Determination of the Safety of Syngenta’s

Corn MIR604

for Direct use as Food, Feed, or Processing

The product dossier of Syngenta’s corn MIR604 was reviewed for safety and nutritional differences compared to the conventional corn. The focus of the food/feed safety assessment is based on the following issues: (a) the nature of the genetic modification; (b) novel protein expression; (c) in vitro digestibility; (d) toxicological assessment; (e) allergenic potential; and (f) compositional and nutritional assessment.

A biosafety permit for corn MIR604 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 March 6, 2018. The permit is valid for five years and shall expire on March 5, 2023 subject to the terms and conditions set forth in DOST-DA-DENR-DOH-DILG Joint Department Circular No. 1 series of 2016. The said 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 or Processing only. This does not include cultivation of MIR604 in the Philippines. Food and Feed use of MIR604 and its by-products is therefore authorized as of March 6, 2018. The biosafety permit (No. 17-005FFP) stated that MIR604 is as safe for human food, livestock feed and for processing as its conventional counterparts.

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

Designation: Corn MIR604

Applicant: SYNGENTA PHILIPPINES, INC.

12th Flr., Two World Square,

Upper McKinley Rd., Mckinley Town Center

Fort Bonifacio, Taguig City

Plant Species:

Name: Corn (Zea mays)

Parent Material: Corn MIR604

Center of Origin: United States

Toxic Factors/Allergen(s): Phytic acid, raffinose and trypsin inhibitor

Trait Description: Insect (Coleopterans) resistance

Trait Introduction Method: Agrobacterium tumefaciens-mediated transformation

**Donor Organisms***:**Bacillus thuringiensis* subsp.tenebrionis is not known to be a source of allergenic proteins.

 *Escherichia coli* is not known to be a source of allergenic proteins.

 Pathogenicity: The mcry3A and pmi sequences have been described. The mcry3A gene is a modified version of a native cry3A gene, which is a member of a class of cry genes found in Bacillus thuringiensis subsp. tenebrionis. On the other hand, the pmi gene came from Escherichia coli. In general, bacteria, including B. thuringiensis and E. coli, are not known to be sources of allergenic proteins

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

## Background Information

Syngenta Philippines Inc. has filed an application with attached technical dossiers to the Bureau of Plant Industry on July 19, 2017 for a biosafety permit for direct use as food, feed or for processing under the DOST-DA-DENR-DOH-DILG Joint Department Circular No. 1 series of 2016 (JDC No.1 s2016).

In accordance with Article VII. Section 20 of the JDC, no regulated article, whether imported or developed domestically, shall be permitted for direct use as food and feed, or for processing, unless: (1) the Biosafety Permit for Direct Use has been issued by the BPI; (2) in the case of imported regulated article, the regulated article has been authorized for commercial distribution as food and feed in the country of origin; and (3) regardless of the intended use, the regulated article does not pose greater risks to biodiversity, human and animal health than its conventional counterpart.

The BPI Biotech Office provided the assessors, except for the SEC expert, the complete dossier submitted by Syngenta. The SEC expert, on the other hand, was provided with a questionnaire on socio-economic, ethical and cultural considerations that have been addressed by Syngenta in relation to their application.

Extensive safety evaluation of MIR604 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 Plant Industry- Plant Products Safety Services Division] and a Scientific Technical Review Panel (STRP) following the JDC No. 1 s2016's guidelines for the release of genetically modified organisms. Furthermore, DENR-BC and DOH-BC also did a thorough evaluation of the environmental risk and environmental health risk respectively.

Syngenta provided data on the identity of MIR604, 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 protein was identified, characterized and compared to the original bacterial protein, including an evaluation of their potential toxicity to livestock and non-target organisms. Relevant scientific publications were supplied.

The DA-Biosafety Committee evaluated the assessment of all agencies including the SEC experts and recommended for the approval of the said application.

Food and Feed Safety

## Description of Novel (Introduced) Traits

Corn MIR604 contains the mcry3A gene and pmi gene. The mcry3A gene is a modified version of a native cry3A gene, which is a member of a class of cry genes found in Bacillus thuringiensis subsp. tenebrionis. It confers resistance to coleopteran insects particularly corn rootworm pests by selectively damaging their midgut lining On the other hand, the pmi gene came from Escherichia coli. It metabolizes mannose and allows positive selection for recovery of transformed plants In general, bacteria, including B. thuringiensis and E. coli, are not known to be sources of allergenic proteins.

### Safety of the Expressed Proteins

The novel proteins, mCry3A and PMI, were subjected to digestibility, heat inactivation, oral toxicity and amino acid sequence comparison studies to determine its potential to cause toxicity or allergenicity to humans (Syngenta, n.d.). The biochemical and functional equivalence between mCry3A and PMI proteins produced by MIR604 and test substances MIR604-0102 and MIR604-PMI-0105 were determined through comparing the protein samples in terms of immunoreactivity, molecular weight and enzymatic activity. Results showed that the microbially-produced and plant-produced proteins were biologically and functionally equivalent (Song, 2009).

Results of the digestibility, heat inactivation, amino acid sequence comparison and acute oral toxicity studies indicates that mCry3A and PMI proteins being expressed in MIR604 corn are not toxic or allergenic to humans (Syngenta, n.d.).

## Nutritional Composition (Compositional Analysis)

Compositional analysis was provided by the developer indicating the nutritional data of MIR604 corn in comparison with the conventional corn (Syngenta, n.d.). The compositional analyses were done in two growing season, in 2002 where two transgenic and 2 non transgenic samples were grown in 3 locations; in 2003, one control and transgenic samples were planted in 7 locations while another 1 transgenic and non-transgenic samples were grown in 9 locations. Results of the analysis indicated that there are no differences in the proximate, fiber, mineral, amino acid, fatty acid, vitamins and anti-nutrient of MIR604 and the conventional corn that can be considered biologically relevant.

## Anti-Nutritional Factors

Anti-nutrients, including ferulic acid, p-coumaric acid, furfural, inositol, phytic acid, raffinose and trypsin inhibitor in grain were analyzed and compared with those of commercial corn varieties. Statistically significant differences are noted for both ferulic acid and p-coumaric acid, with lower levels of both in the transgenic samples as compared to the control samples. Other antinutrients analyzed have no statistically significant differences between the transgenic and the control

Therefore, based on the above statements, there is no safety issue related to the consumption of MIR604 seed, since the contents of all anti-nutrients were comparable to the contents in seeds from other commercial corn lines. The relevance of the statistically significant differences found between the non-transgenic and transgenic control and the transgenic event MIR604 was negligible from a biological and nutritional standpoint.

Environmental Risk Assessment

After a thorough scientific review and evaluation of the documents provided by the Bureau of Plant Industry (BPI) to the DENR Biosafety Committee within the prescribed period pursuant to the Joint Department Circular (JDC) No. 1 S 2016 on the application of Syngenta Philippines Inc. for direct use for feed, food or processing of Genetically Modified corn with single-trait product MIR604, along with the submitted sworn statement and accountability of the proponent, a biosafety permit may be issued to the proponent if the conditions set by DENR are followed.

Environmental Health Risk Assessment

After a thorough scientific review and evaluation of the documents, DOH find sufficient evidence that the regulated article applied for direct use will not pose any significant risk to health and environment and that any hazards could be managed by the measures set by DOH.

Socio-economic. Ethical and Cultural Impact Assessment

Based on the assessment of the indicators, the SEC expert does not have any socio-economic, ethical, and cultural issues to raise regarding the approval of the applicant's application for biosafety permit for direct use as food and feed, or for processing of corn MIR604. The expert recommends for the approval of said application.

Regulatory Decision

Based on the results of the risk evaluation of the submitted scientific data and other information relevant to the application of Syngenta Philippines Inc., it is concluded that corn MIR604, 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, is as safe and substantially equivalent to its unmodified counterpart, and is therefore approved for direct use as food, feed or for processing. Syngenta Philippines Inc. 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 import of this product is covered by conditions for approval as provided in the Biosafety Permit.