RISK ASSESSMENT REPORT

OF THE GENETIC MODIFICATION ADVISORY COMMITTEE (GMAC)

FOR

AN APPLICATION FOR APPROVAL FOR RELEASE OF PRODUCTS OF

MON94100 CANOLA FOR SUPPLY OR OFFER TO SUPPLY

NBB REF NO: JBK(S) 600-2/1/26

APPLICANT: BAYER CO. (MALAYSIA) SDN. BHD.

DATE: 29 SEPTEMBER 2022

I - Summary of Assessment Process

On 14 July 2022, the Genetic Modification Advisory Committee (GMAC, please refer to Appendix 1 for details of GMAC), received from the Department of Biosafety an application for the approval for importation for release [sale/placing on the market for direct use as food, feed and for processing (FFP)] of a product of a Living Modified Organism herbicide tolerant MON94100 canola. The application was filed by Bayer. Co. (Malaysia) Sdn. Bhd. (hereafter referred to as "the applicant"). After an initial review, GMAC requested for additional information from the applicant.

A public consultation for this application was conducted from 4 April 2022 to 3 May 2022 via advertisements in the local newspapers, e-mail announcements and social media. Comments were received from Consumers Association of Penang (CAP). GMAC took note of the possibility of this event being combined with other herbicide resistant crops.

GMAC had four (4) meetings pertaining to this application and prepared the Risk Assessment Report and Risk Assessment Matrix along with its recommended decision, for consideration by the National Biosafety Board.

II - Background of Application

This application is for approval to import and release products of a Living Modified Organism herbicide tolerant MON94100 canola. The aim of the import and release is to supply or offer to supply for sale/placing on the market for direct use as food, feed and for processing (FFP). According to the applicant, MON94100 canola has been approved in a few countries for food, feed and for processing. MON94100 canola is approved in the Australia, Canada, Japan, and New Zealand and may be imported, stored and processed for use in food, animal feed and industrial products in the same way as other conventional, non-transgenic canola. The type of expected use of the products derived from MON94100 canola in Malaysia will be the same as the expected usage for products derived from conventional canola.

Canola is primarily grown for its seed oil, which is used as a cooking oil and for other food and industrial applications. The seed meal which remains after oil extraction is used as animal feed. The term canola refers to varieties of *B. napus* that contain less than 2% erucic acid in the oil and less than 30 µmoles/g of glucosinolates in the seed meal, so are considered suitable for human and animal consumption.

Information about MON94100 canola

Genetically modified MON94100 canola was produced by insertion of *dmo* gene from *Stenotrophomonas maltophilia* strain DI-6 into the genome of conventional canola using *Agrobacterium tumefaciens* mediated transformation method. MON94100 canola produces a

dicamba mono-oxygenase (DMO) protein to confer tolerance to dicamba (3,6-dichloro-2-methoxybenzoic acid) herbicide.

III - Risk Assessment and Risk Management Plan

GMAC evaluated the application with reference to the following documents:

(i) CODEX Guideline for the Conduct of Food Safety Assessment of Foods Derived from Recombinant-DNA Plants

(ii) Roadmap for Risk Assessment of Living Modified Organisms, (according to Annex III of the Cartagena Protocol on Biosafety produced by the *Ad Hoc* Technical Expert Group (AHTEG) on Risk Assessment and Risk Management of the Convention on Biological Diversity)

(iii) The risk assessment and risk management plan submitted by the applicant

GMAC also referred to the following recommendations within the AHTEG guidelines:

(i) That the risk assessment exercise be specific to the details of this particular application

(ii) That the risk assessment exercise be specific to the receiving environment in question

(iii) That any risk identified be compared against that posed by the unmodified organism.

In conducting the risk assessment, GMAC identified potential hazards, and then added a value/rank for the likelihood of each hazard as well as its consequences. The likelihood of each hazard occurring was evaluated qualitatively on a scale of 1 to 4, with 1 for 'highly unlikely', and 4 for 'highly likely'. The consequences of each hazard, if it were to occur, were then evaluated on a scale of 1 to 4, with 1 for 'marginal' and 4 to denote a 'major consequence'. A value was finally assigned for the overall risk from the identified potential hazard. The general formula: Overall Risk = Likelihood x Consequence was employed. GMAC also proposed risk management strategies for potential hazards, where appropriate. This methodology of assessment follows the procedure of Risk Assessment in Annex III of the Cartagena Protocol on Biosafety.

The potential hazards were identified in three main areas:

(i) **<u>Effects on human health</u>**

Relevant scientific publications on the genetic modifications were reviewed for potential human health risks and issues pertaining to acute toxicity of novel protein / altering / interference of metabolic pathways, potential allergenicity of the novel protein, reproductive toxicity, potential transfer of antibiotic resistance genes in

digestive tract, pathogenic potential of donor microorganisms, nutritional equivalence and anti-nutritional properties.

(ii) **Effects on animal health**

Relevant scientific publications on the genetic modifications were reviewed for potential animal health risks and issues pertaining to allergenicity, toxicity, survivability and animal product contamination.

(iii) **Effects on the environment**

Relevant scientific publications on the genetic modifications were reviewed for potential environmental risks and issues pertaining to accidental release of seeds, unintentional release and planting, potential of transgenes being transferred to bacteria (soil bacteria, bacterial flora of animal gut), increased fitness, weediness and invasiveness, accumulation of the protein in the environment via feces from animals fed with the GM plant/seed and cross pollination leading to transfer of transgenes.

Based on the above, a final list of 20 potential hazards was identified. Most of these hazards were rated as having an Overall Risk of 1 or “negligible”.

GMAC also took caution and discussed a few of the hazards that required further evaluation and data acquisition. Some of these risks are expected to be managed effectively with the risk management strategies proposed (please refer to section IV of this document).

Some of the potential hazards are highlighted below along with the appropriate management strategies:

a) Accidental release of viable seeds

Seeds may be accidentally released during transportation. These seeds can germinate and grow along transportation routes and in areas surrounding storage and processing facilities. Transportation of the consignment must be in secured and closed conditions. Any spillage shall be collected and cleaned up immediately. Canola is not grown as an economic crop in Malaysia, thus, there is no issue of outcrossing.

b) Planting of seeds

Plants may be grown by uninformed farmers and perpetuated through small scale cultivations. There should also be clear labeling of the product to state that it is only for the purpose of food, feed and processing, and is not to be used as planting material.

c) Nutritional equivalence

The compositional analyses of MON94100 showed no statistically significant differences ($p<0.05$) for 44 of the 45 components analyzed from MON94100 grain. There was one component (sinapine) that showed a statistically significant difference between MON94100 and the conventional control. However, the mean difference between MON94100 and the conventional control was less than the conventional control range and the MON94100 mean component value was also within the range of values observed in the ILSI-CCDB values (Taylor *et al.*, 2020). Therefore, the nutritional quality of MON94100 canola seeds is comparable to conventional canola varieties.

However, applicant is required to update the National Biosafety Board immediately if additional tests indicate potential adverse effects or the possible presence of toxin or allergenic proteins.

IV - Proposed Terms and Conditions for Certificate of Approval

Based on the 20 potential hazards identified and assessed, GMAC has drawn up the following terms and conditions to be included in the certificate of approval for the release of this product:

a) There shall be clear documentation by the exporter describing the product which shall be declared to the Royal Malaysian Customs.

b) There shall be clear labeling of the product from importation to all levels of marketing stating that it is only for the purpose of food, feed and processing, and is not to be used as planting material.

c) Should the approved person receive any credible and/or scientifically proven information that indicates any adverse effect of MON94100 canola, the National Biosafety Board shall be informed immediately.

d) Any spillage (during loading/unloading/transportation) shall be collected and cleaned up immediately.

e) Transportation of the consignment from the port of entry to any destination within the country shall be in secured and closed conditions.

f) Any import or release of products derived from any new genetically modified lines bred using MON94100 canola will require a separate approval from the National Biosafety Board.

V - Other Regulatory Considerations

a) Administrative regulatory procedures shall be arranged between the Department of Biosafety, Royal Malaysian Customs Department and relevant agencies to ensure accurate declaration of product information and clear labeling of the product is implemented.

b) Administrative regulatory procedures shall be arranged between the Department of Biosafety and the Malaysian Quarantine and Inspection Services (MAQIS) to impose post entry requirements for accidental spillage involving the GM product.

c) Administrative regulatory procedures shall be arranged between the Department of Biosafety and the Malaysian Quarantine and Inspection Services (MAQIS) and other competent agencies to impose post entry requirements for food safety compliance.

d) Administrative regulatory arrangements shall be carried out between the Department of Biosafety and the Department of Veterinary Services (DVS) so that any unanticipated adverse effects in animals caused by any consumption of the GM products shall be reported immediately.

e) Administrative regulatory arrangements shall be carried out by Food Safety and Quality of Ministry of Health to monitor compliance to the Food Act 1983 and Food Regulations 1985.

f) Administrative regulatory procedures shall be arranged between Department of Biosafety and Ministry of Health to ensure that herbicide residues in canola consignments are below the acceptable maximum residual level established.

VI - Identification of issues to be addressed for long term use release of this product

a) Continuous monitoring is required from the approved person and any unanticipated adverse effect caused by MON94100 canola shall be reported to the National Biosafety Board.

VII –Conclusion and Recommendation

GMAC has conducted a thorough evaluation of the application for approval for importation for release [sale/placing on the market for direct use as food, feed and for processing (FFP)] of a product of a Living Modified Organism herbicide tolerant MON94100 canola and has determined that the release of this product does not endanger biological diversity or human, animal and plant health. GMAC recommends that the proposed application for release be **APPROVED WITH TERMS AND CONDITIONS** as listed in section IV - Proposed Terms and Conditions for Certificate of Approval.

VIII - Bibliography

1. An, S.-q. and G. Berg. 2018. Stenotrophomonas maltophilia. Trends in Microbiology 26:637-638.
2. Berg, G. and J.L. Martinez. 2015 Friends or foes: can we make a distinction between beneficial and harmful strains of the Stenotrophomonas maltophilia complex? Front. Microbiol. 6:241.
3. Brooke JS, Di Bonaventura G, Berg G and Martinez J-L (2017) Editorial: A Multidisciplinary Look at Stenotrophomonas maltophilia: An Emerging Multi-Drug-Resistant Global Opportunistic Pathogen. Front. Microbiol. 8:1511.
4. Burge, J.J., L.A. Burzio, and J.J. Finnessy. 2010. Assessment of the in vitro Digestibility of the Dicamba Mono-Oxygenase (DMO) Enzyme in Simulated Gastric and Simulated Intestinal Fluids. Monsanto Technical Report MSL0022502. St. Louis, Missouri
5. Crawley, M.J., S.L. Brown, R.S. Hails, D.D. Koh and M. Rees. 2001. Transgenic crops in natural habitats. Nature 409:682-683.
6. Dong, H., C. Zhu, J. Chen, X. Ye and Y.-P. Huang. 2015. Antibacterial activity of Stenotrophomonas maltophilia endolysin P28 against both gram-positive and gram-negative bacteria. Frontiers in Microbiology 6:1299.
7. FAO-WHO. 2001. Evaluation of allergenicity of genetically modified foods. Report of a joint FAO/WHO expert consultation on allergenicity of foods derived from biotechnology. Food and Agriculture Organization of the United Nations, Rome, Italy.
8. Ferraro, D.J., L. Gakhar and S. Ramaswamy. 2005. Rieske business: Structure–function of Rieske non-heme oxygenases. Biochemical and Biophysical Research Communications 338 (2005) 175–190
9. Gu, X. 2021. Updated Bioinformatics Evaluation of CP4 EPSPS Utilizing the AD_2021, TOX_2021, and PRT_2021 Databases. TRR0000766. Bayer CropScience LP.
10. Harayama S and M. Kok. 1992. Functional and Evolutionary Relationships among diverse oxygenases. Annual Review Microbiology 46: 565-601
11. Heller, D., E.J. Helmerhorst, A.C. Gower, W.L. Siqueira, B.J. Paster and F.G. Oppenheim. 2016. Microbial diversity in the early in vivo-formed dental biofilm. Applied and Environmental Microbiology 82:1881-1888.
12. Herman, P.L., M. Behrens, S. Chakraborty, B.M. Chrastil, J. Barycki and D.P. Weeks. 2005. A three-component dicamba O-demethylase from Pseudomonas maltophilia, strain DI-6: Gene isolation, characterization, and heterologous expression. The Journal of Biological Chemistry 280:24759-24767.
13. Krueger, J.P., R.G. Butz, Y.H. Atallah and D.J. Cork. 1989. Isolation and identification of microorganisms for the degradation of dicamba. Journal of Agricultural and Food Chemistry 37:534-538.
14. Lira, F., G. Berg and J.L. Martínez. 2017. Double-face meets the bacterial world: The opportunistic pathogen Stenotrophomonas maltophilia. Frontiers in Microbiology 8:2190.

15. Martín-Hernández, C., S. Bénet and L. Obert. 2008. Determination of proteins in refined and nonrefined oils. Journal of Agricultural and Food Chemistry 56:4348-4351.
16. Mozaffar, S. 2019. Amended from MSL0030665. Assessment of DMO Protein Levels in Treated Canola Tissues Collected from MON 94100 Produced in United States and Canadian Field Trials During 2018. Monsanto Technical Report MSL0030937. Chesterfield, Missouri.
17. Mukherjee, P. and P. Roy. 2016. Genomic potential of Stenotrophomonas maltophilia in bioremediation with an assessment of its multifaceted role in our environment. Frontiers in Microbiology 7:967.
18. OECD. 1997. Consensus document on the biology of Brassica napus L. (oilseed rape). OCDE/GD(97)63. Series on Harmonization of Regulatory Oversight in Biotechnology No. 7. Organisation for Economic Co-operation and Development, Paris, France.
19. 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.
20. OECD. 2011. Revised consensus document on compositional considerations for new varieties of low erucic acid rapeseed (canola): Key food and feed nutrients, anti-nutrients and toxicants. ENV/JM/MONO(2011)55. Organisation for Economic Co-operation and Development, Paris, France.
21. OGTR. 2011. The biology of Brassica napus L. (canola). Australian Government, Department of Health and Ageing, Office of the Gene Technology Regulator, Canberra, Australia.
22. Okuno, N.T., I.R. Freire, R.T.R.S. Segundo, C.R. Silva and V.A. Marin. 2018. Polymerase chain reaction assay for detection of Stenotrophomonas maltophilia in cheese samples based on the smeT gene. Current Microbiology 75:1555-1559.
23. Palleroni, N.J. and J.F. Bradbury. 1993. Stenotrophomonas, a new bacterial genus for Xanthornonas maltophilia (Hugh 1980) Swings et al. 1983. International Journal of Systematic Bacteriology 43:606-609.
24. Raybould, A., G. Graser, K. Hill and K. Ward. 2012. Ecological risk assessments for transgenic crops with combined insect-resistance traits: The example of Bt11 x MIR604 maize. Journal of Applied Entomology 136:27-37.
25. Rantio-Lehtimäki, A. 1995. Aerobiology of pollen and pollen antigens. Pages 387-406 in Bioaerosols Handbook. C.S. Cox and C.M. Wathes (eds.). CRC Press, Inc., Boca Raton, Florida.
26. 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.
27. Scheffler, J.A., R. Parkinson and P.J. Dale. 1993. Frequency and distance of pollen dispersal from transgenic oilseed rape (Brassica napus). Transgenic Research 2:356-364.
28. Schimdt, C.L. and L. Shaw. 2001.A Comprehensive Phylogenetic Analysis of Rieske and Rieske-Type Iron-Sulfur Proteins. Journal of Bioenergetics and Biomembranes, Vol. 33, No. 1, 2001
29. Smedley J.W. 2010. An Acute Toxicity Study of Dicamba Mono-Oxygenase (DMO) Enzyme from MON 87708 Administered by Oral Gavage to Mice. Monsanto Technical Report CRO-09-419. St. Louis, Missouri.

30. Tamis, W.L.M. and T.J. de Jong. 2010. Transport chains and seed spillage of potential GM crops with wild relatives in the Netherlands. COGEM Report: CGM 2010-02. CML Institute of Environmental Sciences, Institute of Biology Leiden, Bilthoven, The Netherlands.
31. Taylor M.L., A.M. Scaife, and S.G. Riordan. 2020. Amended Report for MSL0030455: Compositional Analyses of Canola Seed from MON 94100 Grown in the United States and Canada During the 2018 Season. Monsanto Technical Report TRR0000589. Chesterfield, Missouri.
32. Todaro, M., N. Francesca, S. Reale, G. Moschetti, F. Vitale and L. Settanni. 2011. Effect of different salting technologies on the chemical and microbiological characteristics of PDO Pecorino Siciliano cheese. European Food Research and Technology 233:931-940.

Appendix 1

GENETIC MODIFICATION ADVISORY COMMITTEE (GMAC) MEMBERS INVOLVED IN SPECIFIC RISK ASSESSMENT AREAS FOR THE APPROVAL FOR RELEASE OF PRODUCTS OF MON94100 CANOLA FOR SUPPLY OR OFFER TO SUPPLY

Genetic Modification Advisory Committee (GMAC) members divided the task of looking up more information for the Risk Assessment matrix based on three broad categories which were environment, human health and animal health. Each sub-committee had a nominated leader to coordinate the work and report back to the main GMAC. The GMAC members involved in the risk assessment are as below:

1. **Prof. Dr. Mohd. Faiz Foong bin Abdullah (Universiti Teknologi MARA) (GMAC Chairman)**
2. **Dr. Kodi Isparan Kandasamy (Industry Representative) (Environment sub-committee Leader)**
3. **Madam T.S. Saraswathy (Institute of Medical Research - retired) (Human Health sub-committee Leader)**
4. **Prof. Dr Jothi Malar Panandam (Universiti Putra Malaysia - retired) (Animal Health sub-committee Leader)**
5. **Dr. Rahizan Issa (Institute of Medical Research - retired) (Notification Assessment sub-committee Leader)**
6. Dato' Dr. Sim Soon Liang (Academy of Sciences Malaysia)
7. Prof. Dr. Chan Kok Gan (Universiti Malaya)
8. Assoc. Prof. Dr. Choong Chee Yen (Universiti Kebangsaan Malaysia)
9. Dr. Adiratna Mat Ripen (Institute of Medical Research)
10. Dr. Norliza Tendot Abu Bakar (Malaysian Agricultural Research & Development Institute)
11. Dr. Norwati Muhammad (Forest Research Institute of Malaysia)
12. Dr. Saifullizam bin Abdul Kadir (Department of Veterinary Services)
13. Dr. Teo Tze Min (Entomological Society of Malaysia)
14. Dr. Mohd Hefni Rusli (Malaysian Palm Oil Board)
15. Madam Shafini Abu Bakar (Ministry of Health)
16. Madam Sabariah Kamis (Department of Agriculture)
17. Mr. Harun bin Ahmad (Department of Chemistry Malaysia)
18. Assoc. Prof. Dr. Sharifah binti Syed Hassan (Monash University Malaysia)
19. Dr. Kumitaa Theva Das (Universiti Sains Malaysia)