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Review

Risk assessment of genetically modified organisms (GMOs)

Latifah Amin[1,2]*, Zinatul Ashiqin Zainol[1,3], Noor Sharizad Rusly[1,2], Frank Akpoviri[1,3] and Nik Marzuki Sidik[1,4]

[1]Social Impact of Biotechnology Development in Malaysia Research Group (SIMBIO), Universiti Kebangsaan Malaysia, 43600 UKM Bangi, Selangor, Malaysia.
[2]Centre for General Studies, Universiti Kebangsaan Malaysia, 43600 UKM Bangi, Selangor, Malaysia.
[3]Faculty of Law, Universiti Kebangsaan Malaysia, 43600 UKM Bangi, Selangor, Malaysia
[4]Faculty of Science and Technology, Universiti Kebangsaan Malaysia, 43600 UKM Bangi, Selangor, Malaysia.

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Risk assessment is a procedure normally carried out prior to decision-making on the release of genetically modified organisms (GMOs) into the environment. Most countries dealing with the release of GMOs have appropriate guidelines. The objectives of this paper are to critically examine the risk assessment provisions of the Malaysian Biosafety Act (2007), and to compare it with several risk assessment provisions in the Cartagena Protocol, as well as regulations in developed countries. There are inadequacies in the risk assessment provisions of the Malaysian Biosafety Act (2007 Act), compared to those of the Cartagena Protocol, as well as those found in European Commission Directives. Although the central objective of the 2007 Act was similar to the Cartagena Protocol, the Act was found to be very basic with only a brief provision on risk assessment and there is no specific coverage on the socio-economic and ethical aspects as well as the precautionary approach. It is hoped that these inadequacies will be improved upon, in order to bring the Malaysian Biosafety Act closer to the level seen in the biosafety laws of more developed countries and to ensure adequate level of protection for the Malaysian people against any adverse effects of GMOs and products.

Key words: Risk assessment, biosafety, Malaysian Biosafety Act 2007, genetically modified organisms (GMOs).

INTRODUCTION

Nowadays, with the emergence of new genetically modified organisms (GMOs) into the market, biosafety has become one of the major challenges faced by governments mostly in countries that have to deal with such organisms. There is a need to assess their potential adverse effects on human, as well on the environment. With more and more GMOs entering the world markets or are in the process of authorization (Zel et al., 2008), tracing and identifying them are becoming increasingly complicated tasks. Modern biotechnology has broadened the scope of genetic changes made to foods and food products, and widened their possible sources. Genetically modified (GM) foods are not necessarily less safe than those produced through conventional means. Hence, the assessment of GM foods and food products does not require a substantial change in established principles neither does it require a different standard of safety

*Corresponding author. E-mail: nilam@ukm.my. Tel: +0192726182. Fax: +0689252976.

Abbreviations: **GMOs**, genetically modified organisms; **GM**, genetically modified; **EU**, European Union; **LMOs**, living modified organisms; **NBB**, National Biosafety Board; **DNA**, Deoxyribonucleic acid.

(Miller, 1999). According to Madsen and Sandoe (2007), from the early stages of genetic engineering, legal frameworks were set up to ensure the safe development of this technology.

Risk assessment is one of the major steps that have to be highlighted when dealing with GMOs, especially since they may become deregulated (as in the U.S.), may become authorised for limited use, such as importation for use as food (as in the EU), or specific products derived from specific GMOs may become authorised (as in PR China) (Jensen, 2009). The concept of risk operates as a substantial filter: If it proves riskless enough in a due procedure, an artefact may enter the common market and enjoy active legal protection by the regulator. In this way, the regulator aims at protecting the environment and its citizens from biological pollution whilst at the same time creating a market for GM foods and products (Valve and Kauppila, 2008).

According to Raybould et al. (2010), a risk assessment cannot prove that an activity is safe. However, acceptable risk can be demonstrated by sufficient corroboration of risk hypotheses that postulate the absence of harm resulting from that activity. Risk assessment can be defined as a tool to identify and evaluate the potential adverse effects of living modified organisms on the conservation and sustainable use of biological diversity in the potential receiving environment, taking also into account risks to human health. It can also be used by competent authorities to make informed decisions regarding living modified organisms (Cartagena Protocol on Biosafety, 2000).

Concerns that unintended and unexpected side effects might arise from GMOs, as a result of the genetic modification processes used, thereby adversely impacting human and animal health, have attracted attention from both the scientific community and the general public. However, the potential occurrence of side effects from non-GMOs must also be highlighted (Kok and Kuiper, 2003). Scientists have provided better tools for the assessment and evaluation of novel plant products, now or in the future. These include molecular characterisation, toxicological assessment, nutritional assessment and allergenicity. Molecular characterisation is more focused on the identification of the exact genetic construct that was inserted into the host plant genome and to assess the possibility of insertional mutagenic effects. In toxicological assessment, the main focus is on well-characterised single compounds and, until recently, not so much on complex products (Pryme and Lemboke, 2003). Taking into account these practical aspects, as well as ethical issues that are related to the performance of animal toxicity studies, it is clear that this type of study should only be performed if there are clear-cut questions that form the basis of the study (Kok et al., 2008).

For the time being, GMOs should be assessed within the framework of risk analysis. In addition, the science-based technologies, with well functioning regulatory systems can inject the desired confidence and awareness into the public through risk assessments (Niang, 2004). The main idea of this framework is to decide whether to accept the release of GMOs or not, or about whether or not to allow the GMOs to enter the human food chain and should be based on scientific risk assessment processes. It is internationally accepted that risk assessment of GMOs should focus on two particular areas; human health and environmental hazard. Here, two concepts have to be incorporated into the regulatory frameworks governing GMOs: That *of substantial equivalence*, which is used to assess risks posed to human health (OECD, 1993a), and that of *familiarity*, which is used in environmental risk assessment (OECD, 1993b).

Although, the concept of substantial equivalence in the safety assessment of GM foods is new, the primary concept of comparing newly developed products or techniques to existing ones has long been applied in various fields, including agriculture, and science, and technology (Shauzu, 2000). That notwithstanding, the substantial equivalence concept is seen as a comparative advancement in spotlighting the similarities and differences between GM foods and their conventional equivalents. Concurrently, it conveys the view that the perception of substantial equivalence is neither a safety assessment in itself nor an endpoint. Instead, it is just the starting point of the safety assessment. Miller (1999), also stated that substantial equivalence is a conceptual tool for food producers and government regulators and not a scientific formulation, since there is no specification and limits to the kind or amount of testing needed for new foods. For the first time, the idea of substantial equivalence was practically applied on GMOs in the safety assessment of the Flavr Savr tomato prior to placing them on the U.S. market in 1994. The collected data from field trials and from the analyses of the molecular and chemical composition showed that the GM tomato corresponded to the non-modified parent plant, with the exception of the novel commenced traits, which then became the subject matter of further studies with a view to establishing food safety (Schauzu, 2000).

Despite this focus on risk assessment and prevention, GM crops have given rise to controversies over the last 10 to 15 years. It is argued that one reason for this is that the early regulatory frameworks did not adequately address the concerns that seem to underlie public resistance to GM crops. Some of these concerns are about risks which lie beyond the issues addressed by the authorities that approve GM crops. The objectives of this paper is to critically examine the risk assessment provi-

sions of the Malaysian Biosafety Act (2007), and to compare it with several risk assessment provisions in the Cartagena Protocol (2000), as well as regulations in developed countries.

RISK ASSESMENT IN THE MALAYSIAN BIOSAFETY ACT

The Malaysian Biosafety Act (2007) was drafted to be in line with the National Biodiversity Policy (1998) and the National Biotechnology Policy (2005), and it covers only modern biotechnology activities. Malaysia signed the Cartagena Protocol on Biosafety in the year 2000 and ratified it on September 3, 2003. The protocol took effect on December 2, 2003. Following her ratification of the Cartagena Protocol, Malaysia passed the Biosafety Act on July 11, 2007. The 2007 Act states that before GMOs or related products can be imported, prepared, and placed on the market, they shall go through a scientific risk assessment before approval by the National Biosafety Board (NBB).

The Act, which also established the NBB is meant to regulate the release, importation, exportation and contained use of living modified organisms (LMOs), and the release of products of such organisms. Its objective is to protect human, plant and animal health, the environmental and biological diversity. The Act makes it clear that, where there are threats of irreversible damage, lack of full scientific evidence may not be used as a reason not to take action to prevent such damage, and to provide for matters connected therewith.

The Act consists of seven main parts. Part 1 deals with preliminary issues. Part 2 relates to the establishment of the NBB, whilst Part 3 deals with approval for release and import. Part 4 dwells on notification for export, contained used and import for contained use, and Part 5 concerns risk assessment and management. Part 6 relates to enforcement, whilst the final part, Part 7, is on miscellaneous matters. This paper will discuss Part 5 of the Act, that is, risk assessment and risk management in relation to the Cartagena Protocol, as well as regulations in other developed countries.

Since the Biosafety Act (2007) contains only the core provisions, details of the risk assessment and management procedures are to be developed by the Department of Biosafety, Ministry of Natural Resources and Environment (NRE). The Act provides for the assessment of the risks and adverse effects that LMOs will have, or are likely to have on human, plant and animal health, the environment and biological diversity. It also provides for the proposed measures that should be undertaken to prevent, reduce or control the risks and adverse effects that such LMOs and products of such organisms will have, or are likely to have on human, plant and animal health, on the environmental and biological diversity. Part 5 of the Act also talks about emergency response plans, which provide safety measures and procedures necessary for the protection of human and animal health, the environment and biological diversity against harm or damage caused directly or indirectly by LMO or products of such organisms, as well as all necessary measures to be taken in the event of an emergency.

Due to concerns of possible risks with GMOs, the establishment of the biosafety act in Malaysia is important in advancing the development of modern biotechnology. The Act also contains provisions on the mechanisms and procedures (risk assessment and risk management) by which information about GMOs or their presence in foods or products must be disclosed to importing countries and consumers (such as, labelling and identification). Furthermore, public concern and the unknown risks of the GMOs to humans and environment compel the need for disclosure. It is expected that this Act will eventually cover virtually all forms of biotechnology research and development, and perhaps most food imports, produced and processed in the country. Moreover, the Act should be used to ensure that GMOs and related products are safe for use by humans and animals, and harmless to the environment (Mirandah, 2009).

CARTAGENA PROTOCOL ON BIOSAFETY

It has long been recognized that any successful sustainable development strategy has to strike a balance between the interests of trade and concern for the environment. The adoption of the Cartagena Protocol on biosafety represents a significant achievement in trying to reconcile these various concerns, and in assessing the safety of GMOs for release into environment. The Protocol is significant in regulating products of modern biotechnology. But its effectiveness with regard to the protection of biodiversity and human health depends on its ability to adapt to, and catch up with rapid changes in biotechnological research and commercialization.

The key objective of this Protocol is to ensure an adequate level of protection in the areas of safe transfer, handling and use of LMOs that may have adverse effects on the conservation and sustainable use of biological diversity, taking also into account risks to human health, and specifically focusing on transboundary movements (Cartagena Protocol on Biosafety, 2000).

Based on the provisions of the Cartagena Protocol on biosafety (2000), the following general principles can be deduced:

The assessment of risks should be done in ways that are scientifically acceptable and verifiable, and due atten-

tion should be paid to the advice of relevant experts and international organizations.

Uncertainties or disagreements should not be taken to mean the absence of risk in any particular GMO, or that the degree of risk associated with it is tolerable.

The risks associated with GMOs or products derived from them, which have detectable new combinations of replicable genetic materials that have been obtained through the means of modern biotechnology, should be considered in the next generation of the risks posed by the non-modified recipients or parental organisms in the likely potential receiving environment.

Risk assessment, as well as the nature and scope of information required should be based on the particular circumstances of each case, including the particular type of GMO involved, the use for which it is intended, and the environment where it is to be received.

The protocol also includes some methodologies obtained from pre-existing guidelines in some countries. The methodologies generally explain that the process of risk assessment may, on the one hand, give rise to a need for further information about specific subjects, which may be identified and requested during the assessment process, whilst, on the other hand, information on other subjects may not be relevant in some instances. The following are the appropriate risk assessment steps provided in the protocol:

An identification of any novel genotypic and phenotypic characteristics associated with the LMO that may have adverse effects on biological diversity in the likely potential receiving environment, taking also into account risks to human health;

An evaluation of the likelihood of those adverse effects being realized, taking into account the level and kind of exposure of the likely potential receiving environment to the LMO.

An evaluation of the consequences should those adverse effects be realized.

An estimation of the overall risk posed by the LMO, based on the evaluation of the likelihood and conesquences of the identified adverse effects being realized.

A recommendation as to whether or not the risks are acceptable or manageable, including, where necessary, identification of strategies to manage those risks.

Where there is uncertainty regarding the level of risk, it may be addressed by requesting further information on the specific issues of concern or by implementing appropriate risk management strategies and/or monitoring the LMO in the receiving environment.

CODEX ALIMENTARIUS COMMISSION

Global guidelines for risk analysis and risk assessment of GMOs have been developed by the Codex Alimentarius Commission (CAC) in several documents. One of those documents, “The Principles Document”, advocates that a new GM food product should be assessed for its safety by comparing it with food that has an established history of safe consumption, in order to identify potential hazards requiring further considerations. As noted earlier on, this view is typically referred to as the “concept of substantial equivalence”. This document also stresses that risk managers should take into account uncertainties identified in the risk assessment and implement appropriate measures to manage them (Codex, 2003).

EUROPEAN UNION REGULATIONS ON BIOSAFETY

Presently, within the European Union (EU), seven legal instruments, comprising both directives and regulation, govern the use of GMOs in areas pertaining to food and feed (Table 1). The three central legal frameworks directly related to food and feed are Council Directive 2001/18/EC on the deliberate release into the environment of GMOs, Regulation (EC) No. 1829/2003 on GM food and feed, and Regulation (EC) No. 1830/2003 pertaining to the traceability and labelling of GMOs and the traceability of food and feed products, produced from GMOs (EC, 2001, 2003a, b). The first two of these legal instruments stipulate a pre-market assessment of GMOs and aims at securing market by releasing only those GMOs that are safe for humans, animals and the environment (Alderborn et al., 2010). The following table shows the key EU Directives and Regulations of relevance to the growth and marketing of GMOs.

According to EU legislation, the key elements in granting authorization to place a GMO intended for food and feed use on the common market include a safety assessment carried out by the European Food Safety Authority (EFSA), and the availability of validated event specific detection methods (European Commission, 2003a; European Commission, 2002). Mehmet (2011) notes that: Article 12 of the New GMO Regulations allows the Biosafety Council to conduct a simplified authorization procedure by taking into consideration a ‘socio-economic assessment’, provided that the application is accompanied by previously conducted environmental risk assessments, and is supported by information indicating that there exists no possibility of any harm deriving from the GMOs and products derived from them, to human, animal and plant health, nor to the environment or biodiversity.

By contrast, under the relevant EU legislation, in respect of genetically modified food and feed for placing on the market, Regulation 1829/2003 prescribes a standard authorization procedure, a simplified procedure is applicable where the deliberate release into the environment

Table 1. Key EU directives and regulations of relevance to the growth and marketing of GMOs.

Legal framework	Coverage
Directive 98/81/EC	On the contained use of GMOs. Applies to research stages of product development
Directive 2001/18/EC	On the deliberate release into the environment of GMOs and repealing Council Directive 90/220/EEC
Regulation (EC) No. 1829/2003	On GM food and feed. Specifies authorization procedure and labelling requirements
Regulation (EC) No. 1830/2003	Concerns the traceability and labelling of GMOs and of derived food and feed products. Specifies amendments of Directive 2001/18/EC
Regulation (EC) No. 1946/2003	On transboundary movements of GMOs. Implements the Cartagena Protocol on Biosafety
Regulation (EC) No. 641/2003	On detailed rules for GMO authorization with respect to documentation on detection and identification methodology
Regulation (EC) No. 65/2003	On the development and assignment of unique identifiers for GMOs

Sources: Alderborn et al., 2010.

of genetically modified plants is concerned (Article 7(6), Directive 2001/18).

In the authorization of GMO releases, this may be far from being a straightforward process. GMOs are exceptionally politicized objects of environmental regulation. Moreover, as components of hybrid networks of primary production, GMOs have no predetermined boundaries. Proceduralization aims to promote legal flexibility and reflexivity by increasing the scope of case specific discretion. Such space is essential for meaningful public participation and for the integration of general policy goals and particular environments. In practice, proceduralization shifts the regulatory focus from substantive ends to knowledge generation and decision-making procedures (Valve and Kauppila, 2008).

DISCUSSION

In this paper, comparison has been made between the Malaysian Biosafety Act (2007 Act) and the Cartagena Protocol and the EC Directives. Compared to the Cartagena Protocol on Biosafety, the central objective of the 2007 Act is broadly the same, which is ensuring adequate level of protection: Safe transfer, handling and use of living modified organisms (LMOs) that may have adverse effects on the conservation and sustainable use of biological diversity, taking also into account risks to human health, and specifically focusing on transboundary movements (Cartagena Protocol on Biosafety, 2000).

Risk assessment in the 2007 Act is very basic compared to that of the Cartagena Protocol and the European Commission. Although risk assessment is one of the main foci of the Act, the relevant provisions are very brief, and there is no specific indication of the actual procedures that should be taken. Since the advances in gene technology have led to speculation and fears in the public regarding its potential risks, the regulatory guidelines related to the release of recombinant Deoxyribonucleic acid (DNA) in the environment have been riddled with inconsistencies (Haguenauer, 1996). Such processes have been harmonized in Europe through the implementation of the European Commission (EC) biotechnology directives. These regulations are applied to preclinical research that mainly relates to the use of GMOs. Wynne (2005) notes that risk assessments are, as a rule, presented as open scientific knowledge, but in practice, always framed in a way that supports social control and authority.

Although, scientific knowledge produces, and is used in a context of political decision-making, embodies traditional scientific characteristics, it also holds additional properties linked to its influence on social, political and economic relations. Therefore, the significance of uncertainty cannot be assessed based on quality criteria that refer to the scientific content only. Uncertainty must also include quality criteria specific to the properties and roles of this scientific knowledge within political, social, and economic contexts and processes (Maxim and van der Sluijs, 2011). Failure to consider scientific uncertainty at the interface between science and policy has led to numerous controversies with consequences (Keepin and Wynne, 1984; Van der Sluijs, 2002).

As mentioned earlier, the Malaysian Biosafety Act consists of 7 main parts. Amongst those, risk assessment has become the significant part, which also has an equivalent in the Cartagena Protocol. However, the major difference between those two procedures is that the Cartagena Protocol is more concise and exhaustive in explaining and describing the risk assessment procedure compared to the Malaysian Biosafety Act. Apart from risk assessment and risk management, the 2007 Act does not cover socio-economic, and ethical issues, as well as precautionary principles. Instead, the Act only focuses on

approval for release and import, as well as notification for export and import for contained use.

Against this background, it may be suggested that socio-economic and ethical requirements, as well as precautionary principles should be highlighted and properly addressed, since all these aspects have considerable impact in shaping public, and, in particular, consumer perception and acceptance of GMOs. The inadequacies and ambiguities of the Act on these matters lead to practical problems in its implementation. However, compared to the Act, the Cartagena Protocol, whilst addressing socio-economic issues, is patchy in precautionary principles and ethical issues, thus making it difficult to adopt the guidelines and references without having any difficulty to recognize it as one major protocol.

The Protocol states the importance of socio-economic issues in consistence with the impact of LMOs on the conservation and sustainable use of biological diversity especially with regard to the value of biological diversity to indigenous and local communities. From the legal provisions of the 2007 Act, it can be observed that all the prescriptions will be made by the NRE, based on the necessity and needs perceived by the Act with regard to GMOs in Malaysia.

Since the 2007 Act and regulations follow the Australian regulations, particularly, the Gene Technology Regulation (2001), it demonstrates some similarities with the regulations of the developed countries, such as those of the EU and the UK. Even though risk assessment and risk management are not detailed out in the Act, the procedures for actions to be taken in the release of GMOs can be seen in the forms supplied by the Department of Biosafety, NRE, which is the government body that is responsible for management of the biosafety aspects of GMOs and GMO-related products, as well as all matters generally connected with the modern biotechnology process.

However, there are two situations that should be concerned when dealing with risk assessment of GMOs. According to Sparrow (2010), the regulation of GMOs can be divided into two parts: 1) contained use and 2) deliberate environmental release (non-contained use). The questions asked in all GM risk assessments will be similar for both contained and non-contained use; however, the depth of supporting information and detail will be far greater for the latter". It should be clarified here that contained use is the production of GMO in the laboratory, and typically, that covers work in laboratories, greenhouses, and closed industrial production facilities. On the other hand, deliberate environmental release relates to experimental release and placing on the market.

The 2007 Act dwells upon the two main situations mentioned above, but it is not as detailed as the equivalent provisions in the EC Directives, except for those aspects concerning release activities of LMOs for research and development purposes in all field experiments, or importation of LMOs. As mentioned already, these procedures are implicitly contained in the risk assessment forms supplied by the Department of Biosafety, NRE. The Act also highlights export and import for contained use, but for general information purposes only. The Act is more focussed on the notification of the relevant requirements, compliance with the requirements of the importing country, specific measures to be taken with regard to contained use and the role of the NBB and the NRE in handling these situations.

Similar observations can be made about the Cartagena Protocol. Whereas the Protocol does mention the subject of risk assessment, its provisions on contained use are very limited compared to the EC directives. The Protocol is more focussed on the procedures for LMOs intended for direct use as food or feed, or for processing. This is a sharp contrast from the Act in which contained use is the major point of concern.

CONCLUSION

The risk assessment procedures that have been implemented worldwide are important. They are needed in order to overcome the problems emanating from GMOs or related products. In addition, they can improve the safety level of GM products intended for public use. Hence, they also can help to clarify the objective that underlies the production of GMOs. Apart from the risk assessment procedures, there are several other methods of testing meant to identify and improve the quality as well as the safety of GMOs. These tests or methods, which have been developed by renowned scientists, include the nutritional assessment test, the allergenicity test, the toxicity test and the compositional studies. These are the well-known tests that GMOs have to go through in order to ensure that the safety of the products is acceptable to all consumers and members of the general public. These procedures if followed appropriately will be able to raise the confidence of all parties concerned.

There are inadequacies in the risk assessment provisions of the Malaysian Biosafety Act, compared to those of the Cartagena Protocol, as well as those found in the regulations of more developed countries. It is hoped that in the future, those inadequacies will be improved upon, in order to bring the Malaysian Biosafety Act closer to the level seen in the biosafety regulation of more developed countries, such the EC directive. More rigorous and clear coverage of the socio-economic, ethical and religious aspects regarding GMOs should be

taken into account to harmonise the Malaysian Biosafety Act. Although, the genetic modification has the potential to benefit Malaysia and its people, it should be adopted under conditions that avoid any potential risks to human and to the environment, in accordance to the norms and religious acceptance of the people. Adequate regulations are necessary to avoid possible environmental and safety problems, while caution (precautionary principle) is necessary in the face of scientific uncertainties related to GMOs which can jeopardize the expected benefits of this new science.

It would also be helpful to carry out more studies in other important fields in order to develop more useful techniques aimed at improving the reliability of GM food safety assessment. Furthermore, the development of new techniques could be useful to the improvement and assessment of GM crops. More systematic measures and research work are required in order to ensure that GM foods do not cause or aggravate health problems. There should be effective agencies with appropriate authority that are charged with the approval of GM foods and products. The decisions of such agencies should be based on the recommendations of specialized committees, organized by or working in conjunction with the agencies. In addition, proper consideration should be given to expert views disseminated in scientific publications.

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