STRP's Assessment

1. Gene Interaction

a. There are no plausible interactions among the novel proteins when produced in the soybean plant.[1].

b. There is an insignificant probability of interaction in which a new allergen or new toxin will be produced, and pose any adverse effect in humans, animals, and the environment.[1].

c. The resulting novel proteins will accumulate in the chloroplast of the transgenic stacked soybean plant cells. Despite the co-localization, the gene products (Cry1A.105, Cry2Ab2, Cry1Ac, DMO, and CP4 EPSPS proteins) act on the different metabolic pathways and do not share any intermediate metabolites in the biochemical pathways that the proteins act on or interfere with.[1].

d. Due to lack of interaction, there is no expected adverse effect on the target trait that the transgenes confer, more so, no new allergen nor toxin will be produced.[1].

2. Metabolic Pathways

a. Cry1A.105, Cry2Ab2, Cry1Ac, DMO, and CP4 EPSPS proteins, would not act on the same metabolic pathways and do not share any intermediate metabolites in the biochemical pathways that the proteins act on or interfere with. Due to lack of interaction, there is no expected adverse effect on the target trait that the transgenes confer, more so, no new allergen nor toxin will be produced.[1].

b. Cry1A.105, Cry2Ab2, Cry1Ac proteins have similarities on the end-results and their modes of action, and differ only on the receptors sites in the insect gut. Although specificity at the molecular level is very much distinct among the three Cry proteins.[1].

c. There are no unintended or unexpected effects on the metabolism upon the novel gene introduction.[1].

3. Gene Expression

a. Enzyme-linked immunosorbent assay (ELISA) and subsequent analysis showed that the novel proteins have no significant difference in the expression levels and were found to be not biologically different between the stacked transgenic plant and its parental genotypes.[1].

b. There is a low expression of the novel proteins in the stacked transgenic plant under evaluation and its parental genotypes.[1].

c. The marker gene, *cp4 epsps* is not transferred and expressed in the stacked transgenic plant.[1].

d. Among the introduced novel proteins, there is no possible interaction and the stability of the genome/partial genome was validated. The parentals' genetic material containing the novel gene were stably incorporated in soybean MON 87751 × MON 87701 × MON 87708 × MON 89788.[1].

STRP's Conclusion

After a thorough and scientific review and evaluation of the documents provided by Monsanto Philippines, Inc. relevant to soybean MON 87751 ×MON 87701 × MON 87708 × MON 89788, the STRP found scientific evidence that the regulated article applied for direct use as food, feed, and or processing (FFP) has no evidence of interaction on the resulting gene products.

BAI's Assessment

1. Gene Interaction

a. It is improbable for Cry1A.105, Cry2Ab2, Cry1Ac, DMO, and CP4 EPSPS proteins to interact with each other and affect the stability of expression level of each gene, since they have different modes of action, substrates or targets and specificity.[1].

b. There are no mechanism and interaction which will possibly lead to production of new allergens or toxin products in the stacked event.[1].

c. Cry1A.105, Cry2Ab2, Cry1Ac, DMO, and CP4 EPSPS proteins are expected to accumulate in the chloroplast.[1].

2. Metabolic Pathways

a. There is a different metabolic pathway and modes of action for each gene product.[1].

- Cry1A.105, Cry2Ab2, and Cry1Ac proteins act through a toxic action in the gut of specific lepidopteran insects.[1].
- DMO catalyzes the demethylation of dicamba to the non-herbicidal compound.[1].
- CP4 EPSPS are enzymes involved in producing aromatic amino acids in biochemical shikimic acid pathway in the chloroplasts of plants.[1].

b. Unexpected effects of the genes and gene products on metabolism of the plant is highly unlikely. The protein expression analysis showed that Cry1A.105, Cry2Ab2,

Cry1Ac, DMO, and CP4 EPSPS proteins were expressed and functioning properly in the combined trait.[1].

3. Gene Expression

a. Cry1A.105, Cry2Ab2, Cry1Ac, DMO, and CP4 EPSPS proteins were expressed properly and at low levels in the combined trait product MON 87751 × MON 87701 × MON 87708 × MON 89788.[1].

b. The marker gene was not transferred and expressed in plants containing the stacked genes.[1].

c. It is improbable for any gene interaction between the two genes will affect the stability of expression, since Cry1A.105, Cry2Ab2, Cry1Ac, DMO, and CP4 EPSPS proteins have distinct modes of action. Moreover, there are no reported instances that the two genes interacted to produce a product that could possibly cause an adverse effect in animals.[1].

BAI's Conclusion

After a thorough and scientific review and evaluation of the documents provided by Monsanto Philippines, Inc. relevant to soybean MON 87751 × MON 87701 × MON 87708 × MON 89788, BAI found scientific evidence that the regulated article applied for direct use as food, feed, and or processing (FFP) has no evidence of interaction on the resulting gene products.

BPI PPSSD's Assessment

1. Gene Interaction

a. The presence of five proteins (Cry1A.105, Cry2Ab2, Cry1Ac, DMO and CP4 EPSPS) will likely not cause interaction to produce new allergen or toxins due to the difference in their mode of actions.[1].

b. The gene products are likely to accumulate in the chloroplast of the soybean cells.[1].

2. Metabolic Pathways

a. Each gene product demonstrated different metabolic pathways and modes of actions.[1].

- The Cry1A.105, Cry2Ab2, and Cry1Ac proteins are insect control proteins and act through a toxic action in the gut of specific lepidopteran insects.[1].

- DMO is an enzyme classified as mono-oxygenase that catalyzes the demethylation of dicamba to the non-herbicidal compound.[1].
- The CP4 EPSPS enzyme decreases binding affinity for glyphosate and confers resistance to glyphosate herbicide and it is involved in the penultimate step of the biochemical shikimic acid pathway producing aromatic amino acids in the chloroplasts of plants.[1].

b. There are no possible unexpected effects of the stacked genes on the metabolism of the plant due to the distinct modes of action and the protein expression. The proteins, Cry1A.105, Cry2Ab2, Cry1Ac, DMO, and CP4 EPSPS are expressed properly to the combined trait product as in its relevant single events.[1].

3. Gene Expression

a. The expression of the novel proteins in MON 87751 x MON 87701 x MON 87708 x MON 89788 is comparable to the corresponding single events. Moreover, the proteins are expressed at low levels in the plant.[1].

b. The marker genes are not transferred and expressed in MON 87751 x MON 87701 x MON 87708 x MON 89788.[1].

c. The difference in the mode of action of the novel proteins and the presence of five proteins (Cry1A.105, Cry2Ab2, Cry1Ac, DMO and CP4 EPSPS) will not likely to cause interaction that can affect the stability and expression level of either one of the genes.[1].

BPI-PPSSD's Conclusion

After a thorough and scientific review and evaluation of the documents provided by Monsanto Philippines, Inc. relevant to soybean MON 87751 x MON 87701 x MON 87708 x MON 89788, the BPI-PPSSD found scientific evidence that the regulated article applied for direct use as food, feed, and or processing (FFP) has no evidence of interaction on the resulting gene products.

DENR-BC'S Assessment

a. The individual events of the stacked Soybean MON 87751 x MON 87701 x MON 87708 x MON 89788 have approved biosafety permits. Therefore, each event has undergone rigorous safety assessment, and is considered safe to the environment and biodiversity particularly on non-target organisms. Similarly, it is less likely to pose any significant adverse effect on the environment.[2];

b. The incorporation of gene stacked event is through conventional breeding, which is regarded as innocuous for its long history of safe use. Furthermore, the method of crossing individual transgenic parents is similar with that of non-transgenic parents. This method does not introduce any greater variation in the genome beyond what is obtained [2]; and

c. The project description report (PDR) discusses the specified environmental management plan indicating the possible risk and harm to the environment and biodiversity particularly on non-target organisms as well as the mitigating measures and contingency plan. Furthermore, the chances of unintended release or planting of the regulated article is very minimal and will not cause any damaging and lasting effects because the receiving environment (areas near the port, roads, railways, etc.) is not conducive for plant growth. Also, soybeans are generally very highly domesticated and do not survive well without human intervention.[3].

DENR-BC's Conclusion

Based on the evaluation and review of literature cited, the DENR-BC considered soybean MON 87751 x MON 87701 x MON 87708 x MON 89788, safe to the environment and biodiversity.

DOH-BC's Assessment

a. The Cry1A.105, Cry2Ab2, Cry1Ac, DMO, and CP4 EPSPS proteins show no amino acid sequence homology to known protein toxins, and are rapidly degraded with loss of functional activity under conditions that simulate mammalian digestion. There were no indications of toxicity as measured by treatment-related adverse effects in mice administered Cry1A.105, Cry2Ab2, Cry1Ac, DMO, and CP4 EPSPS protein by oral gavage.[1][4].

b. The *cry1A.105*, *cry2Ab2*, *cry1Ac, dmo*, and *cp4 epsps* genes were not derived from an allergenic source, and the Cry1A.105, Cry2Ab2, Cry1Ac, DMO, and CP4 EPSPS proteins do not pose immunologically relevant sequence similarity with known allergens or pose the characteristics of known protein allergens.[1][4].

c. Compositional data confirmed that soybean MON 87751 × MON 87701 × MON 87708 × MON 89788 was not a major contributor to variation in the nutritional component levels in soybean seed or forage and confirmed the soybean MON 87751 × MON 87701 × MON 87708 × MON 89788 plants are as safe and nutritious as conventional soybean varieties.[1][4].

DOH-BC's Conclusion

After a thorough review and evaluation of the documents provided by the proponent Monsanto Philippines, Inc., in support of their application for approval for direct use as food, feed or for processing (FFP) of stacked trait product MON 87751 x MON 87701 x MON 87708 x MON 89788. DOH-BC found that the regulated article is safe as its conventional counterpart and shall not pose any significant risk to human health.

SEC Expert's Assessment

a. Soybean is widely produced, consumed and is a significant component of global trade of agricultural commodities. Local production of soybean meal and soybean oil is minimal and used mainly in food production. There are strong demands for soybean meal for the feed industry and soybean oil for the food industry, supply for these soybean products are mostly from importation.[5][6][7][8].

b. Approval of soybean MON 87751 × MON 87701 × MON 87708 × MON 89788 for direct use as food, feed or for processing (FFP) will not result to drastic changes in the current patterns of production, consumption and utilization, but will help in maintaining global trade and ensure food security of soybean in the country.[6][7][8][9].

c. Since soybean MON 87751 × MON 87701 × MON 87708 × MON 89788 is applied for direct use as food, feed, and or processing (FFP), and is not intended to be commercially grown or marketed for propagation and cultivation, the cultural practices of specific ethnic and cultural groups will not be affected.[10].

SEC Expert's Recommendation

After a thorough and scientific review and evaluation of the documents provided by Monsanto Philippines, Inc., relevant to combined trait soybean MON 87751 × MON 87701 × MON 87708 × MON 89788, the SEC expert recommended for the approval and issuance of biosafety permit of the said GM product.

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