ASSESSORS' CONSOLIDATED REPORT ON DOW AGROSCIENCES' APPLICATION FOR DIRECT USE AS FOOD AND FEED, OR FOR PROCESSING OF SOYBEAN DAS-81419-2 × DAS-444Ø6-6

EXECUTIVE SUMMARY

On March 10, 2020, Dow AgroSciences filed for application of soybean DAS-81419-2 × DAS-444Ø6-6 for direct use as food and feed, or for processing, as original application under the DOST-DA-DENR-DOH-DILG Joint Department Circular (JDC) No. 1 Series of 2016. After reviewing the Risk Assessment Report and attachments submitted by the applicant, the assessors namely: Scientific and Technical Review Panel (STRP), BPI Plant Products Safety Services Division (BPI-PPSSD) and Bureau of Animal Industry- Biotech Team (BAI-BT), concurred that soybean DAS-81419-2 × DAS-444Ø6-6 is as safe for human food and animal feed as its conventional counterpart.

The Department of Environment and Natural Resources – Biosafety Committee (DENR-BC), after a thorough scientific review and evaluation of the documents related to Environmental Risk along with the submitted sworn statement and accountability of the proponent, recommended 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 documents related to Environmental Health Impact, concluded that soybean DAS81419-2 x DAS44406-6 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. DOH-BC also recommended for the issuance of biosafety permit for the transformation event.

Furthermore, the Socio-economic, Ethical and Cultural (SEC) Considerations expert also recommended for the issuance of biosafety permit for this regulated article after assessing the socio-economic, social and ethical indicators for the adoption of Genetically Modified Organisms.

BACKGROUND

In accordance with Article VII. Section 20 of the JDC, 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 the complete dossier submitted by Dow AgroSciences Philippines Inc. The SEC expert, on the other hand, was provided with a questionnaire on socio-economic, ethical and cultural considerations that have been addressed by Dow AgroSciences Philippines Inc. in relation to their application. These assessors were given thirty (30) days to submit their independent assessment to BPI Biotech Secretariat.

STRP'S ASSESSMENT

1. Gene Interaction

a. There is no evidence that the novel proteins in DAS-81419-2 × DAS-444Ø6-6 soybean could interact to result in the formation of a new allergen or a new toxin. [1]
b. Crop improvement through conventional breeding have had little, if any, effect on the allergenic potential of our major foods. [2]
c. DAS-81419-2 × DAS-444Ø6-6 soybean has been produced through conventional breeding. DAS-81419-2 and DAS-444Ø6-6 soybean have already been assessed and approved for food and feed use in the Philippines. [3][4][5]
d. Cry1F, Cry1Ac PAT, and AAD-12 proteins are likely to accumulate in the cytoplasm.

2. Metabolic Pathways

a. DAS-81419-2 Cry1F and Cry1Ac proteins have specific mode of action on target lepidopteran insects. Both produce resistance to lepidopteran pests by damaging the midgut lining of the pest. DAS-44406-6 expresses the 2mEPSPS protein, which confers tolerance to glyphosate-based herbicides, the AAD-12 protein, which confers tolerance to 2,4-D herbicides. DAS-81419-2 and DAS-444Ø6-6 PAT proteins eliminates herbicidal activity of glufosinate (phosphinothricin) herbicides by acetylation. [4]
b. The products are not involved in the same metabolic pathway. [7][8]

3. Gene Expression

a. The overall result of the study showed consistency with the natural variability observed in the historical expression ranges. Hence, no biological relevant difference in expression of the proteins in DAS-81419-2 × DAS-444Ø6-6 sprayed with 2,4-D, glyphosate and glufosinate compared with the protein expression in unsprayed DAS-81419-2 or DAS-444Ø6-6. [9]
b. Both proteins are expressed at low level in different plant parts of DAS-81419-2 × DAS-444Ø6-6 soybean. [9]
c. There is no evidence of interaction between and among the cry1Ac, cry1F, pat, aad-12, and 2mepsps genes and their gene products that would affect the stability and expression level of the individual genes. The genes are inserted to provide specific mode of action. [7][8][9]

STRP'S RECOMMENDATION

Find scientific evidence that the regulated article applied for direct use has no evidence of interaction on the resulting gene products.

BAI'S ASSESSMENT

1. Gene Interaction

a. There are no published literatures to prove interactions exist among inserted genes that can form a novel toxin or allergen in stacked events. The transgenes of DAS-81419-2 × DAS-444Ø6-6 were previously described from individually approved single events, elucidating the different mode of actions of the gene and its products, its genetic stability across generations, and rigorous allergenicity and toxicological assessments of the proteins. Any effect in the nutrient intake or in the normal growth of the poultry or in livestock when it is used as animal feed ingredient is very unlikely. [7][8][10][11][12]
b. 2mEPSPS is expressed in the plastids since 2mEPSPS is flanked with the chloroplast-transit peptide. The genes for proteins Cry1Ac, Cry1F, AAD12, and PAT do not have this component in the vector plasmid and will only be accumulated in the cytoplasm. [9][10]

2. Metabolic Pathways

a. Proteins have different mode of action. The Cry1Ac and Cry1F proteins are intended for pest-resistance. The PAT, AAD-12, and 2mEPSPS are intended for herbicide resistance but differ in their target substrates. The PAT on the other hand was used as a selective marker of the plant which has all the stacked traits. [7][8]
b. There are no possible unintended effects of the stacked genes in the plant since they have different roles in the plant's physiology. Other published articles on stacked genes have elucidated that there is a possibility of synergistic or antagonistic interaction among two or more transgene products, but it does not equate to adverse effects to safety. Also, these transgenes have long established its history of safe use in other genetically-modified crops. [1][7][8][11][13]

3. Gene Expression

a. The expression levels of the gene products are relatively the same although it was observed that there are statistical differences in the obtained values of the stacked transgenic plant compared to the single event. This was observed in the protein concentrations of PAT in the stacked plant compared to the single events. This might be due to the two copies of PAT originating from two single events that were conventionally bred. Such significant difference does not pose any biological importance to safety. [7][8][9]
b. The Cry1F, Cry1AC, AAD-12, PAT, and 2mEPSPS are expressed at low levels in leaves, roots, and grains of the transgenic plant. (ng/mg dry weight of sample). [7][8][9]
c. Cry proteins, PAT, 2mEPSPS, and AAD-12 differ in metabolic pathways and stable within the transgenic plant's genome. It is highly unlikely for synergistic or antagonistic interactions to occur among them. Any effect in the nutrient intake or in the normal growth of the poultry or in livestock when it is used as animal feed ingredient is also unlikely. [10][11]

BAI'S RECOMMENDATION

Find scientific evidence that the regulated article applied for direct use has no evidence of interaction on the resulting gene products.

BPI-PPSSD'S ASSESSMENT

1. Gene Interaction

a. The difference in the modes of action and metabolic pathways of Cry1Ac, Cry1F, AAD12, 2mEPSPS and PAT proteins present in DAS 81419-2 x DAS 44406-6 indicates that the proteins are not likely to interact to produce any new allergen or toxins. Compositional analysis indicated that the protein levels of DAS 81419-2 x DAS 44406-6 is within the range of reference values from non-transgenic soybean. [7][8][14][15][16][17][18][19][20]
b. The 2mEPSPS protein is targeted to accumulate in the chloroplast via chloroplast transit peptide while the Cry1Ac, Cry1F, AAD-12 and PAT proteins, which are not regulated by a transit peptide, is likely to accumulate in the cytoplasm. [7][8][21][22]
c. The proteins have different modes of action. [7][8]

2. Metabolic Pathways

a. The products are not involved in the same metabolic pathway. CP4 EPSPS proteins are involved in the shikimic acid pathway producing aromatic amino acids. Cry proteins are not involved in metabolic pathways in plants. PAT proteins are involved in the synthesis of phosphinothricin while AAD-12 proteins are mainly involved in the degradation of 2,4D herbicides in plants. [7][8][14][15][16][17][18][19][20][21]
b. Compositional analysis indicates that the composition of DAS 81419-2 x DAS 4406-6 is comparable to the reference values from non-transgenic soybean. This implies that the stacked genes have no significant impact to the metabolism of the plant with reference to its nutritional composition. [9][16]

3. Gene Expression

a. The expression of the proteins in DAS 81419-2 x DAS 44406-6 is comparable to the corresponding levels in single events. Results indicated that the proteins are expressed similarly to the combined trait product as in its corresponding single events. Their distinct mode of action, involvement 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. [9][16]
b. The protein expression analysis provided by the developer indicated that 2mEPSPS, Cry1Ac, Cry1F, PAT and AAD-12 proteins are being expressed at low levels in the plant. [9]
c. The presence of the novel proteins will not likely to cause interaction that can affect the stability and expression level of either one of the genes.

[7][8][14][15][16][17][18][19][20][21]

BPI-PPSSD'S RECOMMENDATION

Find scientific evidence that the regulated article applied for direct use has no evidence of interaction on the resulting gene products.

DENR BC'S ASSESSMENT

After a comprehensive review and evaluation of the documents and scientific evidence from literature submitted by Dow AgroSciences B.V. Philippines concerning its application for direct use for food, feed, or for processing of Soybean DAS-81419-2 x DAS-44406-6, the DENR-BC considered that the regulated article poses no significant adverse effect to the environment on the following bases:

a. The regulated article is considered substantially equivalent to its conventional counterpart for its history of safe use as food in seven (7) countries and as feed in six (6) countries. It has also been approved for cultivation in two (2) countries.
b. The proteins expressed by the introduced genes *aad-12, pat,* and *2mepsps* do not display any characteristics of any known toxin or allergens and are less likely to harm other organisms in case of unintended release. Furthermore, the gene products of *cry1Ac* and *cry1F* have no potential adverse impacts to non-target organisms and beneficial insects in case of unconfined release;
c. Both individual events in the stack have already undergone thorough risk assessment and have been individually approved for direct use in the Philippines. The stacked genes were also introgressed through conventional plant breeding methods, which has a history of safe use; and
d. 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. However, the regulated article is less likely to survive in non-cultivated land in the event of unintended release. There is a low possibility that the crop will persist or become invasive in unmanaged habitats.
[4][5][23][24][25]

DENR BC'S RECOMMENDATION

Based on the evaluation and review of literatures cited, the DENR-BC considered the regulated article safe to the environment, particularly on biodiversity and non-target organisms.

DOH BC'S ASSESSMENT

Soybean DAS4406-6 x DAS81419-2 is as safe as its conventional counterpart for Direct Use as Food, Feed or for Processing (FFP). Use of this event in its usual context is not expected to pose any new or additional risk to human and animal health and environment.

The following are the observations and recommendations:

1. Scientific pieces of evidence from Toxicity studies and references, find that the regulated article will not cause significant adverse health effects to human and animal health.
2. Dietary exposure to the regulated article is unlikely to result in allergic reaction.
3. The regulated article is as safe as food or feed derived from conventional soybean varieties.
4. The regulated article is not materially different in nutritional composition from that of the non-transgenic soybean or the conventional soybean. [7][8][26]

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

1. The Philippines has been a growing consumer of soybean for processing, animal feed and food especially with recent increasing demand for tofu, meat substitutes and other soy-based products (soy milk, coffee, taho, etc.).Soybean supply utilization has been primarily for processing but net food disposable has been increasing since 2014 based on Philippine Statistics Authority. [27]
2. The application is only for direct use for food, feed or for processing. Changes that may happen in patterns of production, consumption and trade are neither drastic nor attributable to importation of the subject GM soybean alone. Soybean production has not been sufficient to meet local demand in the past years. [27]
3. In any case, possible effects on the use of the GM crop for food, feed and processing on specific ethnic or cultural groups should be best understood in the context of engagement and participation. Evaluation of Applicant's response should be done alongside results of the procedures for Public Participation for Direct Use under Sec. 22 of JDC 1-2016. [28]

SEC EXPERT'S RECOMMENDATION

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

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