RISK ASSESSMENT REPORT

OF THE GENETIC MODIFICATION ADVISORY COMMITTEE (GMAC)

FOR

AN APPLICATION FOR APPROVAL FOR RELEASE OF PRODUCTS OF MS8FR3 OILSEED RAPE FOR SUPPLY OR OFFER TO SUPPLY

NBB REF NO: JBK(S) 602-1/1/28

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

DATE: 10 AUGUST 2016

I - Summary of Assessment Process

On 5 November 2015, 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, glufosinate ammonium herbicide tolerance and fertility restored MS8RF3 oilseed rape. 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 18 January 2015 to 18 February 2015 via advertisements in the local newspapers. There were no comments received via the public consultation.

GMAC had 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 glufosinate ammonium herbicide tolerance and fertility restored MS8RF3 oilseed rape. 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, MS8RF3 oilseed rape has been registered in a number of countries for cultivation as well as for food, feed and for processing. MS8RF3 oilseed rape is approved in Australia, New Zealand, China, European Union, India, Japan, Korea, Mexico, South Africa, Taiwan, Canada and United States of America 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 oilseed rape. Malaysia uses rapeseed oil (as food ingredient) and meal (feed ingredient). According to the applicant, there will be no difference in use of oilseed rape compared to conventional oilseed rape already in the market.

Oilseed rape differed from most other edible oils in having a high percentage of long carbon chain monoenoic fatty acids, eiconsenoic (C20:1) and erucic (C22:1). This oil was found nutritionally superior to the high erucic oil and provided to be an excellent liquid and salad oil, as well as a suitable ingredient for margarine and shortening manufacture. This new natural oil is called "canola oil" in most countries of the world. The fatty acid composition of canola oil met or exceeded the nutritional requirements of a superior edible oil. Harvested oilseed rape grain will be put in the downstream chain for processing into oils for human consumption and meal for animal feed.

The applicant claims that the raw agricultural commodities derived from event MS8RF3 oilseed rape are compositionally equivalent to conventional oilseed rape.

Information about oilseed rape

The recipient or parental plant is *Brassica napus* L. (oilseed rape). There are two types of *B. napus*: 1) oil-yielding oleiferous rape, of which one subset with specific quality characteristics is often referred to as "canola" (vernacular name), and 2) the tuber-bearing swede or rutabaga. It is now grown primarily for its seeds which yield between 35 % to over 45 % oil. Cooking oil is the main use but it is also commonly used in margarine. After oil is extracted from the seed, the remaining by-product, canola seed meal is used as a high protein animal feed. China, India, Europe and Canada are now the top producers, although this crop can be successfully grown in the United States, South America and Australia, where annual production has increased sharply over the last few years. The optimum temperature for maximal growth and development of spring-type oilseed rape is just over 20C, and it is best grown between 12 and 30C. Flowering periods of *Brassica rapa* and other species, such as *Brassica napus*, *Brassica nigra*, are critical for hybridization events to occur. Flowering periods, which are largely environmentally influenced, must overlap at least partially. To evaluate hybridization potential, it is important to know the flowering chronology of both the cultivated plant and related species, physical distance between species with potential to hybridize; occurrence of vectors for pollination, and in the case of pollination by insects, the frequency of the potential pollination, activity and behavior. For a trait to become incorporated into a species genome, recurrent backcrossing of plants of that species by hybrid intermediaries, and survival and fertility of the resulting offspring, is necessary. After emergence, seedlings prefer relatively cool temperatures up to flowering. Under field conditions the fertilization of ovules usually results from self-pollination, although outcrossing rates of 5-30 per cent have been reported. Recent field surveys conducted across Canada, found volunteer canola still present in fields 4 - 5 years after a canola crop had been grown, albeit at low densities (Legere *et al.* 2001).

Information about MS8RF3 oilseed rape

The lines MS8 and RF3 were developed using genetic engineering techniques to provide a pollination control system for the production of hybrid oilseed rape (MS8xRF3) expressing male sterility and tolerance to glufosinate ammonium. The novel hybridization system involves the use of two parental lines, a male sterile line MS8 and a fertility restorer line RF3. The transgenic MS8 plants do not produce viable pollen grains and cannot self-pollinate. In order to completely restore fertility in the hybrid progeny, line MS8 must be pollinated by a modified plant containing a fertility restorer gene, such as line RF3. The resultant F1 hybrid seed, derived from the cross between MS8 x RF3, generates hybrid plants that produce pollen and are completely fertile.

The male-sterile trait was introduced in MS8 by inserting the *barnase* gene, isolated from *Bacillus amyloliquefaciens,* a common soil bacterium that is frequently used as a source for industrial enzymes. The *barnase* gene encodes for a ribonuclease enzyme (RNAse) that is expressed only in the tapetum cells of the pollen sac during anther development. The RNAse affects RNA production, disrupting normal cell functioning and arresting early anther development, thus leading to male sterility.

The transgenic line RF3 was produced by genetically engineering plants to restore fertility in the hybrid line. Transgenic RF3 plants contain the *barstar* gene, also isolated from *Bacillus amyloliquefaciens*. The *barstar* gene codes for a ribonuclease inhibitor (barstar enzyme) expressed only in the tapetum cells of the pollen sac during anther development. The ribonuclease inhibitor (barstar enzyme) specifically inhibits barnase RNAse expressed by the MS8 line. Together, the RNAse and the ribonuclease inhibitor form a very stable one-to-one complex, in which the RNAse is inactivated. As a result, when pollen from the restorer line RF3 is crossed to the male sterile line MS8, the resultant progeny express the RNAse inhibitor in the tapetum cells of the anthers, allowing hybrid plants to develop normal anthers and restoring fertility.

Both transgenic lines MS8 and RF3 were also engineered to express tolerance to glufosinate ammonium, the active ingredient in phosphinothricin herbicides (Basta®, Rely®, Finale®, and Liberty®). Glufosinate chemically resembles the amino acid glutamate and acts to inhibit an enzyme, called glutamine synthetase, which is involved in the synthesis of glutamine. Essentially, glufosinate acts enough like glutamate, the molecule used by glutamine synthetase to make glutamine, that it blocks the enzyme's usual activity. Glutamine synthetase is also involved in ammonia detoxification. The action of glufosinate results in reduced glutamine levels and a corresponding increase in concentrations of ammonia in plant tissues, leading to cell membrane disruption and cessation of photosynthesis resulting in plant withering and death.

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 took cognizance of the following as suggested 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.

A Risk Matrix was prepared based on an assessment mechanism developed by Office of the Gene Technology Regulator, Australia (OGTR, 2009). In applying this matrix, 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 Risk Assessment was conducted over a series of 4 meetings. To start with, the possible pathways to risk/hazard arising from release of the products were identified and listed. The potential hazards were identified in three main areas:

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

Issues pertaining to acute toxicity of novel protein / altering / interference of metabolic pathways, potential allergenicity of the novel protein, production of proteins or metabolites with mutagenic / teratogenic / carcinogenic effects, reproductive toxicity, potential transfer of antibiotic resistance genes in digestive tract, pathogenic potential of donor microorganisms and nutritional equivalence.

(ii) **<u>Effects on animal health</u>**

Issues pertaining to allergenicity, toxicity, anti-nutritional content, survivability and animal product contamination.

(iii) **<u>Effects on the environment</u>**

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, cross pollination leading to transfer of transgenes, toxic effect on non-target organisms were examined.

Based on the above, a final list of 21 potential hazards was identified. All 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. Oilseed rape 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) Compromised Nutritional Content

The potential risk of MS8RF3 oilseed rape was evaluated in equivalence to, and above any potential risk reported for unmodified oilseed rape

Analyses of seed and forage from several studies demonstrate that MS8RF3 oilseed rape is nutritionally and compositionally similar to, and as safe and nutritious as conventional soybean

However as a precautionary measure GMAC recommends that the proposed terms and conditions under section IV should be adhered to.

IV - Proposed Terms and Conditions for Certificate of Approval

Based on the 21 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 down 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 MS8RF3 oilseed rape, the National Biosafety Board shall be informed immediately (for a review as in Section 18 of the Biosafety Act).

d) Any spillage (during loading/unloading) 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.

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 (Amendment) Regulations 2010 for labelling of GM food.

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

a) Continuous monitoring is required from the approved person to report any unanticipated adverse effect caused by the MS8RF3 oilseed rape.

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 glufosinate ammonium herbicide tolerance and fertility restored MS8RF3 oilseed rape 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.

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Appendix I

GENETIC MODIFICATION ADVISORY COMMITTEE (GMAC) MEMBERS INVOLVED IN SPECIFIC RISK ASSESSMENT AREAS FOR THE APPROVAL FOR RELEASE OF PRODUCTS OF MS8RF3 OILSEED RAPE 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. The scope of research aspects for each group is as listed below. Each sub-committee had a nominated leader to coordinate the work and report back to the main GMAC. The respective leader contacted the sub-committee members and discussed the work process with their members. The groupings of GMAC sub-committee members and their assigned tasks are as below:

1. ENVIRONMENT

- **Assoc. Prof. Dr. Mohd. Faiz Foong bin Abdullah (Universiti Teknologi MARA) (Leader)**
- Dato' Dr. Sim Soon Liang (Sarawak Biodiversity Centre)
- Dr. Kodi Isparan Kandasamy (Malaysian Biotechnology Corporation Sdn. Bhd.)
- Madam Atikah binti Abdul Kadir Jailani (Department of Agriculture)
- Dr. Norliza Tendot Abu Bakar (Malaysian Agricultural Research & Development Institute)
- Assoc. Prof. Dr. Choong Chee Yen (Universiti Kebangsaan Malaysia)

2. HUMAN HEALTH

- **Madam T.S. Saraswathy (Institute of Medical Research) (Leader)**
- Dr. Rahizan Issa (Institute of Medical Research)
- Dr. Adiratna Mat Ripen (Institute of Medical Research)
- Madam Laila Rabaah Ahmad Suhaimi (Ministry of Health)
- Assoc. Prof. Dr. Chan Kok Gan (Universiti Malaya)
- Prof. Dr. Abd Rahman Milan (Universiti Malaysia Sabah)

3. ANIMAL HEALTH

- **Prof. Dr Jothi Malar Panandam (Universiti Putra Malaysia) (Leader)**
- Dr. Ahmad Parveez bin Hj Ghulam Kadir (Malaysian Palm Oil Board)
- Dr. Norwati Muhammad (Forest Research Institute of Malaysia)
- Prof. Madya Dr. Zunita Zakaria (Universiti Putra Malaysia)
- Dr. Teo Tze Min (Entomological Society of Malaysia)