute pirate bugs (*Orius insidiosus*), assassin bugs (Reduviidae), damsel bugs (Nabidae), Ichneumonid and Braconids (parasitic wasps), damselflies and dragonflies, and spiders. Visual counts showed no significant differences between the number of arthropods collected in TC1507 maize and the non-transgenic isolines with two exceptions. There was a significantly greater number of lady beetles in the 1507 line (1.2 per test plant vs. 0.6 per control plant), and significantly more Orius were found in the 1507 line than the non-transgenic line on two of the three sample dates. In summary, these field studies demonstrated that Cry1F had neither a direct nor an indirect effect on the beneficial arthropod populations.

Specific feeding trials were also carried out with a number of non-target species, including honeybee larvae and adults, green lacewing, parasitic hymenopterans, ladybird beetles, daphnia (aquatic invertebrates), earthworm, and collembola (soil dwelling invertebrates). In all cases there were no observable adverse effects.

An additional study was conducted on the effect of Cry1F on neonate monarch butterfly larvae when fed a 10,000 ng/mL diet dose. First instar larval weight and mortality were recorded after seven days of feeding. Although there was some growth inhibition, there was no mortality to monarchs fed the 10,000 ng/mL diet, the highest rate tested. Since pollen doses equivalent to 10,000 ng/mL diet are not likely to occur on milkweed leaves in nature, it can be concluded that Cry1F protein will not pose a risk to monarchs.

Impact on Biodiversity

TC1507 has no novel phenotypic characteristics that would extend its use beyond the current geographic range of maize production. Since the risk of outcrossing with wild relatives in Canada and the United States is remote, it was determined that risk of transferring genetic traits from TC1507 maize to species in unmanaged environments was insignificant.

Other Considerations

In order to prolong the effectiveness of plant-expressed *Bt* toxins, and the microbial spray formulations of these same toxins, regulatory authorities in Canada and United States have required developers to implement specific Insect Resistant Management (IRM) Programs. These programs are mandatory for all transgenic *Bt*-expressing plants, including TC1507 maize, and require that growers plant a certain percentage of their acreage to non-transgenic varieties in order to reduce the potential for selecting *Bt*-resistant insect populations. Details on the specific design and requirements of individual IRM programs are published by the relevant regulatory authority.

:: Food Safety Considerations

Nutritional Data

Forage and grain from TC1507 maize were analyzed for nutritional composition and compared to the nutritional composition of non-transgenic versions of the same maize hybrids. With respect to forage, there were no significant differences in the respective levels of protein, fat, neutral detergent fibre (NDF), or ash between the transgenic or non-transgenic control lines. The level of acid detergent fibre (ADF) in TC1507 was lower than the control line, but remained within the range of values reported in the scientific literature. Analyses of calcium and phosphorus in forage from TC1507 and the control non-transgenic line were determined to be 0.22 and 0.23 per cent, and 0.25 and 0.24 per cent, respectively.

Grain from TC1507 was found to have similar levels of protein, ADF, NDF and ash as grain from non-transgenic maize hybrids, however, the level of fat was significantly lower. This lower fat content was not considered biologically significant as it was still within the range of values reported for other commercial maize varieties. In examining the fatty acid profile, it was determined that the transgenic line had lower levels of stearic and oleic acid but higher levels of linoleic and linolenic acids than the non-transgenic control. Although differences were noted, they remained within the normal range of variation reported for maize grain. The levels of calcium, phosphorus, copper, iron, magnesium, manganese, and zinc in TC1507 grain were similar to levels measured in grain from the non-transgenic control line. The levels of essential amino acids in TC1507 grain were within the norms reported in the literature. With respect to vitamins, TC1507 had lower levels of vitamin B1 but higher levels of total tocopherols than the non-transgenic control. Although different, these values were within published ranges.

There were no differences in the levels of phytic acid between the transgenic and non-transgenic lines, and the level of trypsin inhibitor in both TC1507 and the non-transgenic control was below the threshold of detection (2000 TIU/g).

:: Summary of Regulatory Approvals

Country	Environment	Food and/or Feed	Food	Feed	Marketing
Canada	2002		2002	2002	
Japan	2002		2002	2002	
United States	2001	2001			

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

:: Links to Further Information

Canadian Food Inspection Agency, Plant Biosafety Office  [PDF Size: 43059 bytes]

Decision Document DD2002-41: Determination of the Safety of Dow AgroSciences Canada Inc. and Pioneer Hi-Bred International's Insect Resistant and Glufosinate - Ammonium Tolerant Corn (*Zea mays* L.) Line 1507.

Food Standards Australia New Zealand  [PDF Size: 455928 bytes]

Draft assessment report, application A446: food derived from insect-protected and glufosinate ammonium-tolerant corn line 1507.

Impact of Bt corn pollen on monarch butterfly populations: A risk assessment  [PDF Size: 166577 bytes]

Mark K. Sears, Richard L. Hellmich, Diane E. Stanley-Horn, Karen S. Oberhauser, John M. Pleasants, Heather R. Mattila, Blair D. Siegfried, and Galen P. Dively (2001). *Proc. Natl. Acad. Sci. USA Early Edition*

Office of Food Biotechnology, Health Canada  [PDF Size: 144926 bytes]

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

Swiss Federal Office of Public Health  [PDF Size: 100246 bytes]

Information to the Swiss authorities on the potential environmental impact of genetically modified plants in accordance with Annexes IIB and III of Directive 90/220/EEC (August 14, 2001)

US Environmental Protection Agency  [PDF Size: 669353 bytes]

Biopesticide Registration Action Document: *Bacillus thuringiensis* Cry1F Corn.

US Food and Drug Administration  [PDF Size: 89238 bytes]

Memorandum to file concerning insect resistant and herbicide tolerant maize line 1507

USDA-APHIS Environmental Assessment  [PDF Size: 449681 bytes]

USDA/APHIS Decision on Mycogen Seeds c/o Dow AgroSciences LLC and Pioneer Hi-Bred International, Inc. Petition 00-136-01P Seeking a Determination of Nonregulated Status for Bt Cry1F Insect Resistant, Glufosinate Tolerant Corn Line 1507

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