

**CONSOLIDATED REPORT ON SYNGENTA'S APPLICATION FOR DIRECT USE AS FOOD AND
FEED, OR FOR PROCESSING OF COMBINED TRAIT PRODUCT CORN *Bt11 x MIR162 x
MIR604 x TC1507 x 5307 x GA21***

EXECUTIVE SUMMARY

On December 1, 2016, Syngenta Philippines Inc. applied the stacked trait product corn *Bt11 x MIR162 x MIR604 x TC1507 x 5307 x GA21* 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 proteins involved in the combined trait product: *Cry1Ab, Vip3Aa20, mCry3A, Cry1F, eCry3.1Ab, mEPSPS, PAT and PMI*, 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 human, 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 *Bt11 x MIR162 x MIR604 x TC1507 x 5307 x GA21* genome.

After thorough scientific review and evaluation of Syngenta'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 corn *Bt11 x MIR162 x MIR604 x TC1507 x 5307 x GA21* 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 corn *Bt11 x MIR162 x MIR604 x TC1507 x 5307 x GA21* 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, PPSSD AND BAI ASSESSMENT

Bt11 x MIR162 x MIR604 x TC1507 x 5307 x GA21 is a glyphosate and glufosinate ammonium herbicide tolerant and insect resistant corn developed by Syngenta Philippines Inc., through conventional breeding techniques from the single event products *Bt11*, *MIR162*, *MIR604*, *TC1507*, *5307* and *GA21*.

The safety of each single event, *Bt11*, *MIR162*, *MIR604*, *TC1507*, *5307* and *GA21* has recently been assessed and renewed for direct use for food and feed, or for processing (FFP) by the Bureau of Plant Industry in 2013, 2015, 2018, 2013, 2015 and 2013, respectively.

Gene Interaction

Based on the documents provided by the developer, the STRP, PPSSD and BAI concurred that the eight (8) proteins being expressed in the combined trait product, *Cry1Ab*, *Vip3Aa20*, *mCry3A*, *Cry1F*, *eCry3.1Ab*, *mEPSPS*, *PAT* and *PMI*, will not produce new or identified allergen or toxin because they are unlikely to interact due to the different mode of action of each protein. The safety of each protein were assessed using different comprehensive bioinformatics analyses and showed that these proteins have no significant homology and similarity to any known allergen and toxins that could lead to potential adverse effect on human and animal health.

In terms of accumulation, the gene products are likely to accumulate in different subcellular components of the corn plant. For *Bt11*, the *cry1Ab* and *pat* gene expressions are both driven by the 35S promoter, for *MIR162*, the *vip3Aa20* and *pmi* expressions are both driven by ZmUbilnt promoter, for *MIR604*, the *mcry3A* gene expression is driven by the MTL promoter, *MIR604 pmi* gene expression is driven by the ZmUbi, for *TC1507*, the *cry1F* and *pat* gene expression are driven by the maize Ubi1ZM and 35S promoters, respectively and for *5307*, *ecry3.1Ab* expression is driven by CMP promoter and *5307 pmi* is driven by ZmUbilnt promoter and are intended to accumulated at the cytoplasm because no cellular localization sequences are present.

Modified EPSPS enzyme in *GA21* or otherwise, is known to accumulate in the chloroplast. A chloroplast transit peptide that directs the protein to the chloroplast is included in the gene that codes for *mEPSPS*. The transit peptide is cleaved off of the protein when it is transferred into the chloroplast. The indication that all proteins have been immediately imported to the chloroplast upon synthesis is when the protein is isolated from the plant, only the cleaved version of the protein will be found.

Metabolic Pathways

The mode of action and metabolic pathways of each protein are significantly different from each other. *Cry* proteins such as *Cry1Ab*, *mCry3A*, *Cry1F* and *eCry3.1Ab* specifically binds to a specific sites localized in the midgut of susceptible insects which leads to swelling of cells or disruption of midgut ion flow and eventually death of the insect. *Cry1* proteins confer resistance against certain Lepidopteran insects while *Cry3* proteins confer resistance against certain Coleopteran insects. *Cry* proteins are not involved in a metabolic pathway. *Vip3Aa20* binds to specific receptors in the midgut epithelium of susceptible insects which leads to formation of selective ion channels in epithelial membranes causing cell lysis and death. Lee et al, 2003 showed that *Vip* and *Cry* proteins bind to different receptors. *Modified EPSPS (mEPSPS)* is involved in the shikimic pathway of aromatic amino acid biosynthesis. *Phosphinothricin-N-acetyl transferase (PAT)* detoxifies glufosinate ammonium through acetylation of phosphinothricin to N-acetylglufosinate, 3-methylphosphinopropionic acid (MPP) and 3-methylphosphinicoacetic acid (MPA). *PMI* convert mannose to fructose-6-phosphate improving energy status of the cells and preventing accumulation of derivatized mannose. It was being used as selectable marker employed only during selection of transformed cells in culture.

Gene Expression

The genetic stability of each genes, in the single events were already demonstrated in the previous evaluations and has been approved by the Bureau of Plant Industry for Biosafety Permit for food and feed, or for processing. Since the inserted DNA are combined in corn *Bt11 x MIR162 x MIR604 x TC1507 x 5307 x GA21* through conventional breeding, the genetic stability of the genes in the combined trait product was assessed through determining the concentration of each protein using Enzyme-linked Immunosorbent Assay (ELISA) to determine if the combined genes are present. The concentrations of *Cry1Ab*, *Vip3Aa20*, *mCry3A*, *Cry1F*, *eCry3.1Ab* and *mEPSPS* proteins in tissues of the stacked-trait *Bt11 x MIR162 x MIR604 x TC1507 x 5307 x GA21* maize hybrid were similar to those of the corresponding single event maize hybrids *Bt11*, *MIR162*, *MIR604*, *TC1507*, *5307*, and *GA21*. These concentrations were determined and quantified using ELISA. As expected, *PAT* concentrations in tissues of the stacked-trait were higher than those from each of the component single event hybrid due to the presence of 3 copies of the *pat* gene in the stacked-trait hybrid, while *Bt11*, *DAS-59122-7*, and *TC1507* maize hybrids each contain 1 copy of the *pat* gene.

For the marker genes, Southern Blot Analysis showed that *pat* and *pmi* marker genes are transferred and expressed in *Bt11 x MIR162 x MIR604 x TC1507 x 5307 x GA21* stack. History of safe use was attributed with *pat* and *pmi* genes. Comprehensive bioinformatics analyses showed that these proteins have no significant homology and similarity to any known allergen and toxins that could lead to potential adverse effect on human and animal health.

Conclusion

The STRPs, PPSSD and BAI concluded that after a thorough and scientific evaluation of the documents provided by Syngenta Philippines Inc. and other related literature, scientific evidence indicates that the stacked genes of corn *Bt11 x MIR162 x MIR604 x TC1507 x 5307 x GA21* applied for direct use as food and feed or for processing has no evidence of interaction on the resulting gene products and as safe as its conventional counterpart.

DENR 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 Corn resistant to insects and tolerant to glyphosate herbicide and gluphosinate herbicide stacked trait product corn *Bt11 x MIR162 x MIR604 x TC1507 x 5307 x GA21*, 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 corn *Bt11 x MIR162 x MIR604 x TC1507 x 5307 x GA21* 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 RECOMMENDATION

After a thorough review and evaluation of the documents provided by the proponent, Syngenta Philippines Inc., through the Bureau of Plant Industry (BPI), in support of their application for approval for Direct Use for Food and Feed or for Processing (FFP) of *Bt11 x MIR162 x MIR604 x TC1507 x 5307 x GA21*. We find that the regulated article applied for Direct Use for Food and

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. Find that the regulated article applied for Direct Use for food and feed or for processing (FFP) does not require changes in the usual practices in unloading, hauling, transport and 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. literature show that regulated article applied for direct use as 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 the Bureau of Plant Industry (BPI) ensure the following:

a. Strict monitoring of the regulated article from the port of entry to the trader's/importer's storage/warehouse as stated in Section 32 of the JDC No.1 S2016;

b. The BPI to include in the issuance 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 labelling 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.

Based on the above considerations and with the submitted sworn statement and accountability of the proponent, this recommendation is being submitted to BPI to the processing and issuance of biosafety permit for direct use for food and feed or for processing (FFP) of Bt11 x MIR162 x MIR604 x TC1507 x 5307 x GA21.

SEC RECOMMENDATION

In terms of production, consumption and trade, Bt11 x MIR162 x MIR604 x TC1507 x 5307 x GA21 corn will only be imported for direct use as food, feed, and for processing and will not be produced/propagated in the Philippines. Use of imported corn for food, feed and processing in the Philippines will not be affected by importation of the stacked product.

Corn importations in the Philippines totalled to about 458,968 metric tons in 2015 (Global Trade Atlas, 2016). Typically, corn is both used as food and as a major feed ingredient for livestock and poultry. With this, Bt11 x MIR162 x MIR604 x TC1507 x 5307 x GA21 corn importation for direct use as food, feed and for processing is significant to continue supplying corn and corn products to feed millers, for use in poultry, livestock, aquaculture, and other industries (e.g. paper, plastic and cosmetics).

In addition, no drastic change on trade is expected. Worldwide market conditions will continue to be factors for international corn prices and trade, without the presence or absence of this stacked corn on the market.

There are only two basic SEC questions asked of technology developer for SEC approval of the proposed GM product for direct use as FFP. These questions relate to supply-demand of the product (GM and non-GM), implication to trade particularly as it relates to imports, and how domestic production of the GM affect the domestic production of the non-GM product. Given that Bt11 x MIR162 x MIR604 x TC1507 x 5307 x GA21 stacked corn is non-intended for commercial propagation but only for food, feed and or for processing, there is no problem of approving the SEC requirement for this stacked corn given the widely known trade and production trends of GM corn in the Philippines for the past 15 years.

Thus, after a thorough and scientific review and evaluation of the documents provided by Syngenta Philippines Inc., relevant to Bt11 x MIR162 x MIR604 x TC1507 x 5307 x GA21, the SEC expert recommended the approval and issuance of biosafety permit of the said GM product.