SAFETY ASSESSMENT OF GENETICALLY MODIFIED FOOD IN INDONESIA*

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ABSTRACT

Through the use of recombinant DNA (rDNA) techniques, modern biotechnology is changing the ways that strains of micro organisms, plant and animals are developed and used. The DNA of interest is cloned on vectors and transferred to the plant or other cells. For example, genes encoding insecticidal toxins from *Bacillus thuringiensis* (Bt) have been introduced into maize, potato and other plants to produce transgenic insect-resistant plants.

Safety assessment of GM foods should take place with "case-by-case" variations, taking into account the conventional counterpart's long history of safe use. Specifically, safety assessment of GM foods should include the following: identification of the organism that has been modified and the source organism of the introduced gene; identification of the gene products, including description of characteristics of the inserted gene; and evaluation of the safety of expected novel substances in the food. One approach taken by regulatory bodies is to obtain data on the composition of a GM food in relation to its conventional counterpart.

Proteins have the potential to cause allergic reactions. Food allergens are typically large proteins often glycosylated, and are relatively stable to food processing and digestion. Safety assessments of GM foods usually include assessment of the allergenic potential of the newly introduced proteins. One proposed approach to assessing the allergenic potential of new proteins in foods derived from GM plants is using the FAO/WHO decision-tree. Recently software became available to predict spatial protein structures from linear amino acid sequences. This may allow for comparisons of the studied proteins with the secondary and tertiary structures of known allergens

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Assessment of GM Food in Indonesia adopt principle of precautionary approach. Structured systems had been developed through several Decrees and Regulations on the biological and food safety which had been issued by Ministries and BPOM. The regulations cover requisites data for safety of GMF, procedure and mechanism of food safety assessment, and decision on the GMF proposed.

Propose of distribution of any GMF (local or imported) in Indonesia has to submit basic information which indicate and ensure its safety. The information cover ruethodology of genetic engineering performed which has to follow scientifically valid standard procedures. Other information is the nutrient content of the GMF which has to be substantially equivalent with the non GMF counterpart, including the macro and micronutrient (carbohydrate, lipid, protein, ash, minerals, amino acid, fatty acids), content of toxicant, anti nutrient and possible allergen (if any), information on the protein expressed from the inserted gene which should be proven non allergenic.

Several parameters/questions which should be answered by Applicants include those of general biology and food aspects, genetic aspects and food safety. The General information include name/species of GMF, physical properties, nutrient characteristics and stability, and information weather the GMF proposed has been consumed in other countries, and data on the substantial equivalent of the GMF. The Genetic aspect include data on characteristics of DNA insert, sources and function, information weather the GMF source and insert contain gene encoding or gene which can induce allergenic protein and toxic substances, description of the transformation system and gene introduction, cloning, expression vectors, and selection methods. In some cases data on animal studies using GMF can support the food safety aspect.

INTRODUCTION

Genetically modified food (GMF) are food produced from genetically modified organisms (GMO). The genome of those organisms are altered through genetic engineering. The insert DNA taken from another organism is added to the organism's genome to produce both new and useful modified traits or phenotypes. This leading technology facilitates major innovation in health care chemical, agricultural and food sectors. The genetically modifying technique facilitates the combination of DNA which will not occur naturally.

One of the **examples** of **GMO** is **the** GM corn. **A** series of Bt gene from B. *thuringiensis* **is** excised by enzymes. The Bt gene is then inserted into corn expression cassette with promoter and terminator at each end. That cassette is then inserted into **a ylasmid** vector. The vector with transgene is multiplied in bacteria and the foreign genes is inserted into corn cell genome to give GM corn. The CM corn is able to produce Bt protein crystal which acts as pesticide that deters any insects from eating the crop.

Other example is golden rice which was introduced with 3 genes simultaneously so the paddy can produce 3 enzymes which assist in the beta carotene synthesis (phytoene synthase, phytoene desaturase, lycopene β-cyclease). The resulting rice is yellow golden in colour and is high in beta carotene. **As** of April *2002*, there are fifty products of GM foods evaluated by FDA. The total number *of* modified attributes **is** 62 because several products were modified with multiple attributes. According to GMO Compass (2008), in 2007 the cultivation of GM plants was done in **23** countries, twelve of which are developing nations. The greatest increase **was** shown by maize which added 1 million hectares to its area. Some products that are genetically modified is listed on the table below.

Table 1. The traits and sample products of GMO

Trait	Advantage	Sample Product
Pest-Resistance	Less damage by insect, virus, bacteria, etc.	Corn
Herbicide-Resistance	Herbicides will kill only weeds, not crops	Cotton
Delayed Ripening	Can be shipped with less damage	Tomato
Miniature Size	Improved eating quality	Watermelon
Improved Sweetness	Better tasting	Sweet peas
Cold-Resistance	Withstands freezing and thawing	Strawberries
High Starch	Absorbs less oil when fried	Potato
Polyester Gene Added	Better fiber properties	Cotton
Growth Hormone Added	Faster growth	Salmon
Hepatitis B Virus Protein Added	May provide immunity to Hepatitis	Banana

GMF REGULATION

The commercialization of GMF is under tight regulation by national and international bodies. The industries are required to submit complete experimental data of their products to ensure the safety of GMF consumption. There are a lot of parameters that the industries need to provide to be able to meet national regulation procedures. The parameters are nutrition composition, antinutrition , and toxic substance (required in Argentina, USA, Canada, UK, Australia and Japan),information on insert DNA, host characteristics, stability of gene modification, natural allergenicity and allergenicity of new protein (required in USA, Canada, UK, Australia and Japan), quantity and type of new protein expressed in GMO (required in UK and Australia), amino acidsequence homology between new expressed protein and known allergen data base (require in Argentina and Japan), characteristics and suitability of GMO for human and animal consumption (Argentina), and changes in use and processing of GMO(Canada and Japan).

In Indonesia, the principle taken to regulate the GMF is precautionary approach. There was a need of structured system which will analyse possible risks. The basic rule for biological safety assessment of GM products were the decree from Ministy of Agriculture number 856/Kpts/HK.330/9/1997. It was later revised as decree of 3 Ministries (Agriculture:Horticulture Section, Forestry, and Health) No. 998.1/ Kpts/OY.210/9/99; 790.a/Kpts-IX/1 999; 1145NMENKES/SKB/IX/199; 015A/Nmeneg PHORI 09/1999. The assessment of GM products need to follow the standard protocol. Government Regulation No. 21, 2005 is regarding the biological safety of GM products. Rule and regulation in relation with safety assessment GMF has to be followed by Proponents and Technical Team involved in Assessment. The regulations cover the requisites data for safety of GMF, procedure and mechanism of food safety assessment, and decision on the GMF proposed.

The necessary basic information which indicate and ensure the safety of GMF in Indonesia must be provided. The information includes the methodology of genetic engineering performed (has to follow standard procedures which are scientifically valid), the nutrient content of the GMF has to be substantially equivalent with the non GMF counterpart (carbohydrate, lipid, protein, ash, minerals, amino acid, fatty acids), the content of toxicant, antinutrient and allergen (if any) has to be substantially equivalent with those in the Non GMF counterpart, the protein expressed from the inserted gene should not be allergenic, and there should be a destruction mechanism/methodology followed if there is any alteration/deviation found in the future.

The mechanism of proposal of GMF assessment is as follow. Institution interested to distribute GMF should submit written proposal to Committee of Food Safety of the Ministry/BPOM. Proponents need to fill in a specific form and answers all the questions asked in the form (non satisfactory data will be returned). Proponents should complete the data required and resubmit within 14 days of announcement.

For assessment, the Committee of Food Safety will appoint Technical Team to conduct desk evaluation. Any inappropriate case/indication related to religious, ethical, social/culture and esthetical aspects found will result in negative recommendation. Technical Team will conduct desk evaluation and when needed can

ask additional independent laboratory analysis. Assessment is conducted within 56 days which then will be reported to the committee as consideration for further recommendation. The process and result of technical evaluation will be given to the proponents and announced to public to give a chance for community 's participation. The information announced exclude those related with commercial aspects or Intellectual Property rights. If within 60 days, there is no public response, the Committee will assume that there is public acceptance of the recommended GMF. Committee will give recommendation to Ministry/Head of BPOM based on evaluation by Technical Team and Public participation. GMF will be given certificate of safety by related Ministry/BPOM. GMF which does not pass the safety evaluation will be reported to the Ministry/BPOM. Certificate and recommendation is the basis for GMF distribution in Indonesia.

The Government Regulation No. 69/1999 Article 35 regulates the food labeling and advertisement. The safety assessment labeling of GMF is needed to provide consumer information about food whether it contains GMO or not. The consumers have a right to choose the food they like. There is no relation between GMO labeling with the safety of the GMO in the packaged food. The food is labeled only when the content of GMO in the packaged product exceeds the threshold level (5 %).

There are 3 main parameters or questions that should be answered by the GMF distributor applicants in Indonesia. The first one is general biological and food aspects. The applicant needs to specify the name/species of GMO (scientific name, taxonmical classification), physical properties, nutrient characteristics (main nutrient, antinutrition, allergen and toxic substances) and stability and answer to these questions:

- Has this GMO has been previously applied in Indonesia ?
- Any recorded advantageous and disadvantageous?
- Has this GMO been consumed elsewhere ?
- Is there any other country which reject this GMO ?
- What were the basis for rejection ?
- Are there factors which possibly (potentially) related to any risk of the GMO consumption in Indonesia compared with in other countries?
- Is this GMF imported ?

- Any legal document for GMO evaluation from the country of origin ?
- What is the aim of applicants to produce or import GMO ?
- What are the advantages of this GMF compared with the conventional counterpart ?
- Is the GMO prepared for any specific group ? (babies, children, elderly) If yes,please explain.
- Has the donor organism been used to produce food or used as food ? If yes, what is the consumption levels, and what type of food processing was used before consumption ?? If not please explain
- If this is a mixed product, what is the percentage of GMF?

The second parameter is the genetic information. There should be explanation of the genetic sources and DNA inserted that includes the description of characteristics of component of DNA insert, sources and function, possibility of GMF source contain gene encoding allergen protein and toxic substances, the vector construct, transformation and selection method, the phenotypic and genotypic characteristics of the modified organism compared with the conventional counterpart/sources. There should be explanation of the possibility that the inserted DNA can be transferred to other organism (if yes, to which organisms, the mechanism of transfer, the result of this transfer), and the possibility of GMF mixtures which contain more than 1 products can induce interaction which affect the food safety (if yes, mention the possible effects). Comparable data (non significance difference) should be reported on growth and developmental characteristics, plant and ear morphology, plant health and vigor indicators and pest susceptibility, yield characteristics, and survival capacity. The data should infer that GMF does not differ in biological fitness, reproduction, and dissemination if compared to the natural organism. Information on the transferred gene (stability, the phenotype expression, allergenicity, consumption of gene and the products) needs to be documented. The description of the methodologies used (DNA extraction, DNA quantitation and restriction enzyme digestion, Southern blot analysis, Determination of insert number and copy number, the integrity of inserted gene cassettes, selection following gene insertion. Other methodologies needed are the description of the transformation system and gene introduction, method to isolate cut and inserted gene fragment,

cloning and expression vectors, characteristics, functional gene used to construct the gene, gene map, method of transformation) for GMF is necessary too.

The third parameter is food safety. If there are any changes in the nutrient content, explain the changes in the document. Some analysis that can be done are proximate analysis, composition of other relevant nutrient, anti-nutrition and allergen substances analysis.

Other data for evaluation of proposed GMF in Indonesia needed are bioinformatic evaluation, sequence similarity using FASTA and ALLERGENSEARCH, biologically relevant sequence similarities to allergens or toxins, and short (eight amino acid) polypeptide matches shared between the new protein sequence and proteins in the updated allergen database.

FOOD ALLERGY IN GMF

Food allergy is one of the principal safety concerns of GMF. The Codex Alimentarius Commission and EFSA recommend procedures to assess new proteins in GMF which are likely to cause allergy.

All proteins are made up of a long chain of amino acid folded into three-dimensional structure. The allergenic properties are determined by only a few amino acids that form the docking point for antibody. If antibody can bind themselves to a new protein, there is a high chance of allergic reaction. The method is to find the homology of the amino acid sequences and compare those with known allergens. Indications of allergic potential is the correspondence of four to eight consecutive amino acids or correspondence of 35 percent over a span of 80 amino acids. The databases containing amino acid sequences of numerous allergens are available. Powerful computers can make a more precise evaluation on the massive amount of information collected on protein. If there are negative reaction tests with blood serum and the GMF proteins do not break down easily in the digestive tract, there might only be a small chance that the GMF contains allergens. Some methodologies to test the allergenicity are protein electrophoresis, western blotting and animal testing.

CONCLUSION

The regulations have clearly stated and specified the necessary requirements for GMF introduction in Indonesia. If a distributor fulfill all the requirements for GMF and the BPOM approves the application, the GMF is safe to be consumed by the consumers across Indonesia. Indonesia is ready to carry out the safety assessment of genetically modified food.