

**CONSOLIDATED REPORT ON SYNGENTA'S APPLICATION FOR DIRECT USE AS FOOD AND
FEED, OR FOR PROCESSING OF COMBINED TRAIT PRODUCT CORN 3272 x Bt11 x MIR604 x
TC1507 x 5307 x GA21**

EXECUTIVE SUMMARY

On December 16, 2016, Syngenta Philippines Inc. applied the stacked trait product corn 3272 x Bt11 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: *Amy797E* in 3272, *Cry1Ab* in Bt11, *mCry3A* in MIR604, *Cry1F* in TC1507, *eCry3.1Ab* in 5307, *mEPSPS* 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 3272 x Bt11 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 3272 x Bt11 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 3272 x Bt11 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, BAI, PPSSD ASSESSMENT

3272 x Bt11 x MIR604 x TC1507 x 5307 x GA21 is a glyphosate and dicamba herbicide tolerant soybean developed by Syngenta Company through conventional breeding techniques from the single event products *3272, Bt11, MIR604, TC1507, 5307* and *GA21*.

The safety of each single event, *3272, Bt11, MIR604, TC1507, 5307* and *GA21* has recently been assessed and approved for direct use for food and feed, or for processing (FFP) by the Bureau of Plant Industry in 2013, 2013, 2012, 2013, 2015 and 2013, respectively.

Gene Interaction

Based on the documents provided by the developer, the STRP, BAI and PPSSD agreed that the eight (8) proteins being expressed in the combined trait product, *DMO and CP4 EPSPS*, 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.

Amy797E in *3272*, *Cry1Ab* in *Bt11*, *mCry3A* in *MIR604*, *Cry1F* in *TC1507*, *eCry3.1Ab* in *5307*, *mEPSPS* in *GA21*, *PAT* in *Bt11* and *TC1507*, and *PMI* in *3272, MIR604* and *5307* 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.

These proteins are also unlikely to accumulate in the same subcellular components of the corn genome. For *Bt11*, the *cry1Ab* and *pat* gene expressions are both driven by the 35S promoter, for *3272*, the *amy797E* gene expression is driven by maize gamma-zein (GZein) promoter. This promoter provides endosperm-specific expression in *Zea mays*. The gene includes 19 amino acid N-terminal maize gamma-zein signal sequence (GZein ss) and a C-terminal SEKDEL endoplasmic reticulum retention signal (ER rs) and *pmi* expressions of *3272* is 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 accumulate 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 assessors also agreed that 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. The protein, *amy797E* was derived from alpha-amylase genes from three (3) hyperthermophilic microorganism of the archael order Thermococcales. Alpha amylase catalyzes hydrolysis of starch by cleaving the internal α -1,4-glucosidic bonds into dextrans, maltose and glucose.

Cry proteins selectively binds to a specific sites localized in the midgut cells of susceptible insects which leads disruption of midgut ion flow or swelling of cells and eventually death of insect. *Cry1* proteins are known to cause toxicity against certain Lepidopteran insects while *Cry3* protein are known to be specific against Coleopteran insects.

Modified EPSPS is involved in the shikimic pathway of aromatic amino acid biosynthesis. *Phosphinothricin-N-acetyl transferase* detoxifies glufosinate ammonium through acetylation of phosphinothricin to N-acetyl-glufosinate, 3-methylphosphinicopropionic 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 concentrations of *Cry1Ab*, *Amy797E*, *mCry3A*, *Cry1F*, *eCry3.1Ab* and *mEPSPS* proteins in tissues of the stacked-trait *3272 x Bt11 x MIR604 x TC1507 x 5307 x GA21* maize hybrid were similar to those of the corresponding single event maize hybrids *3272*, *Bt11*, *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 2 copies of the *pat* gene in the stacked-trait hybrid, while *Bt11*, *MIR604* and *TC1507* maize hybrids each contain 1 copy of the *pat* gene. Southern Blot Analysis showed that the marker genes, *pat* and *pmi*, are transferred and expressed in *3272 x Bt11 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. Since the hybridization bands detected were of the expected sizes, this demonstrated that *3272 x Bt11 x MIR604 x TC1507 x GA21* corn contains 1 copy per genome of *pmi* from *3272* corn, 1 copy per genome of *pmi* from *MIR604*, and 1 copy per genome of *pmi* from *5307* corn, as expected. The DNA hybridization patterns for *3272 x Bt11 x MIR604 x TC1507 x GA21* corn corresponded to the hybridization bands observed for *3272*, *MIR604*, and *5307* corn, with all the restriction digestion enzymes used.

Conclusion

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 soybean *3272 x Bt11 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 Syngenta Philippines, Inc. for direct use for feed, food or processing of Genetically Modified Corn resistant to glufosinate herbicide stacked trait product 3272 x Bt11 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 3272 x Bt11 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 proponent, Syngenta Philippines Inc., through the Bureau of Plant Industry (BPI) in support of their application for approval for direct use as food and feed or processing of corn. DOH find that the regulated article applied for direct use as food and feed or processing 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 regulated article applied for direct use for food and feed or for processing (FFP) does not require changes in the usual practices in unloading, loading, transport, 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. literatures show that regulated article applied for direct use as food and feed or for processing (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 Bureau of Plant Industry (BPI) ensure the following:
 - a. Strict monitoring of the regulated article from port of entry to the trader's / importer's storage/warehouse as stated in Section 32 of the JDC No. 1 series, 2016.
 - b. The BPI to include in the insurance 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 labeling 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.
4. Based on the above considerations and with the submitted sworn statement and accountability of the proponent, this recommendation is being submitted to BPI related to the processing and issuance of a biosafety permit for direct use as food and feed or for processing of corn 3272 x Bt11 x MIR604 X TC1507 x 5307 x GA21.

SEC ASSESSMENT

The Philippines produces 90-98% of the corn and corn products that are consumed each year with an increasing demand from 2 to 10% of the corn for food, feed, or for processing being imported from 2012 to 2016. The volumes of corn starch, groats and corn meal, corn oil, and corn flour, imported in the Philippines are also shown in Table 1.

Table 1. Philippine production, import, and export volume for corn and corn products from 2011 to 2016.

Commodity	Unit	Year				
		2012	2013	2014	2015	2016
Corn Production	Metric Ton	7,406,830	7,377,293	7,770,603	7,518,756	7,218,817
Corn Import	Metric Ton	179,219	359,640	589,650	458,968	817,577
Import Percent Total*	%	2	5	7	6	10
Corn Export	Metric Ton	862	751	906	667	475
Corn Starch Import	Metric Ton	30,709	12,365	8,507	20,760	29,300
Groats and Corn Meal Import	Metric Ton	2,186	2,307	2,829	3,476	4,234
Corn Oil Import	Metric Ton	2,096	1,333	1,410	1,965	1,576
Corn Flour Import	Metric Ton	382	473	195	341	835
Groats and Corn Meal Export	Metric Ton	822	385	52	114	95
Corn Starch Export	Metric Ton	2	2	0	0	0
Bran Sharps and Other Corn Milling Residues Export	Metric Ton	0	19	0	0	0

*Import Percent Total = (Corn Import/(Corn Production + Corn Import)) x 100

Reference:

Philippine Statistic Authority. 2017. <http://nap.psa.gov.ph/i-stats/makro/tables/Agriculture.asp?xu=&yp=&lang=>.

The importation of 3272 x Bt11 x MIR604 x TC1507 x 5307 x GA21 corn as raw materials for the food and feed industry will help meet local requirements while maintaining the trade between Philippines and US and other trade partners.

The importation of corn in the Philippines has increase from 179,219 metric tons in 2012 to 817,577 metric tons in 2016, with only a slight decrease of the total import of 7% in 2014 to 6% in 2015. Please refer to Table 1 for the trend of importation from 2012-2016.

3272 x Bt11 x MIR604 x TC1507 x 5307 x GA21 corn will be imported and will not be propagated in the Philippines. The use of imported corn for food, feed and processing in the Philippines will not be affected by importation of this stack. 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 stack corn on the market.

Thus, the SEC expert recommends the approval and issuance of biosafety permit of the said GM product Syngenta 3272 x Bt11 x MIR604 x TC1507 x 5307 x GA21.