

Determination of the Safety of Syngenta's
Corn BT11 (Insect-resistant and herbicide-tolerant Corn)
for Direct use as Food, Feed, and for Processing and for Propagation

Food and Feed and Environmental Safety

The product dossiers on Bt 11 Corn 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, the following conclusions were made: Bt 11 Corn is as safe as the conventional corn taking into account dietary impact of any changes in nutritional content or value. Bt 11 is safe to humans, animals, non-target organisms and as nutritious as ordinary corn. Bt 11 is safer than chemical insecticides. Bt 11 is very effective in controlling Asiatic corn borer

Biosafety permits for Bt 11 Corn 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 and for propagation were issued to SYNGENTA Philippines Inc. on July 22, 2003 and April 14, 2005 respectively. The permits for direct use and for propagation are valid for five years and shall expire on July 21, 2008 and April 13, 2010, respectively, subject to the terms and conditions set forth in DA Administrative Order No. 8, Series of 2002. The said Bt 11 Corn was included in the Lists of Approval Registry (Delisting) prepared by the Department of Agriculture- Bureau of Plant Industry.

This approval is for use as food, feed and for processing and for cultivation of Insect-resistant and herbicide tolerant Bt 11 Corn in the Philippines. Food and feed use and Cultivation of Bt 11 Corn and its by-products is therefore authorized as of July 22, 2003 and April 14, 2005 respectively. The biosafety permit (No. 03-001) for direct use and biosafety permit (No.003-05) for propagation stated that "Insect-resistant and herbicide tolerant Bt 11 Corn is as safe for human food, livestock feed and for processing and propagation as its conventional counterparts" respectively.

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

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| Designation: | Insect-Resistant and Herbicide Tolerant Corn (Bt 11) |
| Applicant: | SYNGENTA Philippines, Inc. Building 1-B, Sunblest Compound, Km.23 West Service Road, Cupang, Muntinlupa City |
| Plant Species: | |
| 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), is a potential toxicant but it declines rapidly as the plant grows |
| Trait Description: | Insect-resistance and herbicide tolerance |
| Trait Introduction Method: | Protoplast transformation |
| Donor Organisms: | <i>Bacillus thuringiensis var kurstaki</i> , source of <i>cryIAb</i> gene which produces crystal protein effective as insecticide against specific group of insects and <i>Streptomyces viridochromogenes</i> which produces the <i>pat</i> gene encoding an enzyme, the |

phosphinotricin-N-acetyl transferase that detoxifies glufosinate ammonium

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

Streptomyces viridochromogenes has no known pathogenicity and allergenicity to humans, animals and non-target organisms.

Proposed Use: For direct use as food, feed and for processing and for propagation.

II. Background Information

Syngenta 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 Bt 11, 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, Bt 11 was transformed with a gene that confers tolerance to the herbicide glufosinate ammonium.

On April 16, 2003, and on January 15, 2005, Syngenta Philippines, Inc. submitted applications to the Bureau of Plant Industry, requesting for biosafety permits under Administrative Order (AO) No. 8 for Bt 11 Corn for direct use as food, feed, or for processing and for propagation, respectively. Bt11 has been genetically modified for insect resistance and herbicide tolerance.

Syngenta Philippines Inc has provided data on the identity of Bt 11, 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.

Bt 11 Corn has been evaluated according to BPI's safety assessment by concerned agencies [Bureau of Animal Industry (BAI), Bureau of Agriculture, Fisheries, and Product Standards (BAFPS), Bureau of Plant Industry (BPI) and Fertilizer and Pesticide Authority (FPA)], and a Scientific Technical Review Panel (STRP). The process involves an intensive analysis of the nature of the genetic modification together with a consideration of general safety issues, toxicological issues and nutritional issues and environmental issues associated with the modified corn

The petitioner/applicant published the application for direct use on two widely circulated newspapers: Manila Standard and Manila Times on May 26, 2003 for public comment/review. The Public Information Sheet for the application for propagation was published also on two widely circulated newspapers: Manila Times and Malaya on January 28, 2005 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

Bt 11 Corn and all corn lines/hybrids derived from this Event 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 insect damage. When eaten by the insects and corn pests, 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 cell membrane, making it leaky, and stops the larva in its tracks.

This corn event also contains the marker gene *pat* derived from the soil bacterium *Streptomyces viridochromogenes*. The *pat* coding sequence encodes for the production of phosphinotricin 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.

Safety of the Expressed Proteins

Mammalian toxicity studies conducted using Btk and PAT test material did not reveal any harmful effects. The amino acid sequence of the truncated Btk protein expressed in Bt 11 Corn is closely related to the sequence of the same proteins that are present in strains of *B. thuringiensis* that have been used as commercial organic microbial insecticides. An analysis of the amino acid sequences of the inserted Btk and PAT proteins did not show homologies with known mammalian protein toxins and they are not assessed to have any risk for human toxicity.

The truncated *Btk* and PAT proteins expressed in Bt 11 Corn do not possess characteristics typical of known protein allergens. There were no regions of homology when the sequences of these introduced proteins were compared to the amino acid sequences of known protein allergens. Unlike known protein allergens, both of these proteins are rapidly degraded by acid and/or enzymatic hydrolysis when exposed to simulated gastric fluids. The Btk and PAT proteins are extremely unlikely to be allergenic.

IV. Nutritional Composition (Compositional Analysis)

The grain analysis, protein, oil, starch and fiber content of the ACB resistant maize lines were shown to be substantially equivalent to the untransformed maize. The proximate analysis (protein, fat, fiber and starch.) of the ACB resistant maize hybrids gave values well within the published range for traditional maize cultivars.

Under the same agronomic condition, the analysis of nutrients (the levels of protein, calcium, magnesium, phosphorus and potassium) from Bt 11 Corn and its conventional counterpart did not reveal any significant differences.

V. Anti-Nutritional Factors

Few anti-nutrients have been reported to occur in corn which has no relevance for its food use. Regarding the feed use of corn, phytic acid reduces the availability of phosphorus, especially in mono-gastric animals.

There are no toxic or anti-nutritional factors present in corn which would need to be controlled by a specification. Though trypsin inhibitor, phytic acid, and secondary metabolites such as raffinose, ferulic acid and p-coumaric acid have been established as anti-nutrients in corn, they are present in very low amount and are below the thresholds considered to raise a food safety concern. The amount of anti-nutrients present in Bt1116 corn fell within the range found in non-transgenic corn.

Results of animal feeding studies demonstrated similar performance between animals fed with Bt11 maize and conventional maize. Feeding studies done with cattle showed that there was no effect on dry matter intake, milk production, milk composition or a number of rumen parameters relating to feed utilization. Similarly, there were no significant differences observed for feed intake, bodyweight, egg production and egg weight in laying hens.

VI. Environmental Assessment

Adoption of Bt-11 maize will not alter cultivation practices so as to pose any environmental consequences. The Bt gene is very specific on the control of the Asiatic corn borer but is known not to affect non-target arthropods, mammalian and avian wild life. The accompanying *pat* gene has been shown in many studies to be of no consequence to the environment.

The genetic modification for increased resistance in Bt-11 corn is specific only to lepidopteran insects like the Asiatic corn borer. Multi-location tests conducted by the Applicant in the Philippines showed high incidence of other pests and diseases on both Bt-11 and other non-transgenic counterparts.

The incidence of pests like plant hoppers and seedling maggots and diseases are the same on both Bt-11 and conventional corn entries. The out-crossing of Bt-11 corn with other corn varieties in the farming communities will be a real one but introgression of the *cry1Ab* gene into varieties does not pose any liability but may be an advantage. There are no relatives of corn that are sexually compatible in the Philippines. *Coix lacryma* (Tigbi) and corn are not sexually compatible. Hence, outcrossing will not produce offspring. Out-crossing is possible only with other corn varieties. Considering the average farm size owned by corn farmers, distance isolation is not possible. To prevent out-crossing with other corn varieties planted in adjacent fields, time isolation of about 20-

25 days is possible based on the biology and reproductive cycle of the corn plant. This was demonstrated in the multi-location trial.

Corn varieties have been cultivated in the country for very long years now, however, to date, there is no record to show that these varieties or the corn plant became weeds in the wild. It has been thoroughly domesticated that it cannot survive without the aid of man.

Utilization and planting of Bt-11 corn in the Philippines is safe for human and animal health. It is also safe to non-target insects, earthworms and birds. The human and environmental safety of Bt protected crops is supported by the long history of safe use for Bt microbial pesticides around the world (Betz, *et al* 2000). The possible development of resistance of Asiatic corn borer to Bt corn is currently mitigated by the implementation of a scientifically sound and practical Insect Resistance Management (IRM) strategy.

For MRL establishment, the Cry1Ab protein has no identified toxic dose based from acute toxicity studies in experimental animals. It is reported to be easily digested in the stomach and has no identified receptor sites in experimental animals and humans in the gastrointestinal tract. Both Yieldgard corn and conventional corn are considered “substantially equivalent” based from analytical studies. Due to these findings, additional chronic studies are expected to be useless. In addition, the amino acid sequence has no similarity with identified toxins and allergens. Furthermore, the Bt bacteria had already been registered as a microbial insecticides for many years here (by FPA) in the Philippines and worldwide and are used to control diamond-back moth in cabbages and mosquitoes with an excellent historical safety record. For this reason, even the WHO and the organic food producers have endorsed these microbial insecticides as much less toxic compared to most conventional chemical pesticides. The *pat* gene, derived from *Streptomyces viridochromogenes* strain Tu494, which confers resistance to herbicide glufosinate does not produce any significantly toxic or pesticidal compounds for FPA to be concerned.

Due to the absence of known toxicity of the Cry1Ab and PAT proteins in experimental animals and humans and other safety related data, said substance can be exempted from MRL establishment

VII. Regulatory Decision

After reviewing the scientific data and information relevant to the application of Syngenta Philippines, Inc., it is concluded that Bt 11 Corn 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 or feed or for processing is as safe and substantially equivalent to its unmodified counterpart, and is therefore approved for direct use as food, or feed or for processing and for propagation. Syngenta shall duly inform the public of the approval for direct use 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. For propagation approval, Syngenta must comply with Insect Resistance Management Strategy.