CONSOLIDATED REPORT FOR MONSANTO PHILIPPINES INC.'S CORN MON 810

(APPLICATION FOR COMMERCIAL PROPAGATION)

EXECUTIVE SUMMARY

On August 2, 2017, Monsanto Philippines Inc. submitted corn MON810 for Commercial Propagation, as original application under the DOST-DA-DENR-DOH-DILG Joint Department Circular (JDC) No. 1 Series of 2016.

The said transformation event had obtained Biosafety Permit under the rules and regulations of the Department of Agriculture Administrative Order No. 8, Series of 2002 for commercial propagation on December 3, 2007. The said Biosafety Permit for commercial propagation expired last December 2, 2012 hence this application represents Monsanto Philippines Inc.'s submission for renewal of these permits under the JDC.

This application was assessed in accordance with the *Article VI. Commercial Propagation of Regulated Articles* of the JDC No.1. This Article covers the basic biosafety policies, procedural requirements and guidelines in carrying out the risk assessment of plants carrying single transgene for Commercial Propagation. Focus of the risk assessment is on food and feed safety of the GM product.

Under the JDC, the assessors for Monsanto Philippines Inc.'s corn MON810 for Commercial Propagation were the following:

- Two (2) members of the Scientific and Technical Review Panel (STRP) – for evaluation of the Applicant's submitted risk assessment report.
- Department of Environment and Natural Resources (DENR) – for the determination of the environmental impact of the said application.
- Department of Health (DOH) - for the determination of the environmental health impact of the said application.
- Insect Resistance Management Team (IRMAT) – for review and evaluation of the application for any IRM related concerns and issues.
- Fertilizer and Pesticide Authority (FPA) – for the determination if the applicant is duly licensed as a pesticide handler in accordance with Presidential Decree No.1144 and if tolerance levels and good agricultural practices have been established for registration for the transformation event.
- Socio-economic, ethical and cultural (SEC) Expert – to evaluate SEC impact of the said application

After reviewing the documents submitted by the applicant, the two members of the STRP find scientific evidence that the regulated article applied for Commercial Propagation is as safe for human and animal health, and the environment as its conventional counterpart, while DOH, DENR, and SEC expert recommended for the issuance of Biosafety Permit for corn MON810. In addition, FPA found that Monsanto Philippines Inc. is a duly licensed pesticide importer, exporter, indentor and national distributor of agricultural pesticides.

BACKGROUND

In accordance with Article VI. Section 15 of the JDC, 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, except for the SEC expert, 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.

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.

I. THE HOST ORGANISM

Maize is a good source of carbohydrates, proteins and lipids. It contains 61-78% starch (which includes amylose and amylopectin) found primarily in the endosperm. It also has non-starch polysaccharides such as cellulose (22%) and hemicellulose (70%) found in corn kernels and corn brans. The seed coat is a good source of dietary fibers. In addition, it has 6-12% protein content principally found in its endosperm and germ. However, maize is lysine deficient. It is composed of 3-6% lipids concentrated in its germ. Among its lipid contents were triglycerides, polar lipids, sterols, free fatty acids and some trace amounts of carotenoids and wax. Maize is consumed as an alternative for rice since it contains high amounts of carbohydrates and dietary fiber, which is beneficial for those who are trying to lose weight. It is also rich in Vitamin A. Not only is it a staple food of the human diet but also a main component in animal feeds (Ai and Jane, 2016).

Okechuwu et al., 2013 reported that phytic acid is said to be present to maize. Phytic acid reduces phosphorus availability especially in mono-gastric animals. Other reported anti-nutrients include raffinose and trypsin inhibitor; however, these have a minimal effect on nutrition. Maize also contains trace amounts of saponin, phenol, flavonoid, and alkaloids.

On the other hand, 2,4-Dihydroxy-7-methoxy-2H-1,4-benzoacin (DIMBOA) found in maize leaves and roots has been reported as a potential toxicant. However, there were no reported effect on humans consuming maize. Maize, similar to majority of other crops, contains natural toxicants such as cyanogenetic glycosides. Cyanogenetic glycosides (HCN) is present in a concentration of 29.16±0.03mg/100g dried sample. The fatal dose of HCN in man is 1.5mg/kg b.w. (Onojah and Odin, 2015).

The STRP also cited Hefle et al., 1996 that maize has also been considered as a less common allergenic food, but it does not mean that it is completely non-allergenic. It was reported by Hefle (1996) that there were allergic reactions coming from two major food allergens in maize: a 9-kd lipid transfer protein (LTP) and a 16-kd trypsin inhibitor. However, the clinical relevance of these findings was uncertain.

Filipinos consumes boiled maize as an alternative for rice, especially sweet corn. It is also processed and canned or made into cereals, soups, edible oils, chips (kornik), popcorn, powdered flour, corn syrup and starch. White corn is also consumed raw or even processed as "binatog". Maize is also known to be processed and distilled as bourbon.

The STRP also agreed that maize is mainly consumed by people who have more access to corn than other staple food like rice. It is traditionally consumed in Mexico and Central America in the form of tortillas. Only about 20% of the Philippine population use corn as staple food since rice is more popular. Most maize corn is used as feedstuff. Aside from food and feeds, maize is also used for industrial purposes such as biodegradable paper and plastics, and cosmetics. There are varieties intended for animal feeds, plus corn by-products from processing are used as animal feedstuffs. Maize is processed and sometimes mixed with other feedstuffs, depending on the feed requirement of the animal.

II. THE TRANSGENIC PLANT

Monsanto Company has developed insect-protected corn event MON810 by inserting Cry1Ab gene which naturally produces *Bacillus thuringiensis* (Bt) protein in the maize. MON810 is protected from feeding damage by *Asian corn borer*, *European corn borer*, the *Southwestern corn borer*, and the *Pink borer*.

The benefits of planting the transgenic corn are: 1) a reliable means to control these major pests; 2) control target insects while not harming beneficial species; 3) reduced chemical pesticide usage; 4) reduced exposure of applicator; 5) a fit with the Integrated Pest Management (IPM) and sustainable agricultural systems; 6) reduced fumonisin mycotoxin level in corn kernels; and 7) no additional labor or machinery required, allowing both large and small growers to maximize hybrid yields. Additional to this, the quality of produce would be maintained and crop damage would be reduced thus more produce could be sold.

The gene of interest was isolated from the *Bacillus thuringiensis* var. *kurstaki* HD-1 strain found in DIPEL, the leading microbial insecticide in agricultural use. This gene was bombarded in the embryonic corn tissue with plasmid PV-ZMBK07. Southern blot analysis of MON810 corn demonstrated that a single functional copy of the cry1Ab coding sequence was integrated into the corn genome and that coding sequence is inherited in the expected Mendelian pattern.

The Cry1Ab protein shows no amino acid sequence homology to known protein toxins, and is rapidly degraded with loss of insecticidal activity under mammalian digestion condition. There were no toxicity indications during administration of Cry1Ab oral gavage. The cry1Ab gene was not derived from an allergenic source. The protein does not have immunologically relevant sequence similarity with known allergens or possess characteristics of known protein allergens. It was also reported to have no harmful effects on other types of organisms.

Compositional analyses were performed. The compositional values of MON810 corn were compared with that of the control line, as well as published literature values. Compositional data confirmed that MON810 corn is substantially equivalent to the parental hybrid as well as traditional corn hybrids. It was also confirmed that MON810 corn plants are as safe and nutritious as conventional corn varieties.

A comprehensive phenotypic, agronomic, environmental interaction assessment was conducted which included the evaluation of characteristics for seed germination, disease and pest susceptibilities and yield characteristics. Results indicate that MON810 does not possess weediness potential, increased susceptibility or tolerance to specific abiotic stresses, diseases, or arthropods, or characteristics that would confer a plant pest risk compared to conventional corn.

Even if MON810 was shown to be compositionally equivalent to conventional corn with similar genetic background, there were slight changes in consumption amount by humans or animals due to different beliefs with regards to GMO products.

III. THE DONOR ORGANISM

Bacillus thuringiensis subsp. *kurstaki* has been commercially used in the United States to produce the main component of microbial-derived insecticide. This type of insecticide had a long record of safe use for agricultural pest control. These microbial pesticides were subjected to extensive toxicity testing and were reported to have no adverse effect on human health. Also, no confirmed cases of allergic reactions to Cry proteins in microbial-derived *B. thuringiensis* products reported.

The assessors concur that Cry1Ab protein shows no amino acid sequence homology to known protein toxins, and is rapidly degraded with loss of insecticidal activity under mammalian digestion condition. There were no toxicity indications during administration of Cry1Ab oral gavage. The cry1Ab gene was not derived from an allergenic source. The protein does not have immunologically relevant sequence similarity with known allergens or possess characteristics of known protein allergens. It was also reported to have no harmful effects on other types of organisms.

All potentially inserted regulatory sequences have been adequately described. Description for each component includes the size, orientation, function and location. The complete description for each component was presented in the dossier.

Two plasmid vectors were used for MON810 maize: PV-ZMBK07 and PV-ZMGT10. PV-ZMBK07 contains the cry1Ab gene. This vector contains the enhanced CaMV 35S promoter (0.6 Kb), heat-shock protein hsp70 gene (0.8 Kb), cry1Ab gene (3.46 Kb), nopaline synthase sequence (0.26 Kb), a partial E. coli lacl coding sequence lacZ (0.24 Kb), origin of replication ori-pUC (0.65 Kb), and nptII terminator (0.79 Kb).

PV- ZMGT10 contains the gox and cp4 epsps genes. This vector contains the enhanced CaMV 35S promoter (0.6 Kb), heat-shock protein hsp70 gene (0.8 Kb), chloroplast transit peptide CTP2 (0.31 Kb), CP4 EPSPS gene (1.4Kb), chloroplast transit peptide CTP1 (0.26 Kb), gox gene (1.3 Kb), nopaline synthase sequence (0.26 Kb), a partial E. coli lacl coding sequence lacZ (0.24 Kb), origin of replication ori-pUC (0.65 Kb), and nptII terminator (0.79 Kb). In addition, Cry1Ab is the only expressible sequence in the event.

Bacillus thuringiensis subsp*. kurstaki* is the donor organism of cry1Ab gene. It is not known to be toxic or allergic. Cry1Ab protein is encoded by the Cry1Ab protein. They also concur that it is not known to be toxic or allergic.

IV. THE TRANFORMATION SYSTEM

The transformation method used is the particle acceleration method. This method is more effective for monocot crop like maize. The target of genetic modification is the Nuclear DNA. Nuclear DNA is more appropriate to modify than mitochondrial DNA since it codes for proteins of all functions; unlike the mitochondrial DNA which only codes for metabolic processes. Also, rate of mutation is higher in mitochondrial DNA than in nuclear DNA.

The assessors also agreed that the experimental protocol was completely provided in MSL14204 MON 810 Molecular Characterization section. The protocol included the materials, reagents, and step-by-step process. The genetic components were summarized in tabular form provided in the dossier. Carrier DNA and helper plasmids were not used.

V. THE INSERTED DNA

The DNA from the control and MON810 plants were digested with a variety of restriction enzymes and subjected to Southern hybridization analyses to characterize DNA insert. Southern hybridization analysis is used to assess insert number, copy number, and integrity of the insert. After performing Southern blot analysis and quantitative real-time Polymerase Chain Reaction, the STRPs affirm that it was found to have only on insertion site.

The integrity of each inserted gene was examined by Southern blot analysis, PCR, and Nucleotide Sequencing. After digesting and probing, an expected fragment the same size as the gene of interest was produced for the positive control while no fragment was produced in the negative control. MON810 contains one band relatively similar to the positive control. The backbone integrity of both plasmid PV-ZMBK07 and PV-ZMGT10 was also determined using Southern Blot analysis. There were no identified/determined truncations, deletions, or rearrangements.

According to Khachatourians et al., 2002, cry1Ab gene has been inserted and expressed in cotton, potato, rice, soybean, tobacco, sweet corn, tomato, white clover, and white spruce plant. This was approved by many regulatory agencies in the world.

Backbone sequences are absent as confirmed by Southern blot analysis. The presence of the plasmid backbone in MON810 was tested through restriction fragment analysis and Southern blot analysis. Results obtained showed that the plasmid backbone, alongside with the other genetic elements used for the insertion (CP4 EPSPS gene, gox and nptII/ori-pUC) was not present in the transformant as supported by the Southern blot results (Agriculture and Biotechnology Strategies, 2001).

VI. GENETIC STABILITY

The integrity of the insert has been demonstrated through at least seven generations of crossing. The cry1Ab gene in MON810 was determined stable after generations of crossing to the recurrent parent (B73) and six generations of crosses to second, unrelated inbred (Mo17). The Chi-square tests for all of the backcrosses with B73 and Mo17 did not deviate from each other. The segregation and stability data are consistent with only one active insertion site of the gene into the genomic DNA of MON810.

Segregation data for BC0F1 plants, BC1F1 plants, and BC1F2 progeny from crossing individual BC0F2 plants by non-trasgenic tester and subsequent generation ear to row analysis. The results in all four cases are consistent with only one active insert segregating according to Mendelian genetics.

VII. EXPRESSED MATERIAL

The levels of the expressed proteins were evaluated in young leaves, grain, whole plant and pollen tissues collected from six field locations using Enzyme Linked Immuno-Sorbent Assay (ELISA) and western blot analysis. CP4 EPSPS and GOX genes were not present in any plant tissue, thus the gene is absent in the integrated DNA. Cry1Ab gene was constitutive.

The appearance of a color response in an ELISA indicates the presence of the target molecule in the sample. ELISAs have been used for detecting various proteins, identifying viruses and bacteria, and determining the presence of low-molecular-weight compounds in a wide range of biological samples. To increase the specificity of the primary antibody and to ensure the reliability of the antibody preparation, monoclonal antibodies are often used for diagnostic ELISAs.

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The STRPs also affirmed that the expression of the cry1Ab gene did not alter the original metabolism of maize or the other agronomic characteristics of maize. This gene was expressed for the purpose of insect resistance and antibiosis for some Lepidopteran species.

VIII. TOXICOLOGY and ALLERGINICITY ASSESSMENT

For toxicological and allergenicity assessment, simulated mammalian gastric fluid was prepared. Pepsin is the enzyme used in the digestibility test. The trypsin-resistant core of Cry1Ab protein was used in the simulated digestion study since this was the active insecticidal form of the protein. The protein was rapidly degraded under gastric conditions; more than 90% was degraded under two minutes of incubation. These results were determined by Western Blot analysis for protein quantification.

Further, the assessors agreed that corn mash was incubated at 70ºC, 80ºC, and 90ºC; the starting concentration was approximately 160 pbb. Cry1Ab protein was undetectable (< 3.8 pbb) after incubation at 70ºC for 30 minutes, 80ºC for 15 minutes, and 90ºC for about 3 minutes. More than 50% was detected at 70ºC for 30 minutes. These data showed that immunodetectability of the Cry1Ab protein is reduced or eliminated after heat treatment at 70ºC or higher.

Also, the STRPs stated that after running Protein Blast for amino acid sequence comparison of Cry1Ab, there is no biologically significant homology with known toxins and allergens. In addition, acute oral gavage was performed on mice. Doses of 0, 400, 1000, and 4000 mg Cry1Ab/kg body were administered on the mice. A mice control group was dosed with Bovine serum albumin (BSA) at 4000 mg/kg. Seven days after dosing, there were no statistically significant differences among treatments in terms of mortality, body weights, cumulative body weight or total food consumption. It was concluded in the test that the Cry1Ab protein has no adverse effect in mammals.

The acute oral toxicity was conducted with E. coli-produced Cry1Ab protein, which is the chemical and functional equivalence of the Cry1Ab protein in Insect-Protected maize plants in terms of molecular weight, immunoreactivity and insecticidal activity. Lastly, maize does not contain any known allergens or produce significant quantities of toxins or anti-nutritional factors warranting analytical or toxicological tests.

IX. NUTRITIONAL DATA

Forage and grain were used as samples in the proximate analysis. All assessors concurred that there were no statistically significant differences between the control and MON 810 for the parameters protein, fat, ash, neutral detergent fiber, acid detergent fiber and carbohydrates. They also reported that there are statistically significant differences observed for crude fiber in the 1994 U.S. trials and for moisture in 1995 E.U. trials. However, these parameters could be influenced by external factors and their differences have no biological significance since the reported values are still within the range of literature values. Furthermore, the assessors have also reported that all data derived from the test (transgenic) line were within the reported range.

The assessors have also agreed with the statement of the proponent that the significant differences observed in crude fiber in seed and protein in forage are unlikely to be biologically meaningful since it was within the range of historical conventional control values.

In the amino acid composition analysis of grain, the assessors concurred that the values for 15 of 18 amino acids were within the range of published literature values. They stated that the values for cystine, histidine and glutamic acid were slightly higher than the published literature range for both MON 810 and the control line. This is most likely due to differences in analytical methodology. Furthermore, in the grain from 1994 U.S. trials, there were no statistically significant differences between MON 810 corn and the control line for 10 of 18 amino acids. Eight amino acid values (cysteine, tryptophan, histidine, phenylalanine, alanine, proline, serine and tyrosine) were significantly higher in MON 810 compared to the control line. In the grain from 1995 E.U. field trials, there were no statistically significant differences for 16 of 18 amino acids. However, Only two amino acid values (methionine and tryptophan) were significantly higher in the control line than in MON 810. They reported that these differences measured were minor, and except for tryptophan not consistent across multiple years and geography. Tryptophan values in MON 810 corn grain were significantly higher than those in control grain from 1994 U.S. trials but significantly lower in control grain from 1995 E.U. trials. Therefore, these inconsistent differences are unlikely to be of biological significance.

In the fatty acid composition for the grain, they stated that most of the fatty acids were excluded since their quantities were almost beyond detection. There were no significant differences with the rest of the tested fatty acids.

In the mineral components, the values for phosphorus and vitamin E were within the published literature values while calcium values for both MON 810 and control line were lower than the published literature values. Calcium values were most likely influenced by phosphorus level. There was no biological significance in the difference of values since the values were within published literature values.

Furthermore, all test values of proximate were within the published literature range, except cystine, histidine, glutamic acid and calcium. The values for cystine, histidine and glutamic acid were slightly higher than the published literature range for both MON 810 and the control line. This is most likely due to differences in analytical methodology. The calcium values for both MON 810 corn and control were below the published literature range. The assessors agreed that this may be attributed to differences in analytical methods with older procedures subject to interferences from elements such as phosphorus.

The assessors agreed that the significant differences observed in Methionine, Tryptophan, Palmitic acid and Calcium in grain have no biological significance since it was within the range of historical conventional control values and/or it was not consistent across multiple-year data.

In addition, a thorough description of the anti-nutrients present in corn (seed) has been presented in the OECD Consensus Document (OECD, 2002). These anti-nutrients include phytic acid, 2,4-Dihydroxy-7-methoxy-2H-1,4-benzoxazin-3(4H)-one (DIMBOA), raffinose, and low levels of trypsin and chymotrypsin inhibitors. Neither of which is considered nutritionally significant (White and Pollak, 1995).

X and XI. THE HOST PLANT ENVIRONMENT and CONSEQUENCES OF OUTCROSSING

According to one of the assessors, maize is normally cross pollinated but it can be self-pollinated at about 5% rate. The tassel bears the pollen and is located at the top most portion of the plant. Pollen shedding can last for about 14 days. Pollen viability is affected by change in relative humidity but insensitive to solar radiation. Under certain conditions pollen will remain viable from 20 minute to 24 hours. They added that although maize is visited by insects such as honeybees, no insect pollination in corn has yet been reported. Pollination in corn is generally wind driven.

The assessors also described the potential for pollen mediated gene flow. According to the assessor, pollen mediated gene flow is a process whereby one or more genes successfully integrate into the genome of a recipient plant. Introgression is affected by both biotic and abiotic factors such as plant biology, pollen biology/volume, plant phenology, overlap of flowering times, proximity of the pollen source and sink, ambient conditions such as temperature and humidity, and field architecture. Because gene introgression is a natural biological process, it does not constitute an environmental risk in and of itself. Gene introgression must be considered in the context of the transgenes inserted into the biotechnology derived plant, and the likelihood that the presence of the transgenes and their subsequent transfer to recipient plants will result in increased plant pest potential.

According to the assessors, corn is not sexually compatible to any cultivated species in the country. Maize is sexually compatible with certain subspecies of annual teosinte. However, teosinte is not present in Philippines as it's primarily native to Mexico and Central America (OECD, 2003). However, the risk of loss of this wild species due to the development of the GM variety is very low. As maize is the product of domestication it does not have a natural habitat. Maize's closest wild relative, teosinte, is native to Mexico and Central America. Teosinte tends to thrive in areas that are seasonally dry and receive summer rain (Wilkes, 1972).

In terms of agricultural practices, the assessors reported that there is no adverse environmental impact expected from the introduction of MON 810 on current cultivation and management practices for corn. MON 810 has been shown to be no different from conventional corn in its phenotypic, ecological, and compositional characteristics. Thus, MON 810 is expected to be similar in its agronomic characteristics as in current commercial corn, except for the introduced trait of enhanced protection from feeding damage caused by lepidopteran pests.

Furthermore, the assessors stated that the genetic modification has resulted in an altered reaction to pests and/or diseases. The novel variety produces a truncated version of the insecticidal protein, Cry1Ab, derived from *Bacillus thuringiensis*. This protein is potent to the European corn borer (ECB), *Ostrinia nubilalis*. Delta-endotoxin such as Cry1Ab act by selectively binding to specific sites localized on the brush border midgut epithelium of ECB. Following binding, cation-specific pores are formed that disrupt midgut ion flow causing paralysis and death.

For the list of common associated pests and diseases of corn, the assessors reported that rusts, smuts, leaf blights, and stalk rots are among the more common diseases of microbial origin. The primary insect pests of maize belong to the orders Lepidoptera and Coleoptera. Lepidopterans feed on leaves and stalks as larvae and ears as adults. Examples include the European corn borer (*Ostrinia nubialis*), the Asian corn borer (*O. furnacalis*), the spotted stem borer (*Chillo partellus*), fall army worm (*Spodoptera frugiperda*), and members of the genus *Diatrea*. Coleopterans feed on roots and stalks as larvae and silks, pollen, and leaves as adults. Examples include the northern corn rootworm (*Diabrotica barberi*), the western corn rootworm (*D. vergifera vergifera*), and the southern corn rootworm (*D. undecimpunctata*) (Dicke and Guthrie, 1988).

XII. WEEDINESS POTENTIAL

For the known modes of dissemination of the crop, the assessors stated that under natural conditions, maize reproduces only by seed production. The dissemination of maize plants occurs exclusively through the seed, but human assistance is needed, because natural seed dispersal of kernels does not occur due to the protective structure of the ears of maize.

On the other hand, germination tests showed that all seed samples demonstrated high rates of germination, there were no differences observed between MON 810 and the control line. Thus, there is no difference in germination and dormancy between transgenic and non-modified plants.

XIII. SECONDARY AND NON-TARGET EFFECTS

For the analysis on secondary and non-target effects, the indicator species are as follows:

A. Honeybee Larvae
The assessor reported that the maximum hazard dose was used. Larvae were treated with 20 ppm of B.t.k. protein in distilled water along with control groups. Surviving larvae from the dosing to capping were counted. Also, adult survival from emergence up to the trial termination was accounted. NOEL is reported to be greater than or equal to 20 ppm. There is no significant effect on the survival of honey bee larvae.

B. Honeybee Adult
The assessor reported that the maximum hazard dose was used. Adults were treated with 20 ppm of B.t.k. protein in honey-water solution along with control groups. Adult survival were counted and observed for 30 days. NOEL is reported to be greater than or equal to 20 ppm. There is no significant effect on the survival of honey bee adult.

C. Green Lacewing larvae (*Chrysopa carnea)*, a beneficial predatory insect
The assessor reported that 20 ppm of the protein was coated into moth eggs (natural diet of green lacewing). Larvae were observed for signs of mortality. NOEL is reported to be greater than or equal to 16.7 ppm. No adverse effects were observed on Green lacewing larvae fed with moth eggs coated with B.t.k. HD-1 protein.

D. Brachymeria intermedia, a beneficial parasite of housefly, hymenoptera

The assessors cited that parasitic Hymenoptera were exposed to activated B.t.k. HD-1 protein at 20 ppm concentration in a honey-water solution. Mortality was observed for 30 days.m NOEL is reported to be greater than or equal to 20 ppm. No adverse impact on Brachymeria intermedia, a beneficial parasite of housefly.

E. Ladybird beetle (Hippodamia convergens) a beneficial predaceous insect

It was stated that the Ladybird beetle were exposed to activated B.t.k. HD-1 protein at 20 ppm concentration in a honey-water solution. Mortality was observed for 9 days. NOEL is reported to be greater than or equal to 20 ppm. No adverse impact observed on Ladybird beetles.

F. Earthworms (*Eisenia fetida*)

Two hundred milligrams of Cry1Ab protein per kilogram of soil was used as treatment. All surviving worms were counted at day 7 and 14 of the test. Worms were not fed during the duration of the test. Another set of worms were treated with chloroacetamide as a positive control. Behavior, mortality and average body weights were noted in all test and control groups. NOEL is reported to be greater than or equal 200 mg/kg dry soil. Treatment of Cry1Ab up to 200 mg/kg of soil did not affect the burrowing behavior and the over-all survival of the test organism.

G. Collembola (*Folsomia candida*)

The assessor reported that Juvenile collembola were exposed to diets amended with lyophilized MON 810 (with Cry1Ab protein) and MON 823 (without Cry1Ab protein) maize leaves in three treatment levels (50%, 5% and 0.5%). As a reference, another group was exposed to thiodicarb, an insecticide, in their diet with 5 treatment levels (10,000; 1000; 100; 10; and 1 ppm). As a negative control, another group was fed with 100% baker's yeast (natural diet of collembola). Bioactivity and stability of the protein was checked. Mortality and reproduction patterns were noted in each group. NOEL is reported to be 50.6 μg/g leaf tissue. Exposure to the leaves with Cry1Ab protein did not have any effect in the survival and reproduction of collembola, a beneficial invertebrate in soil ecosystems.

H. *Daphnia magna*, an aquatic species

The assessors cited that Daphnids were exposed to a single dose of maize pollen (100mg pollen/ liter) with and without Cry1Ab protein. Test and control substances were added directly to the well water prior to the addition of Daphnids. Test solutions were renewed daily for two days. Dead and/or immobilized Daphnids were counted during 2 hours, 24 hours and 48 hours exposure to the test solutions. NOEL is reported to be 100 mg test pollen/L. At $p>0.05$ there were no significant differences in the survival of the daphnia neonates treated with pollen with Cry1Ab protein and the controls. There is no treatment-related effects observed at the 100 mg test pollen/L limit concentration.

I. *Coleomegilla maculata, Orius insidiosus* and *Chrysoperla carnea*

The assessors reported that no acute detrimental effects were observed when the said species were exposed to pollens of plants expressing Cry1ab.

For the field study, target organism used is the Asian Corn Borer (*Ostrinia furnacalis Guenee*). The assessors reported that six sites were used during the Wet Season: Ilagan, Isabela; Cauayan, Isabela; Echague, Isabela; Sta. Maria, Pangasinan; Tigaon, Camarines Sur; and Kibawe, Bukidnon.

While for the dry season, ten sites were used: Batac, Ilocos Norte; Ilagan, Isabela; Cauayan, Isabela; Echague, Isabela; Sta. Maria, Pangasinan; Tigaon, Camarines Sur; Dangcagan, Bukidnon; Kibawe, Bukidnon; Koronadal, South Cotabato; and Tampakan, South Cotabato. The field study was reported to be conducted for 3 seasons, 1 Wet season and 2 Dry seasons during years 2000, and 2001 to 2002. Furthermore, it was cited that at selected stages of growth of corn plants, the following data were collected: leaf feeding damage, tassel breakage, borer holes, number of tunnels, tunnel lengths.

The assessors confirmed that corn MON810 performed generally similar as their isohybrid counterparts with respect to selected agronomic parameters. During the said seasons, MON810 has shown excellence resistance against natural field populations of Asiatic Corn Borer.

Furthermore, non-target organisms such as: green lacewing, spiders; coccinellid beetles; various phytopagous, neutrals, predators and parasitoids; derbid planthoppers - proutista moesta; leafhoppers – empoasca ricei; n. viresecns; n. nigropictus, coccinellids – micraspis crocea; and earthworms were used for the field study. Six sites were used during the Wet Season: Ilagan, Isabela; Cauayan, Isabela; Echague, Isabela; Sta. Maria, Pangasinan; Tigaon, Camarines Sur; and Kibawe, Bukidnon. Ten sites were used during the Dry Season: Batac, Ilocos Norte; Ilagan, Isabela; Cauayan, Isabela; Echague, Isabela; Sta. Maria, Pangasinan; Tigaon, Camarines Sur; Dangcagan, Bukidnon; Kibawe, Bukidnon; Koronadal, South Cotabato; and Tampakan, South Cotabato. The field study was done for 3 seasons, 1 Wet season and 2 Dry seasons during years 2000, and 2001 to 2002.

The assessors stated that the sampling protocols used were sweep net sampling, Erline funnel, and soil sampling. The MON 810 has no adverse impact on non-target organisms. There is no difference between the insect fauna populations in both Bt and non-Bt field. The assessors reported that based on the study, Bt corn has no difference with conventional corn in terms of the safety of the non-target organisms.

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DOH RECOMMENDATION

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 Commercial Propagation (CP) of CORN MON810. I/We,

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: unloading and loading, hauling and transport, unloading and storage, harvest and postharvest stage. 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 significant cause adverse health effects to human and animal health.
3. Dietary exposure to the regulated article is unlikely to result 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 provided references i.e. literatures show that regulated article applied for Commercial Propagation is as safe as conventional counterpart and shall not pose any significant risk to human and animal health and on the environment.
6. 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 Series 2016,
   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.
7. 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 Commercial Propagation (CP) of CORN MON810.

DENR RECOMMENDATION

After a thorough and scientific review and evaluation of the documents provided by the Bureau of Plant Industry (BPI) on the application of Monsanto Philippines, Inc. for Commercial Propagation of Corn MON810, here under are the observations:

1. Evaluation of the application and project description report (PDR) submitted by the proponent, including the scientific evidences from provided references, literature and other related studies, the Committee accepts that the commercial propagation of the regulated article will not cause any significant adverse effect on the environment (land, air and water) and on non-target organisms, to wit:

- The regulated article has a history of safe use as food and twenty-one (21) countries and as feed in eighteen (18) countries. It has also been previously approved for commercial propagation in fourteen (14) countries.
- The genetic stability in the transgenic crop over several generations is tested and ensured under contained use (2000) and field trial conditions (conducted year 2001 and 2002), such that no unintended horizontal gene transfer shall occur to unrelated species.
- The protein product produced by the transgenic crop will degrade upon exposure to the natural environment.
- Characterization of the inserted gene has shown that the protein product will not increase the weediness potential of the transgenic crop nor will it give the crop characteristics of a pollutant.
- No significant differences were observed between the regulated article and conventional corn hybrids. This indicates that MON810 has no negative effects on the corn-associated arthropod biodiversity of corn fields.
- Diversity analyses from other peer-reviewed studies observed no significant differences in the non-target arthropod diversity and insect community structure. This study also observed no differences in the earthworm population.
- The adoption of the transgenic plant in agriculture will not result in significant changes in cultivation practices that may adversely affect the environment.

The data evaluated supports the conclusion that the regulated article is as safe as its conventional counterpart.

2. The Bureau of Plant Industry (BPI) to further assist in the dissemination of information on the appropriate Insect Resistance Management (IRM) Plan for Corn MON810 for proper implementation and adherence by growers of the said crop.

The DENR-BC find scientific evidence that the regulated article applied for Commercial Propagation is as safe as its conventional counterpart, and is not expected to pose any significant risk to the environment and to non-target organisms. Any hazards and risks could be managed by the abovementioned measures. Based on the above considerations and with the proponent's sworn statement of accountability, we hereby submit our evaluation relative to Monsanto Philippines, Inc. MON810 application for biosafety permit for commercial propagation.

IRMAT

In a meeting held on November 24, 2017 at BPI Post Entry Quarantine Station, the Insect Resistance Management Advisory Team (IRMAT) reviewed the issuances related to the guidelines for the renewal of permits for commercial propagation of GM products.

The IRMAT suggested that Memorandum Circular (MC) No. 6, Series of 2004 entitled "Risk Assessment of Plants Carrying Stacked Genes for Release into the Environment" requiring the renewal of single events that has been stacked be revisited. Moreover, the committee feels that the application for renewal of **MON810 is not necessary** per provisions of MC No. 8 Series of 2013 entitled "Coverage of Biosafety Approval of Multiple-stacked Events". Thus, the permit of the stacked products should not be cancelled based on non-renewal or expiry of single/intermediate events.

Thank you very much.

SEC CONSIDERATIONS

GM corn is widely produced and consumed and is a significant component of global trade of agricultural commodities. From 2010-2013, the Philippines saved Php 60 billion (US$1.3 billion) of national corn imports by (a) planting high-yielding corn seeds on 62% of yellow corn areas and (b) using insect protection & weed management tactics. Furthermore, Philippines became an exporter of corn silage for the first time in 2013 because of increased corn productivity.

In 2014, the Bureau of Plant Industry reported an aggregated GM Corn adoption of 707,003 hectares by almost half million Filipino farmers. Since 2002, the stacked version of corn MON810 has been significantly contributing to the growing yellow corn production of the country.

The SEC expert affirmed that GM corn product will not drastically change current patterns of production, consumption/utilization and trade. While MON 810 singles is no longer being cultivated in the country, the adoption of MON810 x NK603 contributes to the increasing trend of yellow corn production in the country. By 2013, the National Corn Competitiveness Board reported that biotech corn has contributed to feedstock-supply security and helped in food self-sufficiency. Such impact in the country's Feeds industry has been significant as half of the weight of feed is contributed by yellow corn.

The availability of yellow corn as feeds material is vital to the competitiveness of the Philippine livestock and poultry sector. The "Philippine Agriculture: 2020" reports that the country is projected to have deficits of 683,000 metric tons of pork, 308,400 metric tons of broiler and 30,000 metric tons of eggs by 2020. Among other things, the MON810 x NK603 and the rest of the approved GM corn hybrids in the country can aid reduce projected deficit and minimize imports, both in livestock produce and feeds materials.

The SEC expert also concur that a socio-economic impact study of this technology on smallholder corn farmers in the Philippines from 2003-2008 revealed that MON810 and its stacked version (MON810 x NK603) registered yield advantages of up to 34% (1,298 kg/ha) over open-pollinated variety. It then explained that the main contributing factors to this yield advantage were economies of scale in corn production among average to high yielding farms and labor savings from skipping insecticide applications (and weeding operations for the stacked versions). This increase in yield, coupled with resource use efficiencies, resulted to an income advantage of up to 75% over open-pollinated seeds.

The GM corn product does not require drastic changes in farm management to attain higher yields. Good agricultural practices such as pest control (except on ACB as target pest), soil fertility, etc that would be practiced for non GM corn would be the same practices used for this GM corn. MON810 is characterized for having insect resistance. Chemical and microbial insecticide application as pest management technique against Asian Corn Borer (ACB) will be eliminated or significantly reduced due to insect resistance trait of MON810. The reduction in the use of insecticides should also reduce the threat to many beneficial insects that may in turn, suppress other insect pests. Hazards to ground water, surface water, honey bees, and farm workers brought by insecticide exposure will greatly be reduced or diminished. To optimize yield potential, farmer can employ glyphosate spray to eliminate weeds which easily compete with the crop for fertilizer, soil nutrients, sun light and other resources.

In addition, the SEC expert affirmed that GM corn does not require different farm management practices other than the elimination of extensive pesticide spray, and laborious manual weeding with its stacked corn version. Good agricultural practices such as weed control, soil fertility, etc. that would be practiced for non-GM corn would be the same practices used for this GM corn. For the stacked version, farmer can employ glyphosate spray to eliminate weeds which easily compete with the crop for fertilizer, soil nutrients, sun light and other resources.

This GM corn product potentially decreases the cost of production. In the Philippines, a Monsanto Survey on Farmer Practice during 2009 Dry Season and 2010 Wet Season confirmed that replacement cost for ACB insecticide and labor is valued at P2,000 per hectare compared to non-Bt corn farms. This result is consistent with the STRIVE Foundation study where average cost savings of using stacked corn seeds in terms of pesticide application including weeding costs (manual weeding) compared to non-Bt seeds was P1,984/ha during the wet season and P1,866/ha during the dry season.

There is no standard cost of a GM corn hybrid. Cost of seed varies with specific GM hybrids, much the same as the cost of a non-GM corn hybrid varies depending on the value of the specific hybrid. A market survey by STRIVE Foundation in 2003-2008 found that MON 810 corn was around 40% more expensive than open pollinated corn. While it was understandably more expensive due to its insect resistance trait, it was with the same reason that 49-57% of farmers who were yet to plant Bt Corn indicated pesticide reduction –related statements as their major reason for adopting.

Studies from many countries confirm that this GM corn increases farm yield and contributes to greater efficiency in the use of land, water, fertilizer, pesticide and energy. In the Philippines, a study by STRIVE Foundation analyzed data from corn production in nine major corn producing provinces for six growing seasons and concluded that genetically improved corn hybrids (MON 810 and MON 810 x NK603 included) provided superior performance compared to non-genetically engineered corn hybrids in terms of yield, farm production cost, net farm income, subsistence level carrying capacity, global competitiveness and return on investment.

MON810 has consistently improved farmer profitability compared to non-GM corn in numerous studies around the world. Corn MON810 with its insect resistance traits brings forth positive impact to farmers' income derived from the enhanced productivity and efficiency gains. MON 810 users achieved superior performances over conventional seeds in terms of yield, farm production cost, net farm income, subsistence level carrying capacity, global competitiveness, and return on investment indicators.

Studies from many countries confirm that this GM corn increases farm yield and contributes to greater efficiency in the use of land, water, fertilizer, pesticide and energy. In the Philippines, a study by STRIVE Foundation analyzed data on corn production in nine major corn producing provinces for six growing seasons and concluded that genetically improved corn hybrids (MON 810 and MON 810 x NK603 included) provided superior performance compared to non-genetically engineered corn hybrids in terms of yield, farm production cost, net farm income, subsistence level carrying capacity, global competitiveness and return on investment. This has impacted positively the competitiveness of the small scale farmers in many areas.

A collaborative study of ISAAA, SEARCA and UPLB-CDC on adoption and uptake pathway of GM crops in the Philippines reveals that significant increase in farmers' income can be attributed to GM corn adoption which consequently resulted to changes in several aspects of their lives including their capacity to pay loans and debts, send children to school, acquire home appliances, support other relatives, make farming activities easier and simpler, and engage in other livelihood sources.

After a thorough and scientific review and evaluation of the documents provided by MONSANTO (technology developer) relevant to Corn MON 810 (YieldGard Corn) (transformation event).

I recommend for the approval and issuance of biosafety permit of the said GM product.

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