

Determination of the Safety of Monsanto's
Corn DLL 25 (Herbicide Tolerant Corn)
for Direct Use as Food, Feed and For Processing

Food and Feed Safety

The product dossier on Corn DLL 25 were reviewed for safety and nutritional differences compared with the conventional corn. The focus of the review was on any new or altered expression trait and changes in composition and nutritional content or value relative to the conventional corn. At the end of the safety assessment, a conclusion was made that the corn event DLL 25 is as safe as the conventional corn taking into account dietary impact of any changes in nutritional content or value.

A biosafety permit for corn event DLL 25 and all progenies derived from crosses of the product with any conventionally-bred corn and corn containing approved-biotech events for direct use as food, feed or for processing was issued to Monsanto Philippines, Inc. on November 20, 2003. The permit is valid for five years and shall expire on November 19, 2008 subject to the terms and conditions set forth in DA Administrative order No. 8, Series of 2002 The said corn event DLL 25 will be included in the Lists of Approval Registry (Delisting) being prepared by the Department of Agriculture-Bureau of Plant Industry.

This approval is for use as Food, Feed and Processing only. This does not include cultivation of Phosphinotricin Tolerant Corn DLL 25 in the Philippines. Food and Feed use of Corn Event DBT 418 and its by-products is therefore authorized as of November 20, 2003. The Biosafety Permit (No.03-010) stated that "Phosphinotricin Tolerant Corn Event DLL 25 is as safe for human food, livestock feed and for processing as its conventional counterparts".

I. Brief Identification of the Genetically Modified Organism (Living Modified Organism)

Designation:	Corn DLL 25
Applicant:	MONSANTO PHILIPPINES, INC. 7 th Floor, Ayala-FGU Center Alabang-Zapote Rd., cor Acacia Avenue Madrigal Business Park Alabang 1770 Muntinlupa City Philippines
Plant Species:	
Name:	Corn (<i>Zea mays</i> L.)
Center of Origin:	Mexico, Central America, and South America
Toxic Factors / Allergen(s):	Trypsin inhibitor, phytic acid, and secondary metabolites such as raffinose, ferulic acid and p-coumaric acid are present in low amount 2-4 dihydroxy-7-methoxy-2H-1, 4 benzoxazin- 3(4H)- one

(DIMBOA) a potential toxicant but declines rapidly as the plant grows.

Parent Material:	Proprietary corn inbreds and hybrids
Trait Description:	Herbicide - Tolerance
Trait Introduction Method:	Microparticle bombardment
Donor Organism:	<i>Streptomyces hygrosopicus</i> , source of the <i>bar</i> gene produces the PAT protein, responsible for glufosinate tolerance
Pathogenicity:	The PAT protein was derived from the soil microorganism <i>Streptomyces hygrosopicus</i> . This organism is not a food source and the primary amino acid sequences of the PAT protein is only homologous to other PAT proteins and demonstrates a low level of homology to other bacterial acetylase enzymes. Therefore, the PAT protein is not substantially similar to an edible protein.
Proposed Use:	For direct use as food, feed and for processing

II. Background Information

Monsanto Philippines, Inc. has developed a Phosphinothricin Tolerant Corn. This corn line, designated Corn Event DLL 25, has been transformed using Microprojectile Bombardment Transformation, to produce a Glufosinate tolerant corn that can tolerate the effect of herbicide phosphinothricin.

On June 17, 2003 Monsanto Philippines, Inc submitted an application to the Bureau of Plant Industry requesting for biosafety permit under Department of Agriculture AO#8 for corn event DLL 25 which has been genetically modified for phosphinothricin herbicide tolerance. The rigorous assessment was done by the concerned agencies: [Bureau of Animal Industry (BAI) and Bureau of Agriculture, Fisheries and Product Standards (BAFPS)] and a Scientific Technical Review Panel (STRP) giving emphasis on the nature of the genetic modification, toxicological evaluation, nutritional assessment, substantial equivalence and general safety issues of the modified corn.

Monsanto Philippines, Inc. has provided data on the identity of Corn DLL 25, a detailed description of the transformation method, data and information on the gene insertion sites, copy number and levels of expression in the plant, the role of the inserted genes and regulatory sequences in donor organisms and full nucleotide sequences. The novel proteins were identified, characterized and compared to the original bacterial proteins, including an evaluation of their potential toxicity to livestock and non-target organisms. Relevant scientific publications were supplied.

The petitioner/applicant published the said application in two widely circulated newspapers (Malaya and Daily Tribune) on July 23, 2003 for public comment/review. BPI received no comment on the petition during the 30-day comment period.

Review of results of evaluation by the BPI Biotech Core Team in consultation with DA-Biotechnology Advisory Team (DA-BAT) completed the approval process.

III Description of Novel (Introduced) Traits

The DLL 25 corn line was produced by microprojectile of embryogenic corn cells with plasmid vector comprising the *bar* gene isolated from *Streptomyces hygroscopicus*, which gene encodes the enzyme phosphinothricin-N-acyltransferase (PAT). The PAT enzyme catalyzes the acetylation of the herbicide phosphinothricin, thereby inactivating the herbicide and consequently protecting the plant. This protein does not regulate normal metabolic pathways of plants, hence, it will neither alter nor interfere with the normal growth of the plant. The only significant agronomic difference between corn hybrids containing the DLL25 transformation event and nontransformed counterpart hybrids is the resistance to glufosinate herbicide that is present in corn hybrids containing the DLL25 transformation event.

Safety of the Expressed Protein

The PAT protein was derived from the soil microorganism *Streptomyces hygroscopicus* which is not a food source. The primary amino acid sequences of the PAT protein are only homologous to other PAT proteins and demonstrate a low level of homology to other bacterial acetylase enzymes. Therefore, the PAT protein is not substantially similar to an edible protein.

The introduced protein is not likely to be a macroconstituent in the human or animal diet. Relatively low level of PAT protein was found present in corn grain (0.13% of the total protein) and in corn plant (0.35% of the total protein). The protein is heat labile or does not possess the proteolytic or heat stability characteristic of toxic compounds, the process of ensiling destroys low levels of protein present in the plant. Thus, PAT protein will be present in the grain, but most likely absent in the silage. As an animal feed, the PAT protein is degraded in gastric and intestinal fluids of the digestive organs of the animals.

DEKALB Genetics has demonstrated that PAT has no activity on the mixture of amino acids present in a casein hydrolysate mixture. Amino acid acetyltransferase activities are common in living organisms and therefore, PAT does not represent a novel type of enzyme activity. A protein sequence homology search demonstrated that the protein sequence of the PAT protein does not exhibit homology to any known toxic protein and allergens. Allergens are commonly acid stable and able to survive in animal digestive system but PAT protein is acid labile.

The primary exposure of animals and humans to glufosinate resistant corn will be through oral ingestion. In corn DLL25, there is no evidence for expression of the β -lactamase gene and the gene itself is truncated and does not encode a functional protein. Therefore, there is no anticipated exposure of animals and humans to β -lactamase in corn DLL25. As proteins are water soluble, it is not anticipated that the PAT protein will be present in corn oil.

IV Nutritional Composition (Compositional Analysis)

Expression of the PAT enzyme in corn is not expected to alter the nutritional value of corn, because the enzyme is highly specific in its substrate specificity and does not use naturally occurring amino acids or other cell metabolites as substrate.

No significant difference was observed in terms of chemical composition, nutritional and safety aspects. Amino acid comparison of the DLL 25 corn grain and the counterpart untransformed corn grain showed comparable composition except for tryptophan, cystine and praline which are acid labile. However, the nutrient composition of DLL25 corn fell within the range of variability for the relevant nutrients reported in corn. The use of corn products derived from DLL25 was not anticipated to have any significant impact on the nutritional quality of the food supply.

No statistical significant differences were observed between DLL25 transformed corn hybrids and the counterpart untransformed hybrids with regards to moisture content, protein, fat, fiber, ash and carbohydrate.

The nutritional equivalence of DLL25 corn to conventional corn was confirmed in numerous feeding studies with broiler chickens and rats which included clinical and histological evaluations. The environmental impact of DLL25 corn is also comparable to conventional corn.

V. Anti-Nutritional Factors

The anti-nutrients, trypsin inhibitor and phytic acid are known to be present only in very small amount in corn. Concentration of phytic acid was below 0.02% in both DLL25 corn hybrids and counterpart untransformed hybrids.

VI. Regulatory Decision

Based on the assessment of submitted scientific data and other information relevant to the application of Monsanto Philippines, Inc., it is concluded that Corn DLL 25 and all progenies derived from crosses of the product with any conventionally-bred corn, and corn containing approved-biotech events for direct use as food, feed and for processing is as safe and substantially equivalent as its unmodified counterpart, and is therefore approved for direct use as food, feed and for processing. Monsanto shall duly inform the public of this approval by way of publishing in any one (1) of the top three (3) leading newspapers in the country that imports of this product is covered by conditions for approval as provided in Department of Agriculture memorandum Circular No. 8, Series of 2003.