

**ASSESSOR'S CONSOLIDATED REPORT ON MONSANTO PHILIPPINES'
APPLICATION FOR DIRECT USE AS FOOD AND FEED, OR FOR PROCESSING OF
COTTON MON531 X MON1445**

EXECUTIVE SUMMARY

On December 13, 2019, Monsanto Philippines submitted cotton MON531 x MON1445 for direct use, 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 Scientific and Technical Review Panel (STRP), Bureau of Animal Industry, and BPI Plant Products Safety Services Division concurred that cotton MON531 x MON1445 is as safe as its conventional counterpart.

The Department of Health – Biosafety Committee (DOH-BC), after a thorough scientific review and evaluation of documents related to Environmental Health Impact, concluded that cotton MON531 x MON1445 is safe as its conventional counterpart and shall not pose any significant risk to human health.

The Department of Environment and Natural Resources – Biosafety Committee (DENR BC), after a thorough scientific review and evaluation of documents and scientific evidence from literature of Cotton MON531 x MON1445, considered the regulated article safe to the environment, particularly on biodiversity and non-target organisms.

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 Monsanto Philippines. The SEC expert, on the other hand, was provided with special questionnaire on socio-economic, ethical and cultural considerations that have been addressed by Monsanto Philippines in relation to their application.

STRP's Assessment

1. Gene Interaction

- a. There is no plausible interaction of the resulting novel protein products, in which a new allergen or a new toxin could be produced. CP4 EPSPS, Cry1Ac and NPTII proteins indeed do not act on the same physiological pathways and do not share any intermediate metabolites in the processes that the proteins act on or interfere with. Without the lack of interaction, there will be no expected adverse effect on the target trait that the transgenes confer, more so, no new allergen nor toxin will be produced [1].
- b. The resulting novel protein products, will accumulate in the different parts of the host plant cell. Due to this distinct localization, CP4 EPSPS, Cry1Ac and NPTII proteins will indeed have very low probability of acting on the same physiological pathways and would not share any intermediate metabolites in the pathways that the proteins act on or interfere with [1].

2. Metabolic Pathways

- a. The explanation and the references provided are sufficient to support the proponent's answer regarding the mode of action of CP4 EPSPS, Cry1Ac and NPTII proteins [1].
- b. The mode of action of the resulting novel protein products, CP4 EPSPS, Cry1Ac and NPTII proteins are distinct. These novel proteins indeed do not act on the same physiological pathways and do not share any intermediate metabolites in the processes that the proteins act on or interfere with. Without the 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].
- c. The resulting novel protein products, CP4 EPSPS, Cry1Ac and NPTII are involved in distinct metabolic pathways. Moreover, these novel proteins do not share any intermediate metabolites in the processes that the proteins act on or interfere with. Without the 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].
- d. There are no unintended nor unexpected effects on the metabolism of the plant when the novel genes are introduced in it. The experiments done by the proponents and the data analyses that they performed are scientifically and statistically sound. The data presented herein indeed depicts that the various agronomic characteristics of the stacked trait plant is statistically significantly different when compared to the conventional untransformed counterpart, although the values obtained are well within the range of accepted values from that of reference varieties of cotton [1].

3. Gene Expression

- a. The expression levels of the novel proteins were not biologically different between the stacked transgenic plant under evaluation and its parental genotypes. The measurements done by the proponents using ELISA and subsequent statistical analysis clearly demonstrated that there is indeed no significant difference among the expression levels of the novel proteins. Lastly, even though there are five statistically significant difference found, it is indeed acceptable because it does not imply biological significance when viewed in the data presentation and analysis [1].
- b. There is a low expression of the novel proteins in the stacked transgenic plant under evaluation and these levels are comparable to the single transformant parental genotypes. Lastly, protein level measurements done by the proponents using ELISA and subsequent statistical analysis clearly demonstrated that there is indeed no significant difference among the expression levels of the novel proteins in the parentals and the transgenic stacked cotton. Lastly, even though there are statistically significant difference found, it is indeed acceptable because it does not imply biological significance when viewed in the box-plot perspective and is well within the technical variability of the ELISA method [1].
- c. The selectable marker gene, *nptII*, is transferred and expressed in the stacked transgenic plant being evaluated at hand. Although expressed in the regulated article, the measurements of NPTII protein levels, done by the proponents, was demonstrated to be in very low undetectable concentrations in the leaf of the plant [1].
- d. There is no possible interaction among the novel proteins introduced in the stacked transgenic article evaluated at hand. Moreover, the proponents were also able to comprehensively demonstrate the stability of the genome/partial genome of the parentals in the stacked transgenic crop. The genetic material of the parentals, containing the novel genes, were indeed stably incorporated in Cotton MON 531 × MON 1445. Lastly, protein level measurements done by the proponents using ELISA and subsequent statistical analysis clearly demonstrated that there is indeed no significant difference among the expression levels of the novel proteins in the parentals and the transgenic stacked cotton [1].

STRP's Conclusions

Find scientific evidence that the regulated article applied for direct use is as safe as its conventional counterpart and is not expected to pose greater risk to human and animal health.

After a thorough and scientific review and evaluation of the documents provided by Bayer Crop Science, Inc. relevant to Cotton MON 531 × MON 1445, the STRP found that the new studies submitted by the applicant will not affect the safety of Cotton MON 531 × MON 1445 [17][18][19].

BAI's Assessment

Metabolic Pathways

- a. Description and nature of the gene products were described in the technical dossier provided and there are published literatures available to further support the information of the developer [1].
- b. All genes have different modes of action.
 - *Cp4 epsps* – is known to be a catalyst of the shikimate pathway of the plant cell and decreases the binding affinity of glyphosate (active ingredient of most herbicides), conferring to its resistance to the compound.
 - Cry1Ac – is a crystallized protein (derived from the bacteria *Bacillus thuringiensis*) that is known to be toxic to insects and lyses their midgut epithelial cells.
 - NPTII - a marker protein that confers resistance to kanamycin and neomycin. Usually flanked with the gene of interest to the select transformed plant cells.
 - AAD – enzymes that contribute resistance of the plant to aminoglycosides spectinomycin and streptomycin. It is also a selection marker of transgenic plants [1][6][7][8][9].
- c. These proteins have different involvements in the metabolic pathway. CP4-EPSPS catalyzes the shikimate pathway that enables the plant to produce its aromatic acids and compounds. Cry proteins are responsible for insect-resistance and do not produce any metabolites that are potential allergens or toxins. NPTII and AAD are marker proteins that solely for the selection of transformed cells [1][6][8][10].
- c. The stacked genes will unlikely express unintended allergens or toxins since the inserted genes are of different modes of action and will not adversely affect the metabolism of the plant. The single events that were used (MON 531 and MON 1445) have undergone rigorous safety assessments and was proven to be safe for direct use [1].
- d. The research articles on new studies for Cotton MON531 x MON1445 submitted by the applicant tackled more on plant physiology, plant-insect symbiosis on natural mortality factors, and a long-term study of ecological and economic impacts of transgenic cotton. These peer-reviewed publications do not report any adverse effects regarding food or feed safety [17][18][19].

BAI's Conclusions

Find 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.

After a thorough review of the new studies submitted by Monsanto Philippines, Inc. for Cotton MON531 x MON1445 application for Direct Use as Food and Feed, or for Processing, BPI-PPSSD found that the new studies submitted by the applicant will not affect the safety of (MON531 x MON 1445) [17][18][19].

BPI PPSSD's Assessment

Metabolic Pathways

- a. The developer provided a complete description of the mode of action of CP4 EPSPS, Cry1Ac and NPTII proteins. CP4 EPSPS and Cry1Ac has also been previously described in published literatures [2][3][4][5].
- b. The proteins have different mode of actions. 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 mechanism is being inhibited with glyphosate binding which blocks the binding of EPSPS to PEP. CP4 EPSPS, on the other hand, has higher affinity for PEP thus allowing the catalysis. 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) [5].
- c. 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. NPTII protein, as a marker protein, catalyzes the phosphorylation of the hydroxyl group of aminoglycosides in aminoglycoside antibiotics such as neomycin and kanamycin [1][2][3][4][5].
- d. 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 [1][2][3][4][5].

BPI PPSSD's Conclusions

Find scientific evidence that the regulated article applied for direct use has no evidence

of interaction on the resulting gene products.

After a thorough review of the new studies submitted by Monsanto Philippines, Inc. for Cotton MON531 x MON1445 application for Direct Use as Food and Feed, or for Processing, BPI-PPSSD found that the new studies submitted by the applicant will not affect the safety of (MON531 x MON 1445) [17][18][19].

ANNEX IV

DOH-BC's Assessment

After a thorough review and evaluation of the documents provided by the proponent, Monsanto Philippines, Inc., through the Bureau of Plant Industry (BPI), in support of their application for approval for Direct Use as Food, Feed or for Processing (FFP) of Cotton MON531 x MON1445. The DOH-BC, found that the regulated article applied for Direct Use as Food, Feed or for Processing (FFP) 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. 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 cotton varieties.
4. The regulated article is not materially different in nutritional composition from that of the non-transgenic cotton or the conventional cotton.
5. Based on the above considerations and with the submitted sworn statement and accountability of the proponent, we hereby submit our evaluation to BPI relative to the application of a Biosafety Permit for Direct Use as Food, Feed, or for Processing (FFP) of Cotton MON531 x MON1445.

DOH-BC's Conclusions

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.

After a thorough review of the new studies submitted by Bayer CropScience, Inc. for Cotton MON531 x MON1445 application for Direct Use for Food and Feed, or for Processing, the DOH-BC found that the new studies submitted by the applicant will not affect the safety of Cotton MON531 x MON1445 [17][18][19].

ANNEX V

SEC Expert's Assessment

1. Cotton is widely produced and consumed and is a significant component of global trade of agricultural commodities. However, Philippines is producing a very minimal quantity of cotton. Thus, the Philippines textile industry was highly dependent on imported cotton as local production is very negligible relative to the demand of the textile industry. Philippines was producing an average of 14.09 metric tons of cotton annually from 2015-2019 with annual growth rate of 63%. However, this production was not enough to meet the requirement of the Philippine Textile Industry. In terms of area planted, the average hectarage planted to cotton from 2015-2019 was 13.83 hectares only with an average yield of 1.12 metric tons per hectare.
2. The applicant provided a data on production, exports, and imports of cotton by the Philippines from 2015-2019. As discussed by the applicant, the Philippines was highly dependent on imported cotton as implied in the increasing trend of import of cotton from 49 units in 2015 to 65 units in 2019 with an annual average of 61 units. On the other hand, the export data of the Philippines (applicant's Table 2) shows zero (0) export from 2015-2019. This implies that the Philippine Textile industry was highly dependent on Cotton imports to meet the domestic demand for Cotton. The importation of Cotton resulted to the stabilization of prices of cotton in the domestic market. [13][14][15].
3. Based on the data provided by the applicants, the granting of permit to import Cotton MON 531 × MON 1445 will not drastically affect the current patterns of consumption, production, and trade of cotton. As mentioned earlier, Philippine is an insignificant producer of cotton, thus rely greatly in imported cotton to meet domestic demand. Granting permit to import MON 531 × MON 1445 cotton may help stabilize supply and prices of cotton. Philippine cotton production had decreased by 15.23% from 2018-2019 and possibly more in 2020 due to the COVID-19 pandemic and numerous strong typhoons that hit the cotton producing regions of the Philippines. The granting of permit to import MON 531 × MON 1445 cotton for direct use as food and feed, or processing will help stabilize the supply and prices of cotton in the Philippine. With stable prices, consumption will also be stabilized. Domestic production of products that utilizes cotton as one of the raw materials may increase due to the availability of raw materials, which in turn may improve the domestic trade in the Philippines. However, the global trade of cotton will not be affected since Philippine imports of cotton is very minimal relative to global trade.
4. Granting permit to import MON 531 × MON1445 cotton will not affect the cultural practices of any ethnic and cultural groups in the Philippines since the permit will just for direct use for food, feed and/or processing and not for local cultivation.

SEC Expert's Recommendation

The SEC expert recommends for the approval and issuance of the biosafety permit of cotton MON531 x MON1445.

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