

**Determination of the Safety of Syngenta's
Corn 5307
For Direct use as Food, Feed, or for Processing**

Food and Feed Safety

The product dossier on Corn 5307 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 the corn 5307 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 5307 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 Syngenta Philippines Inc. on June 11, 2015. The said Corn 5307 will be included in the Lists of Approval Registry prepared by the Department of Agriculture- Bureau of Plant Industry.

This approval is for use as food, feed or for processing only. This does not include cultivation of Corn 5307 in the Philippines. Food and feed use of Corn 5307 and its by-products is therefore authorized as of June 11, 2015. The biosafety permit (No. 15-082) stated that "Corn 5307 is as safe for human food, livestock feed or for processing as its conventional counterparts".

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

Designation:	Insect Resistant Corn (5307)
Applicant:	SYNGENTA PHILIPPINES, INC. 12th Floor, Two World Square #22 Upper McKinley Rd. Fort Bonifacio, Taguig City
Plant Species	
Name:	Corn (<i>Zea mays</i>)
Parent Material:	immature NP2222 embryo
Center of Origin:	Corn originated in the highlands of Mexico from 7,000 to 10,000 years ago.
Toxic Factors/Allergen(s):	Corn is not a common allergenic food. Allergies to corn are rare (less than six in over one hundred patients referred to a pediatric allergy specialty center for grain allergy)
Trait Description:	insect – protected maize
Trait Introduction Method:	<i>Agrobacterium</i> -mediated transformation
Donor Organisms:	<i>Bacillus thuringiensis</i> – source of <i>ecry3.1Ab</i> gene which provides protection against coleopteran insect pests <i>Escherichia coli</i> – source of <i>phosphomannose isomerase (pmi)</i> gene which was used as a selectable marker in the production of Event 5307 corn
Pathogenicity:	<i>B. thuringiensis</i> has no known pathogenicity and allergenicity to human, animals and non-target organisms. It has been in commercial use as a microbial pesticide on food crops, including fresh vegetables, for over 30 years. <i>Escherichia coli</i> is ubiquitous in the digestive system of vertebrates.

Proposed Use:

For direct use as food, feed or for processing

Background Information

On April 17 2012, Syngenta Philippines submitted an application to the Bureau of Plant Industry requesting for biosafety permit under Administrative Order (AO) No. 8 Part 5 for Corn 5307 which has been genetically modified for insect resistance.

Syngenta Philippines Inc. has provided data on the identity of corn 5307, a detailed description of the modification method, data and information on the gene insertion sites, copy numbers 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. Relevant scientific publications were also supplied.

The petitioner/applicant published the said application on two widely circulated newspapers: Manila Standard Today and The Manila Times on August 3, 2012 for public comment/review. During the 30-day comment period, BPI had not received comment on the said application.

Description of Novel (Introduced) Traits

Corn 5307 has been evaluated according to BPI's safety assessment by concerned agencies [Bureau of Animal Industry (BAI), Bureau of Agriculture and Fisheries Standards (BAFS) and a Scientific and Technical Review Panel (STRP)]. The process involves an intensive analysis of the nature of the genetic modification together with the consideration of safety assessment paradigm, which includes molecular characterization, protein characterization, and food/feed composition.

Syngenta has developed product corn 5307 which was genetically modified using *Agrobacterium tumefaciens*-mediated transformation. It contains two novel genes. The first, *ecry3.1Ab* gene consists of a fusion between mCry3A, a protein derived from the native Cry3A protein from *B. thuringiensis subsp. tenebrionis*, and Cry1Ab protein from *B. thuringiensis subsp. kurstaki* HD-1.

The second gene, *pmi*, which was derived from *Escherichia coli* is present as a selectable marker and encodes the enzyme phosphomannose isomerase.

Safety of the Expressed Proteins

The species-specific insecticidal mode of action of eCry3.1Ab and its similarity to other Cry proteins for which human safety has previously been established (e.g., mCry3A, Cry3A, and Cry1Ab) support the prediction that no adverse health effects will result from exposure to the eCry3.1Ab protein present in corn 5307.

No toxicity to mammals was observed following oral exposure to high doses of eCry3.1Ab, and the properties of this protein do not indicate allergenic potential. The eCry3.1Ab protein does not share significant amino acid sequence similarity to known protein toxins and no adverse test-substance-related effects were observed in mice administered a single high dose (2000 mg/kg body weight) of eCry3.1Ab protein. Therefore, eCry3.1Ab is considered nontoxic.

Bioinformatic analyses also demonstrated that the PMI amino acid sequence (391 amino acids) has no significant sequence similarity to any toxins. This comparison was conducted using a 2010 posting of the National Center for Biotechnology Information (NCBI) Entrez® Protein Database (NCBI 2010b), and searching the database using the Basic Local Alignment Search Tool for Proteins (BLASTP) program.

The weight-of-evidence indicates that eCry3.1Ab amino acid is not likely to be a food allergen.

- eCry3.1Ab is not derived from a known source of allergenic proteins
- eCry3.1Ab does not have any significant amino acid sequence similarity to known or putative allergenic proteins.
- eCry3.1 is rapidly degraded in SGF
- eCry3.1Ab is inactivated, and thus denatured, at temperature of 95°C

A standard weight-of-evidence analysis for allergenic potential (Codex 2009) indicates that PMI is unlikely to be a food allergen and is unlikely to be cross-reactive to known allergens:

- PMI is not derived from a known source of allergenic proteins.
- PMI does not have any significant amino acid sequence similarity to known or putative allergenic proteins with implications for its allergenic potential.
- PMI is rapidly degraded in simulated mammalian gastric fluid containing pepsin
- PMI is labile upon heating at temperatures of 65°C and above
- PMI is not glycosylated in corn.

Nutritional Composition (Compositional Analysis)

Analysis of key nutritional components of forage and grain from corn 5307 showed that no biologically significant changes in composition occurred as an unintended result of the transformation process or expression of the transgenes in corn 5307. Forage and grain from corn 5307 are considered similar in composition to forage and grain from conventional corn. In addition, a 49-day feeding study demonstrated that there were no adverse dietary effects on broiler chickens consuming diets prepared with corn 5307 grain when compared with those consuming diets prepared with non-transgenic, control corn grain, either as a direct effect of the transgenic proteins in the diet or as a result of any unintended compositional changes in the grain that may have altered its nutritional value. These results support the conclusion that corn 5307 is nutritionally comparable to and as safe as conventional corn.

Corn 5307 is not intended to change the nutritional status of individuals/ populations/ livestock or to result in products with enhanced functionality. Compositional analysis and whole food and safety tests have demonstrated that no unexpected alterations in nutrients and other food components have occurred and that no nutritional imbalances were introduced.

Anti-Nutritional Factors

Phytic acid is an anti-nutrient in plants including corn or maize. The use, however, of enzymes like phytase solves this problem. This is a common practice in formulating diets in simple-stomach animals. Other anti-nutrients such as raffinose and trypsin inhibitor are not considered nutritionally significant in maize.

Regulatory Decision

After reviewing the scientific data and information relevant to the application of Syngenta Philippines Inc., it was concluded that Corn 5307 and all progenies derived from crosses of this product with any conventionally-bred corn except when such cross involves another transformation event is as safe and substantially equivalent to its unmodified counterpart, and is therefore approved for direct use as food, or feed or for processing.

Syngenta 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 are covered by conditions for approval as provided in Department of Agriculture Memorandum Circular No. 8, Series of 2003.