

Determination of the Safety of Pioneer Hi-Bred
Corn Event TC1507 (Insect-Protected and Herbicide Tolerant Corn)
for Propagation

Food and Feed and Environmental Safety:

The product dossiers on Corn Event TC1507 were reviewed for safety and nutritional differences compared with the conventional corn. The focus of the review was on any potential new or altered expression trait, agronomic characteristics, composition and nutritional content or value relative to the conventional corn. At the end of the safety assessment, the following conclusions were made: Corn Event TC1507 is as safe as the conventional corn taking into account dietary impact of any changes in nutritional content or value. Corn Event TC1507 is as safe to humans, animals, non-target organisms and as nutritious as ordinary corn. Corn Event TC1507 is effective in controlling Asian corn borer (*Ostrinia furnacalis*).

A biosafety permit renewal of Corn Event TC1507 for direct use as food and feed or for processing (FFP) was issued to Pioneer Hi-Bred and Dow Agro Sciences of the Philippines on October 7, 2013 and a biosafety permit for propagation was issued to Pioneer Hi-Bred on December 9, 2013. The permits for renewal for direct use and for propagation are valid for five years and shall expire on October 6, 2018 and on December 8, 2018, respectively, subject to the terms and conditions set forth in DA Administrative Order No. 8 (DA AO8), series of 2002. Corn Event TC1507 was listed in the Biotech Approval Registry prepared by the Department of Agriculture-Bureau of Plant Industry.

This approval is for propagation of insect-protected and herbicide tolerant Corn Event TC1507 including all progenies from crosses of this product with any conventionally-bred corn and corn containing biotech events approved for propagation in the Philippines. Propagation of Corn Event TC1507 is therefore authorized as of December 9, 2013. The biosafety permit for propagation (Permit No.13-0010) affirms that Corn Event TC1507 is as safe for human food, livestock feed, processing and for propagation as its conventional counterparts.

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

Designation:	Corn Event TC1507 (Herculex®)
Applicant:	PIONEER HI-BRED PHILIPPINES INC.(PHPI) 8F iSquare Building, 15 Meralco Avenue, Ortigas Center, Pasig City 1605 Philippines
Plant Species:	
Name:	Corn, Maize (<i>Zea mays</i>)
Parent Material:	Inbred corn lines developed and produced by Pioneer Hi-Bred 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 concentrations, 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 protection against 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 and feed or for processing (FFP); and for propagation.

II. Background Information

Pioneer Hi-Bred Philippines Inc. (PHPI) submitted an application to the DA Bureau of Plant Industry (BPI) on June 28, 2013 requesting for biosafety permit under DA AO8 for Cry1F insect-protected, glufosinate-tolerant maize line containing transformation event TC1507. Corn Event TC1507 was developed to provide a method to prevent yield losses from larval feeding damage caused by the Asian corn borer (ACB) without the use of conventional pesticides. In addition, it was transformed with a gene that confers tolerance to the herbicide glufosinate. The glufosinate tolerance trait in TC1507 is utilized as a selectable marker.

PHPI has 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 Bt Cry 1F maize line TC1507 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 and Fisheries Product Standards (BAFPS), Bureau of Plant Industry (BPI) and Fertilizer and Pesticide Authority (FPA)] and a Scientific and Technical Review Panel (STRP) following the DA AO8 guidelines for the release of genetically modified organisms.

The Public Information Sheets (PIS) of the said applications for FFP and propagation were published in two widely circulated newspapers to solicit public comments/review. The PIS for FFP was published in Malaya Business Insight and The Daily Tribune on August 16, 2013; while the PIS for propagation was published in Malaya Business Insight and The Daily Tribune on August 20, 2013 and August 22, 2013, respectively. 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) and DA- Insect Resistance Management Advisory Team (DA-IRMAT) completed the approval process.

III. Description of Novel (Introduced) Traits

The corn transformation event designated as TC1507 was modified using a *cry1F* gene derived from *Bacillus thuringiensis* var. *aizawai* PS811. It produces an insecticidal protein (delta-endotoxin) that is selective in toxicity to specific organisms. Upon ingestion by susceptible insects, these proteins are processed by proteases to release the active core protein. The activated Bt proteins bind to a specific receptor on the apical microvillae of the 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 TC1507 has shown effectiveness against Asian corn borer.

The *pat* gene, which encodes the enzyme phosphinothricin acetyltransferase is also present in Bt Cry1F maize line TC1507. The *pat* gene is a modified version of the native *pat* gene from *Streptomyces viridochromogenes*. Expression of the PAT protein confers tolerance to glufosinate-ammonium herbicide which was used as a selectable marker for transformation. The PAT enzyme catalyzes the conversion of L- phosphinothricin, the active ingredient in glufosinate-ammonium, to an inactive form and thereby providing tolerance to 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 certain species of insects belonging to the Lepidopteran order. The protein expressed by the *pat* gene 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 proteins that regulate the normal metabolic pathways of plants. There is no evidence that the inserted genes will 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 TC1507. 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.

IV. Nutritional Composition (Compositional Analysis)

The key nutrients present in Corn Event TC1507 and non-transformed corn are comparable. The levels in maize line TC1507 of protein, fat, fatty acid, vitamins, minerals, ADF, NDF and ash were all within the literature ranges for maize grain. A small increase in the levels of a non-essential amino acid was reported. However, it would not likely 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 TC1507 and isoline were below the limit of quantification. This confirms that no unusually high levels of trypsin inhibitor are present in maize line TC1507.

VI. Environmental Assessment

Based from the multi-location field trials in the Philippines, the TC1507 corn has been shown to be efficacious against Asian corn borer. The agrophenotypic characteristics of TC1507 corn were found to be generally similar to the non transgenic corn and the commercial corn product. The tolerance of TC1507 corn to different diseases was found to be similar to the non-transgenic corn.

TC1507 maize does not exhibit characteristics that cause it to be more competitive or weedy than other cultivated corn. Cultivated maize is sexually compatible to varying degrees with other members of the genus *Zea* (teosinte) and to a much lesser extent with members of the genus *Tripsacum*. *Teosinte* is not present in the Philippines. *Tripsacum* species have been introduced in the Philippines, however outcrossing with *Tripsacum* species is unlikely under natural field conditions. Therefore, there is no risk of gene flow or introgression of insect resistance or glufosinate resistance traits from TC1507 into wild or weedy species.

The result of the field study demonstrates that the abundance of non target arthropods observed in TC1507 maize was comparable to those of the non transgenic corn of similar genetic background.

Data collected from six field test sites in two cropping seasons demonstrate that agrophenotypic characteristics, disease tolerance and abiotic stress response (e.g. winds, drought conditions) of TC1507 corn is similar to non transgenic corn. The results support the conclusion that the risk associated with propagation of TC1507 corn in the Philippines is low.

VII. Regulatory Decision

After reviewing the scientific data and information relevant to the application of Pioneer Hi-Bred Philippines, Inc., it is concluded that Corn Event TC1507 and all progenies derived from crosses of the product with any conventionally-bred corn, and corn containing approved biotech events for propagation is as safe and substantially equivalent to its unmodified counterpart, and is therefore approved for propagation. Pioneer Hi-Bred Philippines, Inc. must comply with approved stewardship program consisting of enhanced Insect Resistance Management (IRM) Strategy, a valid Plant Incorporated Protectant (PIP) permit from the Fertilizer and Pesticide Authority, other approved monitoring activities, regular reporting of seed sales and conduct of required technical studies.