

**RISK ASSESSMENT REPORT
OF THE GENETIC MODIFICATION
ADVISORY COMMITTEE (GMAC)
FOR
AN APPLICATION FOR APPROVAL FOR
RELEASE OF PRODUCTS OF
MON87751 SOYBEAN FOR SUPPLY OR
OFFER TO SUPPLY**

NBB REF NO: JBK(S) 600-2/1/8

**APPLICANT: MONSANTO (MALAYSIA)
SDN. BHD.**

DATE: 13 JANUARY 2021

I - Summary of Assessment Process

On 18 August 2020, 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 MON87751 soybean. The application was filed by Monsanto (Malaysia) Sdn. Bhd. (hereafter referred to as “the applicant”). After an initial review, GMAC decided to request for additional information from the applicant.

A public consultation for this application was conducted from 11 March 2020 to 24 April 2020 via advertisements in the local newspapers, e-mail announcements and social media. Comments were received from Consumers Association of Penang (CAP). GMAC took into consideration the comments from CAP regarding safety assessment of the Bt toxin, potential allergenicity and unintended effects of the MON87751 soybean to human health, composition of the MON87751 product compared to the conventional soybean, as well as animal toxicity studies.

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 MON87751 soybean. 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, MON87751 soybean has been registered in a number of countries for cultivation as well as for food, feed and for processing. MON87751 soybean is approved in the United States of America, Australia, New Zealand, Brazil, Canada, Colombia, Indonesia, Japan, Korea, Mexico, Nigeria, Philippines and Taiwan 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 soybean. The type of expected use of the products derived from MON87751 soybean in Malaysia will be the same as the expected usage for products derived from conventional soybean. This application does not cover environmental release and MON87751 may be imported to Malaysia as food or feed products or for further processing.

Information about MON 87751 soybean

The recipient or parental plant is *Glycine max* (soybean). Soybean has a long history of domestication and consumption by humans, and foods containing soybean-derived products are consumed by a large proportion of the global population. (Liu, 2004).

MON87751 was developed using *Agrobacterium tumefaciens*-mediated transformation of soybean A3555 meristem tissue by inserting *cry1A.105* and *cry2Ab2* that produce CryIA.105 and Cry2Ab2 insecticidal (Cry) proteins, respectively. Cry1A.105 is a modified Cry1A protein derived from *Bacillus thuringiensis* and Cry2Ab2 is derived from *B. thuringiensis* subsp. *kurstaki*. The CryIA.105 and Cry2Ab2 proteins confer resistance to feeding damage caused by targeted lepidopteran insect pests such as fall armyworm, velvetbean caterpillar, soybean looper and corn earworm.

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, reproductive toxicity, potential transfer of antibiotic resistance genes in digestive tract, pathogenic potential of donor microorganisms, nutritional equivalence and anti-nutritional components.

(ii) **Effects on animal health**

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

(iii) **Effects on the environment**

Issues pertaining to accidental release of seeds, unintentional release and planting, weediness and invasiveness, increased fitness due to genetic modification, potential of transgenes being transferred to bacteria (soil bacteria, bacterial flora of animal gut), accumulation of the proteins 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 20 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. Soybean 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

No major significant differences between MON87751 and conventional soybean were observed from proximate analysis, analysis of fibre, amino acids, key nutrients and anti-nutrients present in soybean. The composition of MON87751 is comparable to that of the conventional soybean control.

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 MON87751 soybean, 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 MON87751 soybean 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; and GM food labelling guidelines.

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 MON87751 soybean 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 MON87751 soybean 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. Barlow, R, R. Wang and R. Hernan. 2013. Assessment of the in vitro Digestibility of the Cry1A.105 Protein in Simulated Gastric and Simulated Intestinal Fluids. Monsanto Technical Report MSL0024977. St. Louis, Missouri.
2. 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
3. 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.
4. Bonnette, K.L. 2005. An Acute Toxicity Study in Mice With Cry1A.105 Protein. Monsanto Technical Report CRO-2005-050. St. Louis, Missouri.
5. Bonnette, K.L. 2005. An Acute Toxicity Study in Mice With Cry2Ab2 Protein. Monsanto Technical Report CRO-2005-049. St. Louis, Missouri.
6. Cannon, R.J.C. 1993. Prospects and progress for Bacillus thuringiensis-based pesticides. Pesticide Science 37:331-335
7. 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.
8. de Alencar, E.R., L.R.D.A. Faroni, A.F. de Lacerda Filho, L.G. Ferreira and M.R. Meneghetti. 2006. Influence of different storage conditions on soybean grain quality. Pages 30-37 in 9th International Working Conference on Stored Product Protection, Campinas, São Paulo, Brazil.
9. 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.
10. Kang. H.T and A. Silvanovich. 2013. Bioinformatics Evaluation of the Cry1A.105 Protein in MON 87751 Utilizing the AD_2013, TOX_2013 and PRT_2013 Databases. Monsanto Technical Report MSL0024925. St. Louis, Missouri.
11. Levya-Guerrero, E., K. D. Miller and R. Sorbet. 2014. Amended Report for MSL0024609: Compositional Analyses of Soybean Forage and Seed Collected from MON 87751 Grown in United States during 2012 Season. Monsanto Technical Report MSL0026251. St. Louis, Missouri.
12. Liu, K. 2004. Soybeans as Functional Foods and Ingredients (1st ed.). AOCS Publishing. <https://doi.org/10.1201/9781003040286>
13. Liu, J., B. Zhou, C.-y. Yang, Y.-r. Li, L.-x. Jiang, M.-c. Zhang, B. Tao and L.-j. Qiu. 2012. Gene flowing of genetically modified glyphosate-resistant soybean with EPSPS. Soybean Science 31: 517-521.

14. Lusas, E.W. 2004. Soybean processing and utilization. Pages 949-1045 in Soybeans: Improvement, Production, and Uses. Third Edition. H.R. Boerma and J.E. Specht (eds.). American Society of Agronomy, Inc., Crop Science Society of America, Inc., Soil Science Society of America, Inc., Madison, Wisconsin.
15. Mbofung, G.C.Y., A.S. Goggi, L.F.S. Leandro and R.E. Mullen. 2013. Effects of storage temperature and relative humidity on viability and vigor of treated soybean seeds. *Crop Science* 53: 1086–1095.
16. 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.
17. Mendelsohn, M., J. Kough, Z. Vaituzis and K. Matthews. 2003. Are Bt crops safe? *Nature Biotechnology* 21:1003-1009.
18. Mozaffar, S.2013. Amended Report for MSL0024805: Assessment of Cry1A.105 and Cry2Ab2 Protein Levels in Soybean Tissues Collected from MON 87751 Produced in U.S. Field Trials during 2012. Monsanto Technical Report MSL0025199. St. Louis, Missouri.
19. Owen, M.D.K. 2005. Maize and soybeans—Controllable volunteerism without fertility? Pages 149-165 in *Crop Fertility and Volunteerism*. J. Gressel (ed.) Taylor & Francis, Boca Raton, Florida.
20. OECD. 2000. Consensus document on the biology of *Glycine max* (L.) Merr. (Soybean). ENV/JM/MONO(2000)9. Series on Harmonization of Regulatory Oversight in Biotechnology No.15. Organisation for Economic Co-operation and Development, Paris, France.
21. 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.
22. Silvanovich, A. and H.T. Kang. 2013. Bioinformatics Evaluation of the Cry2Ab2 Protein Utilizing the AD_2013, TOX_2013 and PRT_2013 Databases. Monsanto Technical Report MSL0024926. St. Louis, Missouri.
23. U.S. EPA. 2001. Biopesticides registration action document - *Bacillus thuringiensis* plantincorporated protectants. U.S. Environmental Protection Agency, Washington, D.C. http://www.epa.gov/pesticides/biopesticides/pips/bt_brad.htm
24. U.S. EPA. 2005. *Bacillus thuringiensis* Cry3Bb1 protein and the genetic material necessary for its production (Vector ZMIR13L) in event MON 863 corn & *Bacillus thuringiensis* Cry1Ab delta-endotoxin and the genetic material necessary for its production in corn (006430, 006484) fact sheet. U.S. Environmental Protection Agency, Washington, D.C. http://www.epa.gov/pesticides/biopesticides/ingredients_keep/factsheets/factsheet_006430-006484.htm
25. U.S. EPA. 2008. Administrative revisions to plant- incorporated protectant tolerance exemptions. *Federal Register* 72: 20431-20436.
26. U.S. FDA. 1992. Statement of policy: Foods derived from new plant varieties. *Federal Register* 57:22984-23005.

27. U.S. FDA. 2001. Premarket notice concerning bioengineered foods. Federal Register 66:4706-4738.
28. Wang, R. and R. Hernan. 2013. Assessment of the in vitro Digestibility of Cry2Ab2 Protein in Simulated Gastric and Simulated Intestinal Fluids. Monsanto Technical Report MSL0025099. St. Louis, Missouri.
29. WHO. 1999. Microbial pest control agent: *Bacillus thuringiensis*. Environmental Health Criteria 217. World Health Organization, Geneva, Switzerland. <http://www.inchem.org/documents/ehc/ehc/ehc217.htm>

GENETIC MODIFICATION ADVISORY COMMITTEE (GMAC) MEMBERS INVOLVED IN SPECIFIC RISK ASSESSMENT AREAS FOR THE APPROVAL FOR RELEASE OF PRODUCTS OF MON87751 SOYBEAN 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:

- **Prof. Dr. Mohd. Faiz Foong bin Abdullah (Universiti Teknologi MARA) (GMAC Chairman)**
- **Dr. Kodi Isparan Kandasamy (Industry Representative) (Environment sub-committee Leader)**
- **Madam T.S. Saraswathy (Institute of Medical Research - retired) (Human Health sub-committee Leader)**
- **Prof. Dr Jothi Malar Panandam (Universiti Putra Malaysia - retired) (Animal Health sub-committee Leader)**
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