Read only:

Biotech crops in the last 22 years of commercialization have brought immense economic benefits, health improvement and social gains which should be shared with the global community. Accurate information on the benefits and potentials of biotech crops will allow farmers and consumers to make informed-choice in what crops to grow and consume, respectively; policy makers and regulators to craft enabling biosafety guidelines for commercialization and adoption of biotech crops; and science communicators and the media to facilitate dissemination of the benefits and potentials of the technology.

The International Service for the Acquisition of Agri-biotech Applications (ISAAA) has been publishing the annual series of Global Status of Commercialized Biotech/GM Crop since 1996 (ISAAA Brief 53-2017).

Highlights of the 2017 adoption of biotech crops

On the 22nd year of commercialization of biotech/GM crops in 2017, 24 countries (19 developing and 5 industrial) grew 189.8 million hectares of biotech crops – an increase of 4.7 million hectares (11.6 million acres) or 3% from 185.1 million hectares in 2016. Except for the 2015 adoption, this is the 21st series of increases every single year; and notably 12 of the 18 years were double-digit growth rates.

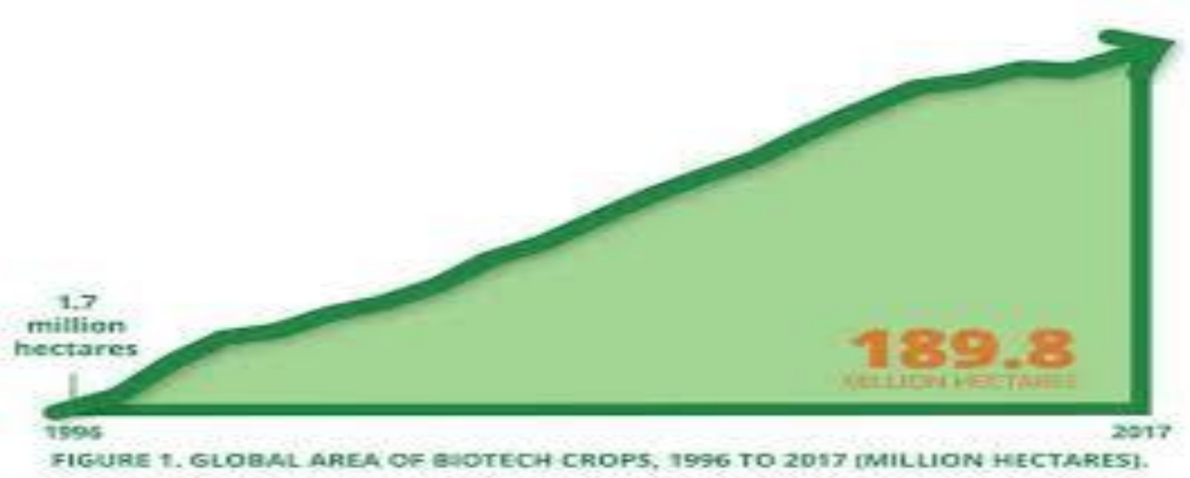
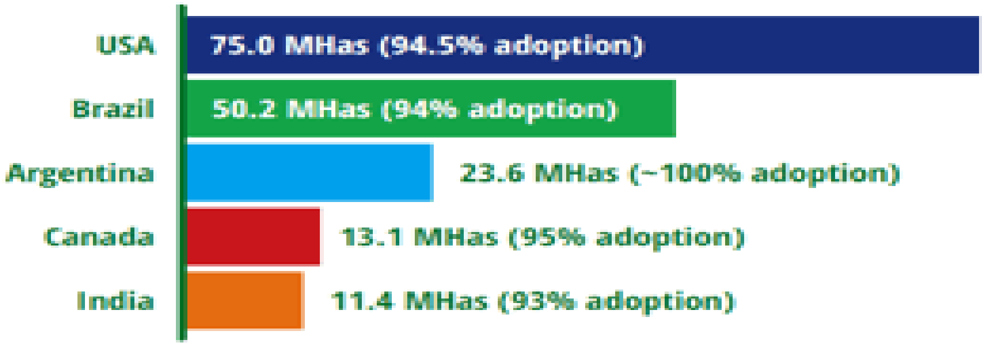


FIGURE 1. GLOBAL AREA OF BIOTECH CROPS, 1996 TO 2017 (MILLION HECTARES).
Source: ISAAA, 2017

Top five countries (USA, Brazil, Argentina, Canada and India) planted 91.3% of the global biotech crop area of 189.8 million hectares. USA at 94.5% (average for soybeans, maize and canola adoption), Brazil (94%), Argentina (~100%), Canada (95%), and India (93%). Expansion of biotech crop areas in these countries would be through immediate approval and commercialization of new biotech crops and traits to target problems related to climate change and emergence of new pests and diseases.



TOP 5 COUNTRIES THAT PLANTED BIOTECH CROPS IN 2017 (AREA AND ADOPTION RATE)

Source: ISAAA, 2017

FIGURE 2.
DISTRIBUTION OF BIOTECH CROPS IN DEVELOPING AND INDUSTRIAL COUNTRIES IN 2017

Source: ISAAA, 2017

The area of biotech crops planted in 2017 in the United States of America (USA) remained the highest globally at 75.04 million hectares, comprised of 34.05 million soybeans, 33.84 million hectares maize, 4.58 million hectares cotton, 1.22 million hectares alfalfa, 876,000 hectares canola, 458,000 biotech sugar beets, 3,000 hectares biotech potato, and some 1,000 hectares each of biotech apples, squash and papaya. Generally, the area planted to biotech crops increased in the USA except for maize and sugar beets. The lesser drought incidence and lesser storms that bypassed the crop growing areas across the country as well as the favorable and profitable prices for soybeans, cotton, and canola, were enough incentives for farmers to increase the area of these three biotech crops. The average near saturation biotech adoption rate of 94.5% from the three major crops: maize, soybeans, and cotton may mean minimal increases expected in the coming years. Thus, further expansion in biotech crop area depends on the adoption of other biotech crops: canola, alfalfa, sugar beets, potato, and apples. The USA leads the bandwagon in the discovery, development, and commercialization of biotech crops. The current revamp on biotech regulations of the three government regulatory agencies should reflect the country's leadership in acceptance and recognition of the scientific basis of the technology. Expeditious approval of new products of agri-biotechnology benefits not only the USA, but also the global community.

Table 1. Global Area of Biotech/GM Crops in 2017: by Country (Million Hectares)**

Rank	Country	Area (million hectares)	Biotech Crops
1	**USA***	**75.0**	Maize, soybeans, cotton, canola, sugar beets, alfalfa, papaya, squash, potato, apples
2	**Brazil***	**50.2**	Soybeans, maize, cotton
3	**Argentina***	**23.6**	Soybeans, maize, cotton
4	**Canada***	**13.1**	Canola, maize, soybeans, sugar beets, alfalfa, potato
5	**India***	**11.4**	Cotton
6	**Paraguay***	**3.0**	Soybeans, maize, cotton
7	**Pakistan***	**3.0**	Cotton
8	**China***	**2.8**	Cotton, papaya
9	**South Africa***	**2.7**	Maize, soybeans, cotton
10	**Bolivia***	**1.3**	Soybeans
11	**Uruguay***	**1.1**	Soybeans, maize
12	**Australia***	**0.9**	Canola, cotton
13	**Philippines***	**0.6**	Maize
14	**Myanmar**	**0.3**	Cotton
15	**Sudan***	**0.2**	Cotton
16	**Spain***	**0.1**	Maize
17	**Mexico***	**0.1**	Cotton
18	**Colombia***	**0.1**	Maize, cotton
19	**Vietnam**	**<0.1**	Maize
20	**Honduras**	**<0.1**	Maize
21	**Chile**	**<0.1**	Maize, canola, soybeans
22	**Portugal**	**<0.1**	Maize
23	**Bangladesh**	**<0.1**	Brinjal/Eggplant
24	**Costa Rica**	**<0.1**	Cotton, pineapple
	Total	189.8	

*18 biotech mega-countries growing 50,000 hectares, or more, of biotech crops
**Rounded-off to the nearest hundred thousand.

For the past six years, developing countries have planted more biotech crops than the industrial countries (Figure 2). In 2017, 19 developing countries planted 53% (100.6 million hectares) of the global biotech hectares, while 5 industrial countries took the 47% (89.2 million hectares) share. This trend is expected to continue in the upcoming years due to the increasing number of countries in the southern hemisphere adopting biotech crops and the commercialization of new biotech crops such as rice, which is mostly grown in developing countries.

Global Adoption of Biotech Soybean, Maize, Cotton, and Canola

he most planted biotech crops in 2017 were soybean, maize, cotton, and canola. Although there was only 3% increase in the planting of biotech soybean, it maintained its high adoption rate of 50% of the global biotech crops or 94.1 million hectares. This area is 80% of the total soybean production worldwide (Figure 3).

FIGURE 3. GLOBAL ADOPTION RATES (%) FOR TOP 4 BIOTECH CROPS (MILLION HECTARES)
Source: ISAAA, 2017

Biotech maize occupied 59.7 million hectares globally, which was 32% of the global maize production in 2017. A slight decline (1%) in the biotech maize area from 2016 is due to the unfavorable weather conditions in Latin America, low market price, lesser pest incidence, high year-end stocks and the problem of counterfeit seeds in the Philippines.

Biotech cotton was planted to 24.1 million hectares in 2017, which indicates a decrease by 8% from 2016. The 8% increase in total biotech cotton area globally was due mainly to the improved global market value and the high adoption rate of insect resistant/herbicide tolerant cotton in 2017.

Biotech canola increased by 19% from 8.6 million hectares in 2016 to 10.2 million hectares in 2016. This raise is attributed to the two-digit increases in biotech canola plantings in the USA, Canada, and Australia, addressing the demand for edible oil.

In 2017, farmers in the USA and Canada planted biotech alfalfa. Approximately 1.14 million hectares of herbicide tolerant alfalfa and 80,000 hectares of low lignin alfalfa were planted in the US, while Canada planted 3,000 hectares low lignin alfalfa. Low lignin alfalfa was first commercialized in 2016, and offers 15 to 20% increase in yield.

Aside from soybean, maize, cotton, canola, and alfalfa, the following biotech crops were also planted in different countries: sugar beet, squash, papaya, eggplant, potato, and apple.

The Global Value of Biotech Crops

According to Cropnosis, the global market value of biotech crops in 2017 was US$17.2 billion. This value indicates that there was a 9% increase in the global market value of biotech crops from 2016, which was US$15.8 billion. This value represents 23.9% of the US$70.9 billion global crop protection market in 2016, and 30% of the US$56.02 billion global commercial seed market. The estimated global farmgate revenues of the harvested commercial "end product" (the biotech grain and other harvested products) are more than ten times greater than the value of the biotech seed alone.

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Frequently asked questions on genetically modified foods

18 questions and answers have been prepared by WHO in response to questions and concerns from WHO Member State Governments with regard to the nature and safety of genetically modified food.

1. What are genetically modified (GM) organisms and GM foods?

Recombinant DNA technology or "genetic engineering" allows selected individual genes to be transferred from one organism into another. Genetically modified organisms (GMOs) are organisms (i.e. plants, animals or microorganisms) in which the genetic material (DNA) has been altered in a way that does not occur naturally. Foods produced from or using GM organisms are often referred to as GM foods.

2. Why are GM foods produced?

GM foods are developed – and marketed – because there is some perceived advantage either to the producer or consumer of these foods. Several publications are now available for using recombinant DNA technology for the following purposes (and others):

a) Insect Resistance

The genetic engineering of crop plants to produce functional insecticides makes it possible to develop crops that are intrinsically resistant to insect predators and do not need to be sprayed (often six to eight times during a growing season) with costly and potentially hazardous chemical pesticides. *Bacillus thuringiensis*, commonly known as *Bt*, is a gram-positive bacterium that occurs naturally in the soil around the world. For decades, bacteriologists have known that some strains of *Bt* kill certain insects and that the toxic substance responsible for the insects death is a protein. When certain insects ingest either the bacterium or the protein produced by the bacterium (the protein is called d-endotoxin), the function of their digestive systems is disrupted, eventually resulting in death. When the dose is high, sudden death occurs. The use of *Bt* as a biopesticide was discovered in the first decade of this century when larvae of flour moths died suddenly. Research into their deaths led to the discovery that the presence of *Bt* was responsible for the death.

The *Bt* protein is not harmful to mammals, birds or fish, nor to beneficial insects. Mammals, including humans, do not have d-endotoxin receptors in their guts and all

Bt proteins tested so far are degraded within 20 seconds in the presence of mammal digestive juices. *Bt* is not effective against all insects; however different *Bt* strains are effective against specific species. The major families of insects that respond to *Bt* are:

- *Lepidoptera* (caterpillars; e.g. European corn borer or cotton bollworm).
- *Coleoptera* (beetles; e.g. Colorado potato beetles).
- *Diptera* (flies and mosquitoes).

This Bt-based biopesticides also have several disadvantages. The production of the biopesticide is relatively expensive; its application requires the use of agricultural machinery; most applications need to be repeated several times per season; sunlight breaks down the active ingredient; and water (rain or dew) washes the protein from the plants, thus limiting the time when insects are exposed to it. Biopesticides therefore must be applied where and when the target insects are feeding. Most of these difficulties are overcome with transgenic insect resistant crops.

With the emergence of biotechnology, the development of insect resistant plants by transferring the gene that produces the *Bt* toxin became possible and this procedure is now well established. The strain of *Bt* that is active against a target insect is identified and the gene producing it is isolated and transferred to the crop to be resistant. The most critical component of the process is to use the gene that is effective against the target insect. Many companies and universities have been working on identifying novel *Bt* genes and have sought appropriate patent protection.

b) Disease Resistance

- **Resistance to Viral diseases**

Plant viruses often cause considerable crop damage and significantly reduce yields. When transgenic plants express the gene for a coat protein (which usually is the most abundant protein of a virus particle) of a virus that normally infects those plants, the ability of the virus to subsequently infect the plants and spread systemically is often greatly diminished. The mechanism by which the presence of coat protein genes inhibits viral proliferation is thought that it likely works through the generation of RNAi. With this approach, researchers have developed virus-resistant transgenic plants for a number of different crops. Although complete protection is not usually achieved, high levels of virus resistance have been reported. In addition, a coat protein gene from one virus sometimes provides tolerance for a broad spectrum of unrelated viruses.

In both eukaryotes and prokaryotes, an RNA molecule that is complementary to a normal gene transcript (mRNA) is called antisense RNA. The mRNA, being translatable, is considered to be a sense RNA. The presence of antisense RNA can decrease the synthesis of the gene product by forming a duplex molecule with the normal sense mRNA, thereby preventing it from being translated. The antisense RNA–mRNA duplex is also rapidly degraded, a response that diminishes the amount of that particular mRNA in the cell. Theoretically, it should be possible to prevent plant viruses from replicating and subsequently damaging plant tissues by creating transgenic plants that synthesize antisense RNA that is complementary to viral coat protein mRNA.

- **Resistance to fungal and bacterial diseases**

Extensive damage and loss of crop productivity are caused by phytopathogenic fungi and bacteria. At present, the major way of controlling the damage and losses to crop plants that result from infection is through the use of chemical agents that may persist and accumulate in the environment and that are subsequently hazardous to animals or humans. It would therefore be beneficial if a simple, inexpensive, effective, and environmentally friendly nonchemical means of preventing fungal and bacterial damage to crop plants could be found.

Plants often respond to fungal or bacterial pathogen invasion or other environmental stresses by converting a conjugated storage form of salicylic acid (salicylic acid 2-*O*-β-d-glycoside) to salicylic acid, which induces a broad systemic defense response in the plant. This "systemic acquired resistance" to pathogens extends to plant tissues that are far from the site of the initial infection and may last for weeks to months. It results from the synthesis of a group of proteins called pathogenesis-related (PR) proteins. Engineering plants with broad-spectrum disease resistance involves overproducing salicylic acid. Theoretically, this can be done by transforming plants with bacterial genes that encode the enzymes isochorismate synthase and isochorismate pyruvate lyase, which catalyze salicylate synthesis.

The *NPR1* gene from the plant *A. thaliana* encodes a “master” regulatory protein that controls the expression of the PR proteins, and it can be activated or induced by the addition of salicylic acid. Overexpression of the *NPR1* gene can lead to the generation of broad-spectrum disease resistance against both fungal and bacterial pathogens. It was observed that overproduction of this “master switch” is an effective strategy in several plants eg: *A. thaliana*, including rice, sugar beet, apple, and corn.

To develop plants resistant to fungal pathogens, researchers have attempted to utilize parts of the systemic acquired resistance system. The PR proteins include chitinases that protect the plant-invading pathogens. Transgenic plants that constitutively express high levels of chitinase, which can hydrolyze the β-1,4 linkages of the *N*-acetyl-d- glucosamine polymer chitin, a major component of many fungal cell walls, have been engineered.

c) Herbicide Resistance

Weeds compete with crops for water and nutrients and, as a result, decrease farming yields and productivity. The development of selective herbicides is not an easy task. Given that each weed requires a different herbicide, herbicide application has been frequent, in large volumes and very costly. Bialaphos is a biodegradable herbicide, which displays low levels of toxicity, till to date, and weeds have shown minimal resistance to its repeated applications. The *bar* (for bialaphos resistance) gene encodes a phosphinothricin acetyl transferase (PAT) that detoxifies bialaphos. Genetically modified plants carrying a *bar* gene do not affected with the wide spectrum herbicide bialaphos, so can help in protection against weeds without affecting the cultivated crops or environment.

d) Resistance to abiotic stresses as salinity

Considerable efforts have been made to increase salt tolerance of crops through transferring foreign genes into them. Various genes induced by salt stress are grouped into two categories, namely *single-function genes* and *regulatory genes*.

Genes of first category generally facilitate production of: protective metabolites, which include osmolytes, transporters/channel proteins, antioxidative enzymes,…..etc:

- **Protective metabolites,** which include osmolytes: These compounds facilitate both water uptake and retention and also protect and stabilize cellular macromolecules from damage by high salt levels. Some well-known osmoprotectants are sugars alcohols, the amino acid proline, and quaternary ammonium compounds (eg: betane).

- **Transporters/channel proteins:** sequester sodium ions in the large intracellular vacuole (eg: Na^+/H^+ antiport protein).
- **Antioxidative enzymes:** Scavengers for Reactive oxygen species (ROS) associated with salt stress.

The second category includes genes for regulatory proteins that regulate gene expression and signal transduction in the stress response eg: transcription factors. The complexity and multigenic nature of salt tolerance trait makes it better to manipulate more than one gene simultaneously. Fortunately, most controls of stress responses appear to be through the transcriptional regulation of genes via an array of transcription factors. Consequently, genetic engineering of plants for a multigenic trait like salt tolerance could be better to achieve through regulating the expression of genes encoding stress-inducible transcription factors that in turn would regulate a set of stress tolerance genes.

Transcriptional factors are important regulatory proteins that are able to regulate the expression of target genes by specifically binding to the cis-acting elements of interactional genes. Transcriptional factors are regarded as master switch that regulate stress-response genes and function in establishing stress tolerance. Based on the structure of their DNA binding domains, these transcriptional factors can be classified into various families. DREB (Dehydration responsive element-binding protein) are an important class of transcription factors that activate the expression of a number of stress responsive genes by binding to cis acting dehydration responsive elements (DRE) with a core motif of A/GCCGAC in their promoters. They participate in stress response to drought, salinity and freezing, and improve stress resistance in plants. DREBs were found to activate many genes involved in production of antioxidant enzymes eg SOD and catalase and accumulation of compatible solutes eg proline and soluble carbohydrates. Thus different DREBs may perform different functions in plants and may be involved in several pathways and/or participate in crosstalk between pathways during the course of abiotic stress.

Transformation with different DREBs may lead to various abiotic tolerances in transgenic plants. For example over-expression of OsDREB2A improved salinity and drought tolerance in rice, DREB2A from *Pennisetum glaucum* was used to enhance salt and dehydration tolerance in tobacco. Over-expression of CKDREB from *Caragana korshinski* enhanced salt tolerance in tobacco.

e) Improvement in Yield Quantity

In general, potential yield may be raised by improving the efficiency of photosynthesis, improving the efficiency of resource use by the plant, or enlarging resource allocations to the food/feed components of the crop, all of which have been targets of research for many years. Some of genes that have been explored for their ability to increase yield and that have wide-ranging effects on plant metabolism include *fasciated ear2* (*fea2*), which controls branching and seed number; *Phytochrome B* which regulates plant light responses; and CDK (proteins controlling cell cycle) inhibitor-like proteins in corn. Some trials are recorded for genes involved in nitrogen assimilation but with little success.

f) Improvement in Yield Quality

Ex: Rice grains containing pro-vitamin A

Upwards of 3 billion people depend upon rice as their main staple. β-carotene (provitamin A), a natural plant pigment, provides the chemical precursor for the body to produce Vitamin A. In rice, beta-carotene is present only in the outer grain layers. Unfortunately, in order to keep the grain from rotting, these layers are removed during milling and polishing. The kernel that most people eat,the starchy interior called the endosperm, does not contain betacarotene.

Since no species in the entire Oryza family produces beta-carotene in its endosperm, hybridization of Oryza lines—the traditional crop improvement approach—is not considered feasible. In the year 2000, an international group of scientists reported using *Agrobacterium*-mediated transformation to introduce the entire β-carotene biosynthetic pathway into rice. Thus genes for phytoene synthase, phytoene desaturase and lycopene β-cyclase were introduced. The frequency of insertion of all three genes into the rice genome and their subsequent expression were quite high. Thus, the engineered rice produces β-carotene, which, after ingestion, is converted to vitamin A. The transgenic rice that produces β-carotene has a yellow or golden color and has been called "golden rice" by the scientists involved in its development. Unfortunately, the initial version of golden rice, now called golden rice 1, synthesized only 1.6 μg of β-carotene per gram of rice, so that individuals would have had to consume around 3 kg of golden rice 1 each day to reach the recommended minimal daily requirement of vitamin A. However, in 2005, scientists reported replacing the daffodil phytoene synthase gene with a similar gene from corn that produces an enzyme with a higher level of activity, resulting in a variety called golden rice 2 that produces a 23-fold-higher level of β-carotene than golden rice 1.

Generally, plants can be used as bioreactors to produce vitamins, pigments, lipids, proteins…etc. Unlike recombinant bacteria, which are grown in large bioreactors, a process that requires highly trained personnel and expensive equipment, crops can be produced relatively inexpensively by less-skilled workers. In addition, when proteins that are intended for human use are produced in transgenic plants, there is a significantly reduced risk of mammalian virus contamination in comparison to proteins that are produced in animal cells grown in culture.

g) Transgenic Plants as Bioreactors

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Transgenic plants have significant potential in the bioproduction of complex human therapeutic agents due to:

- Ease of genetic manipulation,
- Lack of potential contamination with human pathogens,
- Conservation of eukaryotic cell machinery mediating Protein modification
- Low cost of biomass production.

In addition to food and fiber, plants are exploited for a large variety of commercial chemicals including pharmaceuticals, food colors and flavors, fragrances and sweeteners. Plant tissue culture production methods 0 can be developed to profitably manufacture some of these chemicals. Numerous investigators have reported production of useful compounds in both callus and suspension cultures. Several antibodies of therapeutic and diagnostic value have been expressed in plants eg: **Antibodies for:** *Streptococcus mutans* (a cause of tooth decay), Hepatitis B in tobacco and Herpes simplex virus in soybean. **Human proteins including:** human serum albumin, human α-interferon, human erythroprotein etc are also now produced in transgenic plants or cultured transgenic cells. In some cases production in callus and suspension is **much higher** than that in whole plant of the same species. Understanding the biosynthetic pathways has a great beneficial effect on enhancing production of these compounds.

Over production can be obtained through:

1. Over-expressing the key gene(s) involved in the biosynthetic pathway.
2. Blocking the competitive branches of biosynthesizing target compounds.
3. Blocking the degradation pathways or enhancing the transportation of target compounds.
4. Inhibiting the reproductive growth of plants and increase the biomass of vegetation growth, and increase the production of target compounds.

As a source for commercial chemicals, tissue cultures have the following advantages over field grown plants:

1. The culture system doesn’t need much field which can be used for crop growing.
2. The system is not limited by whether and season changes.
3. The secondary metabolism can be regulated to maximize the production of target compounds.
4. No herbicide and insecticide will be used during the maintaining of the system and therefore, the system is ecofriendly.
5. Once the system is established, the content of useful compounds will be more stable than harvested herbs from different areas, which will facilitate the quality control.

3. Is the safety of GM foods assessed differently from conventional foods?

Generally consumers consider that conventional foods (that have an established record of safe consumption over the history) are safe.

Whenever novel varieties of organisms for food use are developed using the traditional breeding methods that had existed before the introduction of gene technology, some of the characteristics of organisms may be altered, either in a positive or a negative way.

National food authorities may be called upon to examine the safety of such conventional foods obtained from novel varieties of organisms, but this is not always the case.

In contrast, most national authorities consider that specific assessments are necessary for GM foods. Specific systems have been set up for the rigorous evaluation of GM organisms and GM foods relative to both human health and the environment. Similar evaluations are generally not performed for conventional foods. Hence there currently exists a significant difference in the evaluation process prior to marketing for these two groups of food.

The WHO Department of Food Safety and Zoonoses aims at assisting national authorities in the identification of foods that should be subject to risk assessment and to recommend appropriate approaches to safety assessment. Should national authorities decide to conduct safety assessment of GM organisms, WHO recommends the use of Codex Alimentarius guidelines.

- Guideline for the conduct of food safety assessment of foods derived from recombinant-DNA plants.
- Guideline for the conduct of food safety assessment of foods produced using recombinant-DNA microorganisms.
- Guideline for the conduct of food safety assessment of foods derived from recombinant-DNA animals.

4. How is a safety assessment of GM food conducted?

Principles of the Codex Alimentarius are used internationally to guide the risk assessment process for novel foods. The process to evaluate the risk of GM food products is based on the concept of substantial equivalence.

Concept of substantial equivalence

The genetically modified product must be at least as safe as its unmodified counterpart, and it is desirable for the GM food to be at least as nutritious.

The underlying assumption of this comparative approach is that traditionally cultivated crops have a history of safe use for consumers. These traditionally cultivated crops can thus serve as comparators when assessing the safety of GM plants and derived food and feed

The risk assessment starts with: The comprehensive molecular characterisation (MC) of the GM plant in question. Followed by the: Comparative analysis of the relevant characteristics of the GM plant and its comparator(s).

The results of genetic engineering is so unpredictable, with different results produced by each attempt and the products are often unstable. The possibility that an unidentified compound may be present in the GM food. Transferred genes might cause:

- The silencing of genes,
- Changes in their level of expression,
- The turning on of existing genes that were not previously being expressed.

This interaction with the activity of the existing genes and biochemical pathways of plants, may lead to:

- Disruption of metabolism in unpredictable ways
- Development of new toxic compounds or an increase of the already existing ones.

Risk for animal and human health

1. **Recorded Deaths from GMOs**

A number of cases of eosinophiliamyalgia syndrome (an incurable and sometimes fatal flu-like neurological condition) were reported among users of the amino acid tryptophan as a dietary supplement. By mid-1993, 37 deaths had been recorded.
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.

2. **Cancer**

GH is a protein hormone which, when injected into cows stimulates the pituitary gland in a way that the produces more milk, thus making milk production more profitable for the large dairy corporations.

In 1993, FDA approved Monsanto's genetically-modified bovine growth hormone (rBGH), a genetically-altered growth hormone that could be then injected into dairy cows to enhance this feature. Scientists warned that rBGH resulted in an increase of IGF-1 from (70%-1000%). IGF-1 is a very potent chemical hormone that has been linked to a 2.5 to 4 times higher risk of human colorectal and breast cancer. Prostate cancer risk is considered equally serious - in the 2.8 to 4 times range.

3. **Allergenicity**

Allergy is a pathological deviation of the immune response to a particular substance, which affects only some individuals. Symptoms include red eyes, itchiness, and runny nose, eczema, hives, or anasthma attack.

In some people, severe allergies to environmental or dietary allergens or to medication may result in life-threatening reactions called anaphylaxis. Anaphylaxis is a serious allergic reaction that is rapid in onset and may cause death. It typically causes a number of symptoms including an itchy rash, throat swelling, and low blood pressure.





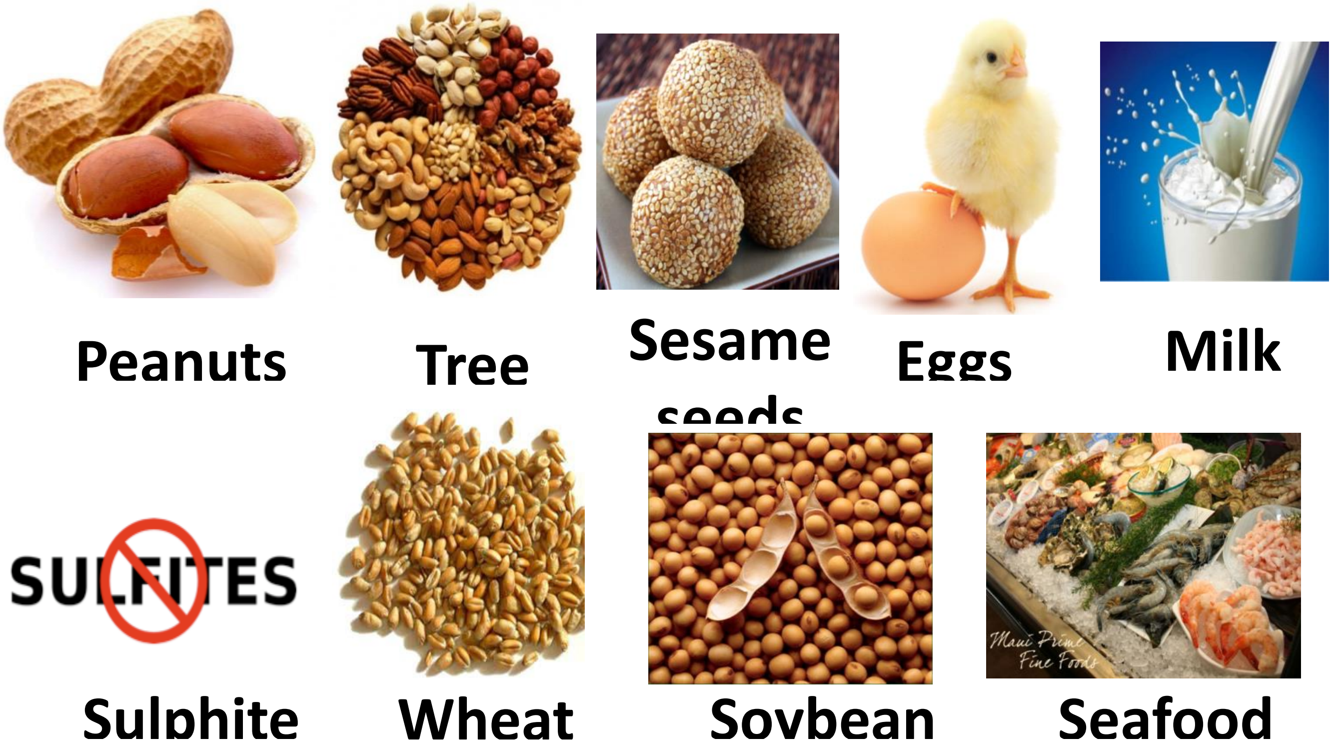
Food allergy can be caused by various immune mechanisms. However, IgE-mediated food allergy represents the main form of food allergy, that causes the most severe reactions and the only form causing life-threatening reactions.

This IgE-mediated food allergy has been the focus in the risk assessment of allergenicity of GMOs.

Importantly, food allergy consists of two separate phases:

- *Sensitisation* where no symptoms occur
- *Elicitation (provocation)* with clinical manifestations.

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 conventional foods.



The introduction of novel proteins into foods such as:

- GM soybean variety expressing methionine from Brazil nut.
- corn variety modified to produce a Bt endotoxin, Cry9C.

may elicit potentially harmful immunological responses, including allergic hypersensitivity.

By testing on rats, the following phenomena appear:

- Stomach erosion and necrosis in rats fed with GM tomatoes.
- GM potatoes expressing Bt toxin caused the disruption, multinucleation, swelling, and increased degradation of ileal surface cells in rats.
- GM soybean cause changes in pancreatic acinar cells of mice.
- Smaller kidneys were developed in rats fed diets containing GM corn.
- Rats fed diets containing GM corn showed a decrease in red blood cell count.
- GM corn caused higher white blood cell levels in male rats.
- An increased mortality was observed in rats fed with GM tomatoes since seven out of forty rats died within two weeks without any explanation.
- Increase in the production of Cry9C-specific IgG and IgG1 in rats and mice fed with GM heat-treated corn.

The safety assessment of GM foods generally focuses on:

- Direct health effects (toxicity).
- Potential to provoke allergic reaction (allergenicity);
- Nutritional effects associated with genetic modification.
- The stability of the inserted gene.
- Any unintended effects which could result from the gene insertion.

5. What are the main issues of concern for human health?

While theoretical discussions have covered a broad range of aspects, the three main issues debated are the potentials to provoke allergic reaction (allergenicity), gene transfer and outcrossing.

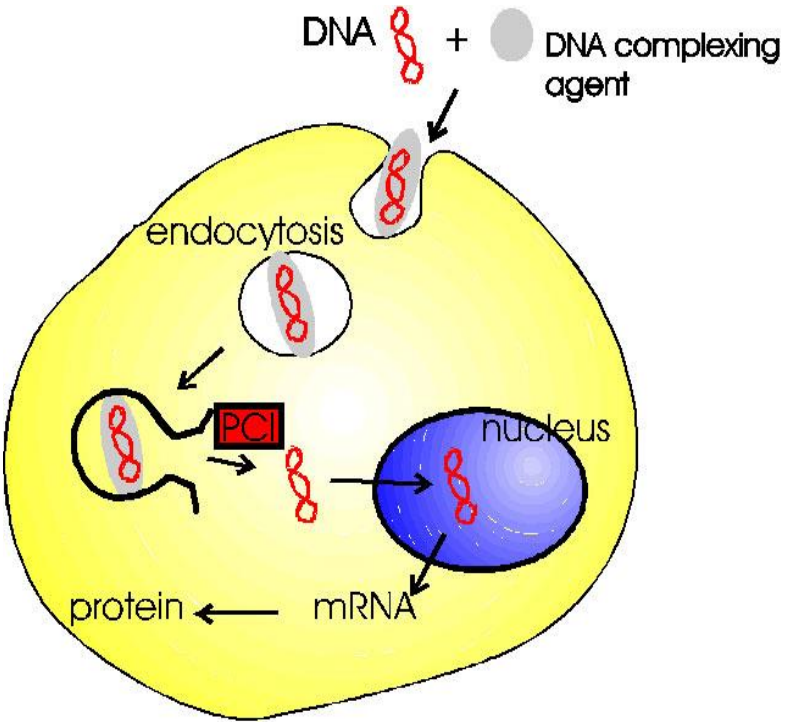
a) Allergenicity (mentioned previously)

b) Gene transfer

Gene transfer from GM foods to cells of the body or to bacteria in the gastrointestinal tract would cause concern if the transferred genetic material adversely affects human health. This would be particularly relevant if antibiotic resistance genes, used as markers when creating GMOs, were to be transferred. Although the probability of transfer is low, the use of gene transfer technology that does not involve antibiotic resistance genes is encouraged.

- *Possible Absorption of Genes Introduced in a GM Plant from the Gut*

One concern associated with GM foods is the possibility that genes introduced into the plant might be taken up by the gut and become incorporated into the genetic make-up of consumers. Short DNA fragments of GM plants have been detected in white blood



cells and in milk of cows and in chicken and mice tissues that had been fed GM corn and soybean, respectively.

- *Possible Transfer of Antibiotic Resistant Genes to Bacteria in the Gastrointestinal Tract*

Antibiotic resistance genes used as markers in transgenic crops may be horizontally transferred to pathogenic gut bacteria, thereby reducing the effectiveness of antimicrobial therapy. Although this probability is considered to be low.

- *Potential Effects on Human Health resulting from the use of Viral DNA in Plants*

Most of the manipulated crops utilize the Cauliflower MosaicVirus 35S promoter (CaMV35S) to switch on the introduced gene. There has been a lot of controversy concerning whether the highly infectious CaMV35S can be horizontally transferred and cause disease, carcinogenesis, mutagenesis, reactivation of dormant viruses and even generation of new viruses. A three-year German study found that herbicide-resistant genes in the canola transferred across to the bacteria and yeast inside the intestines of young bees.

c) Outcrossing

The migration of genes from GM plants into conventional crops or related species in the wild (referred to as "outcrossing"). Several countries have adopted strategies to reduce mixing, including a clear separation of the fields within which GM crops and conventional crops are grown. Escaped genes from GM crops will result in unknown consequences, as most transgenes are transferred to the crops from other organisms.

Gene flow is the movement of genes mediated by pollen flow and seed dispersal.

Gene flow can occur within species (GM crops to the same crop species), between species (GM crops to different plant species), and from GM crops to other organisms such as microorganisms.

Effects of outcrossing on Health, Agriculture and Environment:

- **Risk for animal or human health:**
  - ➢ Toxicity
  - ➢ Allergies,
  - ➢ Food quality
  - ➢ Pathogen drug resistance (antibiotic resistance).
- **Risk for agriculture:**
  - ➢ Superweeds (Superweed is a hybrid plant that contains genes for herbicide resistance: produced by accidental crossing of genetically engineered crop plants with wild plants)
  - ➢ Alteration of nutritional value
  - ➢ Increase of susceptibility to pests
- **Risk for environment:**

➢ <u>Loss of biodiversity:</u> Some weeds are important components of agroecosystems because they positively affect the biology and dynamics of beneficial insects. Non-crop vegetation offers many important resources for natural enemies, such as alternative prey/hosts, pollen, or nectar as well as microhabitats that are not available in weed-free monocultures

- Habitat change: Land use change and agriculture. The most important direct change in terrestrial ecosystems has been land cover change, and in particular conversion to cropland. More than half of the original area of many types of grasslands and forests has been converted into farmland. GM crops will indirectly contribute to forest conservation by allowing marginal land to be cultivated, preventing further deforestation for conversion to cropland. However, actual experiences indicate that GM crop cultivation can accelerate land use change. In a study of deforestation in seasonally dry forests of north-west Argentina, the initial deforestation was associated with black bean cultivation during the 1970s and high soybean prices in the 1980s. The introduction of GM soybean in 1997 stimulated a further increase in deforestation. The possibilities for soil biota to be exposed to transgenic products are high. The insecticidal toxin produced by *Bacillus thuringiensis subsp. Kurstaki* remains active in the soil, where it binds rapidly and tightly to clays. The bound toxin retains its insecticidal properties and is protected against microbial degradation by being bound to soil particles. Bt cotton leaves remained bound in the soil even after 140 days. Transgenic crops substantially alter soil biota and affect processes such as soil organic matter decomposition and mineralization.
- Fresh water ecosystem: Conventional agricultural practices have had an extensive impact on freshwater ecosystems due to large-scale irrigation that reduces river flows as well as pollution from fertilizers and pesticides.

6. How is a risk assessment for the environment performed?

The assessment process includes Evaluation of:

1. The characteristics of the GMO
2. GMO′s effect and stability in the environment, combined with ecological characteristics of the environment in which the introduction will take place.

The assessment also includes unintended effects which could result from the insertion of the new gene.

7. What are the issues of concern for the environment?

The capability of the GMO to escape and potentially introduce the engineered genes into wild populations; The persistence of the gene after the GMO has been harvested; The susceptibility of non-target organisms (e.g. insects which are not pests) to the gene product; The stability of the gene; The reduction in the spectrum of other plants including loss of biodiversity; and increased use of chemicals in agriculture. The environmental safety aspects of GM crops vary considerably according to local conditions.

8. Are GM foods safe?

Individual GM foods and their safety should be assessed on a case-by-case basis. It is not possible to make general statements on the safety of all GM foods. GM foods currently available on the international market have passed safety assessments and are not likely to present risks for human health. In addition, no effects on human health have been shown as a result of the consumption of such foods by the general population in the countries where they have been approved.

9. How are GM foods regulated nationally?

The way governments have regulated GM foods varies:

- In some countries GM foods are not yet regulated.
- Countries which have legislation in place focus primarily on assessment of:

1. Risks for consumer health,
2. Environmental risks,
3. Control- and trade-related issues (such as potential testing and labelling regimes).

10. What kind of GM foods are on the market internationally?

GM crops available on the international market today have been designed using one of three basic traits:

1. Resistance to insect damage;
2. Resistance to viral infections;
3. Tolerance towards certain herbicides.
4. GM crops with higher nutrient content (e.g. soybeans increased oleic acid) have been also studied recently.

11. What happens when GM foods are traded internationally?

The Codex Alimentarius Commission (Codex) is the joint FAO/WHO intergovernmental body responsible for developing the standards, codes of practice, guidelines and recommendations that constitute the Codex Alimentarius, meaning the international food code.

- Principles for the risk analysis of foods derived from modern biotechnology.
- Guideline for the conduct of food safety assessment of foods derived from recombinant-DNA plants.
- Guideline for the conduct of food safety assessment of foods produced using recombinant-DNA microorganisms.
- Guideline for the conduct of food safety assessment of foods derived from recombinant-DNA animals.

12. Have GM products on the international market passed a safety assessment?

The GM products that are currently on the international market have all passed safety assessments conducted by national authorities. These different assessments in general follow the same basic principles, including an assessment of environmental and human health risk. The food safety assessment is usually based on Codex documents.

13. Why has there been concern about GM foods among some politicians, public interest groups and consumers?

Since the first introduction on the market in the mid-1990s of a major GM food (herbicide-resistant soybeans), there has been concern about such food among politicians, activists and consumers, especially in Europe. In the case of food, consumers started to wonder about safety because they perceive that modern biotechnology is leading to the creation of new species.

Where medicines are concerned, many consumers more readily accept biotechnology as beneficial for their health (e.g. vaccines, medicines with improved treatment potential or increased safety). In the case of the first GM foods introduced onto the European market, the products were of no apparent direct benefit to consumers (not significantly cheaper, no increased shelflife, no better taste).

Consumer concerns have triggered a discussion on the desirability of labelling GM foods, allowing for an informed choice of consumers.

14. What is the state of public debate on GMOs?

The release of GMOs into the environment and the marketing of GM foods have resulted in a public debate in many parts of the world.

Debate is usually for:

- Costs and benefits
- Safety issues

15. Are people's reactions related to the different attitudes to food in various regions of the world?

Depending on the region of the world, people often have different attitudes to food. In addition to nutritional value, food often has societal and historical connotations, and in some instances may have religious importance. Technological modification of food and food production may evoke a negative response among consumers, especially in the absence of sound risk communication on risk assessment efforts and cost/benefit evaluations.

16. Are there implications for the rights of farmers to own their crops?

Yes, intellectual property rights are likely to be an element in the debate on GM foods, with an impact on the rights of farmers.

In the FAO/WHO expert consultation in 2003, WHO and FAO have considered potential problems of the technological divide and the unbalanced distribution of benefits and risks between developed and developing countries and the problem often becomes even more acute through the existence of intellectual property rights and patenting that places an advantage on the strongholds of scientific and technological expertise. Such considerations are likely to also affect the debate on GM foods.

17. What further developments can be expected in the area of GMOs?

Future GM organisms are likely to include plants with improved resistance against plant disease or drought, crops with increased nutrient levels, fish species with enhanced growth characteristics. For non-food use, they may include plants or animals producing pharmaceutically important proteins such as new vaccines.

18. What has WHO been doing to improve the evaluation of GM foods?

WHO has been taking an active role in relation to GM foods, primarily for two reasons: on the grounds that public health could benefit from the potential of biotechnology, for example, from an increase in the nutrient content of foods, decreased allergenicity and more efficient and/or sustainable food production; based on the need to examine the potential negative effects on human health of the consumption of food produced through genetic modification in order to protect public health. Modern technologies should be thoroughly evaluated if they are to constitute a true improvement in the way food is produced.

WHO, together with FAO, has convened several expert consultations on the evaluation of GM foods and provided technical advice for the Codex Alimentarius Commission which was fed into the Codex Guidelines on safety assessment of GM foods. WHO will keep paying due attention to the safety of GM foods from the view of public health protection, in close collaboration with FAO and other international bodies.

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