Determination of the Safety of Monsanto's
Soybean MON 87769
for Direct use as Food, Feed, or Processing

Food and Feed Safety

The product dossier of Monsanto's soybean event MON 87769 was reviewed for safety and nutritional differences compared to the conventional soybean. The review was focused on any new or altered expression trait and changes in composition and nutritional content or value relative to the conventional soybean. After thorough evaluation on the safety assessment, the following conclusions were made: Nutrition enhanced MON 87769 soybean is as safe as its conventional counterpart taking into account the safety and nutritional quality of MON 87769.

A biosafety permit for nutrition enhanced soybean MON 87769 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 April 24, 2015. The permit is valid for five years and shall expire on April 23, 2020 subject to the terms and conditions set forth in DA Administrative Order No. 8, Series of 2002, as amended by DA Administrative Order No. 22, Series of 2007 . The said product was included in the Lists of Approval Registry 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 MON 87769 in the Philippines. Food and Feed use of MON 87769 and its by-products is therefore authorized as of April 24, 2015. The biosafety permit (No. 15-080) stated that MON 87769 is as safe for human food, livestock feed and for processing as its conventional counterparts.

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

Designation: MON 87769 Soybean

Applicant: MONSANTO PHILIPPINES, INC.
23rd Floor Tower II
Insular Life Corporate Centre
Insular Life Drive
Filinvest Corporate City
Alabang, Muntinlupa City, 1781
Philippines

Plant Species:

Name: Soybean (*Glycine max)*

Parent Material: Conventional soybean A3525

Center of Origin: Southeast Asia; wild soybean species endemic in China, Korea, Japan and Taiwan

Toxic Factors/Allergen(s): Trypsin inhibitors, lectins, urease, phytoestrogens, stachyose, raffinose and phytic acid.

Trait Description: Nutritional enhancement (High omega-3 fatty acid)

Trait Introduction Method: *Agrobacterium*-mediated transformation

Donor Organisms*:* *Primula juliae,* source of the *Pj.D6D* gene producing the delta 6 desaturase protein which desaturates certain endogenous fatty acids resulting in the production of stearidonic acid (SDA), an omega-3 fatty acid

Neurospora crassa, source of *Nc.Fad3* gene producing the delta 15 desaturase protein which also desaturates certain endogenous fatty acids resulting in the production of SDA, an omega-3 fatty acid

Pathogenicity: *Primula juliae* or primula plant is not a known source of food allergens and has no known pathogenicity to humans, animals, and non-target organisms.

Neurospora crassa is an ubiquitous fungus considered to be non-pathogenic and non-allergenic

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

II. Background Information

Monsanto company has developed Nutrition enhanced soybean event, MON 87769. which was developed by introducing the *Pj.D6D* and *Nc.Fad3* genes to soybean to enhance its nutritional content, specifically long chain omega 3-fatty acids.

Monsanto Philippines, Inc. has filed an application with attached technical dossiers to the Bureau of Plant Industry on March 22, 2010 for a biosafety permit for direct use as food, feed or for processing under Administrative Order (AO) No. 8 Part 5 for MON 87769, A safety assessment of MON 87769 was conducted as per Department of Agriculture Administrative Order No. 8 Series of 2002 and Memorandum Circulars Nos. 6 and 8, Series of 2004.

Monsanto has provided data and/or information on the identity of MON 87769 including a detailed description of the transformation method, the safety of donor organism, the role of the inserted genes and regulatory sequences, the insertion sites, copy number and genetic stability of the insert(s), and the levels of expression in the plant. The introduced protein was identified, characterized and evaluated for their potential toxicity and allergenicity to human and livestock. Relevant scientific publications were supplied.

MON 87769 has been evaluated according to BPI's safety assessment by concerned agencies [Bureau of Animal Industry (BAI), Bureau of Agriculture and Fisheries Standards (BAFS) and a Scientific and Technical Review Panel (STRP)]. The process involved an extensive safety evaluation of the nature of the genetic modification with a consideration of general safety issues, toxicological and nutritional issues associated with the soybean product.

The Public Information Sheet (PIS) of the said application was published in two widely circulated newspapers: Malaya Business Insight and Tribune Publishing on August 14, 2013 for public comments/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 completed the approval process.

III. Description of Novel (Introduced) Traits

Soybean MON 87769 produces the PjΔ6D and NcΔ15D desaturase proteins from *Primula juliae* and *Neurospora crassa*, respectively. MON 87769 contains stearidonic acid (SDA), a sustainable alternate source of an omega-3 fatty acid to help meet the need for increased dietary intake of long chain omega-3 fatty acids. Introduction of *Primulae juliae* Δ6 desaturase (*Pj.D6D*) and *Neurospora crassa Δ15* desaturase (*Nc.Fad3*) resulted to seed-specific production of the PjΔ6D and NcΔ15D proteins. Soybean plants lack the Δ6 desaturase gene, which is a minimal requirement for the production of SDA. However, Δ6 desaturase also converts linoleic acid (LA) to gamma linoleic acid (GLA). The addition of a Δ15 desaturase with temporal expression similar to the Δ6 desaturase increases the flux of alpha-linolenic acid (ALA) to SDA and lowers the substrate pool for GLA production.

Safety of the Expressed Proteins

A history of safe use has been established for MON 87769 PjΔ6D and NcΔ15D proteins. The PjΔ6D and NcΔ15D proteins have been assessed for their potential allergenicity according to the recommendation of the Codex Alimentarius Commission (Codex, 2003). Both proteins are from non-allergenic sources, lack structural similarity to known allergens, are digested in simulated gastric and intestinal fluids, and constitute a small portion of the total protein present in MON 87769 seed.

Exposure to the proteins by ingestion of the seeds is very minimal since these proteins represent only a negligible portion of the total protein present in MON 87769 seeds. The potential for allergenic cross-reactivity between the proteins and known allergens, gliadins and glutenins was assessed using FASTA sequence alignment program sliding window search. Results demonstrate that MON 87769 PjΔ6D and NcΔ15D proteins in MON 87769 are not likely to share biologically-relevant amino acid sequence similarities with known allergens and support the conclusion that both proteins are non-allergenic.

Digestibility studies in SGF and SIF show that PjΔ6D and NcΔ15D proteins were rapidly digestible indicating that it is highly unlikely that these proteins will pose any safety concern to human and animal health.

Finally acute toxicity studies with adult mice found no adverse effects when PjΔ6D and NcΔ15D proteins were administered at dose far exceeding those that would be experienced consuming grain produced by MON 87769.

Based on the weight of evidence, it is concluded that the PjΔ6D and NcΔ15D proteins expressed in MON 87769 is safe and poses no concerns for humans, animals and the environment.

IV. Nutritional Composition (Compositional Analysis)

Detailed compositional analyses in accordance with OECD guidelines were conducted to determine whether levels of key nutrients and anti-nutrients in MON 87769 were comparable to levels present in the conventional soybean control and commercially available soybean varieties.

These compositional comparisons were made by analyzing the seed and forage harvested from five replicated field sites across the United States during the 2006 field season. The analysis included protein, fat, carbohydrates, fiber, ash, moisture, amino acids, fatty acids, vitamins, and anti-nutrients.

Based on the data and information gathered, it was concluded that MON 87769 is compositionally equivalent to conventional soybean control except for the intended fatty acid changes (i.e., the presence of SDA and GLA).

V. Anti-Nutritional Factors

Harvested soybean seeds contain several substances considered to be anti-nutrients (i.e. trypsin inhibitors, lectin, isoflavones (daidzein, genistein and glycitein) and phytic acid). Trypsin inhibitors and lectin are inactivated by proper processing of soybean protein products or soybean meal and their levels are similar to conventional control. The levels of stachyose, raffinose and phytic acid are also similar to conventional control. The mean and range values for three isoflavones, genistein, daidzein, and glycitein, were lower in MON 87769 harvested seed compared to the values in the conventional soybean control. However, the range of values for these three analytes in MON 87769 were all within the 99% tolerance interval for the population of conventional reference varieties, and were also within the range of values found in the published literature and the ILSI Crop Composition Database. . Therefore, these differences were not considered to be biologically meaningful from a food and feed safety and/or nutritional perspective.

VI. Regulatory Decision

Based on the results of the risk evaluation based on the submitted scientific data and other information relevant to the application of Monsanto Philippines Inc., it is concluded that MON 87769, 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 except its intended changes, 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 Department of Agriculture Memorandum Circular No. 8, Series of 2003.