Consolidated Risk Assessment Report of Syngenta's Corn Bt11 Application for Direct Use as Food, Feed or for Processing (FFP)

EXECUTIVE SUMMARY

On March 29, 2018, Syngenta Philippines Inc., submitted corn Bt11 application for direct use as food and feed, or for processing to the Bureau of Plant Industry (BPI) 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 (BAI), concurred that corn Bt11 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, considered the regulated article safe to the environment and biodiversity.

Also, the Department of Health – Biosafety Committee (DOH-BC), after a thorough scientific review and evaluation of documents related to Environmental Health Impact, find scientific evidence that corn Bt11 will not pose any significant risk to health and environment and that any hazards could be managed by the measures set by the department.

Furthermore, the Socio-economic, Ethical and Cultural (SEC) Considerations expert 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 Syngenta Philippines, Inc.

Below is the summary of the evaluation conducted by the STRP and regulatory agencies.

A. STRP, PPSSD, BAI ASSESSMENT

After thorough review of the technical documents submitted by the applicant, the assessors' findings are as follows:

A. Host Organism

Corn is a source of nutrients: carbohydrates, protein, fats, and dietary fiber. This is consumed in larger amounts than rice in some parts of the Philippines. Globally, it is considered a staple food in South America and has been used popularly as cereals. Corn is not specifically consumed as a specific source of nutrients.

Corn contains anti-nutritional factors such as phytic acid, 2,4-Dihydroxy-7-methoxy-2H-1,4-benzoxazin-3(4H)-one (DIMBOA), raffinose and trypsin and

chymotrypsin inhibitors and are known to be present in small amounts in *Zea mays*. History of safe use was attributed to corn (*Zea mays* L.) and it is not known to be associated with any known toxicants (OECD, 2002). It is not a common allergenic food, although in some case-studies, allergenic reactions were reported. Based on the OECD report (2002) and information provided by the developer, maize has been described as a food that is likely to have low allergenicity.

Most of the human consumption of corn is in the form of corn-based ingredients such as high fructose corn syrup, starch, sweeteners, cereals, oil and alcohol. Field maize products are used in food as starch, oil, grits, meal and flour. Sweet maize is used as whole kernel and popcorn maize kernels are used as popcorn and as basis for confections (Morris, 1998; OECD, 2002).

Ground corn is a common principal ingredient in animal feeds, both monogastrics and ruminants. It is incorporated as much as 30-60% of the feed mash. When corn grain is processed for oil, the resulting by-product is corn gluten feed, or corn gluten meal which is a good source of crude protein for animals. Corn bran resulting from polishing whole corn for human consumption is also used in animal feeding. By-products such as green or dry corn stovers are common maintenance feed for ruminants. The corn plant itself is excellent source of roughage for fattening and dairy animals. It is a very suitable material for ensiling.

B. Transgenic Plant

Corn Bt11 has been reviewed and approved for food use in many countries including Argentina (2001), Australia (2001), Brazil (2008), Canada (1996), China (2002), Colombia (2009), European Union (1998), Indonesia (2011), Japan (2001), Malaysia (2012), Mexico (2007), New Zealand (2001), Paraguay (2012), Philippines (2003), Russian Federation (2008), Singapore (2017), South Africa (2002), South Korea (2003), Switzerland (2003), Taiwan (2004), Thailand (2013), USA (2004), Uruguay (2004), and Vietnam (2014).

Furthermore, Bt11 corn has feed approval in the United States, Argentina, Brazil, Canada, China, Colombia, European Union, Japan, Korea, Malaysia, Mexico, Paraguay, Philippines, Russian Federation, Singapore, South Africa, Switzerland, Taiwan, Turkey, Uruguay, and Vietnam

It is not expected that consumption pattern will change with the introduction of Bt11 corn in the market. The amount of corn consumed as food is not likely to change as it is today. Although, in general, increase in consumption is expected due to consistent human population increase.

C. Donor Organism

The *cry1Ab* gene from *Streptomyces viridochromogenes* and *pat* gene from *Bacillus thuringiensis* and *Streptomyces viridochromogenes* were completely described and is not reported to be toxic, pathogenic or allergenic nor could be a source of allergenic properties.

D. Transformation System

The initial parental transformation of the corn lines was accomplished through insertion of the plasmid pZO1502, using a protoplast transformation/regeneration system. The plasmid pZO1502 was digested

with *Not*I to liberate the *bla* gene from a fragment carrying the *cry1Ab* and the *pat* genes prior to transformation. The regenerated transgenic material was grown and crossed/backcrossed to non-transformed Syngenta elite lines, used as parents of commercial hybrids.

The target of the method is the genetic modification of nuclear DNA.

E. Inserted DNA

The multigenerational stability of the DNA insert was demonstrated through Southern blot analyses of two generations, BC3 and BC6, of Bt11using *Eco*R V and *Hin*d III restriction enzymes. Results showed that the DNA insert is stably inherited at a single locus from one generation to the other.

F. Genetic Stability

The segregation of the cry1Ab gene and pat gene was followed over multiple generations. BC2, BC3, BC4, BC6, BC3S1, BC3S2, BC6S2, BC6S2B1, and BC6S2BC2 generations were individually analyzed for the presence of cry1Ab and pat genes. F1 plants were selfed to produce a S1 population. The S1 plants were again selfed after screening for tolerance to ECB and glufosinate ammonium. Seeds were collected from ECB and glufosinate tolerant plants representing different backcross stages and planted in the field. Plants were twice infested with ECB, and were either sprayed with 5 liters BASTA per ha or applied on the leaf tips with a 1% glufosinate solution. This limited application of the herbicide can detect glufosinate tolerance without severely damaging susceptible plants. Non-transgenic plants were used as negative controls. They were also infested with ECB and applied with 1% glufosinate. The results were recorded by visual evaluation.

Results showed that all plants were either tolerant to ECB and glufosinate or susceptible to both. The segregation ratios are consisted with the expected ratio of 1:1, 3:1, or 1:0 for a single dominant locus, depending on the generation studied. It can therefore be concluded that:

- The cry1Ab gene is inherited as a single Mendelian trait in Bt11;
- The pat gene is inherited as a single Mendelian trait in Bt11;
- The cry1Ab and the pat genes are closely linked as they always segregate together;
- The genetic background did not influence the inheritance pattern of the introduced characters.

G. Expressed Material

ELISA methodology was used to determine the concentration of cry1Ab protein in several corn plant tissues derived from Bt 11 corn. Tissues from leaves, roots, kernels, pollen and whole plants were collected from plants representing the two Bt11 corn hybrids and their non-transgenic isoline controls were collected, processed and extracted.

Cry1Ab protein was detected in all Bt11-derived plant tissues analyzed. Levels in pollen were below the lower limit of quantification, < 0.08 ug/g fresh wt. pollen. Across all plant stages, mean Cry1Ab levels measured in leaves, roots and whole plants ranged from ca. 10 - 22 ug/g fresh wt., 2 – 4 ug/g fresh wt., and 4 – 9 ug/g fresh wt., respectively. Mean Cry1Ab levels measured in kernels at seed maturity and senescence were ca. 1 – 2 ug/g fresh wt.

H. Toxicological Assessment and Allergenicity Assessment

Safety of the novel proteins, Cry1Ab and PAT, in Bt11 corn was assessed based on the digestibility, heat inactivation, amino acid sequence comparison and oral toxicity studies and other related scientific literatures provided by the developer. Results of the analyses indicated that the novel proteins are being digested rapidly in mammalian gastric fluid, a characteristic of dietary proteins, are being inactivated by induction of heat which is normally occurring during processing and cooking, and do not cause toxicity on mice via acute oral gavage. Amino acid sequence analysis indicated that Cry1Ab and PAT have no significant homology to any known toxins or allergens.

I. Nutritional Data

Studies were conducted to assess the substantial equivalence of the genetically modified Bt11 corn with non-modified corn. The results from the studies demonstrate that the introduced genetic modification in the Bt11 corn does not alter the composition of the grain. Additionally, the mean levels of all components measured in the Bt11 corn were within the ranges published in the International Life Sciences Institute Crop Composition Database (ILSI 2010). This supports the conclusion that the Bt11 corn is not materially different than the natural variation in non-transgenic field corn.

The assessors find scientific evidence that the regulated article applied for human food and animal feed use is as safe as its conventional counterpart and shall not pose greater risk to human and animal health

B. <u>DENR BC (for Safety of Event to the Environment)</u>

After a comprehensive review and evaluation of the documents including the scientific evidences from provided references and literature submitted by Syngenta Philippines, Inc., on its application for Direct Use as FFP of Corn (Bt11), hereunder are the observations and appropriate actions:

1. The direct use of the regulated article whether for food, feed or for processing will not cause any significant adverse effect on the environment (land, and water) and non-target organisms. The transgenic crop will not increase its weediness potential in case the seeds spill out into the environment because the Cry1Ab and PAT protein products produced by the transgenic crop will degrade upon exposure to the natural environment and general conditions that is high temperature (above 75°C and 55°C, respectively), varying pH, enzyme digestion, etc. (De Luis et al., 2009 and Wehrmann et al., 1996).
2. The protein products Cry1Ab and PAT show no toxicity to mammals nor show similarity with other putative mammalian toxins based on amino acid comparison through Basic Local Alignment Search Tool for Proteins (BLAST) (Forrester, 2017 and Bauman, 2017). Moreover, the in vitro digestibility of the PAT protein was simulated in a mammalian gastric environment, which is also similar with the physiology of digestion of avian gastrointestinal tract, in terms of pH and type of enzyme secreted. The result shows that PAT protein is easily digested and inactivated at acidic pH, similar with the stomach condition according to Privalle (1994a) and Wehrmann, et al. (1996). On the other hand, CrylAb protein, when consumed, has very low potential to be absorbed by the intestinal mucosa due to its susceptibility to the proteases in the mammalian digestive system (Privalle, 1994b).

3. The project description report (PDR) discusses the specified environmental management plan indicating the possible risk and harm to the environment and non-target organisms as well as the mitigating measures and contingency plan. Furthermore, the chances of unintended release or planting of the regulated article is very minimal and will not cause any damaging and lasting effects because the receiving environment (areas near the port, roads, railways, etc.) is not conducive for plant growth. Also, corn is a highly domesticated plant that requires human intervention for it to persist in the environment (OECD, 2003 and Raybould, et al., 2012).

C. <u>DOH-BC (for Environmental Health Safety)</u>

After a thorough review and evaluation of the documents provided by the proponent, the DOH-BC found 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 of the DOH-BC:

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 corn varieties.
4. The regulated article is not materially different in nutritional composition from that of the non-transgenic corn or the conventional corn.
5. 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.
6. 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 Bt11 Corn.

D. <u>SEC Expert (for Socio-economic, ethical and cultural Consideration)</u>

The importation of Bt11 corn will not drastically affect the patterns of consumption of yellow corn. With the granting of permit to import yellow corn, including Bt11, it may slightly increase the supply of yellow corn which might lower its prices. However, being only one of the ingredients in feed formulation for livestock, poultry and aquaculture, it may not have any effect to the current pattern of consumption. With stable supply and prices of yellow corn, the performance of the livestock, poultry and aquaculture sub-sector may improve.

With regards to the patterns of production and trade, definitely it would have a very minimal effects in our domestic production and foreign agricultural trade. In the short-run, domestic production will not be affected because the event will not be propagated domestically. In addition, our agricultural trade will not be affected because we imported very minimal volume of yellow corn (543,770 m.t.). In addition, granting a permit to import Corn Bt11 won't affect the global trade of corn since Philippine importation of yellow corn is very negligible compared to the global trade.

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