

Determination of the Safety of Pioneer Hi-Bred's And Dow Agro Sciences'
Corn 1507 (Insect resistant, herbicide tolerant Corn)
for Direct Use as Food, Feed and For Processing

Food and Feed Safety:

The product dossiers on Corn 1507 was 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 corn 1507 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 1507 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 were issued to Pioneer Hi-bred and Dow Agro Sciences of the Philippines on October 7, 2003. The permit is valid for five years and shall expire on October 6, 2008 subject to the terms and conditions set forth in DA Administrative Order No. 8, Series of 2002. The said corn event 1507 was 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. Food, Feed and use of its by-products is therefore authorized as of October 7, 2003. The biosafety permit (No.03-004) stated that "Insect-resistant, Glufosinate tolerant Corn 1507/Cry1F" 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 1507 (Herculex)
Applicant:	PIONEER HI-BRED PHILIPPINES, INC. (PHI) Anthel Global Bldg., Julia Vargas St., Ortigas Center, Pasig, Metro Manila Philippines and DOW AGRO SCIENCES (DAS) 2 nd Floor Bank of Commerce Building J. Catolico Sr. Avenue, Lagao General Santos City, South Cotabato Philippines
Plant Species:	
Name:	Corn (<i>Zea mays</i>)
Parent Material:	Inbred corn lines developed and produced by Pioneer and Dow Agro Sciences
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)-1 (DIMBOA) is a potential toxicant but declines rapidly as the plant grows.
Trait Description:	Insect Resistance, Herbicide (Glufosinate) Tolerance
Trait Introduction Method:	Microprojectile bombardment
Donor Organism(s):	<i>Bacillus thuringiensis</i> var. <i>aizawai</i> strain PS811, source of <i>cryIF</i> gene which confers resistance to lepidopteran pests. <i>Streptomyces viridochromogenes</i> , source of <i>pat</i> genes which confers tolerance to herbicide (glufosinate).
Pathogenicity:	<i>Bacillus thuringiensis</i> var. <i>aizawai</i> is found naturally in soil worldwide. No known mammalian health effects have been reported. It has been in commercial use as a microbial pesticide on food crops, including fresh vegetables, for over 30 years. <i>Streptomyces viridochromogenes</i> is a non-pathogenic microorganism commonly found in the soil environment. There are no known adverse pathogenic or toxicological effects reported.
Proposed Use:	For direct use as food, feed and for processing

II. Background Information

Pioneer Hi-Bred International, Inc. (PHI) and Dow Agro Sciences (DAS) have developed a corn line resistant to the Asiatic Corn Borer (ACB) larvae, a periodic pest of corn in the Philippines. This corn line, referred to in this document as Cry1F, was developed to provide a method to control yield losses from insect feeding damage caused by the larval stages of ACB, without the use of conventional pesticides. . In addition, Cry1F was transformed with a gene that confers tolerance to the herbicide glufosinate.

PHI and DAS submitted an application to the Bureau of Plant Industry on May 12, 2003 requesting for biosafety permit under Administrative Order #8 for Cry1F insect-resistant, glufosinate tolerant maize line containing transformation event 1507.

PHI and DAS have provided data on the identity of line Cry1F, 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.

Extensive safety evaluation of B.t. Cry 1F maize line 1507 in terms of genetic stability, agronomic characteristics, food compositional analysis, and potential toxicity and allergenicity was undertaken by the concerned agencies [Bureau of Animal Industry (BAI), Bureau of Agriculture, Fisheries and Product Standards (BAFPS)] and a Scientific Technical Review Panel (STRP) following the Department of Agriculture's AO8 guidelines for the release of genetically modified organisms.

The Public Information Sheet (PIS) of the said application was published in two widely circulated newspapers: Malaya and Daily Tribune on July 1, 2003 for public comments/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 corn transformation event designated as 1507 using a modified *cry1F* gene derived from *Bacillus thuringiensis* var. *aizawai* PS811. It produces an insecticidal protein (delta-endotoxins) that is very selective in toxicity to specific organisms. Upon ingestion by susceptible insects, these protein crystals dissolve in the insect gut and are processed by proteases to release the active core protein. The activated Bt proteins bind to specific receptor on the apical microvillae of epithelial midgut cells. Binding is followed by a conformational change of the protein and insertion to the membrane. Protein oligomerization then results in pore formation in the midgut cell membrane and osmotic cell lysis leading to insect death. The Bt Cry1F maize line 1507 has shown effectiveness against certain Lepidopteran larva that is common pest of corn, such as Asiatic Corn Borer (*Ostrinia furnacalis*), true armyworm (*Mythimna separata*), corn earworm (*Heliothis armigera*), common cutworm (*Spodoptera litura*) and corn semi-looper (*Chrysodeixis chalcites*).

The *pat* gene, which encodes the enzyme phosphinothricin acetyltransferase is also present in B.t. Cry1F maize line 1507. The *pat* gene is a modified version of the native *pat* gene from *Streptomyces viridochromogenes*. Expression of the PAT protein confers tolerance to application of glufosinate-ammonium herbicide for purposes of weed control management. The PAT enzyme catalyzes the conversion of L- phosphinothricin, the active ingredient in glufosinate- ammonium, to an inactive form and thereby detoxifies the glufosinate- ammonium herbicide.

Safety of the Expressed Protein

The protein expressed by the *cry1F* gene is non-toxic to plants, animals and humans. Its toxicity is limited only to a certain species of insects belonging to the Lepidopteran order. The protein expressed by the *pat* is an enzyme which is also non-toxic to plants, animals and humans. It specifically modifies certain herbicides making them inactive.

A mouse acute oral toxicity test and a bobwhite quail dietary toxicity study using Cry1F protein were conducted. Similarly, a mouse acute oral toxicity test was performed using PAT protein. No adverse effects were demonstrated on both tests.

The protein products of the inserted genes (*cry1F* and *pat*) are not in any way, proteins that regulate the normal metabolic pathways of plants and therefore will not interfere with the plant's normal growth and development. No nucleic acid sequences that code for a protein toxic to humans or antibiotic resistance were introduced into maize line 1507. Similarly, no significant homology was demonstrated for the *cry1F* and *pat* with known allergens and neither protein was stable in a simulated gastric fluid. Both proteins have little probability of being allergenic. The corn allergenic responsible for food - induced allergic reactions were identified as a lipid transfer protein present only in the pollen.

IV. Nutritional Composition (Compositional Analysis)

The key nutrients present in corn 1507 and non-transformed corn are comparable. The levels in maize line 1507 of protein, fat, fatty acid, vitamins, minerals, ADF, NDF and ash were all within the literature range for maize grain. A small increase in the levels of a non-essential amino acid was reported. However, it would not have a detrimental impact on the nutritional quality of corn.

V. Anti-Nutritional Factors

Two potential anti-nutrients, phytic acid and trypsin inhibitor were found to be within the acceptable range for both conventional and transformed maize grain. Similarly, trypsin inhibitor levels in both maize line 1507 and isolate were below the limit of quantification. This confirms that no unusually high levels of trypsin inhibitor are present in maize line 1507.

VI. Regulatory Decision

Results of the risk evaluation based on the submitted scientific data and other information relevant to the application of Pioneer Hi-Bred's (PHI) and Dow Agro Sciences' (DAS) of the Philippines, it is concluded that Corn 1507 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 to its unmodified counterpart, and is therefore approved for direct use as food, feed and for processing. PHI and DAS 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.