

**RISK ASSESSMENT REPORT  
OF THE GENETIC MODIFICATION  
ADVISORY COMMITTEE (GMAC)**

***FOR***

**AN APPLICATION FOR APPROVAL FOR RELEASE  
OF PRODUCTS OF EVENT 5307 CORN FOR  
SUPPLY OR OFFER TO SUPPLY**

**NBB REF NO: JBK(S) 602-1/1/21**

**APPLICANT: SYNGENTA CROP PROTECTION  
SDN. BHD.**

**DATE: 20 JANUARY 2016**

## ***I - Summary of Assessment Process***

On 17 April 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 rootworm-resistant Event 5307 corn. The application was filed by Syngenta Crop Protection 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 1 October 2015 to 30 October 2015 via advertisements in the local newspapers. Comments were received from Third World Network (TWN). GMAC took into considerations comments regarding the safety of the transgenic protein and the need for thorough molecular characterization of the event.

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 rootworm-resistant Event 5307 corn. 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, Event 5307 corn has been registered in a number of countries for cultivation as well as for food, feed and for processing. Event 5307 corn is approved in Canada, Japan and the 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 corn. The type of expected use of the products derived from Event 5307 corn in Malaysia will be the same as the expected usage for products derived from conventional corn. Potential users of products derived from Event 5307 corn such as grains are feed millers, food processors and other industrial use.

### **Information about Event 5307 Corn**

The recipient or parental plant is *Zea mays* L. spp *mays* (field or sweet corn). Corn is extensively cultivated and has a long history of safe use as a food or feed. It is one of the largest cultivated crop in the world followed by wheat (*Triticum* sp.) and rice (*Oryza sativa* L.) in total global metric ton production (FAOSTAT, 2016).

Event 5307 has active insecticidal properties against certain Coleoptera pests and are protected from damage caused by corn rootworm (CRW) larva. Event 5307 produces eCry3.1Ab protein

which is an engineered chimera of the modified Cry3A and Cry1Ab proteins, from *Bacillus thuringiensis* (Bt), which confers this protection.

### **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. 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 (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 corn 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 on small scales. Thus, there is a likelihood of outcrossing of the GM corn with these cultivated corns. Repeated cycles of spill-and-growth also increase the likelihood for the development of feral GM populations.

**b) Planting of seeds**

Plants may be grown by uninformed farmers and perpetuated through small scale cultivations. These GM corn 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) Compromised Nutritional Content**

Compositional analyses of the forage and grain samples showed no significant difference in nutritional composition between Event 5307 corn and conventional corn.

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 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 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 receives any credible and/or scientifically proven information that indicates any adverse effect of Event 5307 corn, 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 conditions.

## **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) The Food Safety and Quality Division under the Ministry of Health shall ensure that the labelling of GM food is implemented as required under Food Regulations 1985.

## ***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 Event 5307 corn.

## ***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 rootworm-resistant Event 5307 corn 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. Aalberse, R.C. 2000. Structural biology of allergens. *Journal of Allergy and Clinical Immunology*. 106: 228-238.
2. Astwood, J.D., J.N. Leach and R.L. Fuchs. 1996. Stability of food allergens to digestion in vitro. *Nature Biotechnology*. 14: 1269-1273.
3. Barb, A.W., J.D. Williamson and D.M. Pharr. 2002. Selection for mannose-6-phosphate isomerase activity in tobacco NT1 cultures: Partial physiological and molecular characterization. Direct unpublished submission to GenBank database; Accession no. AAN09933 (see NCBI 2010a).
4. Betz, F.S., Hammond, B.G., Fuchs, R.L. 2000. Safety and advantages of *Bacillus thuringiensis*-protected plants to control insect pests. *Regul. Toxicol. Pharmacol.* 32: 156-73.
5. Bravo, A. 1997. Phylogenetic relationships of *Bacillus thuringiensis*  $\delta$ -endotoxin family proteins and their functional domains. *Journal of Bacteriology*. 179: 2793-2801.
6. Burns, A. and A. Raybould. 2014. Nontarget organism effects tests on eCry3.1Ab and their application to the ecological risk assessment for cultivation of Event 5307 maize. *Transgenic Res.* 23(6):985-94. doi: 10.1007/s11248-013-9778-4. Epub 2014 Jan 10.
7. Canadian Food Inspection Agency (CFIA). 2003. The Biology of *Zea mays* L. (Corn/Maize) - a companion document to the assessment criteria for determining environmental safety of plants with novel traits. Regulatory Directive Dir94-11: <http://www.inspection.gc/english/plaveg/bio/dir/dir9411e.shtml>
8. Chen B.Y., W.K. Heneen and V. Simonsen. 1989. Comparative and genetic studies of isozymes in resynthesized and cultivated *Brassica napus* L., *B. campestris* L. and *B. albuglabra* Bailey. *Theoret Appl Genet* 77:673–679.
9. Conner, A.J., T.R. Glare and J. Nap. 2003. The release of genetically modified crops into the environment. Part II. Overview of ecological risk assessment. *The Plant J* 33: 19–46.
10. Delaney, B., J.D. Astwood and H. Cunny *et al.* 2008. Evaluation of protein safety in the context of agricultural biotechnology. *Food and Chemical Toxicology*, vol. 46, pp. S71–S97
11. FAO-WHO. 1991. Strategies for assessing the safety of foods produced by biotechnology. *Report of joint FAO/WHO consultation*. World Health Organization, Geneva, Switzerland.

12. 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.
13. FAOSTAT. 2016. Food and Agricultural Organization statistical database. Statistics for Most produced commodities in the world (Cereals) from the year 1993-2013 (average in million tonnes) *Food and Agricultural Organization of the United Nations, New York, New York*. <http://faostat3.fao.org/browse/Q/QC/E> [Accessed February 11, 2016].
14. Geiser M, S. Schweizer and C. Grimm. 1986. The hypervariable region in the genes coding for entomopathogenic crystal proteins of *Bacillus thuringiensis*: nucleotide sequence of the *kurhd1* gene of subsp. *kurstaki* HD-1. *Gene* 48:109–118.
15. Gould, F.W. 1968. Grass Systematics p. 1-382. McGraw Hill; N.Y
16. Höfte, H. and H.R. Whiteley. 1989. Insecticidal crystal proteins of *Bacillus thuringiensis*. *Microbiological Reviews*. 53: 242-255.
17. JBK Report No. 4 (2015) Germination Rate of GM Corn and GM Soya seeds that are imported into Malaysia for the purpose of food, feed and processing”
18. Keese, P.2008. Risk from GMOs due to Horizontal Gene Transfer. *Environ Biosafety Res.* 2008;7:123–149. doi: 10.1051/ebr:2008014.
19. Koch, M.S., Ward, J.M., Levine, S.L., Baum, J.A., Vicini, J.L., Hammond, B.G. 2015. The food and environmental safety of bt crops. *Front Plant Sci* 6: 283.
20. Lee, B.T. and N.K. Matheson. 1984. Phosphomannoisomerase and phosphoglucoisomerase in seeds of *Cassia coluteoides* and some other legumes that synthesize galactomannan. *Phytochemistry* 23:983–987.
21. Malvolti, M.E., M. Paciucci, F. Cannata and S. Fineschi. 1993. Genetic variation in Italian populations of *Juglans regia* L. *Acta Horti* 311:86–94
22. 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.
23. Mendelsohn, M., J. Kough, Z. Vaituzis and K. Matthews. 2003. Are *Bt* Crops Safe? *Nature Biotechnology* 21 (9) 1003- 1009.

24. Metcalfe, D.D., J.D. Astwood, R. Townsend, H.A. Sampson, S.L. Taylor and R.L. Fuchs. 1996. Assessment of the allergenic potential of foods derived from genetically engineered crop plants. *Critical Reviews in Food Science and Nutrition*. 36: S165-S186.
25. Murray, E.E., J. Lotzer and M. Eberle. 1989. Codon usage in plant genes. *Nucleic Acids Res* 17:477–498.
26. Negrotto, D., M. Jolley, S. Beer, A.R. Wenck and G. Hansen. 2000. The use of phosphomannose isomerase as a selectable marker to recover transgenic maize plants (*Zea mays* L.) via *Agrobacterium* transformation. *Plant Cell Reports* 19:798-803.
27. Nelson, A. 2009. In Vitro Digestibility of Phosphomannose Isomerase (PMI) as Contained in Test Substance PMI-0105 Under Simulated Mammalian Intestinal Conditions. Syngenta Report no. SSB-036-07.
28. Nelson, A. 2009. In Vitro Digestibility of Phosphomannose Isomerase (PMI) as Contained in Test Substance PMI-0105 Under Simulated Mammalian Gastric Conditions. Syngenta Report No. SSB-034-07 A1.
29. Newcomb, M.D. 1995. *Corn and animal nutrition in the United States*. U.S. Food and Drug Administration, Washington, D.C.
30. OECD. 2002. Consensus document on compositional considerations for new varieties of maize (*Zea mays*): Key food and feed nutrients, anti-nutrients and secondary plant metabolites. ENV/JM/MONO (2002)25. *Series on the Safety of Novel Foods and Feeds*, No. 6. Organisation for Economic Co-operation and Development, Paris, France.
31. OECD. 2003. Consensus document on the biology of *Zea mays* subsp. *mays*. Series on Harmonisation of Regulatory Oversight in Biotechnology” (Number 27).
32. OGTR. 2008. The Biology of *Zea mays* L spp *mays* (maize or corn). Document prepared by the Office of the Gene Technology Regulator, Canberra, Australia <http://www.ogtr.gov.au>
33. Owen, M.D.K. 2005. Maize and Soybeans-Controllable Volunteerism without ferality? In: *Crop Ferality and Volunteerism*. Gressel, J. (ed.) Boca Raton, F.L., CRC Press. pp. 149-165
34. Pigott, C.R., Ellar, D.J. 2007. Role of receptors in *Bacillus thuringiensis* crystal toxin activity. *Microbiol Mol Biol Rev* 71: 255-81.
35. Sauve, A.K., Brake, J.T., 2010. Evaluation of Event 5307 Transgenic Maize Grain in a Broiler Chicken Feeding Study. Syngenta Report no. SSB-211-10

36. Seastrum, L. 2010. In vitro Digestibility of eCry3.1Ab Protein as Contained in Test Substance ECRY3.1AB-0208 Under Simulated Mammalian Intestinal Conditions. Syngenta report no SSB-015-09 A1
37. Shearer, J. 2011. Event 5307 Maize Grain - 13 Week Whole Food Safety Study in Rats. Syngenta Report no. 30373.
38. Sjoblad, R.D., J.T. McClintock and R. Engler. 1992. Toxicological considerations for protein components of biological pesticide products. *Regulatory Toxicology and Pharmacology*. 15: 3-9.
39. Song, S. 2010. In vitro Digestibility of eCry3.1Ab Protein under Simulated Mammalian Gastric Conditions. Syngenta study no TK0028111
40. U.S. EPA. 1995a. Plant pesticide *Bacillus thuringiensis* CryIIIA delta-endotoxin and the genetic material necessary for its production; Tolerance exemption. *Federal Register*. 60: 21725-21728.
41. U.S. EPA. 1995b. Plant pesticide *Bacillus thuringiensis* CryIA (b) delta-endotoxin and the genetic material necessary for its production (Plasmid vector pCIB4431) in corn. *Federal Register*. 60: 42443-42446.
42. U.S. EPA. 2001b. *Biopesticides registration action document: Bacillus thuringiensis (Bt) plant-incorporated protectants* (October 15, 2001). U.S. Environmental Protection Agency, Washington D.C. [http://www.epa.gov/pesticides/biopesticides/pips/bt\\_brad.htm](http://www.epa.gov/pesticides/biopesticides/pips/bt_brad.htm).
43. Van Mellaert, H., J. Van Rie, C. Hofman and A. Reynaerts. 1988. Insecticidal crystal proteins from *Bacillus thuringiensis*: Mode of action and expression in transgenic plants. Pages 82-87 in *Biotechnology, Biological Pesticides and Novel Plant-Pest Resistance for Insect Pest Management*. Boyce Thompson Institute, Cornell University, New York.
44. Walters, F., C.M. deFontes, H. Hart, G.W. Warren and J.S. Chen. 2010. Lepidopteran-active variable-region sequence imparts coleopteran activity in eCry3.1Ab, an engineered *Bacillus thuringiensis* hybrid insecticidal protein. *Appl Env Microbiol* 76:3082–3088.
45. White, P.J. and E.J. Weber. 2003. Lipids of the kernel. Pages 355-405 in *Corn: Chemistry and Technology*. Second Edition. P.J. White and L.A. Johnson (eds.). American Association of Cereal Chemists, Inc., St. Paul, Minnesota.

**GENETIC MODIFICATION ADVISORY COMMITTEE (GMAC) MEMBERS INVOLVED IN  
SPECIFIC RISK ASSESSMENT AREAS FOR THE APPROVAL FOR RELEASE OF  
PRODUCTS OF EVENT 5307 CORN 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)
- Assoc. Prof. Dr. Zunita Zakaria (Universiti Putra Malaysia)
- Dr. Noor Zaleha binti Awang Saleh (previously from Department of Chemistry)
- Dr. Teo Tze Min (Entomological Society of Malaysia)