*International Journal of Life Sciences Vol. 4. No. 4. 2015. Pp. 240-250*


***Review Paper***

# Genetically Modified Crops- Perceptions, Concerns Assessment and Regulations for Food Safety in the Context of Human and Animal Nutrition

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***Abstract***

*Genetically modified (GM) crops are developed to create biologically more robust plants to protect them from insects and pests and also to meet the nutrient requirements of ever increasing human and livestock population. Around the world, farmers plant more biotech crops, because they are more tolerant to biotic and abiotic stresses. Of late, there is wide spread public concern with regard to safety issues and risks of consumption of GM crops. One group argues that GM crops provide a means to improve the economic status of poor farmer and so compelling clue to mitigate global hunger. Longstanding argument is that GM crops can adversely affect the human or animal health in the form of allergens and transfer of antibiotic resistance. A new platform, FAO-GM foods has been launched along with 36th Codex Alimentarius Commission; to share information on safety of GM crops .Current research indicates that GM crops are likely to be equivalent to that of traditional foods. Generally human consume a minimum of 0.1 to 1 gm of DNA and the possibility of adverse effects arising from transgenic DNA in GM foods /feed is minimal. But allergens and toxins produced are major concerns about GM crops. No single method is available to test allergens in human /animal responses. Only one documented evidence of human allergens to soy bean protein is recorded. At present no toxological or nutritionally significant effects have been noticed in transgenic crops so far marketed as GM foods. No contribution to antibiotic resistance to bacteria arising from antibiotic markers in GM foods has been documented. Nutritional value of plant and animal sources of food derived from biotech crops is not affected, as indicated by feeding studies with animals. Transgene product that is designed for pesticide effect is not going to affect the non- target organisms. But there is a clear need to develop effective protocol to allow the assessment of safety of whole food. In developed countries, exhaustive screening tests are employed to foods derived from GM crops ,for food safety and are compared to traditional non GM foods in terms of molecular, compositional, toxicological and nutritional data for substantial equivalence ( SE). Labeling of GM foods from plant sources as per consumer choice is required in some countries, but in respect of animal products labeling is not practicable. Currently available GM foods/feeds are thoroughly screened to be safe for use or consumption, because they have been evaluated for food safety before introducing into market for commercialization.*

***Key words:*** *GM crops, concerns, perceptions, food safety, assessment, human and animal nutrition*

## Introduction

Genetically modified crops (GM Crops) are those which have had their DNA altered in a way that does not occur naturally. Individual genes which promote durability and nutritive value are transferred from one organism to another to create biologically robust plants. Initially GM crops are developed in response to growing concern about protecting crops from insects, unusual weather pattern and harmful pests. The GM crops offer potential food security by providing balanced diets for an ever increasing human and livestock population around the world. During the years of commercialization (1996-2007) around the world, farmers continued to plant more biotech crops. United State of America tops the world ranking, with 57.7 million hectares (63% biotech maize, 78% of biotech cotton and 37% of all biotech crops) by the year 2007 (James Clive, 2007).Other principal adopters of biotech crops (Soy bean, maize, cotton and canola) are Argentina (19.1 million ha), Brazil (15.0 million ha), Canada (7 million ha), India (6.2 million ha) and China (3.2 million ha). These products have very important features, and future trends, which meet the multiple needs of the farmers and consumers because they are more tolerant to biotic stresses caused by pests, weeds and diseases and biotech stresses like drought, salinity, acidity, water logging ,frost etc. Biotech crops reduce the environment foot prints of agriculture like reduction in use of fertilizers saving on fossil fuel and decreasing carbon dioxide emission. Biotechnology can be used to cost- effectively to optimize the productivity of biomass per unit area of first generation food, feed and fiber crops and second generation energy crops (James Clive, 2007).

**Public perceptions**

Of late, discussions around the world are centered on GM crops, which attracted the attention of public and Governments as well**.** There is widespread popular perception that consumption of genetically modified food is harmful, and based primarily on that concern, but also on wider concerns about the environment, anti-GMO activists have lobbied for restrictions on growing modified crops and on selling such food, and for labels on genetically modified food that is sold. Particular concerns claim that genetically modified food causes cancer and allergies. Leaders in driving public perception of the harms of such food in the media include Jeffrey M. Smith, Dr. Oz, Oprah**,** and Bill Maher; organizations include Organic Consumers Association Greenpeace (especially with regard to Golden rice) and Union of Concerned Scientists. Social science surveys have documented that individuals are more risk averse about food than institutions. There is widespread concern within the public about the risks of biotechnology, a desire for more information about the risks themselves and a desire for choice in being exposed to risk. There is also a widespread sense that social and technological change is speeding up and people feel powerless to affect this change; diffuse anxiety driven by this context becomes focused when it is food that is being changed.

Various religious groups have raised concerns over whether genetically modified food will remain *kosher or halal.* In 2001, no such foods had been designated as unacceptable by Orthodox rabbis or Muslim leaders. However, there are Jewish groups that dispute this designation. Genetically modified organisms have come to be seen by the public as "unnatural" which creates a negative halo affect over food that includes them. Some groups or individuals see the generation and use of such organisms as intolerable meddling with biological states or processes that have naturally evolved over long periods of time, while others are concerned about the limitations of modern science to fully comprehend all of the potential negative ramifications of genetic manipulation. Other people see genetic engineering as a continuation in the role humanity has occupied for thousands of years in selective breeding. There is growing concern among consumers around the world with regard to safety issues of GM crops due to introduction of new genes into plant genome resulting in important doubts in the mind of consumer such as 1.Could the inserted DNA or modified genes or, their products, if transferred to animals ,cause any adverse effects in these animals. 2. Could these DNA fragments or proteins be transferred to and accumulate in the products (milk, meat and eggs) of animals fed GM crops and 3.will consumption of agricultural crop materials or animal products derived from GM crops lead to adverse health effects in human (Beever and Kemp2000) .The general opinion in the case of GM crops hinges on two basic issues: economics and global hunger .The ability to grow and reap abundant crops is the primary propeller of the proponent of GM crops ( Reddy 2011).

***The case for GM crops***

A recent study at George –August University in Germany concluded that GM crops can yield positive economic results. Research conducted for six years in India revealed that using biotech cotton enhanced crop yield by 24%, while profits increased by 50%. Bill and Melinda Gates Foundation sponsored research and development of GM crops argued that these GM crops provide a means for farmers to maintain livelihood in the face of changing climate conditions.

***The case against GM crops***

Long standing argument is that GM crops and the food they produce can adversely affect human health in the form of allergic reactions and transferred antibiotic-resistant genes to the human body. Regarding malpractices among companies who supply GM crops can add further to the apathy. Several countries have requested FAO to facilitate international dialogue on the issue of trade disruptions involving low levels of GM crops in international food and feed trade. Such an initial dialogue would review the extent and pattern of trade disruptions based on reporting from member countries and would explore likely trends. The Technical Consultation aims at facilitating a common understanding of the issue.

A new international Platform has been created to share information on safety assessment of foods derived from recombinant-DNA plants authorized in accordance with the Codex Plant Guideline, entitled “Guideline for the conduct of food safety assessment of foods derived from recombinant-DNA plants (CAC/GL 45-2003, annex III adopted in 2008) ". This Platform also facilitates the effective utilization of food safety assessment in situations of Low Level Presence (LLP) of r-DNA plant materials in food. FAO GM Foods Platform has been officially launched in July 2013 and accessible at http://fao.org/gm-platform. The database will gradually expand as Member countries upload their information in the future. The final report of the launching event (side event to the 36th Codex Alimentarius Commission) is available. In March 2014, Food Safety at FAO Highlight was published on the topic of FAO GM Foods Platform.

The application of modern biotechnology to GM food and feed production (GM food) presents new opportunities and potential benefits, as well as challenges in ensuring consumer protection. Recent developments have posed concerns, both real and perceived, about the safety of these technologies.Member Countries, especially developing ones, look to FAO to provide sound and unbiased advice on the safety of GM food, in collaboration with international bodies such as Codex, has been involved in a wide range of biotechnology related issues, including: Science-based safety evaluation and risk assessment systems to objectively determine the benefits and risks of GM food.

In 1999, the Codex Alimentarius Commission (CAC) established an Ad hoc Intergovernmental Task Force on Foods Derived from Biotechnology to consider the health and nutritional implications of such food. It is tasked with developing standards, guidelines or

recommendations, as appropriate, for foods derived from biotechnology or traits introduced into foods by biotechnology. It provides critical guidance as to the nature of any increased health hazards in the new food. To establish substantial equivalence, extensive comparative studies on the chemical composition, nutritional quality, and levels of potentially toxic components, in both the engineered and conventional crop and animal, are conducted. Notable differences between the existing and new organism would require further evaluation to determine whether the engineered form presents a higher level of risk. Through this approach, the safety of current biotechnology-derived foods can be compared with that of their conventional counterparts, using established and accepted methods of analytical, nutritional and toxicological research is needed.

Results of studies made in this direction, have established that the level of safety to consumers of current genetically engineered foods is likely to be equivalent to that of traditional foods. Currently no verifiable evidence of adverse health effects of GM foods has been reported, although the current passive reporting system probably would not detect minor or rare adverse effects or a moderate increase in effects with a high background incidence.

The alterations in the composition of existing foods produced through biotechnology are quite limited. Assessing safety may be much more difficult in the future if genetic engineering projects cause more substantial and complex changes in food materials. Methods have not yet been developed with which whole foods (in contrast to single chemical components) can be fully evaluated for safety. Progress also needs to be made in developing definitive methods for the identification and characterization of proteins that are potential allergens, and this is currently a major focus of research. Improved methods of profiling plant and microbial metabolites, proteins and gene expression may be helpful in detecting unexpected changes in GM organisms and in establishing substantial equivalence. A continuing evolution of toxicological methodologies and regulatory strategies will be necessary to ensure that the present level of safety of biotechnology-derived foods is maintained in the future.

## Key concerns related to Human/Animal Health with GM Foods

### *Can the transgene be transferred to the Genome of a food Consumer?*

It is reported that humans typically consume a minimum of 0.1 to 1 gram of DNA in their diet each day (Doerfler, 2000). Therefore, the transgene in a genetically engineered plant is not a new type of material to our digestive systems, and it is present in extremely small amounts. In transgenic corn, the transgenes represent about 0.0001% of the total DNA (Lemaux and Frey, 2002). Decades of research indicate that dietary DNA has no direct toxicity itself. On the contrary, exogenous nucleotides have been shown to play important beneficial roles in gut function and the immune system (Carver, 1999). Likewise, there is no compelling evidence for the incorporation and expression of plant-derived DNA, whether as a transgene or not, into the genomes of consuming organisms. Defense processes have evolved, including extensive hydrolytic breakdown of the DNA during digestion, excision of integrated foreign DNA from the host genome, and silencing of foreign gene expression by targeted DNA methylation, that prevent the incorporation or expression of foreign DNA (Doerfler, 1991,2000). Although much remains to be learned about the fate of dietary DNA in mammalian systems (Doerfler, 2000), the possibility of adverse effects arising from the presence of transgenic DNA in foods, either by direct toxicity or gene transfer, is minimal (FAO/WHO, 2000; Royal Society, 2002).

Both WHO (1993) and the US Food and Drug Administration (1992) have earlier concluded that there is no risk in consuming DNA including that derived from GM crops. The basis of their inference was based on the fact that mammals have always consumed significant quantities of DNA from a wide variety of sources, including plants, animals, bacteria, parasites and viruses.

### *Can the Transgene products pose a Risk to Consumers or Handlers?*

The potential toxicity of the transgene product must be considered on a case-by-case basis. Particular attention must be paid if the transgene produces a known toxin (such as the *Bacillus thuringiensis* [Bt] endotoxins) or a protein with allergenic properties.

**Production of toxins and allergens**

The level of risk of these gene products to consumers and those involved in food production can be evaluated by standard toxicological methods. The toxicology testing for the Bt end toxins typifies this approach and has been described in detail by the U.S. EPA (1998) and U.S. EPA (2001). The safety of most Bt toxins is assured by their easy digestibility as well as by their lack of intrinsic activity in mammalian systems (Betz *et al*., 2000; Kuiper *et al*., 2001; Siegel, 2001). The good understanding of the mechanism of action of Bt toxins, and the selective nature of their biochemical effects on insect systems, increases the degree of certainty of the safety evaluations. However, each new transgenic product must be considered individually, based on exposure levels and its potency in causing any toxic effects, as is typical of current risk assessment paradigms for chemical agents.

Allergenicity is one of the major concerns about food derived from transgenic crops. However, it is important to keep in mind that eating conventional food is not risk-free; allergies occur with many known and even new conventional foods. For example, the kiwi fruit was introduced into the U.S. and the European markets in the 1960s with no known human allergies; however, today there are people allergic to this fruit (Pastorello *et al*., 1998). The issues that have to be addressed regarding the potential

**Allergenicity of GM foods**

- Do the products of novel genes have the ability to elicit allergic reactions in individuals who are already sensitized to the same, or a structurally similar, protein?
- Will transgenic techniques alter the level of expression of existing protein allergens in the host crop plant?
- Do the products of novel genes engineered into food plants have the ability to induce *de novo* sensitization among susceptible individuals?

Considerable scientific resources are being utilized to determine the most appropriate and precise approaches for identifying and characterizing potentially allergenic proteins. The first systematic approach to allergenicity assessment was developed by the International Life Sciences Institute (ILSI) in collaboration with the International Food Biotechnology Council and was published in 1996 (Metcalfe *et al*., 1996). The main approaches currently used in the evaluation of allergenicity are:

**Determination of structural similarity, sequence homology, and serological identity**

The objective is to determine to what extent, the novel protein of interest resembles other proteins that are known to cause allergy among human populations. There are essentially three approaches. 1. To examine the overall structural similarity between the protein of interest and known allergens. 2. To determine, using appropriate databases, whether the novel protein is similar to known allergens with respect to either overall amino acid homology, or to discrete areas of the molecule where complete sequence identity with a known allergen may indicate the presence of shared epitopes. 3. To determine whether specific IgE antibodies in serum drawn from sensitized subjects are able to recognize the protein of interest.

***Assessment of proteolytic stability***

There exists a good, but incomplete, correlation between the resistance of proteins to proteolytic digestion and their allergenic potential, the theory being that relative resistance to digestion will facilitate induction of allergic responses, provided the protein possesses allergenic properties (Astwood *et al*., 1996). One approach is to characterize the susceptibility of the protein of interest to digestion by pepsin or in a simulated gastric fluid. However, this approach alone may not be sufficient to identify cross-reactive proteins with the potential to elicit allergic responses in food- or latex-sensitized individuals as in the case of oral allergy syndrome or latex-fruit syndrome (Yagami *et al*., 2000). Nor are considerations of stability to digestion necessarily relevant for allergens that act through dermal or inhalation exposure and that may have significance for workers health. In these cases, other approaches such as structural homology searches and the use of animal models may be effective in identifying potential new allergens.

***Use of animal models***

There are no widely accepted or thoroughly evaluated animal models available for the identification of protein allergens. Nevertheless, progress is being made and methods based on the characterization of allergic responses or allergic reactions in rodents and other species have been described (Kimber and Dearman, 2001).

Although testing strategies for allergens are still evolving and no single test is fully predictive of human responses, the approaches, when used in combination, allow scientists to address questions of potential allergenicity, and these will increase in precision with time. Considerations of this type led U.S. federal agencies to deny approval of StarLink corn for human consumption because of the possibility that its Bt protein, Cry9C, may be a human allergen. This protein had been modified to slow its digestion and prolong its effect in the insect gut and this change rendered the protein less digestible in the human gut as well. After the accidental introduction of Star Link corn into the human food chain, a limited number of illnesses among consumers were reported. These were investigated by the Centers for Disease Control, who found no evidence that the corn products were responsible (CDC, 2001). However, although this study is reassuring, methodological limitations make it less than conclusive (Kuiper *et al*., 2001), and it cannot eliminate the possibility that some adverse effects may have occurred that were not reported. Because of this incident, Star Link corn is no longer marketed. With the exception of Cry9C, none of the engineered proteins in foods so far evaluated through the FDA consultation process has had the characteristics of an allergen.

The only documented case where a human allergen was introduced into a food component by genetic engineering occurred when attempts were made to improve the nutritional quality of soybeans using a Brazil nut protein, the methionine-rich 2S albumin. Allergies to the Brazil nut have been documented (Arshad *et al*., 1991), and while still in pre-commercial development, testing of these new soybeans for allergenicity was conducted in university and industrial laboratories. It was found that serum from people allergic to Brazil nuts also reacted to the new soybean (Nordlee *et al*., 1996). Once this was discovered, further development of the new soybean variety was halted and it was never marketed. This work led to the identification of the major protein associated with Brazil nut allergy, which was previously unknown (Nordlee *et al*., 1996).

## Can Transgene insertion Increase the hazard from Toxins or Pharmacologically Active Substances Present in the Host?

There have been unsubstantiated concerns about the randomness with which genes are inserted into the host by current genetic engineering processes. This could, result in pleiotropic and insertional mutagenic effects. The former term refers to the situation where a single gene causes multiple changes in the host phenotype and the latter to the situation where the insertion of the new gene induces

changes in the expression of other genes. Such changes due to random insertion might cause the silencing of genes, changes in their level of expression, or, potentially, the turning on of existing genes that were not previously being expressed. Pleiotropic effects could be manifested as unexpected new metabolic reactions arising from the activity of the inserted gene product on existing substrates or as changes in flow rates through normal metabolic pathways (Conner and Jacobs, 1999).

Unexpected and potentially undesirable pleiotropic or mutagenic changes in the genome of the host do occur (Kuiper et al., 2001), but these would likely be revealed by their effects on the development, growth, or fertility of the host, or by the extensive testing of its chemical composition compared with isogenic untransformed plants, which is a necessary part of any safety evaluation of transgenic crops.

For instance, in the U.S., since 1987, the USDA Animal and Plant Health Inspection Service has completed over 5000 field trials with more than 70 different transgenic plant species. The only unexpected result was a mutation in a color gene and gene silencing through changes in the methylation status of these genes that led to unexpected color patterns in petunia flowers. Both of these effects are also seen in conventional plant breeding (Meyer *et al*., 1992). While the possibility of an undetected increase in a toxic component in a new food cannot be entirely eliminated, the current safeguards make this unlikely, and no toxicologically or nutritionally significant changes of this type are evident in the transgenic plants so far marketed for food production.

Substantial public concern about the safety of GM products was raised in 1989 when a number of cases of *eosinophilia-myalgia syndrome* (EMS) were reported among users of the amino acid tryptophan as a dietary supplement. By mid-1993, 37 deaths had been attributed to this outbreak (Mayeno and Gleich, 1994). The development of the syndrome appeared among users of some batches of the supplement after a change in the manufacturing process that included the use of a new genetically modified microorganism in the fermentation. However, concomitant with this change were additional alterations in certain filtration and purification steps used previously in the manufacturing process. The exact cause of the outbreak and the nature of the toxic impurity have not been established with certainty. Thus, it is not possible to determine whether the change in purification, the genetic engineering of the organism, or some other factor were to blame (Mayeno and Gleich, 1994). A subsequent investigation revealed that cases of EMS also occurred among consumers of tryptophan before the GM organism was introduced into the manufacturing process, although at a lower incidence. Thus, the genetic modifications might have caused an increase in the level of the agent that was responsible for tryptophan-associated EMS, but it did not create a novel toxicant (Sullivan *et al*., 1996). This event is troubling in that the tryptophan would be regarded as highly purified (99.6% or higher), and no adequate animal model has been found to replicate EMS, a probable autoimmune disease. This illustrates that toxicology has limits in its ability to explain and predict adverse effects in humans.

These examples indicate that careful analysis of the changes in GM organisms is necessary to ensure against unexpected alterations in the levels of toxins, allergens, and essential nutrients. This analysis will be particularly critical if, engineering of the synthetic pathways of secondary metabolites is undertaken in plants, e.g., to increase their resistance to insects and pathogens or to produce compounds of pharmaceutical value. Such changes might create new and unanticipated secondary compounds with unknown toxic properties. New approaches to profiling changes in metabolites, proteins, and gene expression may be helpful in such cases (Kuiper *et al*., 2001).

## Does the Possible Transfer of Antibiotic Resistance Marker Genes from the Ingested GM Food to Gut Microbes Present a Significant Human Hazard?

In medicinal sector, the development of antibiotic resistance among pathogenic bacteria is a significant human/ animal health issue. However, no contribution to antibiotic resistance in gut bacteria arising from antibiotic resistance markers in GM foods has been documented. For several reasons, including the efficient destruction of the resistance gene in the human gut and the very low intrinsic rate of plant–microbe gene transfer, any contribution from this source is expected to be extremely small (Royal Society, 1998). Genes for resistance to kanamycin and related antibiotics already occur quite commonly in the environment, including in the flora of the human gut, which naturally contains about 1 trillion ($10^{12}$) kanamycin- or neomycin-resistant bacteria (Flavell *et al*., 1992). Even if the occasional transfer of resistance from plant to bacterium did occur, the practical impact would be negligible. However, since any increase in antibiotic resistance is recognized as undesirable and the technology is now available to omit the use of such marker genes, future genetically modified organisms are unlikely to contain them (Goldsbrough *et al*., 1996; Koprek *et al*., 2000).

## Can Genetic Transformation Adversely Affect the Nutritional Value of the Host?

By and large, nutritional value of plant and animal sources of food is of paramount important for human and animal health systems across the globe. In the USA, the FDA is entrusted with assuring that the nutritional composition of GM foods is substantially equivalent to that of the no modified food. Studies are made to determine whether nutrients, vitamins, and minerals in the new food occur at the same level as in the conventionally bred food sources (Berberich *et al*., 1996; Sidhu *et al*., 2000). Except for this difference in trypsin inhibitor levels, all other nutritional aspects were equivalent between the transgenic line and the conventional soybean cultivars. Feeding studies demonstrated that there were no evident differences in nutritional value between the conventional and transgenic soybeans in rats, chickens, catfish, and dairy cattle (Hammond *et al*., 1996). Domestic animal feeding studies with a number of other transgenic crops (Kuiper *et al*., 2001) have similarly shown no significant adverse changes in nutritional value.

## Can the Transgene Product Adversely Affect Non target Organisms?

This concern particularly refers to pesticide transgenic products that exhibit resistance to insect pests or diseases. In addition to the general concerns addressed that relate to food safety, additional attention is needed when the gene product is pesticide or otherwise may be toxic to no target organisms that consume it. The effects of each transgene product that is designed for pesticide effects must be evaluated on a case-by-case basis against target and no target organisms under specific field growth conditions for each transgenic crop. The current example of this is the incorporation of Bt genes into crop plants for insect control. The toxic properties of Bt endo toxins to both target and no target species of many kinds are well known (Betz *et al*., 2000). They show a narrow range of toxicity limited to specific groups of insects, primarily *Lepidoptera, Coleoptera, or Diptera*, depending on the Bt strain. Nevertheless, Bt-producing plants have been tested broadly to determine whether any alteration in this limited spectrum of toxicity has occurred, without the discovery of any unexpected results (Gatehouse *et al*., 2002; Lozzia *et al*., 1998; Orr and Landis, 1997; and Pilcher *et al*., 1997). Exotoxins and enterotoxins, which are much more broadly toxic than the endo toxins, are also produced by some Bt strains, but these are not present in the transformed plant, because their genes are not transferred into the crop.

In plants transformed with Bt genes to control lepidopteron, toxicity to no target lepidopteron would be expected if exposure occurs by feeding on the transformed crop. Particular concern has been expressed over the potential toxicity of the Bt toxin in corn pollen to the Monarch butterfly after initial laboratory studies showed increased mortality in larvae fed on leaves dusted with transgenic pollen (Losey *et al*., 1999). However, most transgenic corn pollen contains much lower nonlethal levels of Bt toxins than the strain used in this study, and there is only a limited synchrony between the feeding period of the most sensitive younger larvae and the period when corn pollen is shed. Also, corn pollen does not typically move far beyond the borders of the field, leaving significant amounts of milkweed uncontaminated in many locations. For these reasons, a detailed risk assessment concluded that, it is unlikely that a substantial risk to these butterflies exists in the field since only a negligible portion of the population is exposed to toxic levels of Bt (Gatehouse *et al*., 2002; Sears *et al*., 2001). It is also important to recollect that the common alternative is to spray corn with synthetic insecticides, which are not as selective as the Bt toxin. In a sweet corn field containing milkweed plants and treated with a synthetic parathyroid for insect control, 91–100% of the monarch butterfly larvae placed on the milkweed leaves after spraying was killed. In plots where Bt sweet corn was planted and the pollen fell naturally on the milkweed leaves, larval death rates were much lower (7–20%) and indistinguishable from those in untreated non-Bt corn plots (Stanley-Horn *et al*., 2001).

## Future Challenges in the Assessment of the Safety of GM Foods

As of now, safety assessment methodologies are focused primarily on the evaluation of the toxicity of single chemicals. Food is a complex mixture of many chemicals. Using animal models, the evaluation of most aspects of the safety of single components of the diet, such as a Bt toxin, is possible using widely accepted protocols. Future projects may involve more complicated manipulations of plant chemistry. In this case, safety testing will be more challenging. Whole foods cannot be tested with the high dose strategy currently used for single chemicals to increase the sensitivity in detecting toxic endpoints (MacKenzie, 1999; Royal Society of Canada, 2001). The issues of potential deleterious interactions between new or enhanced levels of known toxic agents in GM foods will undoubtedly be raised. The safety testing of multiple combinations of chemicals remains a difficult proposition for toxicologists. In view of these challenges, there is a clear need for the development of effective protocols to allow the assessment of the safety of whole foods (NRC, 2000; Royal Society of Canada, 2001).

## FAO/WHO Expert Consultations

FAO and WHO have embarked on an initiative to organize a series of scientific expert Consultations to provide scientific and technical advice to their Member States. The scientific advice derived from the Joint FAO/WHO Expert Consultations can be used by the Member States of FAO and WHO directly. It also serves as the scientific foundation for the work of the Codex Alimentarius Commission in their deliberation on risk analysis principles and safety assessment guidelines for foods derived from biotechnology. The chronology of consultations is presented here under.

- FAO/WHO Expert Consultation on the Safety Assessment of Foods Derived from Recombinant-DNA Animals, 26 February - 2 March 2007, Geneva
- Safety assessment of foods derived from genetically modified animals, including fish, a joint FAO/WHO expert consultation on food derived from biotechnology, Rome, Italy, 17 - 21 November 2003.
- Safety assessment of foods derived from genetically modified microorganisms, a joint FAO/WHO expert consultation on foods derived from biotechnology, Geneva, Switzerland, 24 to 28 September 2001.
- Allergenicity of genetically modified foods, a joint FAO/WHO consultation on foods derived from biotechnology, Rome, Italy, 22-25 January 2001.
- Safety aspects of genetically modified foods of plant origin, a joint FAO/WHO consultation on foods derived from biotechnology, Geneva, Switzerland 29 May - 2 June 2000.

In field crop and animal improvement programs across continents, using traditional and modern methods superior plant varieties and cattle breeds are produced with improved characteristics that make them grow better or more desirable to eat. GM crops are developed using the tools of modern biotechnology where precise tools are used to introduce only the desirable traits into a plant. In contrast, in traditional plant breeding, genes from two parents are mixed in many different combinations in the hope of getting the desired trait. Both methods have the potential to alter the nutritional value of plants or lead to unintended changes in concentration of natural

toxicants or anti nutrients. However, these concerns may be less frequent in transgenic plants since only a limited number of genes are transferred during genetic modification, unlike when traditional breeding methods are used.

In general, foods derived from GM crops have undergone more testing than any other food in history. Before entering the marketplace, they are assessed using guidelines issued by several international scientific agencies such as the World Health Organization, the Food and Agriculture Organization, and the Organization for Economic Cooperation and Development. These guidelines include the following:

- GM food products should be regulated in the same way as foods produced by other methods. The risks associated with foods derived from biotechnology are of the same nature as those for conventional foods.
- These products will be judged on their individual safety, allergenicity, toxicity, and nutrition rather than the methods or techniques used to produce them.
- Any new ingredient added to food through biotechnology will be subject to pre-market approval in the same way a new food additive, such as a preservative or food color, must be approved before it reaches the marketplace.

## Assessment of foods derived from GM crops for food safety

Before any GM food can enter the market, it has to be exhaustively tested by the developer and independently evaluated for safety by scientists or experts in nutrition, toxicology, allergenicity, and other aspects of food science. These food safety assessments are based on guidelines issued by competent regulatory agencies of each country and include: a description of the food product; detailed information about its proposed use; and molecular, biochemical, toxicological, nutritional, and allergenicity data.

Typical questions that must be addressed are:

- Does the GM food have a traditional counterpart that has a history of safe use?
- Has the concentration of any naturally occurring toxins or allergens in the food changed?
- Have the levels of key nutrients changed?
- Do new substances in the GM food have a history of safe use?
- Has the food's digestibility been affected?
- Has the food been produced using accepted, established procedures?

Even after these and other questions about the GM food are answered, there are still more steps in the approval process before the GM food can be commercialized. In fact, GM foods are the most studied food products ever produced.

## Issues that need to be addressed

### *Toxicity*

In nature, plants contain low concentration of toxins to protect it from insect pests and diseases. A list of many common plant toxins and anti nutrients is available in the Food and Drug Administration of the USA. It has guidelines that determine the normal and acceptable toxin levels of all crops varieties consumed based on toxicological studies. Natural toxin levels of GM crops are similar to their conventional counterparts.

The protein products of the inserted gene in the commercialized GM plants are evaluated in the toxicological tests. Information on anticipated processing conditions that may result in the removal or denaturation of the proteinaceous material is part of the assessment. GM plant products are subjected to acute toxicity studies based on the premise that the mode of action of many known proteins is through acute mechanisms. High doses of purified transgenic proteins which are expressed in bacteria or plant systems are administered orally. This is sufficient to evaluate the toxic potential of the
New protein

### *Allergenicity*

In human and animal communities one of the consumers concern is related to GM foods is that an allergen (a protein that causes an allergic reaction) could be accidentally introduced into a food product. There are about 500 amino acid sequences of known protein allergens and 90% of all food allergies are associated with only eight foods or food groups – shellfish, eggs, fish, milk, peanuts, soybeans, tree nuts, and wheat. These and many other food allergens are well characterized and so it is extremely unlikely that they would ever be introduced into a GM food. A variety of tests and questions must be considered to determine whether the food poses any increased risk of allergenicity.

Allergens have shared properties, they are stable during digestion and food processing, and are abundant in foods. Proteins introduced into commercially available GM foods do not have any of these properties. They are from sources with no history of allergenicity or toxicity; do not resemble known toxins or allergens biochemically and structurally, and their functions are well understood. They are also present at very low levels in the GM food, are rapidly degraded in the stomach and have been confirmed as safe in animal feeding studies. The novel proteins in these GM crops have a history of safe use with no allergenic concerns. The material (DNA) that encodes

the genetic information is present in all foods, and its ingestion is not associated with any ill effects. In fact, we take in DNA every time we eat as it is present in all plant and animal material even when it is cooked or raw form.

***Antibiotic Resistance***

Some GM crops contain marker genes such as antibiotic resistance genes to identify cells into which the desired gene has been successfully introduced. Concerns have been raised that these marker genes could move from GM crops to microorganisms that normally reside in a person's gut and lead to an increase in antibiotic resistance. There have been numerous scientific reviews and experimental studies of this issue and the following conclusions have been arrived at;

- The likelihood of antibiotic resistance genes moving from GM crops to any other organisms is extremely remote or virtually zero: less than 10-14 to 10-27; and
- Even in the unlikely event that an antibiotic resistance gene is transferred to another organism, the impact of this transfer would be negligible, as the markers used in GM crops have limited clinical or veterinary use.
- Nevertheless, in response to public concerns, scientists have been advised to avoid using antibiotic resistance genes in GM plants. Alternative marker strategies are being used in developing the next generation of GM plants

## Substantial Equivalence (SE) approach to Safety Assessment of GM Foods

Absolute safety is unattainable for any food as people react differently to natural ingredients of food. Substantial equivalence (SE) is an alternative approach used for the safety assessment of genetically modified foods where traditional toxicological testing and risk assessment to whole foods could not be applied. It is based on the idea that existing products used as foods or food sources can serve as basis for comparison. The safety assessment is therefore based on a comparison of the modified food to its traditional (non GM) counterpart in terms of molecular, compositional, toxicological and nutritional data. SE has been used in the safety assessment of GM crops available today.

Mon 810 for example has been compared rigorously as to the levels of major nutritional components (protein, fat, ash, carbohydrates, calories and moisture) with the non transgenic counterpart Mon 818 .and the results showed that the amino acid composition, fatty acids, inorganic composition (calcium and phosphorous), carbohydrate components (starch, sugars and physic acid, crude fiber), and tocopherol content of Mon 810 are within the range of Mon 818.

***Substantial equivalence concept***

This process establishes whether the new plant or animal is significantly different from comparable, no engineered plants or animals used to produce food that is generally considered to be safe for consumers. It provides critical guidance as to the nature of any increased health hazards in the new food. To establish substantial equivalence, extensive comparative studies of the chemical composition, nutritional quality, and levels of potentially toxic components, in both the engineered and conventional crop and animal, are conducted. Notable differences between the existing and new organism would require further evaluation to determine whether the engineered form presents a higher level of risk. Through this approach, the safety of current biotechnology-derived foods can be compared with that of their conventional counterparts, using established and accepted methods of analytical, nutritional, and toxicological research**.**

The guiding principle in the evaluation of GM foods by regulatory agencies in Europe and the U.S. is that their human and environmental safety is most effectively considered, relative to comparable products and processes currently in use. From this arises the concept of "substantial equivalence" If a new food is found to be substantially equivalent in composition and nutritional characteristics to an existing food, it can be regarded as being as safe as the conventional food (FDA, 1992; Kuiper *et al*., 2001; Maryanski, 1995, OECD, 1993) and does not require extensive safety testing. Evaluation of substantial equivalence includes consideration of the characteristics of the transgene and its likely effects within the host, and measurements of protein, fat, and starch content, amino acid composition, and vitamin and mineral equivalency together with levels of known allergens and other potentially toxic components.GM foods can either be substantially equivalent to an existing counterpart, substantially equivalent except for certain defined differences (on which further safety assessments would then focus), or nonequivalent, which would mean that more extensive safety testing might be necessary. The examination of substantial equivalence, therefore, may be only the starting point of the safety assessment. It provides a valuable guide to the definition of potential hazards from GM foods and focus necessary areas for further study (FAO/WHO, 2000).

While there is some concern relative to the meaning of "substantial" and how equivalency should be established, and debate over its use continues (Millstone *et al*., 1999) and following correspondence;(Kuiper *et al*., 2001; Royal Society of Canada, 2001), the concept appears to be logical and robust in assessing the safety of foods derived from both genetically modified plants and microorganisms (FAO/WHO, 2000, 2001a). If it can be established with reasonable certainty that a GM food is no less safe than its conventional counterpoint, it provides a standard likely to be satisfactorily protective of public health. It is also an approach that has the flexibility to evolve in concert with the field of transgenic technology. A recent study of FDA procedures for assessing the safety of GM foods by the U.S. General Accounting Office reviews these procedures and concludes that the current regimen of safety tests are adequate to assess existing GM foods (U.S. General Accounting Office, 2002).

***Labeling***

Labeling of GM food products to provide consumer choice is required in some countries and suitable methods are available to test the products. Threshold limits have been established to designate the limits of labeling GM commodities. But in respect of animal products, whether animals consumed GM crops or not, the relevance and practicability of implementing and enforcing becomes difficult, since protein and DNA consumed by animals from GM crops will be digested .In addition most of GM transgenic proteins are expressed at low concentrations, it is difficult to detect them. The present research findings indicated that the detection of plant proteins from GM crops, in products like meat or milk or eggs, is not detectable by sensitive PCR essays. Therefore, any suggestion to label food products derived from animals fed GM crops could be impracticable or difficult to enforce in the current scenario, In the near future it may be possible with further development of facilities ( Beever and Kempf,2000).

***Safety of food products derived from animals fed GM crops***

Generally two questions will come into the minds of producers, consumers and feed manufacturers.1. Can traces of GM material find their way into animal products like meat, milk and eggs? 2 .Will GM derived foods be acceptable to the consumer all around the world? For the first one, it seems that there is likelihood that the size of DNA is extremely small, no higher than 1 in 10,000 or 0.01% and so not detectable. Regarding the consumer acceptability, survey of European consumers revealed that there is great reluctance to contemplate eating such GM foods, despite assurances that GM foods are safe. But elsewhere it is not so, It may be difficult to obtain a food/feed in U S A totally free from GM material (Beever and Kemp. F, 2000).The rapidity of research in food bio-technology, regulatory issues, legislation and intellectual property rights will enhance discovery and innovations, but public education on awareness about genetically modified (GM) and produced products should be continuously enhanced for its acceptance among the people (Chang, 2001).

## Conclusion

It can be concluded that GM foods pass-through numerous regulatory mandates between the early gene discovery stage and product of commercialization. The products of biotech crops currently sold in the market for food /feed purposes around the world have been subjected to intensive safety evaluations. The safety evaluation of GM foods usually begins with comparison of novel food with its traditional counterpart. The novel food/ feed are comparable with its traditional counterpart except for a few defined differences resulting from the introduction of the particular gene of interest. As a result, the safety assessment is then focused upon the safety of the introduced gene and especially the novel protein produced from the gene. Current genetically modified foods are well documented to be safe for their intended uses under the anticipated conditions of consumptions because they have been subjected to variety of safety evaluations before introduction into market for commercialize.

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