**Determination of the Safety of Monsanto’s**

**Soybean MON 87705**

**For Direct use as Food and Feed, and for Processing**

**Food and Feed Safety**

The product dossier on Soybean MON 87705 was reviewed for safety and nutritional differences compared with the conventional soybean. 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 soybean. At the end of the safety assessment, a conclusion was made that the soybean MON 87705 is as safe as the conventional soybean taking into account dietary impact of any changes in nutritional content or value.

A biosafety permit for Soybean MON 87705 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 and feed and for processing was issued to Monsanto Philippines Inc. on 28 November 2014. The said Soybean MON 87705 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 and feed and for processing only. This does not include cultivation of Soybean MON 87705 in the Philippines. Food and feed use of Soybean MON 87705 and its by-products is therefore authorized as of 28 November 2014. The biosafety permit (No. 14-078) states that “Soybean MON 87705 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:** Improved fatty acids

**Applicant:** **MONSANTO PHILIPPINES, INC.**

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**Plant Species**:

**Name:**  Soybean (Zea maize)

**Parent Material**: soybean variety A3525 developed by Asgrow Seed Company

**Center of Origin:** Soybean originated in the highlands of Mexico 7,000 to 10,000 years ago.

**Toxic Factors/Allergen(s):** Soybean is not a common allergenic food. Allergies to soybean are rare (less than six in over one hundred patients referred to a pediatric allergy specially center for grain allergy)

**Trait Description**: Improved fatty acid profile

**Trait Introduction Method:** *Agrobacterium*-mediated transformation

**Donor Organisms:** *Agrobacterium* sp. - a source of cp4 epsps coding sequence

**Pathogenicity**: The donor organism, *Agrobacterium* sp. strain CP4 encodes CP4EPSPS protein which was used as a selectable marker during transformation. *Agrobacterium* produces a naturally glyphosate-tolerant EPSPS protein which makes the bacterium resistant to glyphosate. *Agrobacterium* species are not known for human or animal pathogenicity, and are not commonly allergenic. In addition, there is no known population of individuals sensitized to bacterial proteins.

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

1. **Background Information**

On 25 June 2010, Monsanto Philippines submitted an application to the Bureau of Plant Industry requesting for biosafety permit under Administrative Order (AO) No. 8 Part 5 for Soybean MON 87705 which has been genetically modified for improved fatty acid profile in soybean oil.

Monsanto Philippines Inc. has provided data on the identity of soybean MON 87705, a detailed description of the modification method, data and information on the gene insertion sites, copy numbers 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. Relevant scientific publications were also supplied.

The petitioner/applicant published the said application on two widely circulated newspapers: Tribune Publishing and Malaya Business Insight on 27 November 2012 for public comment/review. During the 30-day comment period, BPI had not received comment on the said application.

Review of results of evaluation by the BPI Biotech Core Team completed the approval process.

1. **Description of Novel (Introduced) Traits**

Soybean MON 87705 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 involves an intensive analysis of the nature of the genetic modification together with the consideration of safety assessment paradigm which includes molecular characterization, protein characterization, and food/feed composition.

Monsanto has developed an improved fatty acids profile in soybean MON 87705 soybean oil that results in enhanced nutritional characteristics. MON 87705 was produced by *Agrobacterium*-mediated transformation of soybean with the binary vector PV-GMPQ/HT4404 that contains two transfer DNAs (t-DNAs). Both the T-DNA I and T-DNA II contain DNA segments designed to suppress endogenous *FAD2* and *FATB* genes, which encode two key enzymes in the soybean fatty acid biosynthetic pathway. MON 87705 contains two endogenous soybean (*Glycine max*) genes segments, FATB1-A and FAD2-1A assembled in a single suppression cassette under the control of a seed promoter that limits the change in fatty acid profile in soybean seed. The introduced gene segments produce inverted repeat RNAs that form double stranded RNA (dsRNA). The dsRNA suppresses production of endogenous soybean FATB and FAD2 transcripts via the RNA interference (RNAi) pathway, thereby producing the desired fatty acid phenotype.

The T-DNA I contains the sense segments of the *FAD-2A* intron and *FATB1-A 5’* untranslated region (UTR) and plastid targeting sequence while the T-DNA II contain a partial suppression cassette that contains the antisense segments of the FA2-IA intron and FATB1-A 5’ UTR and plastid targeting sequence. T-DNA 1 contains a *cp4epsps* expression cassette under the regulation of a promoter (FMV/Tsf1) active in all tissues. During the plant transformation, the two T-DNAs cointegrated into one locus in the soybean genome creating an insert containing a single *cp4epsps* expression cassette and a single *FAD2-IA/FATB1-A* suppression cassette.

**Safety of the Expressed Proteins**

The cp4epsps expression cassette in MON 87705 produces CP4EPSPS protein that is equivalent to the protein produced in Roundup Ready 2 Yield (MON 89788) and Roundup Ready soybean products.

The donor organism, *Agrobacterium* sp. strain CP4, was isolated based on its tolerance to glyphosate brought about by the production of a naturally glyphosate-tolerant EPSPS protein.

Bioinformatics analyses demonstrated that the CP4 EPSPS protein present in MON 87705 does not share immunologically relevant amino acid sequence similarities with known allergens and, therefore, is highly unlikely to contain immunologically cross reactive allergenic epitopes and based on the evaluation of potential allergenicity on the source of protein, structural similarity to known-allergens, CP4 EPSPS protein does not pose a significant allergenic risk to human and animals.

Digestive fat experiments conducted with the CP4 EPSPS protein demonstrate that the full-length protein is rapidly digested in simulated gastric fluid *in vitro* assay. In addition, the CP4 EPSPS protein represents no more than 0.031% of the total protein in the seed of MON 87705, a relatively low abundance for this protein compared to the rest of the seed protein content. These data support the conclusion that the CP4 EPSPS protein present in MON 87705 is not similar to known allergens and does not pose a significant allergenic risk to humans or animals and is unlikely to pose a human health concern.

An acute oral toxicity evaluation in mice demonstrated that CP4 EPSPS is not acutely toxic and does not cause any adverse effect, even at the highest dose tested. A dietary safety assessment based on the observed expression levels of CP4 EPSPS in the seed of MON 87705, acute toxicity data and soybean product dietary intake patterns show that the margin of exposure (MOE) for the overall US population is >43,600 indicating that there are no meaningful risks to human health from dietary exposure to CP4EPSPS protein derived from MON 87705. Therefore the safety assessment supports the conclusion that CP4 EPSPS protein derived from MON 87705 is safe for human and animal consumption.

Results from an IgE binding study using sera from soybean allergic individuals demonstrate that MON 87705 does not pose an increased endogenous soybean allergenic risk compared to conventional soybean.

The effect of heat treatment on the immunodetectability of CP4 EPSPS in MON 87705 was evaluated using western blot analysis. The results of this study demonstrate that the heat treatment significantly decreased the level of immunodetectable CP4 EPSPS protein present in extracts of heat-treated ground seeds of MON 87705. The level of the CP4 EPSPS protein detected in extracts of heated MON 87705 was below the limit of detection (LOD), indicating a decrease in the immunodetectable protein of at least 98% relative to the protein levels detected in extracts of unheated MON 87705. These results demonstrate that the heat treatment, similar to the treatment utilized in the processing of soybean flour in food preparation, had a significant impact on the immunodetectability of CP4 EPSPS protein in ground seed from MON 87705.

1. **Nutritional Composition (Compositional Analysis)**

MON 87705 was developed to generate soybean oil with lower levels of saturated fatty acids (16:0 palmitic acid and 18:0 strearic acid) and higher levels of 18:1 oleic acid, with an associated decrease in 18:2 linoleic acid, through suppression of *FAD2* and *FATB* RNAs. MON 87705 contains the same major fatty acids that are found in conventional soybean, 16:0 palmitic, 18:0 stearic, 18:1 oleic, 18:2 linoleic and 18:3 linolenic acids in different proportions. MON 87705 has a fatty acid profile comparable to other widely consumed vegetable oils including olive oil and canola oil.

The nutritional impact from the use of MON 87705 soybean oil in targeted foods under the intended conditions of use is estimated to result in changes in fatty acid consumption that are within current dietary guidelines for fatty acid intake.

**V. Anti-Nutritional Factors**

Soybean seed contains several well-described antinutritional factors which include: trypsin inhibitors, phytic acid, lectins, isoflavones (daidzen, glycitein and genistein), raffinose and stachyose. Combined site anlaysis of antinutrients showed no significant differences between MON 87705 and the conventional soybean control. Both trypsin inhibitors and lectins are inactivated during processing of soybean protein products or soybean meal and, when processed appropriately, the final edible soybean fractions should contain minimal levels of these nutrients.

No significant differences in isoflavone and raffinose levels were observed between MON 87705 and the conventional soybean control for the combined-site or individual-site analyses. Stachyose levels showed no differences between MON 87705 and the conventional soybean control in the combined-site analysis, but were significantly different at one site. This difference is not considered biologically relevant because it was observed only at one site and was not observed consistently across all sites.

1. **Regulatory Decision**

After reviewing the scientific data and information relevant to the application of Monsanto Philippines Inc., it is concluded that Soybean MON 87705 and all progenies derived from crosses of this product with any conventionally-bred soybean except when such cross involves another transformation event is as safe and substantially equivalent to its unmodified counterpart, and is therefore approved for direct use as food, or feed or for processing.

Monsanto 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, and that imports of this product is covered by conditions for approval as provided in Department of Agriculture Memorandum Circular No. 8, Series of 2003.