

Decision for the Safety Assessment of  
Syngenta's corn Bt11 x MIR162 x MIR604 x GA21,  
for Direct Use as food and feed or for processing

**Food and Feed Safety**

The product dossiers on Syngenta Philippines' combined trait product corn: Bt11 x MIR162 x MIR604 x GA21 were reviewed for safety and nutritional differences compared with the conventional corn. The focus of the food/feed safety assessment is based on three major issues/concerns regarding stacked genes from different sources namely: a) gene interaction; b) effect on metabolic pathways and c) differential gene expression due to stacking.

A biosafety notification for combined trait product: corn Bt11 x MIR162 x MIR604 x GA21 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 the 28<sup>th</sup> day of July 2010. The notification is valid for five years and shall expire on July 27, 2015 subject to the terms and conditions set forth in DA Administrative Order No. 8 (DA AO8), Series of 2002, and Memorandum Circulars Nos. 6 and 8, Series of 2004. The said combined trait product was included in the Lists of Approval Registry 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 combined trait product corn Bt 11 x MIR162 x MIR604 x GA21 in the Philippines. Food and Feed use of combined trait product corn: Bt11 x MIR162 x MIR604 x GA21 and its by-products is therefore authorized as of 28<sup>th</sup> day of July 2010. The biosafety notification (No. 10-031) stated that combined trait product corn: Bt11 x MIR162 x MIR604 x GA21 is as safe for human food, livestock feed and for processing as its conventional counterparts”.*

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

<b>Designation:</b>	Combined trait product corn: Bt11 x MIR162 x MIR604 x GA21
<b>Applicant:</b>	Syngenta Philippines, Inc.
<b>Plant Species:</b>	
Name:	corn ( <i>Zea Mays</i> )
Parent Material:	Inbred corn lines (and/or isolines) developed and produced by Syngenta
Center of Origin:	Mexico and Central 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

**Trait Description:** Insect resistance and herbicide tolerance

**Trait Introduction Method:** Conventional breeding

**Donor Organisms:** *Bacillus thuringiensis* var *kurstaki*, source of *cryIAb* gene which produces crystal protein effective as insecticide against corn borer

*Streptomyces viridochromogenes* source of the *pat* gene that encodes an enzyme, the phosphinotricin-N-acetyl transferase that detoxifies glufosinate ammonium.

*Bacillus thuringiensis* (*B. thuringiensis*) source of *vip3Aa20* gene that encodes a vegetative insecticidal protein (Vip) that controls several lepidopteran pest of maize including corn earworm, black cutworm, fall armyworm, and western bean cutworm.

*Escherichia coli* (*E. coli*) source of the *phosphomannose isomerase* (*pmi*) gene which encodes the PMI protein for use as a selectable marker during the development of maize event MIR162.

*Bacillus thuringiensis* subsp.*tenebrionis*, source of *cry3A* gene that encodes for a protein that confers resistance to corn rootworm

*Zea mays* L. a source of *mepsps* gene

**Pathogenicity:** *Bacillus thuringiensis* var. *kurstaki* has been shown to be non-toxic to humans, other vertebrates and beneficial insects. *B.t.k.* based foliar insecticides have been registered for over 30 years and have a long history of safe use.

*Bacillus thuringiensis* has no known pathogenicity and allergenicity to humans, animals and non-target organisms.

*Escherichia coli* has no known pathogenicity and allergenicity to humans, animals and non-target organisms.

*Bacillus thuringiensis* subsp. *tenebrionis* is a common soil bacterium with no reported allergenic and toxic responses, establishing basis for the lack of allergenic or toxic concern for the Cry3A protein. Bt-based products have shown that the proteins produce toxic effects only in the gut of chewing insects and are not activated in human digestive tracts.

*Zea mays*, source of *mepsps* gene, has been traditionally used as food and feed for many years and has shown no adverse effect on human/animal health.

**Proposed Use:** For direct use as food, feed or for processing

## II. Background Information

Syngenta Philippines Inc. has filed an application with attached technical dossiers to the Bureau of Plant Industry (BPI) on April 16, 2010 for a biosafety notification for direct use as food, feed and for processing under Administrative Order (AO) No. 8 Part 5 for stacked trait product corn: Bt11 x MIR162 x MIR604 x GA21 which has been genetically modified for insect resistance and herbicide tolerance.

A safety assessment of combined trait product corn: Bt11 x MIR162 x MIR604 x GA21 was conducted as per Department of Agriculture Administrative Order No. 8 Series of 2002 and Memorandum Circulars Nos. 6 and 8, Series of 2004. The focus of risk assessment is the gene interactions between the six (*cry1Ab*, *pat*, *vip3Aa20*, *mcry3A*, *pmi* and *epsps*) transgenes.

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

Maize plants derived from Event Bt 11 contain the *cry1ab* coding sequence derived from *Bacillus thuringiensis* var *kurstaki* which is a common soil bacterium. The *cry1ab* gene encodes for the production of Cry1Ab (*Btk*) protein. This crystal protein protects the plant from specific lepidopteran insect damage. When eaten by the larva, the *Btk* protein is broken down by digestive enzymes in the larva's alkaline intestine, generating a shorter protein that binds to the wall of the intestine. This damages the larva's cell membrane, making it leaky, and stops the larva from feeding that leads to its eventual death.

Corn Bt11 also contains the marker gene *pat* derived from the soil bacterium *Streptomyces viridochromogenes*. The *pat* coding sequence encodes for the production of phosphinothricin acetyl-transferase (PAT) protein. This protein gives the plant tolerance to glufosinate ammonium, an active ingredient in herbicide. The glufosinate ammonium inhibits the glutamine synthetase in plants, resulting in an accumulation of ammonia in plant tissues leading to its death.

Corn MIR162 was produced by *Agrobacterium tumefaciens*-mediated transformation of immature embryos using the plasmid vector pNOV1300. It contains two novel genes. The first, *vip3Aa20* gene derived from *Bacillus thuringiensis* encodes the insecticidal protein, Vip3Aa20. The second gene, *pmi* is present as a selectable marker and encodes the enzyme phosphomannose isomerase derived from *Escherichia coli*. Corn MIR162 has been genetically modified to be resistant to a number of Lepidopteran insects, namely common cutworm (*Spodoptera litura* Fabricius), corn semi-looper (*Chrysodeixis chalcites* [Esper] L.), true armyworm (*Mythimna separata* Walker) and corn earworm.

Maize plants derived from the transformation event MIR604 contains a modified *cry3A* (*mcry3A*) gene, from *Bacillus thuringiensis* subsp. *tenebrionis*, which encodes for a protein for the control corn rootworm and, a phosphomannose isomerase (*pmi*) gene from *Escherichia coli*, as a selectable marker trait which was employed only during selection of transformed plant cells in culture to utilize mannose as a primary carbon source.

Corn event GA21 contains a double mutated 5-enol pyruvylshikimate-e-phosphate synthase (*mepsps*) gene that confers tolerance to glyphosate. The mEPSPS protein shows no significant amino acid sequence homology to known or putative allergenic proteins.

Bt11 x MIR162 x MIR604 x GA21 maize was produced by the combining the Bt11, MIR162, MIR604 and GA21 maize transgenic traits through conventional breeding.

#### **Safety of the Expressed Proteins**

Bt11 x MIR162 x MIR604 x GA21 maize produces the six transgenic proteins (Cry1Ab, PAT, Vip3Aa20, mCry3A, PMI and EPSPS). These proteins show no homology to any known mammalian allergen or toxin. There is no evidence suggesting that the six proteins will interact to form some new allergen or toxin since each has distinct mode of action and are not likely to interact. Allergenicity and toxicity reports on individual proteins in each event were provided when the single events were submitted for biosafety assessment, all of which received biosafety approvals for food, feed and for processing.

Based on the modes of action of the Cry1Ab, PAT, Vip3Aa20, mCry3A, PMI and EPSPS proteins, and the location of these proteins' accumulation in the plant cells, there is no known mechanism of interaction among the gene products that could lead to adverse effects in human and animals

#### **IV. Nutritional Composition (Compositional Analysis)**

The World Health Organization (1995) stated that when two plants that are substantially equivalent to conventional varieties are crosses by conventional breeding techniques, the combined trait product is expected to be substantially equivalent to the single event products.

#### **V. Anti-Nutritional Factors**

Levels of anti-nutritional factors between individual single events and non-transgenic counterparts are not biologically different.

#### **VI. Regulatory Decision**

After reviewing the scientific data and information relevant to the combined trait product corn Bt11 x MIR162 x MIR604 x GA21 application of Syngenta Philippines, Inc., it is concluded that no interaction found between/among the combined traits. Hence, this plant product was found to be as safe as its conventional corn and can substitute for its traditional counterpart for direct use as food, feed and for processing and is therefore approved for direct use as food, or feed or for processing. Syngenta Philippines, Inc. is hereby notified that it may proceed with the activities for the above product for direct use as food and feed or for processing following all existing rules and regulations consistent with DA AO #8.