

**ASSESSORS' CONSOLIDATED REPORT ON MONSANTO'S APPLICATION FOR DIRECT
USE AS FOOD AND FEED, OR FOR PROCESSING OF COMBINED TRAIT PRODUCT
SOYBEAN MON87705 x MON87708 x MON89788**

EXECUTIVE SUMMARY

On December 5, 2016, Monsanto Philippines Inc. applied the stacked trait product soybean MON87705 x MON87708 x MON89788 for direct use as food and feed, or for processing as an original application under the DOST-DA-DENR-DOH-DILG Joint Department Circular No. 1 Series of 2016 (JDC No.1, S2016).

After reviewing the Risk Assessment Report and attachments submitted by the applicant; the Scientific and Technical Review Panel (STRP) member, BPI-Plant Products Safety Services Division (BPI-PPSSD) and Bureau of Animal Industry (BAI) has found no interaction of the resulting gene product of the regulated article applied for direct use as food and feed, or processing based on scientific evidences provided.

The STRP, BAI, and BPI-PPSSD concurred that the likelihood of interaction of the two proteins involved in the combined trait product: DMO and CP4EPSPS is highly unlikely to produce any known allergen or toxins to human and animals because of the difference on their mode of action. There is no known mechanism of interaction among the RNA-based suppression and the proteins that could lead to adverse effects in humans, animals or environment which is not likely to interact. Furthermore, the assessors affirmed that there are no possible unintended effects of stacked genes on the metabolism of the plant based on the previous assessments of individual transformation events. In addition, stability and expression of the gene will never be affected since molecular analyses also indicated the absence of any marker gene in MON87705 x MON87708 x MON89788 genome.

After thorough scientific review and evaluation of Monsanto's duly accomplished Environmental Risk Assessment (ERA) and Project Description Report (PDR) forms, the Department of Environment and Natural Resources – Biosafety Committee (DENR-BC), recommended for the issuance of a biosafety permit for this regulated event provided that the conditions set by DENR are complied. Also, the Department of Health – Biosafety Committee (DOH-BC), after a thorough scientific review and evaluation of the accomplished Environmental Health Risk Assessment form, concluded that soybean MON87705 x MON87708 x MON89788 will not pose any significant risk to the health and environment and that any hazards could be managed by the measures set by the department. Hence, the DOH-BC also recommended for the issuance of biosafety permit for the stacked trait product.

Lastly, after assessing that there will be no negative socio-economic, ethical and cultural concerns that will arise from the adoption of Genetically Modified Organisms, the Socio-economic, Ethical and Cultural (SEC) expert recommended for the approval and issuance of

biosafety permit of soybean MON87705 x MON87708 x MON89788 for direct use as food and feed, or for processing.

BACKGROUND

In accordance with Article VIII, Section 20 of the JDC No.1, S2016, 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 Philippines. The SEC expert, on the other hand, was provided with a separate questionnaire on socio-economic, ethical and cultural considerations that have been addressed by Syngenta Philippines in relation to their application.

Upon receipt of the individual reports from the assessors, the BPI Biotech staff prepared this consolidated risk assessment report for the information of the public.

STRP ASSESSMENT AND RECOMMENDATION

Gene Interaction

MON87705 has the cp4epsps gene for glyphosate tolerance and the inverted repeat of FAD2-1A and FATB1-A which produces ds RNA that suppresses endogenous FATB and FAD 2 RNA levels leading to improve fatty acid profile. MON87708 contains DMO gene that expresses mono-oxygenase that rapidly demethylates dicamba which renders it inactive thereby conferring tolerance to dicamba. Lastly, MON89788 contains cp4epsps which produces CP4EPSPS protein confers tolerance to glyphosate.

The STRP agreed that there is no interaction in the resulting products of the two proteins dmo and cp4epsps because the mode of action is totally different from each other. The STRP also stated that DMO and CP4EPSPS would accumulate in the plastids. These proteins are targeted specifically to the organelle because dmo and cp4epsps genes encodes chloroplast transit peptides that would direct the proteins to the chloroplast.

Metabolic Pathways

As presented in the request for review of MON87705 x MON87708 x MON89788, page 4 (paragraphs 3 to 6), STRP agreed that the technology developer provides the complete description of the mode of action of each gene product. Also, as stated earlier, the mode of action of each gene product is different. The products are not involved in the same metabolic pathway. Each single event will not alter the metabolism of soybean. RNA based suppression of FATB and FAD 2 to improve fatty acid composition is totally independent on

the expression of DMO and CP4EPSPS proteins. Since the DMO and CP4EPSPS proteins are expressed in MON87705 x MON87708 x MON89788, this would indicate that the genes can also function properly in the stacked trait product.

Gene Expression

The expression levels of the individual protein products are the same as the individual approved transformation events as presented in table 2 page 9 of the paper request for review of MON87705 x MON87708 x 89788. It is also shown in the table that the protein level expression is within the range. In addition, the marker genes are not transferred and expressed in the stacked plants. The STRP affirmed that the interaction is unlikely to happen. Stability and expression of the genes will never be affected.

BPI-PPSSD ASSESSMENT AND RECOMMENDATION

Gene Interaction

Based on the documents provided by the developer, the two (2) proteins being expressed in the combined trait product, DMO and CP4 EPSPS, will not interact to produce any known allergen or toxins to human and animals. There is no known mechanism of interaction among the RNA-based suppression and the proteins that could lead to adverse effects in humans, animals or environment which is not likely to interact.

It is also highly unlikely that the RNA-based FAD2-1A/FATB1-A suppression cassette present in MON87705 x MON87708 x MON89788 produces a protein. The gene transcript with an inverted repeat produces double stranded RNA (dsRNA) that, via the RNA interference (RNAi) pathway, suppresses endogenous FATB and FAD2 RNA levels that leads to improved fatty acid composition.

In terms of accumulation, the DMO and CP4 EPSPS proteins would accumulate in plastids because they are targeted specifically to these organelles. The dmo and cp4 epsps genes contained in MON 87705 x MON 87708 x MON 89788 are designed to encode chloroplast transit peptides so that the DMO and CP4 EPSPS proteins are directed to the chloroplast.

Metabolic Pathways

The mode of action and metabolic pathways of each protein are significantly different from each other. DMO belongs to a family of Rieske oxygenase proteins, which is part of a three-component system that includes a ferredoxin, a reductase, and an oxygenase. It catalyzes the NADH-dependent oxidative demethylation of the herbicide dicamba.

The CP4 EPSPS protein belongs to the family of EPSP synthases involved in the penultimate step of the biochemical shikimate pathway producing aromatic amino acids in the chloroplasts of plants.

Gene Expression

Enzyme-Linked Immunosorbent Assays (ELISA) was used to quantify and determine the level of proteins. DMO and CP4 EPSPS proteins were expressed properly in the combined trait product MON 87705 x MON 87708 x MON 89788 and was comparable to each single event. The mean DMO protein levels in MON 87705 x MON 87708 x MON 89788 and MON 87708 were 13µg/g dwt and 19µg/g dwt in seed, respectively. The mean CP4 EPSPS protein levels in MON 87705 x MON 87708 x MON 89788, MON 87705, and MON 89788 are 140µg/g dwt, 130µg/g dwt and 63µg/g dwt in seed, respectively. Molecular analyses also indicated the absence of any marker gene in MON87705 x MON87708 x MON89788 genome.

BAI ASSESSMENT AND RECOMMENDATION

Gene Interaction

The structural differences of DMO and CP4EPSPS proteins as well as the distinct modes of action among these proteins are unlikely to produce a significant interaction. BAI affirmed that this lack of interaction will not lead to production of a new allergen or toxin in the combined trait product. BAI agreed to the information provided by the developer the gene products will accumulate the same subcellular compartments. The dmo and cp4epsps are designed to encode chloroplast transit peptides so that DMO and CP4EPSPS proteins are directed to chloroplast.

Metabolic pathways

BAI agreed that the mode of action has been completely described in the previous safety assessment of each individual single event. CP4EPSPS protein confers tolerance to glyphosate and is involved in an enzymatic pathway producing aromatic amino acids in the chloroplasts of plants. On the other hand, DMO protein catalyzes the NADH-dependent oxidative demethylation of the herbicide dicamba rendering inactive, thereby conferring its tolerance.

The two proteins are structurally and functionally different and not involved in the same metabolic pathway. The inserted genes, which are not designed to alter the plant metabolism are inherited and functioning properly when combined into the breeding stack. It indicates that any mechanisms of interaction between these products are highly unlikely and that each gene product functions independently as in single event.

Gene Expression

In terms of gene expression, results obtained from ELISA performed on seed tissues of MON 87705 x MON 87708 x MON 89788, MON 87705, MON 87708 and MON 89788 collected from five field sites during Argentina field trials show that the proteins were expressed properly in the combined trait product as in its relevant single events. The proteins were expressed at low level also as demonstrated by ELISA. Also, it did not show any indication that the marker genes were transferred and expressed in plants containing the combined genes. Due to the different mode of action, any form of interaction is unlikely.

This means that the stability and expression levels of all the genes will not be significantly affected.

DENR ASSESSMENT AND RECOMMENDATION

After thorough and 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 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 tolerant to glyphosate herbicide stacked trait product MON87705 x MON87708 x MON89788, the following are the observations and recommendations:

1. The effect of the regulated article on the environment depends largely on the viability of the product to be utilized for direct use. If the article is transported in a non-viable form, there is no danger to the environment;
2. Due to the absence of a specified Environmental Management Plan (EMP) by the traders/importers, the Committee would like to recommend that it be added to the requirements for the issuance of an import permit by the Bureau of Plant Industry (BPI) (Article VIII, Section 26 of JDC No,1 s.2016);
3. It is suggested that BPI ensure the following:
 - a) development of guidelines on the EMP in coordination with DENR;
 - b) implementation of the EMP by the traders/importers involved in the import, handling, processing and transport of viable soybean MON87705 x MON87708 x MON89788 commodity products; and
 - c) Strict monitoring of the regulated article from port of entry to the trader's/importer's storage/warehouse (Section 32 of the JDC No. 1 s.2016);

Based on the above considerations and with the submitted sworn statement and accountability of the proponent, a biosafety permit may be issued to the proponent if the abovementioned recommendations are followed.

DOH ASSESSMENT AND RECOMMENDATION

After a thorough review and evaluation of the documents provided by proponent, Monsanto Philippines Inc., through the Bureau of Plant Industry (BPI) in support of their application for approval for direct use as food and feed or processing of soybean MON87705 x MON87708 x MON89788. DOH find that the regulated article applied for direct use as food and feed or processing is safe as its conventional counterpart and shall not pose any significant risk to human and animal health and environment.

The following are the observations and recommendations:

1. Find that regulated article applied for direct use for food and feed or for processing (FFP) does not require changes in the usual practices in unloading, loading, transport, storage and processing. As such, the regulated article is as safe as its conventional counterpart and is not expected to pose any significant risk to human and animal health and environment while in transit, storage and processing.
2. Scientific pieces of evidences from provided references i.e. literatures show that regulated article applied for direct use as food and feed or for processing (FFP) is as safe as its conventional counterpart and shall not pose any significant risk to human and animal health and on the environment.
3. It is suggested that Bureau of Plant Industry (BPI) ensure the following:
 - a. Strict monitoring of the regulated article from port of entry to the trader's / importer's storage/warehouse as stated in Section 32 of the JDC No. 1 series, 2016.
 - b. The BPI to include in the insurance of permit for the release of this product the following conditions:
 - b.1. Any spillage (during unloading and loading/hauling and transport unloading and storage) shall be collected and cleaned up immediately.
 - b.2. Transportation of the consignment from the port of entry to any destination within the country shall be in closed containers.
 - b.3. There shall be a clear labeling of the product from importation down to all levels of marketing stating that it is only for the purpose of direct use for food and feed or for processing and is not to be used as planting materials.
4. Based on the above considerations and with the submitted sworn statement and accountability of the proponent, this recommendation is being submitted to BPI related to the processing and issuance of a biosafety permit for direct use as food and feed or for processing of soybean MON87705 x MON87708 x MON89788.

SEC ASSESSMENT AND RECOMMENDATION

According to the SEC expert, the impact of GM Soybean MON 87705 X MON 87708 X MON 89788 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 87705 X MON 87708 X MON 89788, the SEC expert recommend the renewal of permit of the MON 87705 X MON 87708 X MON 89788. 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. Likewise, food and processing sub-sectors will also benefit the approval of this GM product. However, concern agencies, both government and non-government, should continue monitor and regularly assess the risk of any GM products introduced in the country.