RISK ASSESSMENT REPORT

OF THE GENETIC MODIFICATION ADVISORY COMMITTEE (GMAC)

FOR

AN APPLICATION FOR APPROVAL FOR RELEASE OF PRODUCTS OF LLCotton25 COTTON FOR SUPPLY OR OFFER TO SUPPLY

NBB REF NO: JBK(S) 602-1/1/31

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

DATE: 9 MARCH 2017

I - Summary of Assessment Process

On 27 December 2016, 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 tolerant LLCotton25 cotton. The application was filed by Bayer Co. (Malaysia) Sdn. Bhd. (hereafter referred to as "the applicant").

A public consultation for this application was conducted from 10 October 2016 to 8 November 2016 via advertisements in the local newspapers. Comments were received from Third World Network (TWN). GMAC took into considerations comments regarding the combinatorial/ synergistic effects of the PAT protein and the level of herbicide residue in the plants and whether or not these levels of exposure could cause acute and/or chronic health effects.

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 tolerant LLCotton25 cotton. 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, LLCotton25 cotton has been registered in a number of countries for cultivation as well as for food, feed and for processing. LLCotton25 cotton is approved in Argentina, Australia, New Zealand, Brazil, Canada, China, Colombia, European Union, Japan, Korea, Mexico, South Africa, Taiwan 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 cotton. Among the end products that may be derived from LLCotton25 cotton are processed oil (as food ingredient), meal (feed ingredient), hulls and linters. According to the applicant, there will be no difference in use of LLCotton25 cotton compared to conventional cotton already in the market.

Cottonseed oil was the first oilseed oil produced in the United States (White, 2000). It is the main cotton product used for human consumption. The crude oil contains about 2% nonglyceride materials such as terpenoid phytoalexin, cyclopropenoid fatty acids (CPFA), phospholipids, sterols, resins, carbohydrates and related pigments which are mostly removed during processing.

About 56% of the oil is used for salad or cooking oil, 36% is used for baking and frying fats, and the remaining 8% goes into margarine and other uses.

Cottonseed meal, hulls and linters are by-products of the cottonseed oil processing with cottonseed meal being the most abundant, produced by pressing and solvent extraction. It is produced with and without hulls. Cottonseed meal is an excellent source of protein for ruminant animals and used in animal feeds as a high protein supplement.The protein from cottonseed meal can also be used to form fibrous material for use by the textile industry. Cottonseed hulls are very high in indigestible fiber and are commonly used as roughage in livestock feed products in combination with limited amounts of corn silage or hay. It can also be used as fuel for oil mills, insulation material, soil conditioner, filler for phenolic plastics, cellulose for regenerated fiber production and a source of xylose and furfural. Cottonseed linters are a major source of cellulose for chemical and food use and can be used in packaging products, preparation of regenerated fibers, films, lacquers, plastics and papers to name a few.

The applicant claims that the raw agricultural commodities derived from event LLCotton25 cotton are compositionally equivalent to conventional cotton.

Information about cotton

Cotton is a plant of the genus Gossypium in the family Malvaceae that is cultivated in areas of intense heat (temperate and tropical regions). It is one of the oldest cultivated crops, dating back to some 5000 years and considered the most prominent source of textile fibre in the world. It makes up over 40% of the total fibre used in the world (USDA ERS, 2002).

Although there are over 40 species of cotton, the four (4) main commercially cultivated species of cotton are *G. hirsutum* L. (upland cotton, native to Central America, Mexico, the Caribbean and southern Florida and accounts for 90% of world production) (Jenkins, 2003), *G. barbadense* L. (extra-long staple cotton, native to tropical South America, 5% of world fibre production) (Wu *et. al,* 2005), *G. arboretum* L. (tree cotton, native to India and Pakistan) and *G. herbaceum L.* (Levant cotton, native to southern Africa and the Arabian Peninsula). In the U.S., the two primary types of cotton grown are the *G. hirsutum* L. and *G. barbadense* L. (USDA ERS, 2002).

Cotton is primarily grown as a fibre crop. It is propagated from seed by planting directly in a field with favorable conditions. The optimal temperature for seeds to germinate is 34°C, while the seedlings requires a temperature between 24 and 29°C to grow and develop properly. Cotton will grow on a variety of soils including sandy soil and heavy clay as long as it is water permeable and will grow optimally in a soil with a pH of 5.5–8.5. In addition cotton has a high tolerance for salt. The radicle (root tip) emerges within 2-3 days from the seed and newly germinated seedlings emerge above the soil 5-6 days after emergence of the radicle (Oosterhuis and Jernstedt, 1999). Cotton plant contains a central stem with many branches. The first cotton leaf appears 10-12 days after emergence and leaf development reaches its peak about three weeks after the first buds are formed. The first flower-bud appears on the lowest fruiting branch 35-45 days after emergence, depending upon prevailing temperatures. The other flower buds follow at regular intervals until shortly before flowering ceases. The ovary of the plant develops into a boll which is 2–6 cm (0.8–

2.4 in) long. Mature bolls will split open to reveal the white cotton fibers and seed contained within. The cotton plant can reach heights of 1–1.5 m (3.3–4.9 ft) and is usually cultivated as an annual, surviving only one growing season.

Cotton is predominately a self-pollinated crop though varying degree of cross-pollination has been reported. Cotton pollen is relatively large, heavy, sticky and watery and thus wind is not a factor in the pollination of cotton. The amount of cross pollination depends upon the abundance of pollen-carrying insects. Honey bee (Apis mellifera L.) is the main vector for pollination in cotton. Apart from that, bumble bees (Bombus sp.), leaf cutting bees (Hymenoptera megachilidae) and a few dipterans also help in pollination. Dispersal studies on cotton have consistently demonstrated that when outcrossing occurs, it is localized around the pollen source and decreases significantly with the distance (Thomson, 1966; Galal et al., 1972; Theron & van Staden, 1975; Elfawal et al., 1976; Umbeck et al., 1991; Llewellyn & Fitt, 1996). Fertilization takes place between 24-30 hours after pollination (Govila, 1969).About 40-50 days are required from fertilization to boll bursting, maturation of fibres and seed formation.As cotton does not generally reproduce vegetatively, spread within the environment occurs by seed dispersal. Dispersal of cotton seeds is a physical process. Unprocessed 'seed cotton' that retains all of the fibres attached to the seed coat, also has a high potential for dispersal within the environment.

The cotton which is then ginned to separate the seed and the lint. The long lint fibers are further processed to make yarn which can be used to produce cotton fabrics. De-linted cotton seed (i.e. seed with no lint) is processed into oil, meal and hulls. Cotton seed oil has been used since the 19th century.

Information about LLCotton25 cotton

The recipient or parental plant is *Gossypium hirsutum* (upland cotton). LLCotton25 cotton is tolerant to the action of glufosinate ammonium herbicides as it contains a *bar* gene from *Streptomyces hygroscopicus* which produces PAT protein conferring the glufosinate ammonium tolerant trait.

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.

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, 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) **Effects on animal health**

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

(iii) **Effects on the environment**

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 and toxic effect on non-target organisms were examined.

Based on the above, a final list of 21 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. LLCotton25 cotton 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 growers. 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 LLCotton25 cotton was evaluated in equivalence to, and above any potential risk reported for unmodified cotton seeds.

Analyses of seed and forage from several studies demonstrate that LLCotton25 cotton is nutritionally and compositionally similar to, and as safe and nutritious as conventional cotton seeds.

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 LLCotton25 cotton, the National Biosafety Board authority shall be informed immediately.

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 Regulations 1985 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 LLCotton25 cotton.

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 tolerant LLCotton25 cotton 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 LLCotton25 COTTON 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 Bioeconomy Development 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)
- Madam Elliza binti Mat Noor (Department of Chemistry Malaysia)
- Dr. Teo Tze Min (Entomological Society of Malaysia)