Decision for the Safety Assessment of

SYNGENTA’s Event 176 Corn (Insect-protected Corn)

For Direct use as Food, Feed, and for Processing

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Food and Feed Safety:

The product dossier on Event 176 Corn 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 Bt 176 Corn is as safe as the conventional corn taking into account dietary impact of any changes in nutritional content or value.

A biosafety permit for Event 176 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 were issued to SYNGENTA Philippines. Inc. on October 24, 2003. The said Bt 176 Corn will be included in the Lists of Approval Registry (Delisting) being prepared by the Department of Agriculture.

This approval is for use as Food, Feed and Processing only. This does not include cultivation of Insect-protected Bt 176 Corn in the Philippines. Food and Feed use of Event 176 Corn its by-products is therefore authorized as of October 24, 2003. The biosafety permit (No. 03-008) stated that “Insect-protected Bt 176 Corn is as safe for human food, livestock feed and for processing as its conventional counterparts”.

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

Designation: Bt176 Corn

Applicant: SYNGENTA Phils. Inc. 8th Floor, Salustiana Dee Ty Tower

104 Paseo de Roxas Avenue

Makati City

Philippines

Plant Species:

Name: Corn (Zea mays)

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

Trait Introduction Method: Biolistic method (Microprojectile bombardment)

Donor Organisms: Bacillus thuringiensis var kurstaki strain HD-1(Btk), source of cry1Ab gene which produces crystal protein effective as insecticide against specific group of insects.

Streptomyces hygroscopicus, source of bar gene which produces an enzyme, phosphinothricin acetyl transferase (PAT).

Pathogenicity: Cry1Ab protein, product of a gene derived from Bacillus thuringiensis subsp. kurstaki, has been shown to be non-toxic to humans, other vertebrates and beneficial insects. Bt-based foliar insecticides have been registered for over 30 years and have a long history of safe use.

Streptomyces hygroscopicus is ubiquitous in the soil and there have been no reports of adverse affects on humans, animals, or plants

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

## Background Information

SYNGENTA has developed a corn line resistant to the Asiatic Corn Borer (ACB) larva, a periodic pest of corn in the Philippines.. This corn line, designated Event 176 Bt corn has been transformed using microprojectile bombardment of embryos, to produce an insecticidal protein, from Bacillus thuringiensis ssp. kurstaki, active against certain species of Lepidoptera, an insect order to which butterflies and moths belong, including ACB. This corn line 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

On August 6, 2003, SYNGENTA Phils. Inc. submitted an application to the Bureau of Plant Industry requesting for biosafety permit under Administrative Order (AO) No. 8 Part 5 for Bt- 176 Corn which has been genetically modified for insect resistance (corn borer). Since the validity of the permit is only five years, Syngenta Philippines, Inc. submitted an application for Event 176 renewal to the Bureau of Plant Industry on July 31, 2008.

SYNGENTA Phils. Inc. has provided data on the identity of line Event 176, 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.

Event 176 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)] 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 associated with the modified corn.

The petitioner/applicant published the said application on two widely circulated newspapers: Malaya and Manila Times September 12, 2003 and September 11, 2003 respectively for public comment/review. BPI received no comment on the petition during the 30-day comment period.

Review of the results of evaluation by BPI Biotech Core Team, in consultation with DA-Biotechnology Advisory Team (DA-BAT), completed the approval process.

## Description of Novel (Introduced) Traits

Bt- 176 Corn and all corn lines/hybrids derived from this event contain the Cry1Ab coding sequence from Bacillus thuringiensis var kurstaki strain HD-1 (Btk). The Cry1Ab gene encodes for the production of crystal proteins. These crystal proteins are effective as insecticides after ingestion by specific sensitive insects. The crystal proreins, also called “protoxins” are solubilized by alkaline gut juice and proteolytically cleaved into a smaller active toxic fragment, the core fragments. The activated protein binds to brush border membrane vesicules in the insect midgut inducing the formation of pores, affecting the osmotic balance. The cells swell and lyse, leading to eventual death of the insect. The various crystal proteins produced exhibit specificity for lepidopterans, dipterans, and coleopterans. The CrylAb protein renders the Bt- 176 Corn resistant to specific Lepidopteran insects.

Event 176 Corn also contains the bar coding sequence from Streptomyces hygroscopicus. The bar gene encodes for the production of phosphinothricin acetyl-transferase (PAT) protein. This protein detoxifies glufosinate ammonium, an active ingredient in the herbicide Basta®. The glufosinate ammonium inhibits the glutamine synthetase in plants, resulting in an accumulation of ammonia in plant tissues which leads to its death. The expression of the PAT protein protects the plant from the herbicide glufosinate ammonium.

### Safety of the Expressed Proteins

Toxicity studies conducted using Cry1Ab and PAT test materials did not reveal any deleterious effects. The amino acid sequence of the truncated Cry1Ab protein expressed in Event 176 maize is very similar to the sequence of the same proteins that are present in strains of B. thuringiensis that have been used for over 40 years as commercial microbial insecticides. An analysis of the amino acid sequences of the inserted Cry1Ab protein and the PAT enzyme did not show homologies with known mammalian protein toxins and they are not judged to have any potential for human toxicity.

The truncated Cry1Ab protein and the PAT enzyme expressed in Event 176 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 were rapidly degraded by acid and/or enzymatic hydrolysis when exposed to simulated gastric fluids. The Cry1Ab and PAT proteins are extremely unlikely to be allergenic.

## Nutritional Composition (Compositional Analysis)

Results from proximate analysis, and analyses of fatty acid profiles, carotenoids, and amino acid profiles showed that Event 176 did not differ significantly from non-transformed isogenic lines, and indicated that there were no unintended effects on metabolic pathways. Comparisons of protein, fat, fibre and ash concentration of corn grain and whole plant material from Event 176 and the non-transgenic counterpart showed occasional significant differences in fat and protein content and whole plant ash content. The observed variation described was judged to be normal variation rather than due to the inserted novel trait, and the values are within the published ranged for commercial corn.

## Anti-Nutritional Factors

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 amounts and are below the thresholds considered to raise a food safety concern. The amount of anti-nutrients present in Event 176 corn fell within the range found in non-transgenic corn.

## Regulatory Decision

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After reviewing the scientific data and information relevant to the application of SYNGENTA Phils. Inc., it is concluded that Event 176 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.