RISK ASSESSMENT REPORT

OF THE GENETIC MODIFICATION ADVISORY COMMITTEE (GMAC)

FOR

AN APPLICATION FOR APPROVAL FOR RELEASE OF PRODUCTS OF TC1507 CORN FOR SUPPLY OR OFFER TO SUPPLY

NBB REF NO: JBK(S) 602-1/1/6

APPLICANT: DUPONT MALAYSIA SDN. BHD.

DATE SUBMITTED: 10 MAY 2012

I - Summary of Assessment Process

The Genetic Modification Advisory Committee (GMAC, please refer to Appendix 1 for details of GMAC), under the purview of the National Biosafety Board (NBB), was given the dossier by the Department of Biosafety on 24 May 2012 for an 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 TC1507 corn). The application was filed by Dupont Malaysia Sdn. Bhd. (hereafter referred to as "the applicant"). GMAC members also took the opportunity to obtain further clarification on certain details of the activity. Additional information was provided by the applicant as requested.

A public consultation for this application was conducted from 8 August 2012 to 6 September 2012 via advertisements in the local newspapers. A few technical and scientific issues were raised through the Public Consultation for this application regarding the release. These issues have been considered by GMAC in the risk assessment.

GMAC had three (3) 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 TC1507 (insect-resistant and herbicide-tolerant 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, TC1507 has been registered in a number of countries for cultivation as well as for importation for direct use as feed and for processing corn. TC1507 corn is grown in a number of countries, e.g. United States of America (USA), Canada, Argentina, Philippines, Brazil and South Africa, 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 TC1507 corn in Malaysia will be the same as the expected usage for products derived from conventional corn. Potential users of products derived from TC1507 corn such as grains are feed millers, food processors and other industrial use.

Information about TC1507 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 the world's third leading cereal crop behind wheat and rice.

TC1507 corn has been genetically modified (GM) by incorporation of two bacterial genes: the *cry1F* gene (derived from the soil bacterium *Bacillus thuringiensis* var. *aizawai* strain PS811) which expresses an insect-specific protein toxin, Cry1F, and the *pat* gene (derived from the soil bacterium *Streptomyces viridochromogenes*) which expresses the enzyme phosphinothricin acetyltransferase (PAT), conferring tolerance to glufosinate-ammonium herbicides.

Cry1F protein, as expressed in TC1507 corn, is effective in controlling European Corn Borer (*Ostrinia nubilalis*), southwestern corn borer (*Diatraea grandiosella*), black cutworm (*Agrotis ipsilon*) and armyworms (*Spodoptera* sp.) that are common insect pests of corn in the USA where this variety is intended to be primarily cultivated.

TC1507 is also tolerant to glufosinate-ammonium herbicide through the expression of a bacterial gene from *Streptomyces viridochromogenes*, encoding an enzyme, phosphinothricin acetyltransferase (PAT). This enzyme is able to specifically break down the herbicide in the plant, converting it to an inactive form, thus allowing the plants to grow normally. The production of PAT in the plants allows selection of GM plants in the field as well as providing tolerance to the herbicide when used at agricultural levels.

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 three (3) 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) **Effects on human health**

Relevant scientific publications on TC1507 corn were reviewed for potential human health risks and issues pertaining to acute toxicity of the novel proteins, potential allergenicity, mutagenic/teratogenic/carcinogenic effects, reproductive toxicity, potential transfer of antibiotic resistance genes in the digestive tract, the pathogenic potential of the donor microorganisms and nutritional equivalence.

(ii) **Effects on animal health**

Issues pertaining to allergenicity, toxicity, survivability, horizontal gene transfer, anti-nutritional properties and compromised nutritional content.

(iii) **Effects on the environment**

Issues pertaining to unintentional release and planting, weediness, gene transfer to bacteria, accumulation of toxin, cross-pollination and toxic effects on non-target organisms were examined.

Based on the above, a final list of 22 potential hazards was identified. Most of these hazards were rated as having an Overall Risk of 1 or "negligible". In addition safety assessment reports from several government regulatory agencies, namely Australia/NewZealand, Canada, European Union, Japan and Philippines were referred to. The safety assessment reports were based on studies conducted by independent experts on the molecular characterization, biochemical, toxicological, nutritional, and allergenicity data of the introduced proteins, in accordance with guidelines from World Health Organization (WHO), the Food and Agriculture Organization (FAO) and the Codex Alimentarius Commission. These data have showed the stability of expression of Cry1F and PAT protein. While a number of putative Open Reading

Frames (ORFs) adjacent to the gene insertion site were detected using bioinformatics, none of these appears to encode sequences with similarity to known allergens or toxins. There are also no indications that any of these ORFs are transcriptionally active.

GMAC also took extra caution and further discussed pre-emptive mitigation procedures for hazards where the Overall Risk was estimated to be above the minimal, and also for a few 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).

A few potential hazards where the Overall Risk was found to be 2 or “low” are highlighted below along with the appropriate management strategies.

a) Accidental release of viable seeds

Seeds may be accidentally released during transportation and these spilled seeds may germinate and become established in the ecosystem. Spillage of seed is likely, however, it is unlikely that these spilled seeds will germinate and become established in the ecosystem as the post-harvest drying process of forcing hot air through the grains (seeds) would affect the viability of the seeds. Furthermore, corn generally does not survive well without human cultivation. It is an annual plant. Outcrossing with any locally cultivated corn or wild relative of corn is unlikely as corn is not grown as an economic crop in Malaysia and there is no wild relative. However, as some baby corn and sweet corn are grown in this country, there is a likelihood of outcrossing of the GM corn with these. As spillage of seed during transportation is likely, it is proposed that a post monitoring plan should be implemented and any spillage incident should be managed.

b) Planting of seeds

Plants may be grown through the ignorance of uninformed farmers and perpetuated through small scale cultivations. It is noted that the post-harvest drying process of forcing hot air through the grains, affects the viability of the corn grains. Corn is not a major crop in Malaysia. Nevertheless, there could be persistence of GM crop plants in the environment, albeit at low level. These GM corn may pollinate the non-GM baby corn and/or sweetcorn. It is proposed that a post monitoring plan should be implemented and any spillage incident should be managed. 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

TC1507 corn is as nutritious as the non-GM counterparts (EFSA, 2009). Studies show no statistically significant differences in nutritional performance variables and organ weights were observed between Sprague–Dawley rats fed TC1507 corn grain and those fed three non-GM corn control diets (MacKenzie *et al.,* 2007). Usage of maize silage and maize kernels derived from transgenic TC1507 and non-GM control hybrids showed no significant differences on feed intake and milk production of 20 lactating dairy cows (EFSA, 2005). No significant differences in body weight, body weight gain and feed conversion between broilers fed with TC1507 corn, control hybrid corn Mycogen 7250 and four commercial corn hybrids (EFSA, 2005). However, applicant is required to update NBB immediately if additional tests indicate potential adverse effects or the possible presence of toxin or allergen proteins.

IV - Proposed Terms and Conditions for Certificate of Approval

Based on the 22 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 describing the product by the exporter which shall be declared to the Customs of the importing country.

b) Any spillage (during loading/unloading) shall be collected and cleaned up immediately. The approved person shall submit a yearly report to the National Biosafety Board in compliance with procedures for handling any spillage

c) Transportation of the consignment from the port of entry to any destination within the country shall be in closed containers.

d) A post monitoring plan for reporting adverse health effects in human and animals shall be implemented.

e) Should the approved person receive any scientifically proven information/evidences that confirms any adverse effect of TC1507 corn, the National Biosafety Board authority shall be informed immediately for a review (as in Section 18 of the Biosafety Act).

f) 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.

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) Applicant is responsible to ensure that the user and/or importer of the technology are aware of the Terms and Conditions for Certificate of Approval as given in Section IV.

f) The necessary authorities should conduct regular checks on imported corn, local meat (animals fed on these) and imported meat (from countries with this GMP or importing it) to ensure compliance with safety limits of glufosinate residues. There are legal limits on levels of glufosinate that are allowed. Seeds are exposed less to pesticides. Glufosinate and metabolite MPPA3 (3-methylphosphinicopropionic acid) are neurotoxins. Teratogenic and animal studies show that it has reproductive toxicity; and is a skin and eye irritant. However, it is excreted in urine and faeces. Recommended management strategy is initial checks on random batches for residue levels at port of entry.

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

a) No additional issues have been identified that would be important during the assessment of an application for the long-term usage of this product.

b) Continuous monitoring is required from the approved person to report any unanticipated adverse effect caused by the TC1507 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 feed and for processing (FFP)) of a product of a Living Modified Organism (insect-resistant and herbicide-tolerant TC1507 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. Agodi, A., Barchitta, M., Grillo A. and S. Sciacca S. "Detection of genetically modified DNA sequences in milk from The Italian market". *International Journal of Hygiene and Environmental Health* 209 (2006) : 81-88.

2. Aris, A. and Leblanc, S. "Maternal and Fetal Exposure to Pesticides Associated to Genetically Modified Foods in Eastern Townships of Quebec, Canada". *Reproductive Toxicology* 31 (2011) : 528-533.

3. Aumaitre, A., Aulrich, K., Chesson, A., Flachowsky, G., Piva, G."New feeds from genetically modified plants: substantial equivalence, nutritional equivalence, digestibility, and safety for animals and the food chain" *Livest. Prod. Sci.* 74 (2002): 223–238.

4. Aumaitre, A. "Safety assessment and feeding value for pigs, poultry and ruminant animals of pest protected (Bt) plants and herbicide tolerant (glyphosate, glufosinate) plants: interpretation of experimental results observed worldwide on GM plants" *Ital. J. Anim. Sci*. 3(2004) : 107–121.

5. Australia New Zealand Food Authority "Food Derived From Insect-Protected, Herbicide-Tolerant Corn Bt-11" *Australia New Zealand Food Authority* 10 (2001) : 1-36.

6. Atherton, K.T. "Safety Assessment of Genetically Modified Crops" *Toxicology* 181-182 (2002) : 421-426.

7. Bad Science, Bad Decisions: The evidence against Aventis' GM maize. http://www.foe.co.uk/resource/briefings/bad_science_decisions.pdf

8. Bailey, S.A., Robert, H.Z., and Richard W.P. " Relationship Between Organ Weight and Body/Brain Weight in the Rat: What is the best analytical endpoint? Toxicology Pathology 32 (2004): 32-448.

9. Bauer-Panskus, A and Then, C. “Testbiotech opinion concerning the application for market approval of genetically modified maize” 1507 (DAS-Ø15Ø7-1) (2010) *Testbiotech Institute for Independent Impact Assessment in Biotechnology* 25 pgs.

10. Benachour, N., and Seralini, G.E. “Glyphosate formulations induce apoptosis and necrosis in human umbilical, embryonic, and placental cells” *Chemical Research in Toxicology* 22 (2009) : 97-105.

11. Benachour, N., Siphatur, H., Moslemi, S., Gasnier, C., Travert, C. and Seralini, G.E.“Time- and dose-dependent effects of Roundup on human embryonic and placental cells” *Archives of Environmental Contamination and Toxicology* 53 (2007) : 126-33.

12. Bernstein, I.L., Bernstein, J.A., Miller, M., Tierzieva, S., Bernstein, D.I., Lummus, Z., Selgrade, M.K., Doerfler, D.L. and Seligy, V.L. “Immune responses in farm workers after exposure to *Bacillus thuringiensis* pesticides”, *Environmental Health Perspectives* 107 (1999) : 575-582.

13. BPI, Philippines (2003) “Determination of the Safety of Pioneer Hi-Bred’s And Dow Agro Sciences’ Corn 1507 (Insect resistant, herbicide tolerant Corn) for Direct Use as Food, Feed and For Processing”. http://cera-gmc.org/docs/decdocs/09-131-003.pdf

14. Brake, D.G., and Evenson, D.P.“A generational study of glyphosate-tolerant soybeans on mouse fetal, postnatal, pubertal and adult testicular development” *Food Chem. Toxicol.* 42 (2004) : 29-36.

15. Brake, J.,Faust, M.A., and Stein, J. “Evaluation of Transgenic Event Bt11 Hybrid Corn in Broiler Chickens” *Poultry Science* 82 (2003) : 551-559.

16. Brazil National Technical Biosafety Commission “Technical Opinion no. 2053/2009 - Commercial Release of Genetically Modified Tolerance to Glyphosate Herbicide and Insects Resistant Corn (Zea Mays), namely TC 1507 x NK603 Corn” (2009)

17. Canadian FIA “Decision Document DD2002-41 Determination of the Safety of Dow AgroSciences Canada Inc. and Pioneer Hi-Bred International’s Insect Resistant and Glufosinate - Ammonium Tolerant Corn (*Zea mays* L.) Line 1507” Canadian FIA (2002).

18. Calsamigla, S., Hernandez, B., Hartnell, G.F., and Phipps, R. “Effects of corn silage Derived From a Genetically Modified Variety Containing Two Transgenes on Feed Intake, Milk Production, and Composition, and the Absence of Detectable Transgenic Deoxyribonucleic Acid in Milk in Holstein Dary Cows” *American Dairy Science Assocciation* (2007) : 4718-4723.

19. Chesson, A., and Flachowsky, G. “Transgenic plants in poultry nutrition” *Worlds Poult. Sci. J.* 59(2)(2003): 201–207.

20. Chowdhury, E.H., Kuribara, H.,Hino, A., Sultana, P., Mikami, O., Shimada, N., Guruge, K.S., Saito, M., and Nakajima, Y. “Detection of Corn Intrinsic and Recombinant DNA Fragments and Cry1Ab Protein in The gastrointestinal contents of Pigs Fed Genetically Modified Corn Bt11” *Journal of Animal Science* 81 (2003) : 2546-2551.

21. Cisterna, B., Flach, F., Vecchio, L., Barabino, S.M., Battistelli, S., Martin, T.E., Malatesta, M., andBiggiogera, M. “Can a genetically-modified organism-containing diet influence embryo development? A preliminary study on pre-implantation mouse embryos” *Eur*. *J. Histochem.* 52(4) (2008) : 263-267.

22. Codex CAC/GL “Guideline For The Conduct Of Food Safety Assessment of Foods Derived From Recombinant-DNA Plants” CAC/GL 45 (2003) : 1-18.

23. Department of Agriculture-Bureau of Plant Industry “Determination Of The Safety of Syngenta’s Corn BT11 (Insect-resistant and herbicide-tolerant Corn) For Direct Use as Food, Feed and for Processing and For Propagation” : 1- 4.

24. Donkin, S.S., Velez, J.C., Totten, A.K., Stanisiewski, E.P., and Hartnell, G.F. “Effects of feeding silage and grain from glyphosate-tolerant or insect-protected corn hybrids on feed intake, ruminal digestion, and milk production in dairy cattle”*J. Dairy Sci.* 86 (2003) :1780-1788.

25. Duggan, P.S., Chambers P.A., Heritage, J. and Forbes, J.M. “Fate of genetically modified maize DNA in the oral cavity and rumen of sheep. *British J. Nutrition*; 89 (2003) : 159-166.

26. Duggan, P.S., Chambers, P.A., Heritage, J., and Forbes J.M. “Survival of free DNA encoding antibiotic resistance from transgenic maize and the transformation activity of DNA in ovine saliva, ovine rumen fluid and silage effluent” *FEMS Microbiol. Lett.* 191 (2000) : 71–77.

27. Droge-Laser W., Siemeling U.,Puhler A., and Broer I. “The metabolites of the herbicide L-Phosphinothricin (Glufosinate): Identification, stability and mobility in transgenic, herbicide-resistant and untransformed plants”. *Plant Physiology*; 105 (1994).:159-166.

28. EFSA. *“*Application (EFSA-GMO-RX-1507) for renewal of authorisation for the continued marketing of existing products produced from maize 1507 for feed use, under Regulation (EC) No 1829/2003 from Pioneer Hi-Bred International, Inc./Mycogen Seeds Scientific Opinion of the Panel on Genetically Modified Organisms” *The EFSA Journal* (2009) 1138: 1-11

29. EFSA “Scientific Opinion on Application (EFSA-GMO-UK-2007-43) for the placing on the market of Herbicide Tolerant Genetically Modified Soybean 356043 for Food and Feed uses, import and processing under Regulation (EC) No 1829/2003 From Pioneer” *European Food Safety Authority Journal* 7 (2011) : 1-40.

30. EFSA "Opinion of The Scientific Panel on Genetically Modified Organisms on a Request from the Commision Related to the Notification (Reference C/F/96/05.10) for The Placing on the Market of Insect resistant Genetically modified Maize Bt.11, For Cultivation,Feed and Industrial Processing, under Part C of Directive 2001/181EC from Syngenta Seeds" *The EFSA Journal* 213 (2005) :1-33.

31. Einspanier, R., Klotz, A., Kraft, J., Aulrich., K., Poser, R., Schwagele, F.,Jahreis, G. and Flachowsky, G. "The fate of forage plant DNA in farm animals: a collaborative case study investigating cattle and chicken fed recombinant plant material" *Eur. Food Res. Technol.* 212(2001): 129-134.

32. Einspanier, R., Lutz, B., Rief, S., Berezina, O., Zverlov, V., Schwarz, W., and Mayer, J. "Tracing Residual Recombinant Feed Molecules During Digestion and Rumen Bacterial Diversity in Cattle Fed Transgene Maize" *Eur. Food Res. Technol.* 218 (2004) : 269-273.

33. Flachowsky, G., Halle, I., and Aulrich, K. "Long Term Feeding of Bt-corn- a ten-generation Study With Quails" *Archives of Animal Nutrition* 59 (2005) : 449-451.

34. Flachowsky, G. "Poultry Feed from Genetically Modified Plants" *Lohmann Infromation 46* (2011) : 43-60.

35. Food and Agriculture Organization of The United Nations Rome "GM Food Safety Assessment Tools For Trainers" *Food and Agriculture Organization of the United Nations* (2008) : 190 pgs.

36. Gijs, A., Kleter, G.A., Peijnenburg, Ad A. C.M., and Aarts J.M.H. "Health Considerations Regarding Horizontal Transfer of Microbial Transgenes Present in Genetically Modified Crops". *J Biomed Biotechnol*. 2005(4): 326–352. doi: 10.1155/JBB.2005.326

37. Green, J.M. "Evolution of Glyphosate-Resistant Crop Technology". *Weed Science* 57 (2009):108–117

38. Guertler, P., Paul, V., Albrecht, C. And Meyer, H.H.D "Sensitive and Highly Specific Quantitative Real-Time PCR and ELISA for Recording a Potential Transfer of Novel DNA and Cry1Ab Protein from Feed into Bovine Milk" *Anal. Bioanal. Chem.* 393 (2009) : 1629-1638.

39. Herouet C., Esdaile D. J., Mallyon B. A., Debruyne E., Schulz A., Currier T., Hendrickx K., van der Klis R-J., and Rouan D. "Safety evaluation of the phosphinothricin acetyltransferase proteins encoded by the pat and bar sequences that confer tolerance to glufosinate-ammonium herbicide in transgenic plants". *Regulatory Toxicology and Pharmacology* 41 (2005):134-149.

40. Hofmann, C., Vanderbruggen, H., Hofte, H., Van Rie, J., Jansens, S., and Van Mellaert, H. "Specificity of Bacillus thuringiensis δ-endotoxins in correlated with the presence of high-

affinity binding sites in the brush border membrane of target insect midguts" *Proc. Natl. Acad. Sci. USA* : 7844-7848.

41. Hofmann, C., Vanderbruggen, H., Hofte, H., Rie, J.V., Jansens, S., and Mellaert, H.V. "Endotoxins is correlated with the presence of high-affinity binding sites in the brush border membrane of target insect midguts" *Proc. Natl. Acad. Sci. USA* 85 (1988) : 7844-7848.

42. Hohlweg, U. and Doerfler, W. "On the fate of plant or other foreign genes upon the uptake in food or after intramuscular injection in mice" *Mol. Gen. Genet*. 265 (2001) : 225-233.

43. ILSI Research Foundation Washington D.C. "A Review of the Environmental Safety of the PAT Protein. Center for Environmental Risk Assessment" *ILSI Research Foundation Washington D.C., USA* April 11 (2011).

44. Japan Ministry of Agriculture, Forestry and Fisheries. "Biological Diversity Risk Assessment for Maize resistant to Lepidoptera and tolerant to glufosinate herbicide and glyphosate herbicide (cry1F, pat, cp4 epsps, Zea mays subsp. mays (L.) Iltis) (1507×NK603, OECD UI : DAS-Ø15Ø7-1×MON-ØØ6Ø3-6) for provision as food, provision as feed, cultivation, processing, storage, transportation, disposal and acts incidental to them.

45. Konig, A., Kleter, G., Hammes, W., Knudsen, I., and Kuiper, H. "Genetically Modified Crops in The EU: Food Safety Assessment, Regulation, and Public Concerns" *Biotechnology, Agricultural and Food Research* (2003) : 3-97.

46. Ladics, G.S., Bardina, L., Cressman, R.F., Mattsson, J.L., Sampson, H.A. "Lack of cross-reactivity between the Bacillus thuringiensis derived protein Cry1F in maize grain and dust mite Der p7 protein with human sera positive for Der p7-IgE". *Regulatory Toxicology and Pharmacology* 44(2) (2006), 136-143.

47. Lutz, B., Wiedermann, S., Einspanier, R., Mayer, J., Albrecht, C. "Degradation of Cry1Ab Protein from genetically modified maize in the bovine gastrointestinal tract. Journal of Agricultural and Food Chemistry, 53 (2005) : 1453-145.

48. MacKenzie, S.A., Lamb, I., Schmidt, J., Deege, L., Morrisey, M.J., Harper, M., Layton, R.J., Prochaska, L.M., Sanders, C., Locke, M., Mattsson, J.L., Fuentes, A., and Delaney, B. "Thirteen week feeding study with transgenic maize grain containing event DAS-Ø15Ø7-1 in Sprague–Dawley rats" *Food and Chemical Toxicology* 45 (2007) :551–562.

49. Oberdörfer. **"**Nutritional Composition of Glufosinate-Tolerant Field MaizeTransformation Event T25 Europe 2000". *Bayer CropScience GmbH, Germany* (2002**)**.

50. OGTR. Risk Analysis Framework (2009): 106 pgs

51. Paganelli, A., Gnazzo, V., Acosta, H., López, S.L., and Carrasco, A.E. “Glyphosate-based herbicides produce teratogenic effects on vertebrates by impairing retinoic acid signalling” *Chemical Research in Toxicology* 23 (2010) : 1586-1595.

52. Park, K.W., Lee, B., Kim, C.G, Kim, D.Y., Park, J.Y., Ko, E.M., Jeong, S.C., Choi, K.H, Yoon, W.K., and Kim, H.M. “Monitoring the occurrence of genetically modified maize at a grain receivingport and along transportation routes in the Republic of Korea” *Food Control* 21 (2010) : 456–461.

53. Parrot, W., Chassy, B., Ligon, J, Meyer, L., Petrick, J., Zhou, J., Herman, R., Delaney, B. and Levine, M. “Application of Food and Feed Safety Assessment Principle to Evaluate Transgenic Approches to Gene Modulation in Crops” *Food and Chemical Toxicology* 48 (2010) : 1773-1790.

54. Paul, V., Steinke, K., and Meyer, H.H.D “Development and Validation of a Sensitive Enzyme Immunoassay for Surveillance of Cry1Ab Toxin in Bovine blood Plasma of Cows Fed Bt-Maize (MON810)” *Analytica Chimica Acta* 607 (2008) : 106-113.

55. Paul, V., Guertler, P., Wiedemam, S, and Meyer, H.H.D. “Degradation of Cry1Ab from Genetically Modified Maize (MON810) in Relation to Total Dietary Feed Proteins in Dairy Cow Digestion” *Transgenic Res.* 19 (2010) : 683-689.

56. Philippines Department of Agriculture. Determination for the Safety Assessment of Corn 1507 for Direct Use as Food, Feed and for Processing. (2003)

57. Phipps, R.H., Jones, A.K., Tingey, A.P., and Abeyasekera, S.“Effect of corn silage from an herbicide-tolerant genetically modified variety on milk production and absence of transgenic DNA in milk” *J. Dairy Sci.* 88 (2005) : 2870–2878.

58. Rossi, F., Morlacchini, M., Fusconi, G., Pietri, A., Mazza, R. And Piva, G. “Effect of Bt Corn on Broiler Growth Performance and Fate of Feed-Derived DNA in the Digestive Tract” *Poultry Science* 84 (2005) : 1022-1030.

59. Saturnina, C.H. “How Bt Corn MON810 was Approved*” DA-Biotechnology Technical Advisory Team* : 1-5.

60. Schwarz D., Berger S., Heinzelmann E., Muschko K., Welzel K., and Wohlleben W. (2004). “Biosynthetic gene cluster of the herbicide phosphinothricin tripeptide from *Streptomyces viridochromogenes* Tu494”. *Applied and Environmental Microbiology* 70(12) (2004):7093-7102.

61. Shimada, N., Murata, H., Mikami, O., Yoshioka, M.,guruge, K.S., Yamanaka, N., Nakajima, Y., and Miyazaki, S. “Effects of Feeding Calves Genetically Modified Corn Bt11: A Clinico-Biochemical Study” *Clinical Pathology* (2006) : 1113-1115.

62. Sidhu, R.S., Hammond, B.G., Fuchs, R.L., Mutz, J.N., Holden, L.R., George, B., and Olson, T. “Glyphosate-Tolerant Corn: The Composition and Feeding Value of Grain from Glyphosate-Tolerant Corn Is Equivalent to That of Conventional Corn (*Zea mays* L.)” *J. Agric. Food Chem.* 48 (2000) : 2305-2312.

63. Sjoblad R.D., McClintock J.T. and Engler R. “Toxicological considerations for protein components of biological pesticide products”. *Regulatory Toxicologyand Pharmacology* 15 (1992): 3-9.

64. Syngenta Bt11 Maize for European Corn Borer control “EU File on import, food and feed use:”*Bt11 EU Food and Feed Import Dossier* (2010).

65. Syngenta Seeds Comunication “The Facts About Bt Corn” *Kernel Of Gold* (2003) :1-15.

66. Syngenta “Maize Resistant to Lepidoptera and Tolerant to Glufosinate herbicide” *Biological Diversity Risk Assessment Report Annex List.*

67. Taylor, M.L., Hartnell, G., Nemeth, M., Karunanandaa, K., George, B. “Comparison of broiler performance when fed diets containing corn grain with insect-protected (corn rootworm and European corn borer) and herbicide-tolerant (glyphosate) traits, control corn, or commercial reference corn” *Poult. Sci.* 84 (2005) : 587–593.

68. Weber, T, E., B.T. Richert, D.C. Kendall, K.A. Bowers and C.T. Herr. 2000. “Grower-Finisher Performance and Carcass Characteristics of Pigs Fed Genetically Modified Bt Corn”. Purdue University 2000 Swine Day Report.

69. Weber, T.E. and B.T. Richert. Grower-finisher growth performance and carcass characteristics including attempts to detect transgenic plant DNA and protein in muscle from pigs fed genetically modified “Bt” corn. *J. Anim. Sci. 79* (Suppl. 2) 67. (2001) Abstract 162.

70. WHO. “Safety aspects of genetically modified foods of plant origin”. *Report of a joint FAO/WHO Expert Consultation on Foods Derived from Biotechnology. WHO Headquarters, Geneva, Switzerland.* 29 May- 2 June 2000.

71. Wohlleben W., Arnold W., Broer I. Hillermann D., Strauch E., and Puhler A. “Nucleotide sequence of the phosphinothricin *N*-acetyltransferase gene from *Streptomyces viridochromogenes* Tu494 and its expression in *Nicotiana tabacum”*. *Gene* 70 (1988).:25-37.

Appendix I

GENETIC MODIFICATION ADVISORY COMMITTEE (GMAC) MEMBERS INVOLVED IN SPECIFIC RISK ASSESSMENT AREAS FOR THE APPROVAL FOR RELEASE OF PRODUCTS OF TC1507 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**

   Effect on ecology of receiving environment due to unintentional release and planting (e.g. weediness, gene transfer to bacteria, accumulation of toxin in the environment, cross pollination and toxic effects on non-target organisms)

   - **Assoc. Prof. Dr. Mohd. Faiz Foong bin Abdullah (Universiti Teknologi MARA) (Leader)**
   - Dr. Sim Soon Liang (Sarawak Biodiversity Centre)
   - Dr. Martin Abraham (Malaysian Society of Marine Sciences)
   - Madam Atikah binti Abdul Kadir Jailani (Department of Agriculture)
   - Madam Jasbeer Kaur (Department of Chemistry)
   - Dr. Tan Swee Lian (Academy of Science Malaysia)-plant breeding
   - Dr. Mohamed Mohd Salleh (previously Malaysian Agricultural Research & Development Insitute)

2. **HUMAN HEALTH**

   Effect on human health (e.g. acute toxicity of the novel protein, potential allergenicity, mutagenic/tetragenic/carcinogenic effects, reproductive toxicity, potential transfer of antibiotic resistance genes in the digestive tract, the pathogenic potential of donor microorganisms, nutritional equivalence and anti-nutrient activity)

   - **Madam T.S. Saraswathy (Institute of Medical Research)(Leader)**
   - Madam Hasimah Hafiz Ahmad (Malaysian Agricultural Research & Development Insitute)
   - Dr. Norwati Muhammad (Forest Research Insitute Malaysia)
   - Dr. Norliza Tendot Abu Bakar (Malaysian Agricultural Research & Development Insitute)
   - Dr. Rahizzan Issa (Institute of Medical Research)
   - Mr. Jamal Khair b Hashim (Ministry of Health)

3. ANIMAL HEALTH

Effect on animal health (e.g. allergenicity, toxicity, survivability, horizontal gene transfer, anti-nutritional properties, compromised nutritional content)

- **Prof. Dr Jothi Malar Panandam (Universiti Putra Malaysia) (Leader)**
- Dr. Ahmad Parveez bin Hj Ghulam Kadir (Malaysian Palm Oil Board)
- Prof. Dr. Helen Nair (Academy of Science Malaysia)
- Dr. Kodi Isparan Kandasamy (Malaysian Biotechnology Corporation Sdn Bhd)
- Dr. Fuzina Nor Hussein (Universiti Putra Malaysia)