Determination of the Safety of Monsanto’s

Soybean MON87701

for Direct use as Food, Feed, or Processing

The product dossier of Monsanto’s soybean MON87701 was reviewed for safety and nutritional differences compared to the conventional soybean. 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 soybean MON87701 and all progenies derived from crosses of the product with any conventionally bred soybean and soybean containing approved-biotech events for direct use as food, feed or for processing, was issued to Monsanto Philippines Inc. on June 22, 2018. The permit is valid for five years and shall expire on June 21, 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 MON87701 in the Philippines. Food and Feed use of MON87701 and its by-products is therefore authorized as of June 22, 2018. The biosafety permit (No. 18-010FFP) stated that MON87701 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: Soybean MON87701

Applicant: MONSANTO PHILIPPINES INC.

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Insular Life Corporate Center, Insular Life Drive

Filinvest Corporate City, Alabang, Muntinlupa City

Plant Species:

Name: Soybean (Glycine max)

Parent Material: Cultivar MON87701

Center of Origin: United States

Toxic Factors/Allergen(s): Trypsin inhibitors, lectins, phyto-estrogens, stachyose, raffinose and phytic acid

Trait Description: Lepidopteran insect resistance

Trait Introduction Method: Agrobacterium tumefaciens-mediated plant transformation

**Donor Organisms***:**Bacillus thuringiensis* subsp. Kurstaki strain HD73 is used commercially in the U.S. to produce microbial-derived products with insecticidal activity.

 Pathogenicity: Microbial pesticides containing B. thuringiensis Cry proteins have been subjected to extensive toxicity testing showing no adverse effects to human health. Additionally, there are no confirmed cases of allergic reactions to Cry proteins in microbial-derived B. thuringiensis products during more than 50 years of use.

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

## Background Information

Monsanto Philippines Inc. has filed an application with attached technical dossiers to the Bureau of Plant Industry on December 2, 2016 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 Monsanto. The SEC expert, on the other hand, was provided with a questionnaire on socio-economic, ethical and cultural considerations that have been addressed by Monsanto in relation to their application.

Extensive safety evaluation of MON87701 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.

Monsanto provided data on the identity of MON87701, 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

MON87701 soybean contains cry1Ac gene conferring resistance to lepidopteran insects by selectively damaging their midgut lining.

### Safety of the Expressed Proteins

An evaluation on potential allergenicity of the CryAc protein based on safety of donor organism, structural similarity to known allergens, in vitro digestibility in simulated digestive fluids, CryAc protein as a proportion of total protein in MON 87701 were performed.

The donor organism, Bacillus thuringiensis (Bt) subsp. kurstaki, is a gram-positive bacterium that is commonly found in soil and has been used commercially in agriculture for pest control. Microbial pesticides containing B. thuringiensis Cry proteins have been used for more than 45 years and subjected to extensive toxicity testing showing no adverse effects to human health. There are no known reports of allergies to Bacillus thuringiensis or to the proteins produced by Bacillus thuringiensis.

The CryAc protein represents no more than 0.0012% of the total protein in the seed of MON 87701. Therefore, the CryAc protein would constitute a very small portion of the total protein present in feed and food derived from MON 87701. Bioinformatics analyses demonstrated that the CryAc protein do not share structurally or immunologically relevant amino acid sequence similarities with known allergens. Thus, it is highly unlikely that the CryAc protein contains immunologically cross-reactive allergenic epitopes. Digestive fate experiments conducted with E. coli-produced CryAc demonstrated that the protein is rapidly digested in simulated digestive fluids, a characteristic shared among proteins with a history of safe consumption. Taken together, these data support the conclusion that the CryAc protein presents in MON 87701 is not similar to known allergens and does not pose a significant allergenic risk to humans or animals.

## Nutritional Composition (Compositional Analysis)

Compositional analyses were conducted on the forage and seed collected from MON 87701, the conventional soybean control (A5547), and twenty unique commercial conventional soybean varieties grown at five replicated trial sites in a 2007 U.S. field production. Seeds were planted in a randomized complete block design with three replicates per block for MON 87701, the control, and reference soybean varieties. Samples from all three replicates of MON 87701 and control plots at each site were analyzed, whereas one replicate of the twenty unique commercial conventional soybean varieties planted across sites was analyzed. Analysis of a single replicate from each unique reference variety was sufficient to establish a 99% tolerance interval for each analyte, as described below. All samples were collected from plants grown under normal agronomic field conditions for their respective geographic regions. A total of 64 compositional analytes (seven in forage and 57 in seed) were evaluated.

There were no significant differences in the seven comparisons for forage between MON 87701 and the conventional soybean control in the combined-site analysis. For seed, no significant differences were detected in 27 of 40 nutrient analyte comparisons made between MON 87701 and the conventional soybean control in the combined-site analysis. Statistically significant differences (p<0.05) were detected for 13 analytes in seed: protein, nine amino acids (alanine, glycine, histidine, isoleucine, leucine, lysine, serine, threonine, and valine), 22:0 behenic acid, carbohydrates, and vitamin E. The magnitude of these differences were generally small (most <5%), except in the case of vitamin E. However, these were not observed consistently across all sites (individual-site analyses), and the mean value for MON 87701 were within the calculated 99% tolerance interval for the population of commercial conventional soybean varieties grown concurrently at the same field site.

Therefore, it is concluded that these differences were not regarded as biologically relevant. Soybean seed and forage analyte values were also comparable to values published in the scientific literature and reported in ILSI-CCD. This further supports the conclusion that the soybean seed and forage from MON 87701 are compositionally equivalent to those of conventional soybean.

## Anti-Nutritional Factors

The levels of anti-nutrient in MON 87701 are compositionally equivalent to that of the conventional soybean. In addition, MON 87701 is intended to provide insect protection; therefore, no changes should be anticipated on amount of material consumed, the characteristics of the edible parts of the plant or in the use pattern and processing procedure of MON 87701, compared to conventional soybean.

In general, soybean processing for food use includes various procedures such as steam cooking, baking, drying and cooling, fermenting, roller milling, grinding and etc. Some degree of heating, mechanical and chemical disruption may accompany those processes, which may or may not affect the level of anti-nutrients. Nevertheless, the level of anti-nutrients in processed products of MON 87701 and the conventional control would be expected to be similar, as there was no difference in the levels of anti-nutrients in MON 87701 compared to control soybean.

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 Monsanto Philippines Inc. for direct use for feed, food or processing of Genetically Modified Soybean with lepidopteran insect resjstant trait MON87701, 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

The impact of GM Soybean MON 87701 to the feed industry and ultimately to the livestock, poultry and the aquaculture sub-sectors would be tremendous. Importation of soybeans will save millions of dollars for our country through lower prices.

With the above scenario and observed consequences of MON 87701, the SEC Expert recommends the renewal of permit of the MON 87701. The renewal of the utilization of GM Soybeans would help the feed industry and may result to lower production cost of poultry, livestock and aquaculture products in our country. However, concern agencies, both government and non-government, should continue monitor and regularly assess the risk of any GM products introduced in the country.

Regulatory Decision

Based on the results of the risk evaluation of the submitted scientific data and other information relevant to the application of Monsanto Philippines Inc., it is concluded that soybean MON87701, and all progenies derived from crosses of the product with any conventionally-bred soybean, and soybean 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. Monsanto 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.