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Genetically Modified Food: Its uses, Future Prospects and Safety Assessments

A. Pandey, M. Kamle, L.P. Yadava, M. Muthukumar, P. Kumar, V. Gupta, M. Ashfaque and B.K. Pandey
Central Institute for Subtropical Horticulture, Rahmankhera, Lucknow, 227107, India

Abstract: In the context of the GM food regulations crop improvement via transgenic technology is a new stage of introducing novel food which supercedes over the conventional breeding. It was analyzed that worlds hunger, malnutrition problems, environmental pollution and phytoremediation in agriculture are the challenges for scientist as well as governments those can be combated by application of genetic engineering in crops. Genetically modified microbes/plant/animals or GM microbes/plant/animals results from modification in the genetic make-up of microorganisms, plants and animals using recombinant DNA technology to improve the nutritional requirement, disease resistant traits, increased production and medicinal properties. In many instances, these modification processes represent faster, more efficient mechanisms for achieving changes than traditional breeding. However, a wide variety of modifications are possible through genetic manipulation and the potential for the introduction of toxic compounds, unexpected secondary effects and changes in nutritional and toxicological characteristics may give rise to safety concerns about GM crops. Thus, generation of GM food explores new vistas for future food requirement but the assessment of policy regarding environmental risks is also to be concerned.

Key words: Genetically modified food (GM food), genetic engineering, transgenic, DNA technology

INTRODUCTION

Most of the foods we eat today come from plants and animals that have been grown and bred by humans for countless generations, undergoing substantial genetic changes over several thousand years. Traditionally, plants or animals with the most desirable characteristics were chosen for food and for breeding the next generation. The desirable characteristics arose from naturally occurring variations in the genetic make-up of individual plants or animals. Thus, genetic modification in this sense occurs naturally and forms the fundamental basis of evolution and breeding. The term genetically modified food (or GM food) refers to products developed through biotechnology. Since, biotechnology can include numerous processes and applications the term genetically modified is applied only to products that have been genetically engineered. Genetically Modified (GM) foods are food items that have had their DNA changed through genetic engineering. Unlike conventional genetic modification that is carried out through time-tested conventional breeding of plants and animals as combining genes from different organisms is known as recombinant DNA technology and the resulting organism is said to be genetically modified, or genetically engineered or transgenic. The GM products include vaccines, food ingredients, medicines, feeds and fibres. The use of recombinantly produced chymosin in cheese production since the end of the 1980s represents one of the first applications of genetic engineering in the food industry. The *Flavr Savr* tomato was the first genetically modified product entering commerce that was itself a GMO; it thus brought the consumer into close contact with new plant technology. Since then, at least 42 other genetically engineered agricultural crops have been approved.

It is generally agreed that the application of genetic modification does not inherently increase or decrease the risk associated with an organism. It is now three decades since some of those early promises were made and a decade since Genetically Modified (GM) crops were first grown commercially. But the only substantial way that biotechnology has contributed to the well-being of the hungry is through higher incomes from the production of GM cotton (Huang *et al*., 2002). Only a small set of countries have extended GM food crops and most of them in a relatively minor way (James, 2004, 2005). The first generation of Genetically Modified (GM) crop varieties sought to increase farmer profitability through cost reductions or higher yields. The next generation of GM food research is focusing also on breeding for attributes of interest to consumers beginning with golden rice, (Fig. 1) which has been genetically engineered to contain a higher level of vitamin A and thereby boost the health of unskilled laborers in developing countries. Golden rice is a GM variety that may have no farm productivity attributes but has the potential to improve health

Corresponding Author: B.K. Pandey, Central Institute for Subtropical Horticulture, Rahmankhera, Lucknow, 227107, India

Fig. 1: Comparison of rice (left), Golden Rice 1 (middle) and Golden Rice 2 (right) (Paine *et al*., 2005)

significantly in regions where rice is or could be a dietary staple for poor people through providing pro-vitamin A. (Paine *et al*., 2005). The latter characteristic is the result of golden rice being genetically engineered to contain a higher level of beta-carotene in the endosperm of the grain (Ye *et al*., 2000; Beyer *et al*., 2002).

Transgenic Bt (*Bacillus thuringiensis)* rice varieties that are resistant to rice stem borer and leaf roller were approved for environmental release trials in 1997 and 1998 (Zhang *et al*., 1999). Farmers have successfully resorted to genetically improving their crops through deliberated plant breeding for thousands of years although its scientific basis was not established until classical Mendelian genetics were rediscovered in the early twentieth century (Robinson, 1999; Uzogara, 2000).

Crop development thereby becomes a continuous process of introducing novel traits where transgenic technology is a new stage following and coexisting with conventional crossbreeding. Assessment policy regarding environmental risks is thus being based on the product rather than the process (Brill, 1985, 1986).

Many crop plants that are used to produce food ingredients are now being genetically modified for example soya and maize. Soybeans can be processed to yield many different food ingredients from Soya protein and flour to oil and lecithin used as emulsifiers. Maize can also be processed to yield a variety of ingredients from starch and sugars to oil and flour. Some ingredients derived from crop plants are very highly refined for example sucrose and vegetable oils and these refining processes destroy and remove any genetic material and protein that might be present in the food ingredient. The end product that goes into food is therefore not itself modified and cannot be distinguished from that produced by conventional means. Animals that have been genetically modified to produce pharmaceutical products for use in human therapy do not enter the food chain. No GM animals have so far been approved for food use.

Farmer's practices have led to altering the genetic constitution and evolution of crops. In this sense farmers have been considered to be the first genetic engineers (Jones, 1994; Prakash, 2001). B12 manufactured from Rhone-Poulenc has been recently approved for food use in Switzerland apparently using genetically modified *Agrobacterium radiobacter.* Efforts to produce Vitamin B2 (riboflavin) using a recombinant *Bacillus subtilis* strain has also been reported (Van Loon *et al*., 1996).

GENETICALLY MODIFIED FOODS/CROPS

Genetically modified foods originally derived from *Agrobacterium tumefaciens* is the most frequently used as a terminator in approved transgenic crops (Table 1). Several Biotechnologist and researchers worked on various crops for nutritionally improved traits intended to provide health benefits to consumers with genetically modified foods/crops. They have tried to develop GM crop resistance to certain pesticides and herbicide also e.g., rape seed and soybeans. Genetically modified crop helps in developing male sterile line facilitating production of hybrid cultivars.

IDENTIFICATION OF GENETICALLY MODIFIED FOODS

The ever increasing number of approvals granted spurred strong interest in developing methods for identifying GMOs in food. The availability of suitable identification procedures is necessary also for various food control activities such as the observance of regulations on the labelling on GMOs and of regulations with respect to seed certification. The requirements on the specificity of detection methods will increase significantly with the number of distinct products available the appearance of mixtures of distinct GMO products and increased processing of such products or complex mixtures. The main methods of identification of genetically modified foods are described.

PCR-based methods: This technique has revolutionized molecular biology and many other areas in the biomedical

Table 1: List of important crops genetically modified with nutritionally improved traits intended to provide health benefits to consumers and domestic animals

Crop\species	Trait	Transgene	References
Cereal crops			
Rice	+β-carotene	Phytoene synthase (daffodil) Phytoene desaturase (*Erwinia*) Lycopene cyclase (daffodil)	Ye *et al.* (2000)
	Iron	Ferritin (*Phaseolus*) Metallothionein (rice)	
		Phytase (*mutant, Aspergillus*)	Lucca *et al.* (2002)
	Allergenic protein	Antisense 16 kDa allergen (rice)	Tada *et al.* (1996)
	+Puroindolinone compounds: softer rice kernels, flour yields more finer particles, less damage to starch	Wheat puroindoline genes	Krishnamurty and Giroux (2001)
Wheat	Glutenins	High molecular weight subunit genes	Barro *et al.* (1997) Rooke *et al.* (1999)
	Caffeic and ferulic acids	Wheat gene	UPI (2002)
Maize	Methionine	mRNA stability by intron switiching Dzr1 target	Lai and Messing (2002)
	Fumonisin	de-esterase+de-aminase (mbial)	Duvick (2001)
	Insect resistance	Avidin (chicken)	Kramer *et al.* (2000)
	protein with favorable amino - acid profile	α-Lactalbumin (porcine)	Yang *et al.* (2002)
	Sulfur amino acids	Maize 15 kDa-zein	Dinkins *et al.* (2001)
	Vitamin C	Wheat dehydroascorbate reductase (DHAR)	Chen *et al.* (2003a, b)
Oilseed			
Soybeans	Improved amino acid composition	Synthetic proteins	Rapp (2002)
	Increased sulfur amino acids	Overexpressing the maize 15 kDa zein protein	Dinkins *et al.* (2001)
	Oleic acid	Δ-12 Desaturase (soybean, sense suppression)	Kinney and Knowlton (1998)
	Oleic acid	Ribozyme termination of RNA transcripts down regulate seed fatty acid	Buhr *et al.* (2002)
	Isoflavones	Isoflavone synthase	Jung *et al.* (2000)
Lupin	Methionine	Seed albumin (sunflower)	White *et al.* (2001)
Sorghum	Improved digestibility of livestock feed	Mutated Brown midrib (Bmr) encodes caffeic acid O-methyltransferase (COMT), a lignin-producing enzyme	Bout and Vermerris (2003)
Tuber			
Potato	Starch	ADP glucose pyrophosphorylase (*Escherichia coli*)	Stark *et al.* (1992)
	Very-high-amylose starch	Inhibition of SBE A and B	Schwall *et al.* (2000)
	Inulin molecules	1-SST (sucrose:sucrose 1-fructosyltransferase) and the 1-FFT (fructan:fructan1-fructosyltransferase) genes of globe artichoke (*Cynara scolymus*)	Hellwege *et al.* (2000)
	+Sulphur-rich protein	Nonallergenic seed albumin gene (*Amaranthus hypochondriacus*)	Chakraborty *et al.* (2000)
	Solanine	Antisense sterol glyco transferase (Sgt) gene	McCue *et al.* (2003)
Sweet Potato	Protein content	Artificial storage protein (ASP-1) gene	Prakash *et al.* (2000)
Cassava	Cynaogenic glycosides	?Hydroxynitril lyase	Siritunga and Sayre (2003)
Beet	+Fructans	1-Sucrose:sucrose fructosyl transferase	Smeekens (1997)
Narcotics			
Coffee	Caffeine	Antisense xanthosine-N-7 methyltransferase (coffee)	Moisyadi *et al.* (1998)
Fruit and vegetables			
Tomato	Provitamin A and lycopene	*Lycopene cyclase* (*Arabidopsis*)	Rosati *et al.* (2000)
	Provitamin A	Phytoene desaturase (*Erwinia*)	Fraser *et al.* (2001)
	Flavonoids	Chalcone isomerase (*Petunia*)	Muir *et al.* (2001)
	Lycopene	Engineered polyamine accumulation	Mehta *et al.* (2002)
Other crops			
Alfalfa	+Resveratrol	Resveratrol glucoside	Hipskind and Paiva (2000)
	Lignin	Downregulation of caffeic acid 3-O-methyltrans ferase and caffeoyl CoA 3-O-methyltransferase	Guo *et al.* (2001)
Canola	Vitamin E	γ-Tocopherol methyltransferase (*Arabidopsis*)	Shintani and DellaPenna (1998)
	Lauric acid	Lauroyl ACP thioesterase (California bay tree)	Del Vecchio (1996)
	+β- Carotene	Phytoene synthase (daffodil) Phytoene desaturase (*Erwinia*) Lycopene cyclase (daffodil)	Ye *et al.* (2000)
Cotton	High-oleic and high-stearic cottonseed oils	hpRNA-mediated post-transcriptional gene silencing desaturases	Liu *et al.* (2002)

sciences in the mid 1980s (Saiki *et al.*, 1985). The number of references to PCR in the scientific literature has been estimated to be more than 40,000 (White, 1996).

The high chemical and thermal stability of DNA the high sensitivity of the method, its technical simplicity the vast amount of experience already accumulated with it;

along with the apparent potential for automation (Abramowitz, 1996; White, 1996) are main advantages of this method establishing the current prevalence of PCR-based detection methods. This preference is likely to continue in the foreseeable future.

The sensitivity of a PCR test can be significantly improved by increasing the number of cycles (Meyer *et al*., 1994). The application of magnetic capture-hybridization-technique has also been shown to augment the sensitivity of an assay by two orders of magnitude (Jacobsen, 1995). Using hemi-nested PCRor nested PCR (Brockmann *et al*., 1996; Meyer, 1995; Lunel *et al*., 1995) instead of conventional PCR represents another way of increasing assay sensitivity. Sensitivity may be assessed through a positive control which targets a sequence of similar length expected to be present in similar quantity as the actual target sequence.

Various nucleotide-based amplification methods and their applicability: Most of the nucleotide-based amplification methods have generally not yet been used widely for the identification of genetically engineered food or food stuffs. Therefore, very much restricts itself to survey review articles that may simplify access to additional readings. Some of the techniques may under certain circumstances be appropriate for food analysis.

Protein-based methods: The application of protein-based detection methods for the identification of genetically engineered food products is generally restricted to fresh (or frozen) and unprocessed foods. Protein samples obtained from GMOs can be resolved with one-dimensional SDS-gel electrophoresis. Unfortunately the resolution is not sufficient to clearly distinguish the protein pattern of a GMO from the protein pattern of its conventional counterpart. Two-dimensional gel electrophoresis provides better resolution but still may generally not be able to provide unequivocal identification of a transgene product unless combined with immunological methods. The expression level of transgene products in plants were reported to constitute 0 to 2% of the total soluble protein even when strong constitutive promoters were used to drive expression (Longstaff *et al*., 1995). Provided that specific antibodies against the proteins encoded by the transgenes are available one-dimensional (Padgette *et al*., 1995; Wood *et al*., 1995; Yang *et al*., 1996) and certainly also two-dimensional gel electrophoresis, in combination with Western-blot analysis are suitable detection methods. ELISA can also be an inexpensive but powerful technique (Padgette *et al*., 1995; Wood *et al*., 1995). Recently, developed techniques using immunosensors have up to now mainly been used for the analysis of serum and blood samples (Morgan *et al*., 1996). All immunological methods described above depend on the availability of highly specific antibodies. The latter are commercially available only for a small number of proteins that are the products of transgenes used in approved genetically engineered crops.

Detection of enzymatic activities: The detection methods based on measuring enzymatic activities are limited to the detection of transgenes that represent enzymes. Enzymatic function of a protein depends on the structural preservation of the protein molecule even more than the recognition of the protein by antibodies. Therefore an important restriction of enzymatic methods is the requirement that the sample must be fresh enough to contain enzymatic activity. With this in mind, it seems highly unlikely that detection of certain enzymatic activities e.g., by measuring the enzymatic EPSPS activity (Padgette *et al*., 1987, 1988) will find broad application in the detection of genetically engineered food.

GENETIC MODIFICATION

A transgenic plant is one that has received a segment of DNA or genes from another organism. The nucleic acid preferably DNA that has been transferred using recombinant DNA techniques is known as heterologous or foreign DNA. The foreign DNA is integrated through natural systems present in plant cells into the plant's genome. The newly introduced genes are subsequently inherited in a normal Mendelian manner through pollen and egg cells. The process of introducing DNA into plants is called transformation mainly using the *Agrobacterium* mediated method and it can be achieved both in monocotyledonous plants such as wheat, barley and rice, in dicotyledonous plants such as soyabean, potato and tomato.

Agrobacterium mediated transformation in plants *Agrobacterium tumefaciens* is a soil bacterium that causes crown gall disease on some plants. Many dicotyledonous species are susceptible to infection by this species. In causing crown gall disease *A. tumefaciens* transfers DNA (the transferred DNA or T-DNA) from the bacterium to the plant. In nature the transferred bacterial DNA cause the symptoms associated with crown gall disease. In the early 1980s scientists removed the disease causing genes from this bacterium and the T-DNA is now routinely used to transport foreign genes into plants. *Agrobacterium* cells carrying the foreign genes of interest are incubated with cultured cells of the recipient crop plant and transgenic plants are regenerated from them. Not all cells subjected to this process are successfully modified so it may be necessary to identify the modified

cells using marker genes which are closely linked to the genetic material that is transferred. These selectable marker genes usually confer resistance to an antibiotic such as kanamycin or resistance to an herbicide.

In essence genetic modification involves the identification of the gene coding for a particular desired characteristic and the moving of that gene from one living thing where it occurs naturally to another living thing in which the characteristic is required. Recombinant DNA technology DNA sequencing from genes using DNA markers for constructing genetic maps designing PCR-based methods for selecting and characterizing genes and DNA transfer technologies between different species have all laid the foundations for the modern production of the genetically-engineered plants and crops currently on the market (Conner and Jacobs, 1999).

The following are the steps for the genetic modification:

- Isolation of DNA
- Transfer and modification of DNA
- Multiplication of the desired gene and insertion into the host cell
- Selectable marker genes
- DNA sequences necessary to control gene expression
- Selection and subsequent propagation

More recent developments in the genetic modification of plants are beginning to allow the expression of the gene to be targeted to only certain parts of the plant such as the leaves and roots. This is achieved by careful selection of the promoter switch. For example genes for pest resistance could be expressed only in the parts of the plant susceptible to attack by the pest and not in the parts of the particular plant used for food. A heat-stable form of *Aspergillus fumigatus* phytase has also been engineered which can break down the phytate ingested from other food sources (Prakash, 1997). Moreover transgenic technology has been useful in producing hypoallergenic crops by interfering with the expression of genes encoding major allergens (Bhalla and Singh, 2004; Losada and Fonseca, 2007). A gene encoding *Galanthus nivalis* snowdrop lectin (GNA lectin) has been inserted into a number of different food crops including rice, wheat, potatoes and sugarcane (Stoger *et al*., 1999; Setamou *et al*., 2002; Poulsen *et al*., 2007a, b) to confer resistance to several insect pest species (Gatehouse *et al*., 1998).

MERITS OF GENETICALLY MODIFIED FOODS

The GMOs are approved like many crops previously developed using more conventional plant breeding techniques. The technology does have the potential to produce foods that could be of direct consumer benefit such as:

- Improved nutritional quality like Fruit and vegetables with increased vitamin content, non-allergenic peanuts, potatoes with higher starch content thus resulting in healthier chips, corn with increased essential fatty acid content, wheat with increased levels of folic acid etc.
- Prolonged shelf life with good quality
- Edible vaccines

Nutritional: Malnutrition is common in third world countries where impoverished peoples rely on a single crop such as rice for the main staple of their diet. However, rice does not contain adequate amounts of all necessary nutrients to prevent malnutrition. If rice could be genetically engineered to contain additional vitamins and minerals, nutrient deficiencies could be alleviated. For example blindness due to vitamin A deficiency is a common problem in third world countries. Researchers at the Swiss Federal Institute of Technology Institute for Plant Sciences have created a strain of *golden rice*. Golden Rice a variety of rice engineered to produce β-carotene (pro-vitamin A) has been further improved to produce 23 times more total carotenoids than the previous Golden Rice version produced in 2000 (Paine *et al*., 2005).

Since, this rice was funded by the Rockefeller Foundation a non-profit organization the Institute hopes to offer the golden rice seed free to any third world country that requests it. Plans were underway to develop *golden rice* that also has increased iron content.

However, as discussed in more detail elsewhere (Anderson *et al*., 2004) second-generation GM varieties such as *golden rice* require a treatment different from first-generation GM varieties. Bouis (2002) and Welch (2002) suggest nutritionally enhanced rice and wheat cultivars are more resistant to disease their roots extend more deeply into the soil so they require less irrigation and are more drought resistant they release chemical compounds that unbind trace elements in the soil and thus require less chemical inputs and their seeds have higher survival rates.

Another example of directly improving food micronutrients comes from Iron Rice which is a GM rice having increased iron content obtained by inserting a gene from the *Aspergillus niger* fungus into the rice genome (Prakash, 1997; Lucca, 1999).

Genetic engineering has also enabled improving food and feed protein quality by incorporating genes encoding non-allergenic proteins containing essential amino acids (De Lumen *et al*., 1997; Roller and Hallander, 1998; Chakraborty *et al*., 2000).

Pharmaceuticals: Medicines and vaccines often are costly to produce and sometimes require special storage conditions not readily available in third world countries. Researchers are working to develop edible vaccines in tomatoes and potatoes. These vaccines will be much easier to ship, store and administer than traditional injectable vaccines.

Pest resistance: Crop losses from insect pests can be staggering resulting in devastating financial loss for farmers and starvation in developing countries. Farmers typically use many tons of chemical pesticides annually. Consumers do not wish to eat food that has been treated with pesticides because of potential health hazards and run-off of agricultural wastes from excessive use of pesticides and fertilizers can poison the water supply and cause harm to the environment. Growing GM foods such as *B.t.* corn can help eliminate the application of chemical pesticides and reduce the cost of bringing a crop to market.

Phytoremediation: Not all GM plants are grown as crops. Soil and ground water pollution continues to be a problem in all parts of the world. Plants such as poplar trees have been genetically engineered to clean up heavy metal pollution from contaminated soil.

Approach to the assessment of GM foods in comparison with the evaluation of medicines. It has been suggested that the safety of novel and GM foods should be assessed in a similar way to that used for pharmaceutical products. The ACNFP has recently considered this issue and has advised that long term feeding studies should be carried out where it is relevant and appropriate to do so. However, each case needs to be considered on its merits. Complicating factors in the design and interpretation of long term studies when applied to foods as opposed to pure chemicals mean that it is unlikely that they would give rise to meaningful information in all cases.

Pharmaceutical products are generally well characterized materials of known purity of no nutritional value and human exposure levels are normally low. It is relatively straightforward therefore to feed such compounds to animals at a range of doses some orders of magnitude greater than the expected human exposure levels in order to identify any potential adverse effects of importance to humans. In this way it is possible in most cases to determine levels of exposure at which adverse effects are not present and so set safe upper limits by the application of appropriate safety factors.

Herbicide tolerance: For some crops it is not cost-effective to remove weeds by physical means such as tilling so farmers will often spray large quantities of different herbicides (weed-killer) to destroy weeds a time-consuming and expensive process that requires care so that the herbicide doesn't harm the crop plant or the environment. Crop plants genetically engineered to be resistant to one very powerful herbicide could help prevent environmental damage by reducing the amount of herbicides needed. For example Monsanto has created a strain of soybeans genetically modified to be not affected by their herbicide product Roundup. A farmer grows these soybeans which then only require one application of weed-killer instead of multiple applications, reducing production cost and limiting the dangers of agricultural waste run-off.

Disease resistance: There are many viruses, fungi and bacteria that cause plant diseases. Plant biologists are working to create plants with genetically engineered resistance to these diseases.

Cold tolerance: Unexpected frost can destroy sensitive seedlings. An antifreeze gene from cold water fish has been introduced into plants such as tobacco and potato. With this antifreeze gene, these plants are able to tolerate cold temperatures that normally would kill unmodified seedlings.

Drought salinity tolerance: As the world population grows and more land is utilized for housing instead of food production farmers will need to grow crops in locations previously unsuited for plant cultivation. Creating plants that can withstand long periods of drought or high salt content in soil and groundwater will help people to grow crops in formerly inhospitable places.

DEMERITS OF GM FOODS

Environmental hazards: Unintended harm to other organisms a laboratory study was published in *Nature* showing that pollen from Bt. corn caused high mortality rates in monarch butterfly caterpillars. Monarch caterpillars consume milkweed plants, not corn, but the fear is that if pollen from Bt. corn is blown by the wind onto milkweed plants in neighboring fields the caterpillars could eat the pollen and perish. Reduced effectiveness of pesticides just as some populations of mosquitoes developed resistance to the now banned pesticide DDT many people are concerned that insects will become resistant to B.t. or other crops that have been genetically modified to produce their own pesticides. Gene transfer to non-target species another concern is that crop plants engineered for herbicide tolerance and weeds will cross-breed resulting in the transfer of the herbicide resistance genes from the crops into the weeds. These super weeds would then be herbicide tolerant as well. Other introduced genes may cross over into non modified crops planted next to GM crops. Genes are exchanged

between plants via pollen. Two ways to ensure that non-target species will not receive introduced genes from GM plants are to create GM plants that are male sterile (do not produce pollen) or to modify the GM plant so that the pollen does not contain the introduced gene.

Human health risks: Allergenicity has developed life-threatening allergies to peanuts and other foods among the children's and adults. There is a possibility that introducing a gene into a plant may create a new allergen or cause an allergic reaction in susceptible individuals. Unknown effects on human health is a growing concern that introducing foreign genes into food plants may have an unexpected and negative impact on human health. The most common allergy causing foods are cow's milk, eggs, fish, shellfish, tree nuts, wheat, peanuts, and soybeans etc.

Economic concerns: Bringing a GM food to market is a lengthy and costly process and of course agribiotech companies wish to ensure a profitable return on their investment. Many new plant genetic engineering technologies and GM plants have been patented and patent infringement is a big concern of agribusiness. Yet consumer advocates are worried that patenting these new plant varieties will raise the price of seeds so high that small farmers and third world countries will not be able to afford seeds for GM crops thus widening the gap between the wealthy and the poor. Unfortunately Bt. toxins kill many species of insect larvae indiscriminately but it is not possible to design a Bt. toxin that would only kill crop damaging pests and remain harmless to all other insects.

The fears of the people opposing the technology producing GM crops are associated with a wider spectrum of issues includes that the companies are more interested in increasing their profits than in protecting the environment or alleviating hunger the possibility that transgenic crops may invade wild ecosystems with detrimental effects on biodiversity the unfair competition with other agricultural systems such as organic agro-ecological and traditional ones the negative effects that GM food might produce on human health the possible negative impact of GM crops on food supply safety. The concern that risk-averse poor farmers would be unable to afford to take up the higher cost of GM seeds provided by private biotech firms does not seem to be vindicated by the dramatic take-up of GM cotton in developing countries as soon as it is available and can be seen to be profitable. On the adoption experience in China and India (Pray *et al*., 2003) the part of the reason for that rapid uptake in developing countries may be because of the occupational health benefits for farmers who expose themselves to fewer chemical pesticides with GM cotton (Hossain *et al*., 2004) but mainly it is because of its much greater productivity.

SAFETY ASSESSMENTS TESTS USED FOR GM FOODS

The safety assessment of GM food relies of substantially equivalent to conventional foods when levels of nutrients, allergens, or naturally occurring toxins are not substantially different and there no new allergens or toxins detected. The approach to assessing the safety of genetically engineered food products is to focus on the gene product and its function including the product produced as a result of its function. This includes chemical analysis and evaluation of nutritional composition for proteins, amino acid profiles, fat, carbohydrates, fiber, vitamins and minerals, digestibility tests, toxicity studies, animal feeding studies, phenotypic characteristics, molecular characterization, immunotoxicity, genotoxicity and allergenicity testing. The assessment of the safety of GM organisms addresses both intentional and unintentional effects that may result as a consequence of genetic engineering of the food source. Future transgenic crops are expected to contain fewer or no marker genes in the final products since marker free insertion techniques or methods to eliminate marker genes from transgenic plants. The assessment of safety measures are a lengthy and tedious process (Fig. 2, 3). The nutritional aspects, risk characterization and exposure assessment are preliminary steps being taken. Before hitting the market, all GM products have to pass all the allergic tests and provide the details. Only those products find as possessing no harmful or allergic effects are only recommended.

A number of studies over the past decade have revealed that genetically engineered foods can pose serious risks to humans, domesticated animals, wildlife and the environment. Human health effects can include

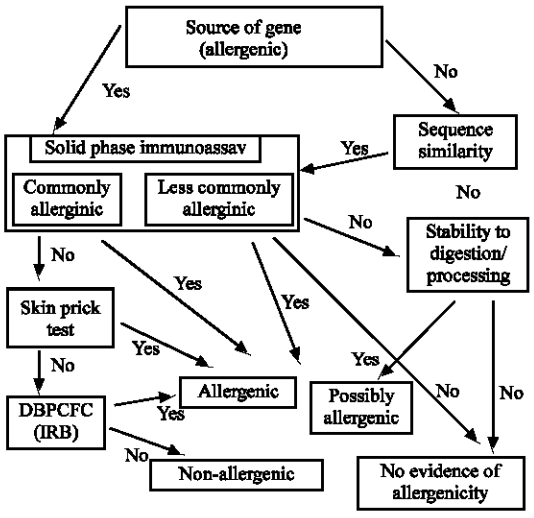

Fig. 2: Assessment of the allergenic potential of foods derived from genetically modified crop plants

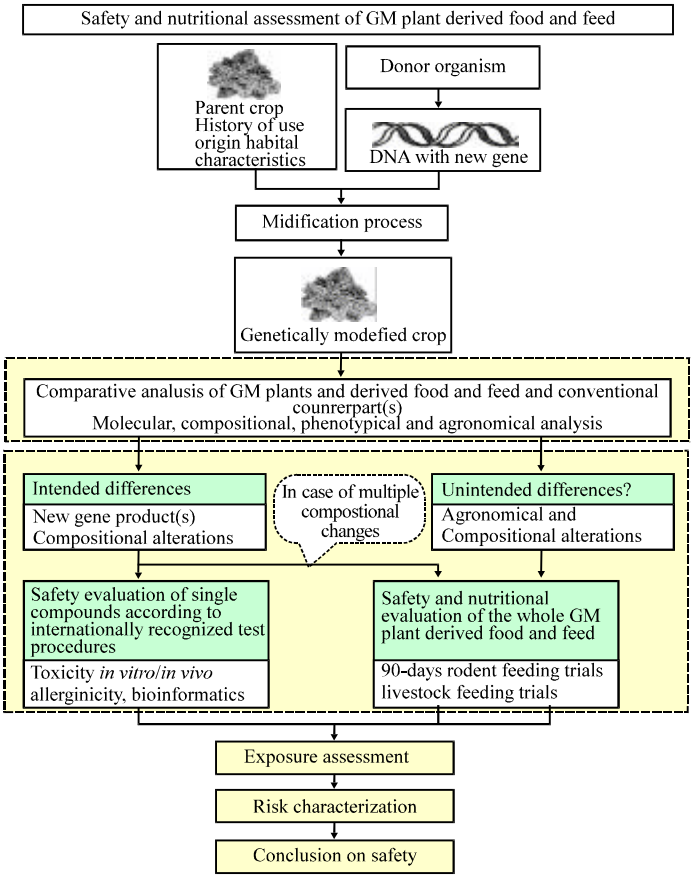

Fig. 3: Strategic scheme for pre-market safety and nutritional testing of genetically modified plant derived food and fed (EFSA GMO Panel Working Group on Animal Feeding Trials, 2008)

higher risks of toxicity, allergenicity, antibiotic resistance, immune-suppression and cancer. As for environmental impacts the use of genetic engineering in agriculture could lead to uncontrolled biological pollution threatening numerous microbial plant and animal species with extinction and the potential contamination of non-genetically engineered life forms with novel and possibly hazardous genetic material. Despite the potential of this achievement as a viable and sustainable alternative contributing towards alleviating Vitamin A deficiency in many poor countries (Mayer, 2007) anti biotech opponents have claimed that Golden Rice is not effective and superfluous (Greenpeace, 2005).

Some Golden Rice critics argue that this GM crop might actually interfere with current vitamin A supplement and fortification programmes (Mayer, 2005). However, opponents of GM technology often ignore the great number of people who are not receiving the benefits of these programmes.

Known food allergens known toxins and nutritional quality can all be evaluated in a straight forward manner employing well established *in vitro* analytical methods. All three testing strategies use the same procedures for this purpose. Assessing unanticipated allergens and toxins is more challenging. It is in this area that the three testing strategies described below differ. These strategies employ various combinations of the following three approaches to detecting and characterizing allergens and toxins:

- *In vivo* testing using small animals and human subjects for the purpose of screening broadly for allergens and toxins
- Molecular characterization of the genetic alterations induced through recombinant DNA modifications
- Controlled and monitored commercial release of recombinant foods

Safety testing of GM foods in laboratory animal species: Examples of safety studies with GM food and feed are given in (Table 2). In different experiments food and feed derived from GM plants, mixed in animal diets have been

Table 2: Safety studies performed on laboratory animals with GM plant derived foods

Plant	Trait	Species	Duration	Parameters	Reference
Rice	Glycinin (Soybean [*Glycine max*])	Rat	28 days	Feed consumption, body weight, blood chemistry, blood cell count, Liver- and kidney histopathology	Momma *et al.* (2000)
	Cry1Ab endotoxin (*Bacillus thuringiensis* Var kurstaki)	Rat	98 days	Feed consumption, body weight, blood chemistry, blood cell count, organ weights, histopathology	Wang *et al.* (2002)
	PHA-E lectin (*Phaseolus vulgaris*)	Rat	90-days	Feed and water consumption, body weight, organ weights Blood cell count, blood chemistry Intestinal microbiology Histopathology	
	Cry1Ab endotoxin (*Bacillus thuringiensis*)	Rat	90-days	Feed and water consumption, body weight, organ weights Blood cell count, blood chemistry Intestinal microbiology Histopathology	Schroder *et al.* (2007)
Sweet pepper, tomato	Cucumber mosaic virus coat protein (CMV-CP)	Rat	30 days	Feed consumption, body weight, organ weights, blood cell count, blood chemistry, histopathology Genotoxicity	Chen *et al.* (2003a)
Tomato	Cry1Ab endotoxin (*Bacillus thuringiensis* var kurstaki)	Rat	91 days	Feed consumption, body weight, organ weights, blood chemistry, histopathology	Noteborn *et al.* (1995)
	Chalcone isomerase *(Petunia)*	Mouse, transgenic for human C-reactive protein	42 days	Feed consumption, body weight gain	Rein *et al.* (2006)
Soybean	CP4 EPSPS *(Agrobacterium)*	Mouse	2–4 generations; 87 days after birth (2nd generation) and 63 days afterbirth 4th generation)	Litter size, body weight, testicular cell populations	Brake and Evenson (2004)
	CP4 EPSPS *(Agrobacterium)*	Rat	91 days	Feed consumption, body weight, organ weights, blood cell count, blood chemistry, urine chemistry, histopathology	Zhu *et al.* (2004)
	CP4 EPSPS *(Agrobacterium)*	Mouse	240 days	Histocytochemistry of hepatocytes, pancreatic acinar and testicular cells Enzyme chemistry of serum, liver and pancreas	Malatesta *et al.* (2002a, b, 2003) Vecchio *et al.* (2004)
	CP4 EPSPS (Agrobacterium)	Mouse	30 days	Histocytochemistry of hepatocytes	Malatesta *et al.* (2005)
	CP4 EPSPS *(Agrobacterium)*	Rabbit	40 days	Body weight, organ weights, serum and tissues enzyme chemistry	Tudisco *et al.* (2006)
Maize	Cry3Bb1 endotoxin (*Bacillus thuringiensis* var kumamotoensis)	Rat	90-days	Feed consumption, body weight gain, organ weights Blood cell count, blood chemistry, urine chemistry Histopathology	Hammond *et al.* (2006a)
	Cry1Ab endotoxin *(Bacillus thuringiensis* var kurstaki)	Rat	90-days	Feed consumption, body weight, organ weights Blood cell count, blood chemistry, urine chemistry Histopathology	Hammond *et al.* (2006b)
	CP4 EPSPS *(Agrobacterium)*	Rat	90-days	Feed consumption, body weight, organ weights Blood cell count, blood chemistry, urine chemistry Histopathology	Hammond *et al.* (2004)
	Cry1Ab endotoxin (*Bacillus thuringiensis* var kurstaki)	Mouse	2-4 generations; 87 days after birth (2nd generation) and 63 days after birth (4th generation)	Litter size, body weight Testicular cell populations	Brake and Evenson (2004)
	Cry1F endotoxin (*Bacillus thuringiensis* var aizawai) and phosphinothricin acetyltransferase *(bar* gene, *Streptomyces viridochromogenes)*	Rat	90-days	Feed consumption, body weight Clinical pathology (serum, blood, urine) Anatomical pathology (organ weights, histopathology)	Mackenzie *et al.* (2007)

Table 2: Continued

Plant	Trait	Species	Duration	Parameters	Reference
	Cry34Ab1 and Cry35Ab1 endotoxins (*Bacillus thuringiensis* Berliner strain PS149B1) and phosphinothricin acetyltransferase (*bar* gene, *Streptomyces viridochromogenes*)	Rat	90-days	Feed consumption/efficiency, body weight/ gain Neurobehavioural and ophthalmological examinations Clinical pathology (hematology, clinical chemistry, coagulation and urinalysis) Pathology (organ weights and gross and microscopic pathology)	Malley *et al.* (2007)
Potato	Lectin (*Galanthus nivalis*)	Rat	10 days	Histopathology of intestines	Ewen and Pusztai (1999)
	Cry1 endotoxin (*Bacillus thuringiensis* var kurstaki HD1)	Mouse	14 days	Histopathology of intestines	Fares and El Sayed (1998)
	Glycinin (Soybean [*Glycine max*])	Rat	28 days	Feed consumption, body weight, blood chemistry, blood count, organ weights, liver and kidney histopathology	Hashimoto *et al.* (1999a) Hashimoto *et al.* (1999b)
	CryV endotoxin (*Bacillus thuringiensis*)	Rat	30 days	Feed consumption, body weight, blood chemistry Organ weights	El Sanhoty *et al.* (2004)
	Phosphinothricin acetyltransferase (*bar* gene, *Streptomyces hygroscopicus*)	Rat	5 generations; 70-day intervals before reproduction	Feed consumption, body weight Reproductive performance, development and viability of progeny Organ weights Skeletal and visceral deformations Histopathology	Rhee *et al.* (2005)
	Polymerase and non-coding DNA sequences derived from potato virus Y (PVY)	Rat	21 days	Serum chemistry, non-specific immunity, caecal wall and digesta characteristics	Zdunczyk *et al.* (2005)
Oilseed rape	High γ-linolenic acid (Δ^6- and Δ^{12}-desaturases from Mortierella alpina)	Mouse	2 generations, 28 days after birth	Maternal characteristics, litter size, pup weight Brain weight and lipid chemistry, pup behaviour Pup maze test	Wainwright *et al.* (2003)

(Data collected by Dr. G. A., RIKILT, partly derived from Kuiper *et al.*, 2003)

fed to rats or mice during different periods of administration, and parameters such as body weight, feed consumption, blood chemistry, organ weights, histopathology, etc., have been measured.

CONCLUSION

Genetically-modified foods have the potential to solve many of the world's hunger and malnutrition problems and to help protect and preserve the environment by increasing yield and reducing reliance upon chemical pesticides and herbicides. Yet there are many challenges ahead for governments especially in the areas of safety testing, regulation, international policy and food labeling. Many people feel that genetic engineering is the inevitable wave of the future and that we cannot afford to ignore a technology that has such enormous potential benefits. It has been estimated that demand placed on world agricultural production by 2050 will double assuming moderately high income growth taken together with expected population growth. However, we must proceed with caution to avoid causing unintended harm to human health and the environment as a result of our enthusiasm for this powerful technology.

Genetic modification has increased production in some crops but the evidence we have suggests that the technology has so far addressed too few challenges in few crops of relevance to production systems in many developing countries. Even in developed countries a lack of perceived benefits for consumers and uncertainty about their safety have limited their adoption.

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