RISK ASSESSMENT REPORT

OF THE GENETIC MODIFICATION ADVISORY COMMITTEE (GMAC)

FOR

AN APPLICATION FOR APPROVAL FOR RELEASE OF PRODUCTS OF

DP910521 MAIZE FOR SUPPLY OR OFFER TO SUPPLY

NBB REF NO: JBK(S) 600-2/1/28

APPLICANT: CORTEVA AGRISCIENCE (MALAYSIA) SDN. BHD.

DATE: 20 FEBRUARY 2025

I - Summary of Assessment Process

On 23 May 2023, 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 insect resistant and herbicide tolerant DP910521 maize. The application was filed by Corteva Agriscience (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 28 December 2022 to 26 January 2023 via advertisements in the local newspapers, e-mail announcements and social media. Comments were received from Malaysian Palm Oil Board (MPOB), Consumers Association Penang and several individuals. GMAC took into consideration comments that were relevant to the risk assessment including the safety of the genes involved and proteins produced, use of genome editing technique for modification, herbicide residue, unintentional release and the lack of safety information about this event, as it is relatively "new".

GMAC had five (5) 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 insect resistant and herbicide tolerant DP910521 maize. 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). DP910521 maize has been approved for use in food and animal feed in the Brazil, Japan, Australia, Canada and South Korea (Biosafety Clearing House and FAO GM Foods Platform). To date, DP910521 maize has not yet been commercialized. The expected use of the products derived from DP910521 maize in Malaysia will be the same as the expected usage for products derived from conventional maize This application does not cover environmental release and DP910521 maize may be imported to Malaysia as food or feed products or for further processing.

Information about DP910521 maize

DP910521 was developed to provide growers an additional tool for controlling targeted pests and weeds. Insect resistant and herbicide tolerant DP910521 maize was developed through site specific integration (SSI) using two sequential transformation steps. The first transformation step involved microprojectile bombardment to insert the integration site sequence ("landing pad"

sequence) at a specific location of the maize genome using CRISPR-Cas9 mediated targeted insertion. The maize plants were regenerated after the first transformation and the line containing the expected “landing pad” sequence was selected for further transformation to create DP910521 maize. The second transformation involved microprojectile co-bombardment to insert the trait genes into the landing pad. Maize plants were regenerated after the second transformation and molecular characterization was conducted.

DP910521 maize was genetically modified to express the proteins Cry1B.34 for protection against certain susceptible lepidopteran pests (insect resistant), phosphinothricin acetyltransferase (PAT) for glufosinate herbicide tolerance and phosphomannose isomerase (PMI) as a selectable marker.

The Cry1B.34 protein is encoded by the *cry1B.34* gene, a chimeric gene comprised of sequences from the genes *cry1B*-class, *cry1Ca1* and *cry9Db1,* all derived from *Bacillus thuringiensis.* The PAT protein is encoded by a maized-optimized version of the *pat* gene (*mo-pat*) from *Streptomyces viridochromogenes* and the PMI protein is encoded by the *pmi* gene from *Escherichia coli.*

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, and

(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.

GMAC has previously evaluated the safety of PAT and PMI proteins in the context of several other applications and found no indication that would suggest an adjuvant effect of the individual proteins or mixture in this event. The Cry1B.34 protein has not been assessed previously by GMAC.

The potential hazards were identified in three main areas:

(i) **Effects on human health**

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, 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, anti-nutritional properties, 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/grain and cross pollination leading to transfer of transgenes.

Based on the above, a final list of 17 potential hazards were 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 (JBK Report Number No. 04, 2015). In the conducive warm and humid climate of Malaysia, there is a high likelihood of these volunteers maturing to the flowering and seed-setting stages. Although maize is not grown as an economic crop in Malaysia and there are no wild relatives, some varieties of baby corn and sweet corn are cultivated in small scales. Thus, there is a likelihood of outcrossing of the GM maize with these cultivated maize. Repeated cycles of spill-and-growth also increase the likelihood for the development of feral GM populations.

Any spillage (during loading/unloading) shall be collected and cleaned up immediately. Transportation of the consignment from the port of entry to any destination within the country must be in secured and closed conditions.

b) Planting of seeds

Plants may be grown by uninformed farmers and perpetuated through small scale cultivations. These GM maize may pollinate the non-GM baby corn and/or sweetcorn.

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) Weediness

The possibility of plants grown unintentionally may develop characteristic of weediness and become invasive was considered. Maize is highly domesticated and its weediness/invasiveness is effectively limited by multiple characteristics, including poor seed dispersal mechanisms and poor competitive ability. Fundamental changes to such limiting characteristics, including competitive ability, would be required for it to become invasive or weedy. DP910521 maize lacks plausible hypotheses under which they would cause such fundamental changes. DP910521 maize does not exhibit characteristics that increase its fitness compared to conventional maize, and is highly unlikely to become weedy or invasive. There are no native Malaysian species sexually compatible to maize. Lepidopteran-protected traits such as DP910521 maize would have little or no impact on non-agricultural habitats that generally do not receive pesticide applications. Any DP910521 maize that invades agricultural habitats could be easily controlled with mechanical cultivation and herbicides.

Any spillage (during loading/unloading) shall be collected and cleaned up immediately. Transportation of the consignment from the port of entry to any destination within the country must be in secured and closed conditions.

IV - Proposed Terms and Conditions for Certificate of Approval

Based on the 17 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 DP910521 maize, 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 condition.

f) Any import or release of products derived from any new genetically modified lines bred using DP910521 maize 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 maize consignments are below the 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 the DP910521 maize 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 insect resistant and herbicide tolerant DP910521 maize 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

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Appendix 1

GENETIC MODIFICATION ADVISORY COMMITTEE (GMAC) MEMBERS INVOLVED IN SPECIFIC RISK ASSESSMENT AREAS FOR THE APPROVAL FOR RELEASE OF PRODUCTS OF DP910521 MAIZE 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. **Dr. Mohd Hefni Rusli (Malaysian Palm Oil Board) (GMAC Chairman)**
2. **Dr. Kumitaa Theva Das (Universiti Sains Malaysia) (Environment sub-committee Leader)**
3. **Dr. Choong Chee Yen (Universiti Kebangsaan Malaysia - retired) (Human Health sub-committee Leader)**
4. **Dr. Teo Tze Min (Entomological Society of Malaysia) (Animal Health sub-committee Leader)**
5. **Dr. Adiratna Mat Ripen (Institute of Medical Research) (Notification Assessment sub-committee Leader)**
6. Prof. Dr. Mohd. Faiz Foong bin Abdullah (Universiti Teknologi MARA)
7. Dr. Kodi Isparan Kandasamy (Industry Representative)
8. Madam T.S. Saraswathy (Institute of Medical Research - retired)
9. Assoc. Prof. Dr. Sharifah binti Syed Hassan (Monash University Malaysia)
10. Dr Jothi Malar Panandam (Universiti Putra Malaysia - retired)
11. Dr. Rahizan Issa (Institute of Medical Research - retired)
12. Dr. Norliza Tendot Abu Bakar (Malaysian Agricultural Research & Development Institute)
13. Madam Shafini Abu Bakar (Ministry of Health)
14. Madam Sabariah Kamis (Department of Agriculture)
15. Mr. Harun bin Ahmad (Department of Chemistry Sabah)
16. Dr. Sara Jane Chiu (Industry Representative)
17. Dr. Yuwana Podin (Universiti Malaysia Sarawak)
18. Prof. Dr. Chan Kok Gan (Universiti Malaya)