FACT SHEET

APPLICATION FOR APPROVAL FOR RELEASE OF PRODUCTS OF MON 95379 MAIZE FOR SUPPLY OR OFFER TO SUPPLY FOR SALE OR PLACING IN THE MARKET

NBB REF NO: JBK(S) 600-2/1/25

The objective of the Biosafety Act 2007 is to protect human, plant and animal health, the environment and biological diversity. Under the Biosafety Act 2007, the National Biosafety Board (NBB) is currently assessing an application for approval submitted by Bayer Co. (Malaysia) Sdn. Bhd.

1. What is the application for?

This application is to import and release MON 95379 maize and its products. The application does not cover deliberate environmental release (i.e. cultivation) in Malaysia.

2. What is the purpose of the import and release?

The purpose of the import and release is to supply or offer for sale/ placing on the market-for direct use as food, feed and for processing (FFP) of MON 95379 maize. This means that MON 95379 maize may enter Malaysia as grain, food ingredients for processing or packaging or as finished products ready for distribution, or as feed meal for animals. The MON 95379 maize is not intended for cultivation in Malaysia.

3. How has MON 95379 maize been modified?

Genetically modified MON 95379 maize was produced by insertion of *cry1B.868* and *cry1Da_7* genes from *Bacillus thuringiensis* (*B.t.*) into the genome of conventional maize using *Agrobacterium*-mediated transformation method. MON 95379 maize produces Cry1B.868 and Cry1Da_7 insecticidal crystal (Cry) proteins that protect against feeding damage caused by targeted lepidopteran insect pests.

4. Characteristics of MON 95379 maize

a. Details of the parent organism

The recipient or parental plant is *Zea mays* (maize), also known as corn. Maize has been a staple of the human diet for centuries and is grown in nearly all areas of the globe. It is the largest cultivated crop in the world followed by wheat (*Triticum* sp.) and rice (*Oryza sativa* L.) in total global metric ton production (FAOSTAT, 2020[1]). However, unlike wheat and rice, the majority of maize produced is consumed as animal feed in the form of grain, forage, or silage.

[1] FAOSTAT. 2020. Food and Agricultural Organization statistical database. Food and Agricultural Organization of the United Nations, Rome, Italy. http://www.fao.org/faostat/en/#data/QC [Accessed June 03, 2020].

b. Donor organism

Characteristics of *Bacillus thuringiensis*

The origin of the *cry1B.868* and *cry1Da_7* genes is from *Bacillus thuringiensis* (*B.t.)*, which is a common soil bacteria*.* Applications of sporulated *B.t.* have a long history of safe use for pest control in agriculture, especially in organic farming. Several different *Bt* subspecies have been subjected to toxicity testing and showed no evidence for adverse effects on human health (Baum *et al.*, 1999; Betz *et al.*, 2000; Federici and Siegel, 2008; Hammond, 2004; McClintock et al., 1995; Mendelsohn et al., 2003; Siegel, 2001; U.S. EPA, 1986; 2001). Additionally, microbial pesticides containing *B.t.* Cry proteins have been subjected to extensive toxicity testing showing no adverse effects to human or animal health (Koch et al., 2015; Moar et al., 2017; OECD, 2010a). There are no confirmed cases of allergic reactions to Cry proteins in microbial-derived *B.t.* products during more than 50 years of use (Hammond, 2004; OECD, 2010b).

c. Description of the trait(s) and characteristics which have been introduced or modified

MON 95379 maize contains *cry1B.868* and *cry1Da_7* genes derived from *Bacillus thuringiensis* that expresses Cry1B.868 and Cry1Da_7 proteins that provides protection against the feeding damage of targeted lepidopteran pests, including Fall Armyworm (FAW; *Spodoptera frugiperda*), sugarcane borer (SCB; *Diatraea saccharalis*) and corn earworm (CEW; *Helicoverpa zea*).

d. Safety of the expressed proteins

Cry1B.868 is a chimeric protein comprised of domains I and II from Cry1Be (*Bacillus thuringiensis*, Bt), domain III from Cry1Ca (*Bt subsp. aizawai*) and C-terminal protoxin domain from Cry1Ab (*Bt subsp. kurstaki*). *Cry1Da_7* is a modified Cry1Da protein derived from *Bt subsp. azawai.* Information and data from studies demonstrate that the Cry1B.868 and Cry1Da_7 proteins are unlikely to be allergens or toxins. This is based on the assessment of the donor organism, *Bacillus thuringiensis* which is not a known human or animal pathogen and have lack of reports of allergies derived from the organism. Additionally, there are no confirmed cases of allergic reactions to Cry proteins in microbial-derived *B. thuringiensis* products during more than 50 years of use (U.S. EPA, 1988; Hammond, 2004; Koch *et al.,* 2015; McClintock *et al.,* 1995). Bioinformatics was used to compare the Cry1B.868 and Cry1Da_7 amino acid sequences against known allergens and toxins and the results showed a lack of significant structural similarity between the Cry1B.868 and Cry1Da_7 proteins and known allergens or toxins (Skottke and Silvanovich, 2021). In addition, studies using the Cry1B.868 and Cry1Da_7 proteins have demonstrated that the proteins were digested rapidly in simulated digestive fluids (Bretsnyder and Wang, 2000; Calcaterra and Wang, 2019), and ingestion of the proteins did not cause acute toxicity in mice (Good, 2019; Good, 2020). These data support the safety for Cry1B.868 and Cry1Da_7 proteins. Detailed safety studies of the expressed proteins information can be obtained from the Department of Biosafety.

e. Utilization of maize

Maize has been a staple of the human diet for centuries, and its processed fractions are consumed in a multitude of food and animal feed products.

Maize is grown globally and is the largest grain crop in the world in total metric ton production, ahead of both wheat (*Triticum sp*.) and rice (*Oryza sativa L*.) (FAOSTAT, 2020). In the 2019/2020 marketing year, world maize area was approximately 192 million hectares (USDA-FAS, 2020).

Food uses of maize include processed products from field maize and direct consumption of sweet maize and popcorn. Food products derived from the wet milling process include starch and sweetener products (e.g., high fructose maize syrup) (May, 1987). Food products derived from the dry milling process include maize grits, maize meal, and maize flour (Watson, 1988). Maize oil may be derived from both wet and dry milling processes (Watson, 1988).

Maize is used extensively as a livestock feed for reasons that include its palatability, digestibility, and metabolizable energy (Loy and Lundy, 2019) and its relatively low cost (OECD, 2002). Animal feed products include maize gluten feed, maize gluten meal, and hominy feed (Loy and Lundy, 2019). Ethanol production from dry milled maize provides distillers grains, another source of animal feed (Loy and Lundy, 2019). Maize can also be fed as a whole plant silage.

MON 95379 maize may enter Malaysia as grain, food ingredients for processing or packaging or as finished products ready for distribution, or as feed meal for animals.

5. Assessment of risks to human health

a. Nutritional data

Data obtained from compositional analyses conducted on the grain and forage of MON 95379 maize showed that there were no statistically significant differences in 43 of the 61 comparisons made between MON 95379 and conventional control. The mean values for the 18 components that showed statistically significant difference between MON 95379 and the conventional control were found to be within the natural variability of these components as published in scientific literature and/or the ILSI Crop Composition Database (ILSI-CCDB)(Bedair *et al,* 2019). Therefore, these statistically significant differences are not considered biologically relevant. This data supports the statement that MON 95379 maize is compositionally equivalent to conventional maize. Detailed MON 95379 maize composition analysis information can be obtained from the Department of Biosafety.

b. Toxicological information

There are no known health hazards associated with the product. Studies conducted using the Cry1B.868 and Cry1Da_7 proteins produced in MON 95379 have shown no toxicity toward mammals (Good, 2019; Good, 2020). Additionally, there are no amino acid sequences

similarities of MON 95379 maize to known toxins (Skottke and Silvanovich, 2021). Detailed MON 95379 maize toxicology information can be obtained from the Department of Biosafety.

c. Pathogenicity

Bacillus thuringiensis is not a known human or animal pathogen and there are no knownreports of allergies derived from the organism (Hammond, 2004; OECD, 2010b).

d. Allergenicity

The Codex guidelines for the evaluation of the allergenicity potential of introduced proteins (Codex Alimentarius, 2009) are based on the comparison of amino acid sequences between introduced proteins and allergens, where allergenic cross-reactivity may exist if the introduced protein is found to have at least 35% amino acid identity with an allergen over any segment of at least 80 amino acids.The bioinformatic results demonstrated there were no biologically relevant sequence similarities to allergens when the Cry1B.868 and Cry1Da_7 proteins sequences were used as a query for a FASTA search of the AD_2020 database. Furthermore, no short (eight amino acid) polypeptide matches were shared between the Cry1B.868 and Cry1Da_7 proteins sequences and proteins in the allergen database. These data show that Cry1B.868 and Cry1Da_7 proteins sequences lacks both structurally and immunologically relevant similarities to known allergens, gliadins, and glutenins. Detailed MON 95379 maize allergenicity information can be obtained from the Department of Biosafety.

6. Assessment of risks to the environment

The application does not cover an environmental release. The application is intended only to cover the import of MON 95379 maize products from countries where maize is already approved and commercially grown, and that may enter Malaysia as grain, food ingredients for processing or packaging or as finished products ready for distribution, or as feed meal for animals. Thus, the potential exposure to the environment is limited to spillage events. On environmental risk assessment of genetically engineered (GE) plants under low-exposure conditions, the loss of imported seeds are most likely to occur near ports or along roads from ports to manufacturing sites (Roberts *et al.,* 2014). Most of the spilled seeds are unlikely to survive for long outside intentional cultivation by the following limiting factors:

i) Seeds not encountering conditions favorable for germination;
ii) The plants germinated in the areas which are often managed (e.g. mowing, cleaning);
iii) Poor competitive ability with native vegetation, maize is not an indigenous species (OECD, 2000), and is not a major economic crop in Malaysia.

Therefore, MON 95379 maize is unlikely to germinate and establish upon accidental spillage in Malaysia.

7. What is the emergency response plan?

MON 95379 maize and food and feed products derived from it have been assessed as being as safe as its conventional non-genetically modified counterparts. Should adverse effects be reported and verified, appropriate follow up action would be taken to investigate these, and if verified, appropriate actions taken.

a. First aid measures

No special first aid measures are required in response for exposure to this product.

b. Accidental release measures

No special measures are required in response to an accidental release. Spilled seeds should be swept, scooped or vacuumed in a manner that avoids dust generation and dust-related hazards.

c. Handling and storage

No special handling and storage procedures are required for this product. MON 95379 maize and its products may be handled and stored as any conventional maize products.

d. Disposal considerations

The same measures for waste disposal and treatment as for conventional maize are valid for MON 95379 maize.

8. How can I comment on this application?

Any member of the public may submit their comments or queries on publicly notified information about the application. Before submission of comments or queries, the person should review the information provided in this Fact Sheet. Your comments or queries on any possible impacts/risks to the health and safety of the people and the environment that may be posed by the proposed release are appreciated. The submission of the comments or queries should be prepared carefully to express your concerns. Even if the submission is not science-based, and focuses on cultural or other values, it should still be developed in the form of a well-founded argument. The submission of comments and clarifications of queries should contribute to the NBB's assessment. Your submission will be given the same scrutiny as the application by the NBB.

Please note that the consultation period closes on 3 May 2022 and written submissions are required before/by that date. Submissions must be addressed to:

Director General,
Department of Biosafe
Ministry of Environment and Water
Level 4, Block F11, Complex F
Lebuh Perdana Timur, Precinct 1
Federal Government Administrative Centre
62000 Putrajaya, MALAYSIA
E-mail: dob@biosafety.gov.my

Please include your full name, address and contact details in your submission.

References

Baum, J.A., T.B. Johnson and B.C. Carlton. 1999. *Bacillus thuringiensis:* Natural and recombinant bioinsecticide products. Pages 189-209 in Methods in Biotechnology: Biopesticides: Use and Delivery. Volume 5. F.R. Hall and J.J. Menn (eds.). Humana Press Inc., Totowa, New Jersey.

Bedair, M.F., J.M. Helm and C. Meng.2019. Amended Report for MSL0029995: Compositional Analyses of Maize Grain and Forage Harvested from MON 95379 Grown in the United States During the 2018 Season. MSL0030947. Monsanto Company.

Betz, F.S., B.G. Hammond and R.L. Fuchs. 2000. Safety and advantages of *Bacillus thuringiensis*-protected plants to control insect pests. Regulatory Toxicology and Pharmacology 32:156-173.

Bretsnyder, E. and R. Wang. 2020. Amended Report for MSL0030730: Assessment of the in vitro Digestibility of Cry1B.868 Protein by Pepsin and Pancreatin. TRR0000667. Bayer CropScience LP.

Calcaterra J. and R. Wang. 2019. Assessment of the in vitro Digestibility of Cry1Da_7 Protein by Pepsin and Pancreatin. MSL0030568. Monsanto Company.

Codex Alimentarius. 2009. Foods derived from modern biotechnology. Second Edition. Codex Alimentarius Commission, Joint FAO/WHO Food Standards Programme, Food and Agriculture Organization of the United Nations, Rome, Italy.

FAOSTAT. 2020. Food and Agricultural Organization statistical database. Food and Agricultural Organization of the United Nations, Rome, Italy. http://www.fao.org/faostat/en/#data/QC [Accessed June 03, 2020].

Federici, B.A. and J.P. Siegel. 2008. Safety assessment of *Bacillus thuringiensis* and Bt crops used in insect control. Pages 45-102 in Food Safety of Proteins in Agricultural Biotechnology. B.G. Hammond (ed.). CRC Press, Boca Raton, Florida.

Good, N.A. 2019. An Acute Oral Gavage Toxicity Study of Cry1B.868 Protein in CD-1 Mice. MSL0030740. Monsanto Company.

Good, N.A. 2020. An Acute Oral Gavage Toxicity Study of Cry1Da_7 Protein in CD-1 Mice. MSL0030741. Monsanto Company.

Hammond, B. 2004. A review of the food/feed safety and benefits of *Bacillus thuringiensis* protein containing insect-protected crops. Pages 103-123 in ACS Symposium, American Chemical Society, Washington, D.C.

Koch, M.S., J.M. Ward, S.L. Levine, J.A. Baum, J.L. Vicini and B.G. Hammond. 2015. The food and environmental safety of *Bt* crops. Frontiers in Plant Science 6:283.

Landin, K.L. 2017. Amended from MSL0027647: An Acute Oral Gavage Toxicity Study of Cry51Aa2.834_16 Protein in CD-1 Mice. MSL0028578. Monsanto Company.

Loy, D.D. and E.L. Lundy. 2019. Nutritional properties and feeding value of corn and its coproducts. Pages 633-659 in Corn: Chemistry and Technology. Third Edition. S.O. Serna-Saldivar (ed.). Woodhead Publishing and AACC International Press.

May, J.B. 1987. Wet milling: Process and products. Pages 377-397 in Corn: Chemistry and Technology. S.A. Watson and P.E. Ramstad (eds.). American Association of Cereal Chemists, St. Paul, Minnesota.

McClintock, J.T., C.R. Schaffer and R.D. Sjoblad. 1995. A comparative review of the mammalian toxicity of *Bacillus thuringiensis*-based pesticides. Pesticide Science 45:95-105.

Mendelsohn, M., J. Kough, Z. Vaituzis and K. Matthews. 2003. Are *Bt* crops safe? Nature Biotechnology 21:1003-1009.

Moar, W.J., A.J. Evans, C.R. Kessenich, J.A. Baum, D.J. Bowen, T.C. Edrington, J.A. Haas, J.-L.K. Kouadio, J.K. Roberts, A. Silvanovich, Y. Yin, B.E. Weiner, K.C. Glenn and M.L. Odegaard. 2017. The sequence, structural, and functional diversity within a protein family and implications for specificity and safety: The case for ETX_MTX2 insecticidal proteins. Journal of Invertebrate Pathology 142:50-59.

OECD. 2000. Report of the task force for the safety of novel foods and feeds. C(2000)86/ADD1. Organisation of Economic Co-operation and Development, Paris, France.

OECD. 2002. Consensus document on compositional considerations for new varieties of maize (*Zea mays*): Key food and feed nutrients, anti-nutrients and secondary plant metabolites. ENV/JM/MONO(2002)25. Series on the Safety of Novel Foods and Feeds, No. 6. Organisation for Economic Co-operation and Development, Paris, France.

OECD. 2010a. Section 1. Cotton (*Gossypium* spp.). Pages 40-83 in Safety Assessment of Transgenic Organisms. Volume 4. Organisation for Economic Co-operation and Development, Paris, France.

OECD. 2010b. Human health assessment. Pages 234-237 in Safety Assessment of Transgenic Organisms. Volume 3. Organisation for Economic Co-operation and Development, Paris, France.

Roberts, A., Y. Devos, A. Raybould, P. Bigelow and A. Gray. 2014. Environmental risk assessment of GE plants under low-exposure conditions. Transgenic Research 23:971-983.

Siegel, J.P. 2001. The mammalian safety of *Bacillus thuringiensis*-based insecticides. Journal of Invertebrate Pathology 77:13-21.

Skottke, K. and A. Silvanovich. 2021. Amended From TRR0000118: Updated Bioinformatics Evaluation of Cry1Da_7 and Cry1B.868 in MON 95379 Utilizing the AD_2020, TOX_2020, and PRT_2020 Databases. TRR0001041. Bayer CropScience LP.

U.S. EPA. 1986. *Bacillus thuringiensis* - Fact Sheet 9/86. U.S. Environmental Protection Agency, Washington, D.C.

U.S. EPA. 1988. Guidance for the reregistration of pesticide products containing *Bacillus thuringiensis* as the active ingredient. 540/RS-89-023. U.S. Environmental Protection Agency, Washington, D.C.

USDA-FAS. 2020. World agricultural production. U.S. Department of Agriculture, Foreign Agricultural Service, Washington, D.C.
https://apps.fas.usda.gov/psdonline/circulars/production.pdf [Accessed June 03, 2020].

Watson, S.A. 1988. Corn marketing, processing, and utilization. Pages 881-940 in Corn and Corn Improvement. Third Edition. G.F. Sprague and J.W. Dudley (eds.). American Society of Agronomy, Inc., Crop Science Society of America, Inc., Soil Science Society of America, Inc., Madison, Wisconsin.