

**ASSESSORS' CONSOLIDATED REPORT ON SYNGENTA PHILIPPINES INC.'S
APPLICATION FOR COMMERCIAL PROPAGATION OF CORN Bt11 x TC1507 x GA21**

EXECUTIVE SUMMARY

On November 29, 2019, Syngenta Philippines Inc. submitted corn Bt11 x TC1507 x GA21 for commercial propagation, as an 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), concurred that corn Bt11 x TC1507 x GA21 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 applicant, recommended the issuance of a biosafety permit for this regulated event provided 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 corn Bt11 x TC1507 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. DOH-BC also recommended for the issuance of biosafety permit for corn Bt11 x TC1507 x GA21

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 Section 15 of the JDC No.1, S2016, no regulated article shall be released for commercial propagation unless: (1) a Biosafety Permit for Commercial Propagation has been secured in accordance with this Circular; (2) it can be shown that based on field trial conducted in the Philippines, the regulated article does not pose greater risks to biodiversity, human and animal health than its conventional counterpart; (3) food and feed safety studies show that the regulated article does not pose greater risks to biodiversity, human and animal health than its conventional counterpart, consistent with CODEX Alimentarius Guidelines on the Food Safety Assessment of Foods Derived from the Recombinant-DNA Plants and protocols of the DOH and BAI on feeding trials; and (4) if the regulated article is a pest-protected plant, its transformation event that serves as plant-incorporated protectant (PIP) has been duly registered with the Fertilizer and Pesticide Authority (FPA).

The BPI Biotech Office provided the assessors the complete dossier submitted by Syngenta 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 Syngenta 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 interaction of the resulting products such that a new allergen or a new toxin could be produced due to the interactions of the genes coding for the four proteins namely: Cry 1Ab, Cry 1F, PAT and mEPSPS. According to Forrester (2017), Cry 1Ab has been shown already not be allergenic or toxic. A similar case was found for the PAT protein, according to Bauman (2017), acetyltransferases are not toxic proteins, hence none of these multiple sequence alignments indicated the potential for PAT to act as a toxin. A similar case holds true for mEPSPS amino acid sequences like the two cases mentioned above, according to Bauman (2016), evaluation of these alignments demonstrated that none of these alignments indicated the potential for mEPSPS to act as a toxin. Hence, this non-toxic protein to start with when it interacts with another non-toxic protein cannot form a product that is toxic and allergenic [1][2].
- b. The gene products will not accumulate in the same or different subcellular compartments of plant parts. In the case of Bt11, carrying the *cry1b* and *pat* gene expressions which are both driven by the 35S promoter, cellular localization of sequences are not present, hence the site for accumulation is the cytoplasm. In the case of the bar gene encoding for PAT proteins, they are also expressed in the cell's cytoplasm. Meanwhile, for TC1507, the *cry1F* gene expression is driven by the UB11ZM promoter and the *pat* gene expression is driven by CaMV 35S promoter, no cellular localization sequences are present, hence again the cytoplasm is the site of accumulation. On the other hand, the modified EPSPS enzyme, whether modified (as in GA21) or otherwise is known to be directed in the chloroplast using the CTP. When this transit peptide is imported into the chloroplast of the cell, this is cleaved off the protein [3].

2. Metabolic Pathway

- a. There is a complete description of the mode of action of each gene product. Historically, a *Bt* isolate that produced the highest level of enterotoxin when fed to rats at 10¹² spores per rat, or when 10⁶ *Bt* spores were injected sub-cutaneously in rats, it was found that there is no evidence of illness and there is no occurrence of weight loss of the experimental rats. Given this information that the original *Bt* do not induce adverse effects, hence a truncated portion of *Bt* that was used in developing the present stack maize, its gene product is unlikely also to cause adverse effects. On the other hand, the mEPSPS protein has low affinity for

glyphosate, thus when the plants expressing the mEPSPS protein are treated with glyphosate, the plants are not affected. Meanwhile, for the PAT, the pat gene encodes an enzyme the phosphinothricin N-acetyl transferase that detoxifies glufosinate ammonium, the active ingredient in the herbicide Basta®. The transgenic plants expressing the pat gene are protected from the herbicide glufosinate ammonium. The PAT enzyme detoxifies glufosinate ammonium (GA) through acetylation of the phosphinothricin that leads to N-acetyl-glufosinate (NAG) and two other metabolites namely 3-methylphosphinicopropionic acid (MPP) and 3-methylphosphinicoacetic acid (MPA) [4][5][6].

- b. As indicated in the sections on gene interaction and metabolic pathways, Cry 1b, Cry1F, PAT and mEPSPS proteins have distinct mode of actions. The mode of action of Cry1b and Cry1F appears to be mechanistically similar. However, there is a strong evidence showing that the modes of action of the two insecticidal proteins are distinct. As reported in several experiments, it was demonstrated that Cry1Ab and Cry1F show high affinity to different protein receptors in the insect midgut. Also in various laboratories, their results support the conclusion that the mode of action for the two Cry1 proteins are not identical, since Cry1Ab-resistant insects do not show high levels of cross resistance to Cry1F [7][8][9][10][11][12][13][14].
- c. The products are not involved in the same metabolic pathway. The Cry1Ab and Cry1F proteins have no enzymatic activities, and therefore they are not involved in any metabolic pathways in the plant metabolism. Also, the PAT protein has no enzymatic activities, and no endogenous substrate has been identified in the corn plant. Lastly, the modified EPSPS enzyme is involved in the production of the aromatic amino acids tyrosine, phenylalanine and tryptophan. In addition, the mEPSPS protein belong to the family of EPSPS synthases, which are enzymes involved in the pinultimate step of the biochemical shikimic acid pathway leading to the synthesis of aromatic amino acids whose site is in the chloroplasts of plants [4][5][6].
- d. There are no possible unexpected effects of the stacked genes on the metabolism of the plant. According to Raper (2014), the possible unexpected effects of the stacked genes on the metabolism of the plant are extremely unlikely which is supported by weight of evidences encompassing the distinct mode of action of introduced proteins and the analysis conducted on protein expression. Evidences support that previously in each single event prior to gene stacking, it has been shown that a single trait is equivalent to conventional corn. Each protein has a different mode of action and that any possible interaction is not known to have an unexpected effect on the metabolism of the corn plant [15].

3. Gene Expression

- a. The expression levels of the individual protein products are the same as in the individual previously approved transformation event. It was found that there is substantial equivalency of the concentrations of Cry1Ab, PAT, Cry1F and mEPSPS in the tissues of the Bt11 x TC1507 x GA21 corn stack plants to those of the tissues of the single event such as Bt11, TC1507 and GA21 corn. The concentrations of PAT proteins, as expected in most of the corn stack hybrid plants were higher than those

of the single event hybrid plants namely: Bt11 and TC1507. The presence of the two copies of the gene pat in the corn stack Bt11 x TC1507 x GA21 corn hybrid plants is most probably the cause of the higher concentration of PAT proteins [15].

- b. Most tissues of the corn stack Bt11 x TC1507 x GA21 corn hybrid plants, the protein concentrations of PAT were higher than those that were found in the tissues of the single-event corn hybrids namely: Bt11 and TC1507. This higher protein concentration is most probably due to the presence of the two copies of the gene pat in the corn stack Bt11 x TC1507 x GA21 corn hybrid, in contrast to the single copy of the gene pat in the individual Bt11 and TC1507 corn hybrids [15].
- c. The marker genes are transferred and expressed also in the plants containing the stacked genes. The Southern blot analyses and protein expression studies showed that the pat marker genes from Bt11 and TC1507 were transferred and expressed in Bt11 x TC1507 x GA21 stack corn hybrid [3].

4. Agricultural Management

The presence of the introduced traits will not cause a change in cultural management of crop except for the intended change. The two introduced traits like resistance to the Lepidopteran insect like the corn borer and tolerance to the glyphosate and glufosinate herbicide are the only changes that are built-in within the corn stack plant. Like the conventional corn, cultural management practices will remain the same for the above-mentioned stack corn and the introduced traits will not affect these management practices. Except for the fact that spraying of insecticides against the Lepidopteran insects like the corn borer will not be done anymore, and herbicide tolerance is expected in this stack corn.

STRP'S RECOMMENDATION

Find scientific evidence that the regulated article applied for commercial propagation 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 Syngenta Philippines, Inc. concerning its application for commercial propagation of Corn (Bt11 x TC1507 x GA21), the DENR-BC considered that the regulated article poses no significant adverse effect to the environment on the following basis:

1. The regulated article is considered substantially equivalent to its conventional counterpart for its history of safe use. It has previously been approved for direct use as food in five (5) countries and as feed in four (4) countries. Its cultivation has also been previously approved in Argentina [33].

2. The individual events for Bt11, TC1507, and GA21 have previously undergone environmental risk assessments and have subsequently been approved for commercial propagation in the Philippines. Since the individual events were considered safe to the environment, biodiversity, and non-target organisms, the regulated article is similarly less likely to pose such significantly negative effects.
3. The development of the corn stack hybrid was through conventional breeding, which is regarded as safe considering its long history of use. The method of crossing individual transgenic parents is also the same to that of non-transgenic parents. This does not give any further genomic variation beyond what is obtained [34].
4. Since maize has lost the ability to survive in the wild during its domestication, it is incapable of continuously reproducing in uncultivated land and less likely to threaten natural habitats. Its weediness potential is also considered negligible.

DENR-BC'S RECOMMENDATION

Based on the evaluation of the documents submitted by the applicant, applicable studies and review of literature, the DENR-BC considers that the regulated article poses no significant adverse effect to the environment, particularly on its weediness and invasiveness potential, and its effects on non-target organisms.

DOH-BC'S ASSESSMENT

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 Commercial Propagation (CP) of Corn BT11 x TC1507 x GA21, the DOH-BC,

Find that the regulated article applied for Commercial Propagation (CP) 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 Commercial Propagation (CP) does not require changes in the usual practices as described in the phases/stages of biotechnology project activities. 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.
2. Scientific pieces of evidences from toxicity studies and references, find that the regulated article will not cause significant adverse health effects to human and animal health.
3. Dietary exposure to the regulated article is unlikely to result in an allergic reaction.
4. The regulated article is not materially different in nutritional composition from that of the non-transgenic corn or the conventional corn.
5. Scientific pieces of evidences from provided references i.e. literatures show that regulated article applied for Commercial Propagation is as safe as its conventional

counterpart and shall not pose any significant risk to human and animal health and on the environment.

DOH-BC'S RECOMMENDATION

It is suggested that the Bureau of Plant Industry (BPI) ensure that any spillage (during unloading and loading/hauling and transport unloading and storage) shall be collected and cleaned up immediately and that transportation of the consignment from the port of entry to any destination within the country shall be in closed containers.

SEC EXPERT'S ASSESSMENT

1. There is a dearth of studies on the socioeconomic aspects of GM corn production in the Philippines. While most studies exhibited increase in productivity of GM corn and a yield advantage of GM corn over conventional hybrid corn, a study by Afidchao (2014) in Isabela province showed that there was no statistical difference in production output between GM and non GM corn though BtHT and HT (herbicide tolerant) corn growers out yielded non-GM corn growers by 8% and 7%, respectively and non-GM corn out yielded Bt corn by 1% [47][48][50][52].
2. Most studies exhibited cost efficiency of Bt corn compared with conventional corn. However, Afidchao (2014) showed a significant difference among corn types in the cost of fertilizer with Bt corn having the highest fertilizer cost efficiency, followed by BtHT, HT and finally non-GM corn [47][48][50][52].
3. Cost of seeds per hectare was far higher for GM corn than for the leading conventional corn hybrids available in the market. Agricultural input cost between GM corn types, i.e. *Bacillus thuringiensis* (Bt) vs. herbicide tolerant (HT) vs. BtHT, did not differ but all these GM corn types differed from non-GM corn with GM corn types exhibiting a higher total input cost compared with its non-GM counterparts [48].
4. Total labor cost per hectare of production showed no difference between corn types [47][48][50][52].
5. In general, farmers who use GM corn obtain higher incomes and show higher economic performance than those who adopt other varieties, as found in past studies in the country. However, the study by Afidchao (2014) in Isabela province found that non-GM corn was not statistically different from GM corn (Bt, BtHT and HT) in terms of production output, net income, production cost ratio and return on investment [47][48][50][52].
6. Monocropping of GM corn and its adoption across the Philippines could potentially diminish crop biodiversity. Other native corn varieties are now at risk of being totally eliminated from the agro-ecosystem. Considering the high economic potential and increasing adoption of GM yellow corn, the seeds of which are incapable of being recycled, traditional varieties are at high risk of extinction [47].

SEC EXPERT'S RECOMMENDATION

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

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