STRP's Assessment

A. Gene Interaction

a. Considering that the modes of action of CPP4 EPSPS and bar gene proteins are different, there is no significant likelihood of interaction such that a new allergen or a new toxin could be produced.[1].

b. The gene product CP4 EPSPS protein is likely to accumulate in the chloroplast of canola cells while, the *bar* gene encoding for PAT proteins is expressed in the cytoplasm of the cell.[1].

B. Metabolic Pathways

a. The gene products have different metabolic pathway and modes of action in the stacked trait and are described below:

- CP4 EPSPS protein belongs to the family of EPSPS synthases, which are enzymes involved in the penultimate step of the biochemical shikimic acid pathway producing aromatic amino acids in the chloroplasts of plants.[1][2][3][4].
- PAT protein is a very specific N-acetyltransferase, which detoxifies phosphinothricin (PPT), the active ingredient of glufosinate-ammonium herbicides. In the presence of acetyl-CoA, the PAT enzyme immediately acetylates PPT to N-acetyl-PPT, which has no inhibitory effect on the glutamine synthetase enzyme (GS). Therefore, this does not disrupt ammonium assimilation in plants.[1][2][3][4].

b. The possible unexpected effects of the stacked genes on the metabolism of the plant are extremely unlikely as supported by weight of evidences encompassing the distinct modes of action of introduced proteins and the protein expression analysis. It was shown that each single event is equivalent to conventional canola.[1].

C. Gene Expression

a. The protein expression analysis showed that CP4 EPSPS and PAT (bar) proteins were expressed properly in the combined trait product canola MON 88302 x RF3 x MS8, indicating that the inserted genes, *cp4 epsps* and *pat* are inherited and functioning properly when combined into the breeding stack.[1].

b. CP4 EPSPS and PAT (bar) proteins both were expressed at low levels in the plant. Also, no marker gene was transferred and expressed in the plants containing the stacked genes.[1].

c. The CP4 EPSPS and PAT (bar) proteins have distinct modes of action, and it was found that no significant interaction will affect the stability and expression levels of each gene, nor will it lead to production of new allergens or toxins in the combined trait product. There is no known mechanism of interaction among these proteins that could lead to adverse effects in humans, animals and environment.[1].

STRP's Recommendation

After a thorough and scientific review and evaluation of the documents provided by Monsanto Philippines, Inc., the STRP found scientific evidence that the regulated article applied for direct use as food and feed or for processing has no evidence of interaction on the resulting gene products.

BAI's Assessment

A. Gene Interaction

a. Any interaction between proteins are unlikely due to their distinct modes of action, or if there is an interaction between proteins, it will not lead to production of new allergen/toxin in the stacked event. There is no reported mechanism of interaction among the proteins that could lead to adverse effects in animals.[1].

b. The genes have different cell localization. The CP4 EPSPS protein will accumulate in the chloroplast while the PAT protein encoded by the bar gene is expressed in the cell cytoplasm.[1].

B. Metabolic Pathway

a. CP4 EPSPS and PAT protein has distinct modes of action and do not belong in the same pathway.[1].

b. The CP4 EPSPS protein or 5-enolpyruvulshikimate-3-phosphate synthase (EPSPS) enzyme catalyzes the sixth step of the shikimate pathway producing aromatic amino acids. It decreases binding affinity for glyphosate, thereby conferring increased tolerance to glyphosate herbicide.[1].

c. PAT protein, on the other hand, eliminates herbicidal activity of phosphinothricin or glufosinate herbicides through acetylation.[1].

d. The protein expression analysis data show unexpected effects of the stacked genes on metabolism of the plant are unlikely to happen.[1].

C. Gene Expression

a. CP4 EPSPS and PAT proteins are expressed at a low level, and no marker gene has been transferred nor expressed in the stacked event.[1].

b. Due to distinct modes of action and cellular localization interaction of proteins are unlikely. If any interaction proceeds it will not affect the stability and expression level of each gene. This is reflected in the protein expression analysis data provided by the applicant.[1].

c. CP4 EPSPS and PAT proteins were properly expressed in the stacked trait product MON 88302 × RF3 × MS8 which implies that the proteins are inherited and functioning thoroughly.[1].

BAI's Recommendation

After a thorough and scientific review and evaluation of the documents provided by Monsanto Philippines, Inc., the BAI found scientific evidence that the regulated article applied for animal feed use is as safe as its conventional counterpart and shall not pose greater risk to animal health.

BPI-PPSSD's Assessment

A. Gene Interaction

a. The presence of CP4 EPSPS and PAT proteins will not interact to produce any new allergens or toxins. This is due to the different modes of action and metabolic pathway which have no known mechanism of interaction that could lead to adverse effects.[1][2].

b. The CP4 EPSPS protein is targeted to accumulate in the chloroplast via chloroplast transit peptide (CTP2) while the PAT protein which is not regulated by a transit peptide, is likely to accumulate in the cytoplasm.[1][5].

B. Metabolic Pathway

a. The proteins CP4 EPSPS and PAT have different modes of action and metabolic pathway.[1].

b. CP4 EPSPS proteins are involved in the biochemical shikimic pathway producing aromatic amino acid in the chloroplasts. It catalyzes the transfer of

enolpyruvyl group from phosphoenol pyruvate (PEP) to the 5-hydroxyl of shikimate3-phosphate (S3P) producing inorganic phosphate and 5 enolpyruvylshikimate-3-phosphate. This enzyme catalyzes the reaction wherein the enolpyruvyl group from phosphoenol pyruvate (PEP) is transferred to the 5-hydroxyl of shikimate-3-phosphate (S3P) to form 5-enolpyruvylshikimate-3-phosphate (EPSPS) and inorganic phosphate (Pi).

c. PAT detoxifies glufosinate ammonium through acetylation of phosphinothricin forming N-acetyl-glufosinate (NAG), 3-methylphosphinicopropionic acid (MPP) and 3-methylphosphinicoacetic acid (MPA).[1][2][3][4].

C. Gene Interaction

a. There is similar expression of proteins in the stacked event as in its corresponding single events. There are no marker genes transferred and expressed in MON 88302 x MS8 x RF3.[1].

b. The protein expression analysis indicated that CP4 EPSPS and PAT in MON 88302 x MS8 x RF3 are being expressed at low levels in the plant.[1].

c. The distinct modes of action of the proteins involved in different metabolic pathways and the protein expression analysis indicates that the possibility of unexpected effects of the stacked genes on the metabolism of the plant is unlikely.[1][2].

BPI-PPSSD's Recommendation

After a thorough and scientific review and evaluation of the documents provided by Monsanto Philippines Inc., the PPSSD found scientific evidence that the regulated article applied for human food use has no evidence of interaction on the resulting gene products.

DENR-BC'S Assessment

a. The individual events of the gene stacked canola MON88302 x RF3 x MS8 have biosafety permits for direct use, which were previously issued. Therefore, each event has undergone rigorous safety assessment, and is considered safe to the environment, particularly on biodiversity. Similarly, it is less likely to pose any significant adverse effect on the environment [1];

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 particularly on biodiversity 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, canola is a poor competitor and non- invasive; it is sensitive to weather changes, early growing conditions, and seedbed conditions thus, need human intervention.[3].

DENR BC's Recommendation

After a thorough and scientific review and evaluation of the documents provided by Monsanto Philippines, Inc., the DENR-BC considered the regulated article safe to the environment, particularly on biodiversity.

DOH-BC's Assessment

a. Scientific evidence from toxicity studies and references, find that the regulated article will not cause significant adverse health effects to human and animal health.

b. Dietary exposure to the regulated article is unlikely to result in allergic reaction.

c. The regulated article is as safe as food or feed derived from conventional canola varieties.

d. The regulated article is not materially different in nutritional composition from that of the non-transgenic canola or the conventional canola.

DOH-BC's Recommendation

It is suggested that the Bureau of Plant Industry (BPI) ensure that there shall be clear instructions that the product is only for the purpose of direct use for FFP and is not to be used as planting materials.

SEC Expert's Assessment

a. The SEC expert examined the trade aspects of the transboundary boundary movements of GM products with the implied assumptions that there are no

violations of the importing and exporting countries on their other equally important international agreements (e.g. GATT-WTO).

b. Data have shown that both non-GM and GM canola are not cultivated in the country. Canola is used as a vegetable oil, which accounts for less than 1% of the total oil consumption.[6][7][8][9][10][11][12].

c. The GM canola product will not drastically change the current patterns of production and consumption.[6].

d. As the application pertains to the importation of FFP and is not intended to be commercially grown and marketed for propagation and cultivation, cultural practices of specific ethnic and cultural groups will not be affected.[12].

e. Canola is not produced domestically in the Philippines. It is a very insignificant component of our vegetable oil consumption, dominated by our coconut oil market. It cannot drastically change the patterns of production trade and consumption.[6].

SEC EXPERT's Recommendation

The SEC expert recommended for the approval and issuance of the biosafety permit of the GM product.

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