

INTER-ACADEMY REPORT ON GM CROPS

Prepared under the auspices of

The Indian Academy
of Sciences

The Indian National
Academy of Engineering

The Indian National Science
Academy

The National Academy of
Agricultural Sciences

The National Academy
of Medical Sciences

The National Academy of
Sciences (India)

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Foreword

We have great pleasure in presenting a report on GM crops prepared under the auspices of the six academies listed below, at the request of Shri Jairam Ramesh, Minister of Environment & Forests and Dr. K. Kasturirangan, Member of Planning Commission. The way the document has been prepared is detailed in the report itself. The report also contains an appraisal of the issue and a set of recommendations. We hope that this document would be useful to decision makers.

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Preamble

In the context of the national debate earlier this year on transgenic crops with special reference to Bt-brinjal, Shri Jairam Ramesh, Minister of Environment & Forests, and Dr. K. Kasturirangan, Member of Planning Commission, expressed their interest in meeting the Presidents of the different National Academies and a few experts to discuss the issue. In pursuance of this suggestion, a meeting was held at the premises of INSA on 19th March. In addition to Shri Jairam Ramesh and Dr. Kasturirangan, the meeting was attended by the Presidents of the three Science Academies and the Academies of Engineering, Agricultural Sciences and Medical Sciences, and officers of the Planning Commission and the Indian National Science Academy and a few experts. In the light of the discussions at the meeting, Shri Jairam Ramesh requested the Academies to provide him and the Planning Commission with a report on the subject of biotechnology in food crops with focus on transgenic crops and on the Biotechnology Regulatory Bill, presently under discussion in the government. This was followed by a letter from Shri Ramesh confirming this request. This letter and the background information were widely circulated among the Fellows of different Academies and their views were solicited. Many Fellows and representatives of Academies sent their comments on the issue. Subsequently, a brain storming meeting was held at INSA on June 1, which was attended by a cross section of Fellows and nominees of the Academies. The meeting involved a few introductory presentations and in-depth discussions. The present document is based on the discussions at this meeting, the written comments given by Fellows and the documents brought to the attention of the meeting by different Fellows.

The National Academy of Agricultural Sciences had already prepared a comprehensive set of suggestions on the Biotechnology Regulatory Bill. The document containing them and the other suggestions on the Bill arising out of the discussions in the brain storming meeting referred to above, have already been sent to Shri Jairam Ramesh. The present document concentrates on GM crops in general and on the specific issue of Bt brinjal in particular.

The issue

Even before the laws of heredity became well-known through the rediscovery of the work of G. Mendel, C. Darwin observed the appearance of ancestral traits of domesticated organisms in the progenies of crosses, leading to the view that human selection is responsible for domestication from wild relatives. The traits helpful in domestication of crops include reduced seed dispersal, plant architecture, increased seed number/size and loss of dormancy. Most of these traits are represented by mutant alleles of pre-existing genes which have their origin in evolution. Thus, many organisms have similar genes. Human beings and rice have been identified to have thousands of similar genes, a few hundreds are shared even by bacteria, but rice genes produce only grain and not a human organ. Essentially, all genes produce proteins or RNAs of variable nature.

Hybrids of organisms contain genomes derived from both parents. For crop improvement, during breeding, selected parents with desirable traits are hybridized allowing recombination of a large number of parental genes. Selection in the subsequent generations for desirable traits leads to the development of a new 'variety' containing stable novel combination of genes. Sometimes, a single gene for known trait is also introduced into the genome of a popular variety by "backcross breeding". Breeding approaches are limited to plants capable of crossing and sexual reproduction. Genetic engineering, having its origin in recombinant DNA technology that evolved in 1970s, allows use of a wider gene pool to produce Genetically Modified Organisms (GMOs), Living Modified Organisms (LMOs) or Transgenics. Even new genes can be generated and tested. Once demonstrated for superior trait, transgenics can be maintained like a variety and used to produce other superior varieties.

The cultivation of transgenic crops started in 1996 in USA and in 2009, about 14 million farmers in 25 countries planted about 330 million acres (134 million hectares) under transgenic crops. India cultivated transgenic Bt cotton in 2002 for the first time and covered 20 million acres in 2009. Concerns about bio-safety, food-safety, environment, economic and social issues have been raised regularly despite the available regulatory system for release of transgenic crops. It was, therefore, important to examine the issue of GM food crops, with special reference to the Indian scenario. Particular attention needed to be paid to Bt brinjal in view of the ongoing discussion on the issue.

The approach

The scientific approach does not involve absolute certainties. Some uncertainties are likely to remain in every conclusion. An action is proposed based on the balance of evidence obtained from experimentation, observation and logical reasoning. Scientific conclusions also do not involve absolute unanimity. There is no central authority which directs or controls scientific pursuit. It is important to minimize uncertainties and to strive towards broad consensus. However, to make action contingent on elimination of all uncertainties and unanimity among scientists, would be a sure prescription for inaction. Most of the scientific advances, which helped to shape the world as we see today, have been accompanied by uncertainties as well as dissenting voices. While inaction is undesirable, as mentioned earlier, it is important to continuously strive to minimize or eliminate uncertainties and to build the broadest possible consensus.

All human activities and beneficial technologies cause some environmental perturbations and also involve some risk. Introduction of agriculture millennia ago certainly affected the natural environment. Modern means of transportation involve elements of risk. There is no drug which is entirely devoid of side effects. Wisdom lies in adopting technologies and practices, the benefits from which far outweigh the harmful effects and in not taking undue risks. Gluten allergy cannot be a reason for stopping cultivation of wheat. We should also remember occasions when unexpected harmful effects ensued from practices which appeared to be almost wholly beneficial to start with. Therefore, utmost caution should be exercised when introducing new practices and technologies. New technologies and practices should be introduced only after ascertaining that the deleterious effects caused by them are well within reasonable limits and are very small compared to the benefits accruing from them.

Any vibrant scientific community is characterized by a measure of plurality in views and approaches around some widely accepted principles. The scientific community of India is no exception to this observation and this plurality was reflected in the written and spoken comments of the Fellows of the Academies. However, the overwhelming common thrust of the views of the Fellows was very clear. This report builds on it while paying adequate attention to all shades of opinions and concerns.

Much has been written and several evidences have been produced for and against GM crops. Different shades of opinion have also been expressed on the subject. It is not necessary to repeat or refer to all of them. The attempt here has been to formulate a set of conclusions and recommendations, based on the approach enunciated above, in the light of the spoken and written comments of the Fellows, and the document brought to attention by them.

How to produce GMOs?

When a piece of DNA capable of producing a protein or RNA is introduced into the genome of an organism thereby allowing the organism to transfer the introduced DNA or gene to its progenies, the organism is known as Genetically Modified Organism (GMO). While introduction of genes occurs in nature or in classical crossing of varieties to generate hybrids, the term GMO has come to signify transgenics generated through the recombinant DNA route. LMO (Living Modified Organism) refers to a GMO that is alive. A gene consists of a transcribed region, normally endowed with the capacity to produce RNA which codes for a protein, a promoter capable of initiating and producing RNA and a terminator responsible for defining the end point of RNA. Living organisms have a large number of genes (up to 50,000) in their genome which control various traits. Recombinant DNA technology allows to clone, modify and multiply a gene. The gene cloned in a vector is maintained in a host cell and monitored using the presence of a marker gene normally capable of coding for antibiotic resistance. A gene or a group of genes can be introduced into plant cell by a physical method (e.g. particle bombardment) or using a bacterium (e.g. *Agrobacterium tumefaciens*). For this, suitable vectors containing gene-of-interest, an easy to follow reporter gene and a selectable marker gene (for antibiotic resistance) are used. The transformed cells containing the introduced DNA in their genome are selected in the presence of antibiotics and regenerated into plants. The number of copies of gene introduced may vary, but generally it is possible to select transgenics with a single copy transgene. Each such transformant is referred to as an Event. The expression of transgene in transgenic plant is monitored by molecular methods. The phenotype of transgenic plant and inheritance of the introduced gene/trait is monitored in subsequent progenies to achieve stable integration of transgene.

How much transgenic crops?

World-wide transgenic crops have been grown in 134 million hectares in 2009 starting from 1.7 million hectares in 1996. The share of developing countries is 46%. Out of 25 countries

growing transgenic crops, the countries growing transgenic crops in more than one million hectare include USA, Brazil, Argentina, India, Canada, China, Paraguay and South Africa. India has grown 8.4 million hectares of transgenic Bt cotton. Six EU countries also planted 94,750 hectares of Bt maize in 2009. The major transgenic crops include soybean, maize, cotton, and canola; and major engineered traits include insect resistance, herbicide tolerance and virus resistance. New trends show the use of stacked genes on 28.7 million hectares (21% area planted under transgenic crops). In USA, maize transgenics with eight different genes for pest resistance and herbicide tolerance have been approved. World-wide, area covered by transgenic soybean, cotton, maize and canola represents 43% of total area covered by these crops. While large numbers of food, feed and fiber crops as well as other plants are being developed as transgenics, in India trials of transgenic crops like brinjal, cabbage, cauliflower, cotton, groundnut, maize, mustard, okra, potato, rice, sorghum and tomato are in progress.

Transgenic crops associated with food products include canola, cotton (oil), maize, papaya, soybean and squash. Recently, transgenic Bt rice and phytase maize were approved by China. However, it would require 2-3 years of the standard field registration trials before a step towards cultivation in farmer's field is taken. Japan initiated commercialization of transgenic blue rose. It must, however, be noted that such crops are grown in green houses. In addition to 25 countries growing transgenic crops, 32 countries (making up a total of 57) have given regulatory approvals for transgenic crops/products for the purpose of food/feed.

Regulatory system

Most countries growing transgenic crops or importing transgenic food or feed have a regulatory system in place. Already, 762 approvals for 155 events in 24 crops have been provided world-wide. These approaches are also influenced by Substantial Equivalence, Principle of Familiarity and Generally Regarded as Safe (GRAS) as working principles as well as by multilateral negotiations related to environmental and human health safety (e.g., Cartagena Protocol on Biosafety, International Plant Protection Convention, Codex Alimentarius) and trade (e.g., Agreement on the Application of Sanitary and Phytosanitary Measures, Agreement on Technical Barriers of Trade, Agreement on Trade-related Aspects of Intellectual Property Rights) and United Nations Convention on Biological Diversity.

The regulatory system in India involves multi-layered recommending and approval committees. The Institutional Bio-safety Committee (IBSC) and Review Committee on Genetic Manipulation (RCGM) concern with laboratory research, green house experiments, contained field trials and multi-location research trials as well as bio-safety. A Monitoring and Evaluation Committee (MEC) monitors multi-location research trials and large-scale field trials and makes an appropriate recommendation to RCGM. The Genetic Engineering Appraisal Committee (GEAC) is responsible for approvals related to large-scale field trials, experimental seed production and commercial release by de-regulation. These committees work on behalf of the Ministry of Science and Technology or Ministry of Environment and Forest or Ministry of Agriculture. The regulatory guidelines, first proposed in 1990, have been up-dated from time-to-time and recently in 2008, Guidelines and standard operating procedures for confined field trials of regulated, genetically engineered (GE) plants, Protocols for food and feed safety assessment of GE crops, and Guidelines for the safety assessment of food derived from genetically engineered plants, were introduced. Further, in 2009, an Event Based Approval Mechanism (EBAM) has been notified. Recently, a blueprint for Biotechnology Regulatory Authority of India (BRAI) has been prepared and made public. Some of the concerns raised are being addressed in the proposed Bill.

World food requirement

In the last century, the major increase in global food production was mainly due to the improvement in yield through green revolution. This involved identification of gene(s) controlling agronomic traits and their introgression into local varieties of staple crops like rice and wheat. At the beginning of 21st century, such efforts could help produce food enough to feed 6 billion people. The number of people is likely to increase to 9 billion by 2050. This necessitates a mega-jump in productivity, with dwindling land reserves, scarce water and nitrogen and daunting challenges of climate change. Malnutrition of a billion people also needs to be addressed urgently for a healthy world. The present growth of agricultural productivity, at the rate of about 2% per year, is much lower in comparison to the 3% growth required for food security.

The food grain production in India has increased four times over the last five decades. But, in India also, the yield of major food grain crops is reaching a plateau although its

population continues to rise and is expected to reach 1.5 billion people in 2050. Also, 27% of world's undernourished people live in India. This requires an increase of more than 50% in agricultural production.

Concerns about transgenics

Fate of transferred DNA

Production of transgenics involves use of constructs which include the target gene, the reporter maker gene, the selectable marker gene with regulatory sequences and backbone DNA. Since transgenic technology allows to cross the barriers of incompatibility, the source of gene (DNA) could be organisms like viruses, bacteria, plants or animals etc. One may like to make a distinction between genes from plants, particularly those in use as food or feed, and those coming from other organisms. Concerns may arise if the target gene influences food quality or confers antibiotic resistance rather than improving traits like drought tolerance. Genes producing a pharmaceutically relevant product in transgenics may elicit a new response. Chemically, however, all DNA are the same. Daily intake of DNA from food source is estimated to be 0.1 – 1g and transgene DNA may represent 0.5 – 5 μ g under average situations. This DNA is mostly degraded in the digestive system and only small fragments of DNA have been detected in body tissue. Regarding the fate of genes, the European Food Safety Authority released the statements “After ingestion, a rapid degradation into short DNA or peptide fragments is observed in the gastrointestinal tracts of animals and humans” and “To date a large number of experimental studies with livestock have shown that rDNA fragments and proteins derived from GM plants have not been detected in tissues, fluids or edible products of farm animals”.

Generation of recombinant viruses

Some viral promoters, e.g. CaMV35S, have been used to drive transgenes. It has been demonstrated that it can be inactivated in transgenics if Cauliflower Mosaic Virus (CaMV) infects. Use of such promoters may require appropriate investigations, particularly in crops susceptible to the viral source. Alternatively, several other promoters allowing expression of gene in the whole plant or in a particular organ or state can be utilized.

It has been noted that infection with multiple viruses results in homologous and nonhomologous recombination between viruses, resulting in new viral strains. Similar to natural situation, recombination with viral genes cannot be excluded altogether. However, it has been

found that most recombinant viruses are compromised in fitness. Although squash and papaya transgenics with virus resistance genes have been grown for some time, no novel viruses have been reported yet. The likelihood of detecting such an event would be high if new virus causes adverse effect. Recently, use of small sequences by way of RNAi technology for viral resistance has been proposed and it is also likely to reduce the chances of recombination.

Antibiotic resistance

A concern about transgenics is related to the use of antibiotic resistance genes as selectable marker genes. In 1999, a report to Food Standards Agency, UK has articulated such concerns and advised against increasing the opportunity of transfer of a resistance gene by way of transgenics. For this to happen, a gene from the ingested plant cell must survive in the digestive system and transform a bacterium. Even if the gene is transferred, it may not express in the recipient. Experimentally, transfer of antibiotic resistance to gut bacteria was not observed in chickens fed on transgenic maize. Still the use of GM food needs to be looked at in the context of living organisms, present in the gut of animals and humans or taken along with food or feed, which might already have acquired such genes due to the wide-spread practice of use of antibiotics in human therapy. Similar concerns have been raised regarding horizontal gene transfer from transgenic plant to soil bacteria. Although certain events of horizontal transfer on evolutionary scale have been observed, transfer of such genes need to be coupled with selection advantage to let the event become prevalent. Under experimental condition of sterile soils, such a transfer was observed at a frequency range of 10^{-8} to 10^{-11} . Lack of a selectable advantage for antibiotic resistance genes in soil further minimizes the risk of its spread. However, the quantum of risk would naturally be dictated by the nature of the gene. Use of genes like phosphomannose and xylose isomerase, co-cultivation strategy, post-transformation excision of antibiotic resistance genes or bombardment with target gene alone is likely to reduce the use of antibiotic resistance genes in future.

Biodiversity

Since the time human beings started to domesticate plants, a huge amount of biodiversity has entered the agri-system and a much larger amount remains in the wild. Subsequent practices of

breeding have yielded mega-varieties which led to monoculture in different regions of the world. This erosion of genetic diversity is a reality and needs to be contained. As a consequence, various nations, including India, have initiated wide collection of land races along with wild species to be conserved and maintained in genebanks. Certain international genebanks have also been established. Over 500 species are cultivated in India and three out of 34 hot spots of biodiversity extend into India. The National Bureau of Plant Genetic Resources (NBPGR) maintains a National Gene Bank system with several thousand accessions of crops (e.g. 88681 for rice and 4350 for brinjal). Such activities need to be intensified. It would be appropriate to consider the deployment of transgenic crops in the above context. If a transgenic crop provides advantage to the farmer, it is likely to be cultivated more extensively as in the case of a mega-variety already in use. An alternative for this could be the use of transgene in suitable local varieties. This would, however, require suitable compensation to industry or intensification of research in public sector. A transgene could contribute to loss of biodiversity only when it enhances the invasiveness or susceptibility of target species through pollen flow. Pollen-mediated transgene flow at low frequency has been observed, but such gene flow is not unique to transgenic crops. Studies on it are part of the assessment of environment risk. Care need to be taken for cultivation of transgenic as well as non-transgenic crops near the centres of crop diversity and impact assessment should be a regular activity. Further, all efforts should be made to minimize flow of transgene that may affect the environment and the farming community should be made aware of the consequences, if any.

Development of resistance in insects

Challenges and competition between living organisms result in selection of mutants capable of facing such challenges and overcoming the competition. Bt toxins and genes of various kind being used in transgenics kill larvae of specific target species and may also have some leaky influence unless selected for high specificity. This precision to kill certain insects and lack of effect in animals and humans is based on the mechanism of action. Exposure to Bt in bacterial spray or transgenics can result in insect resistance in the long run. To delay the emergence of resistance, strategies like plantation of refuge non-transgenic crop along with transgenics or deployment of multiple form of Bt genes have been proposed. Nevertheless, use of Bt genes requires close surveillance and compliance about use of strategies helpful in

suppression and delay of resistance development. Despite this, emergence of field resistance in insects against Bt has been observed. This has led to gene stacking in the next generation techniques. In the long run, this entails search for better strategies like use of insect-bite inducible promoter to drive the gene thereby minimizing the exposure, modification of cry genes, introduction of stacked genes, deployment of RNAi against insects or incorporation of Bt as part of IPM strategy.

Effect on non-target organisms

Concurrent with resistance development is the fear of the adverse effect on non-target organisms. The famous case of monarch butterflies has been followed by several investigations. Such studies show limited influence of Bt and led to a conclusion that Bt corn was not a significant factor in the field death of monarch larvae when compared with other factors like use of pesticides. An analysis of 25 studies similarly revealed no significance of Bt on honeybee survival, which is important for pollination of several crops. Similar influence on soil microbes has not been confirmed by several investigators. Thus, one may like to compare the influence on non-target organisms with those of other prevalent practices. The advantages that accrue from each practice also may be taken into account.

The possibility of transfer of herbicide tolerance to non-target species, wild-types and weeds from transgenic crops has also been considered as it happened with traditionally bred herbicide tolerant crops. This could narrow down the option of certain weed management strategies and utility of certain herbicides. Thus management of herbicide tolerance, e.g. by alternative herbicide usage, may be considered seriously. Wide use of herbicide crops would reduce the weeds some of which serve as habitat or feed to other organisms. However, in a country like India, with multiple cropping patterns and significant uncultivated land area, the effect is likely to be minimal.

Food safety

The issue of food safety from GE organisms is of paramount importance. Even before the advent of transgenic crops, the use of L-tryptophan produced by GE bacteria for treating disease

became highly controversial due to death of people. Subsequently, a change in the process of production was found to be responsible for the contaminant producing this effect. This entails requirement of following safety studies in a larger context. Food safety assessment is generally based on substantial equivalence. This should include qualitative as well as quantitative range. New substances produced require testing in laboratory or animal models. Use of kanamycin resistance gene and its product in Flavr SavrTM tomato was subjected to such testing and approved as having GRAS status in USA which means that the nature of substance does not raise significant safety issues.

Concerns about safety of genes and their products have been raised for various reasons. The use of lectins for insect resistance was criticized due to lesions observed in rats fed on transgenic potatoes. Follow-up scrutiny of data could neither confirm nor disprove the observations as the study was found to lack appropriate controls. Major concerns have been raised regarding safety of food containing Bt gene or protein. Bt as microbial insecticide is in use for several decades and no report of harmful effect have been recorded except for a report on immune response and skin sensitization in 2 out of 123 people after inhalation of spray containing Bt. Since the Bt protein is expressed within the plant and not as an inhaleable particle, the issue of respiratory allergy will not arise. Analysis of several Bt proteins has indicated absence of features similar to protein allergens and toxins. Data on toxicity of Bt in animals have been generated and evaluated in several countries including India. Multi-tiered stepwise assessment for allergenic potential have been carried out, which includes matching the amino acid sequence of the protein with allergen sequence databases and acid and thermal stability ELISA tests for IgE binding. The results have been negative and they do not indicate any allergenic potential for the Bt protein. Excess dose and acute toxicity with certain Bt forms in plants has also not substantiated the safety concerns that have been raised. It may, however, be noted that all Bt are not the same and tests for each Bt protein need to be conducted. For example the Cry9C protein is slow to digest in human and it is also more stable to heat. StarlinkTM corn was recalled after deregulation for animal consumption to establish non-allergenicity of Cry9C. Although certain studies show that the product may not be responsible for the allergenic response, StarlinkTM was removed from market in 2000. Similarly, development of soybean with a methionine-rich 2S albumin protein from Brazil nut was not allowed since the possibility of allergic reaction could not be eliminated. It may be noted that no food can be declared as 100% safe since allergenicity to a large number of natural food items has

been observed including those made from animal (milk, eggs, fish) and plant (peanuts, wheat, soybean) sources. However, a robust testing system with transgenic food items would give the opportunity to eliminate chances of allergenicity or toxicity to a large extent. At the same time, transgenics can be generated with the objective of reducing allergens/toxins in certain crops.

One of the most robust evidences of safety, which has been practiced when any new product or material or crop is brought in for human consumption, is its comparison with already existing known material with established safety. For instance, GM brinjal is compared with its non-GM existing brinjal variety for all identifiable and validated components like macro nutrients, micro nutrients, moisture, minerals, anti nutrients and every known component and when all these are similar and within acceptable variations it can be safely assumed that GM brinjal is similar to the non-GM version except for the presence of the Bt protein whose safety and allergenicity is already established through standardized methods. Even a greater level of safety assurance is that the same Bt protein present in another food crop has been consumed elsewhere in the world with no evidence for any scientifically established negative effect.

While complete safety of transgenic plants and products cannot be guaranteed, the safety levels can be assessed as per existing best practice or a scientifically devised protocol. It cannot be ignored that calculated knowledge-based risks are always taken in the technology intensive present day world, while the individual's acceptance and values are given due freedom and credence. Many regulatory bodies in the world, including RCGM and GEAC, have evolved safety protocols based on a variety of such inputs.

Other applications of transgenics

Transgenic crops are also being raised to provide an alternative to major micronutrient deficiencies like vitamin A, iron and zinc deficiencies. Golden rice is in an advanced stage of development and can potentially provide for up to 50% of requirement of nutrients in children. Such transgenic crops would pose a challenge to science based regulatory process, keeping in view the potential advantages of and reservations against transgenic food crops. Transgenics against abiotic stresses (low rainfall, saline soil) would perhaps demand different parameters for risk evaluation.

Equally engaging and requiring novel ways of regulation would be the use of plants for producing pharmaceutical products with promise to reach common people and make health management cost-effective.

Socioeconomics

Increasing demand for food and nutritional requirements are the major reasons to look for alternative means of efficient food production. This could be coupled with the impact of agriculture on environment, climate change, food pricing, food availability and affordability. Transgenic crops are one possible alternative and complementary technology products which can contribute to the on-going efforts of genetic enhancement of crops. The technology does not replace traditional plant breeding, hybrid seed technology, molecular breeding or organic farming but complements them in the over-all objective of attaining food security. Like any other technology, it comes with some genuine and other perceived risks and affects different social strata and cultures to variable extent. This is the reason for varied, sometimes extreme, response of different social groups, countries and regions of the world to GM crops. This also makes it necessary for the regulatory system for transgenic technology to take into account socioeconomic factors. The system should also identify beneficiaries and losers and provide for remedial action.

For obvious reasons, the socioeconomic issues would remain debatable. It is, however, evident that the farmer could benefit due to improved yield, better protection against yield loss, premium for quality, reduction in pesticide, insecticide or fertilizer use and can suffer due to cost of transgenic seed or loss of market. While transgenic crops for more intrinsic yield are not yet available, protection against yield loss due to pests, weeds or viruses is the primary target of transgenic technology some of which could also contribute by saving cost of in-puts. Transgenics with improved nutrient use efficiency would also benefit farmers as and when produced as would be expected from drought tolerant crops. In any case, proper controls should be in place to evaluate equivalence of yield in transgenics to common local varieties. Also cost of seed should not out do the benefits that may accrue from the use of transgenic technology. A few studies conducted in developed as well as developing nations have shown net benefit to the farmer, but this may depend on prevailing conditions (e.g. high infestation). Thus, farmers should be made aware of cost and benefits.

The desire to recover cost of investment and that for benefits encourage patent regime. Developed nations and industry are in the forefront in this area due to better organization. This makes one wonder if resource poor farmers would ever benefit from transgenic technology. It should, however, be remembered that economics works for large-size consumer as well as large number of consumers. Therefore, in order to protect the farmer and to ensure a level playing field, it is necessary that public sector is encouraged to acquire patents and minimize exclusive licensing. At the same time, suitable humanitarian models for freedom to operate (FTO) could be evolved for the benefit of the society. This is exemplified by 'Golden Rice' and Public Intellectual Property Resource for Agriculture (PIPRA) where multiple technologies were put together for public good willingly at no cost or pooled at appropriate cost and effort. There is also need to give considerable importance and encouragement to indigenous development of transgenics by public sector organizations and through public-private partnerships. Consumer benefit is obviously an equally important issue. This would happen due to increased productivity and even more importantly due to improved nutritive quality of grains. The government does face issues of distribution, access, affordability etc., for which strategies beyond GM technology are needed.

Transgenics in India

Research work on plant transformation in Indian laboratories started in the 1980s and transgenics of certain crop plants were produced in the 1990s. Various crops being targeted for genetic transformation include brinjal, cabbage, cauliflower, cotton, groundnut, chickpea, maize, mustard, Okra, pigeonpea, potato, rice, sorghum, tomato, and wheat. The traits being targeted include insect resistance, virus resistance, fungal resistance, nutritional enhancement, delayed ripening and abiotic stress tolerance. Both public and private sectors are actively engaged in transgenic research. The efforts of public research institutions in the area are summarized in Table 1.

Table 1. Some important transgenic crop plants developed /tested by public research institutions in India

Crop	Trait	Institution
1. Brinjal	Insect resistance	IVRI Varanasi, NRCPB, TNAU, UAS Dharwad
2. Chickpea	Insect resistance	Assam Agricultural University Jorhat, BI, ICRISAT Hyderabad, NRCPB
3. Cotton	Insect resistance	Central Institute of Cotton Research, Nagpur NBRI, UAS Dharwad
4. Groundnut	Disease resistance	ICRISAT, Hyderabad
5. Mustard	Male sterility	DUSC
6. Potato	Disease resistance	CPRI
7. Potato	Cold-sweetening	CPRI
8. Potato	Protein quality	NIPGR
9. Rice	Insect resistance	BI, CU, DRR, NRCPB
10. Rice	Pro Vitamin A	CU, DRR, IARI, TNAU
11. Rice	High iron	CU
12. Rice	Abiotic stress	BI, CU, ICGEB, MSSRF, DUSC
13. Rice	Fungal disease	CU, MKU, TNAU
14. Sorghum	Insect resistance	NRC for Sorghum, Hyderabad
15. Sugarcane	Insect resistance	Sugarcane Breeding Institute, Coimbatore
16. Tomato	Slow ripening	NIPGR, NRCPB
17. Tomato	Virus resistance	IARI
18. Tomato	Edible vaccine	DUSC

BI, Bose institute; CU, Calcutta University; CPRI, Central Potato Research Institute; DRR, Directorate of Rice Research; DUSC, Delhi University South Campus; IARI, Indian Agricultural Research Institute; ICGEB, International Centre for Genetic Engineering and

Biotechnology; MSSRF, MS Swaminathan Research Foundation; NBRI, National Botanical Research Institute; NIPGR, National Institute of Plant Genome Research; NRCPB, NRC on Plant Biotechnology; TNAU, Tamil Nadu Agricultural University

India cultivated its first transgenic Bt cotton crop, which was developed in the private sector, on 0.05 million hectares in the year 2002. In 2009, transgenic Bt cotton was cultivated by 5.6 million farmers on 8.6 million hectares (43% single gene, 57% two genes). Further, commercialization of Bt cotton variety Bikaneri Nerma and hybrid NHH-44, developed in the public sector, has been initiated. In all, six Bt cotton events have been approved. India now occupies second position in terms of global cotton production by turning out 30 million bales of cotton in 2009 which is likely to increase up to 35 million bales in the year 2010. The benefits of Bt cotton include decrease in yield loss which increases over-all yield, decreased production costs, a reduction of at least 50% in insecticide applications resulting in substantial environmental and health benefits to small producers, and significant economic and social benefits. Reduction in use of pesticides leads to less insecticides in aquifers and the environment, reduced farmer exposure to insecticides and improvement of human health, increased populations of beneficial insects, reduced risk for wildlife, reduced fuel and raw material consumption and decreased pollution. Failure of Bt cotton in a few pockets in the country is often due to middle men, but does require a scientific analysis.

Bt Brinjal

Brinjal (*Solanum melongena* L.), commonly known as eggplant, aubergine or guinea squash, is an important vegetable crop of tropical and temperate parts of the world. It is a rich source of vitamins and minerals, especially iron. Genus *Solanum* to which brinjal belongs is predominantly of Central and South American origin; however, the question of centre of its origin is yet to be resolved. Evidences seem to indicate that it originated in Asia. South West Asia including Arabia, Indo-Burma region, Japan and China have been suggested as probable places of origin by different investigators. Germplasm resources and collections have been well-documented, evaluated and conserved throughout the world. Based on fruit shape, brinjal has been divided

into three main types namely, egg-shaped (*S. melongena* var. *esculentum*); long slender shaped (*S. melongena* var. *serpentium*) and dwarf type (*S. melongena* var. *depressum*).

Brinjal has been cultivated for the last 4,000 years in India. Among the Solanaceous vegetables, brinjal is the most common and popular vegetable crop grown in many geographical parts in India. The area under brinjal is estimated at 0.55 million hectares with a total production of 8.2 million tons (<http://faostat.fao.org/>). A total of 1.4 million small, marginal and resource-poor farmers grow brinjal and it is an important cash crop for poor farmers, who produce two or three crops, each of 150 to 180 days duration.

Brinjal cultivars as well as modern varieties have been shown to be susceptible to a variety of stress conditions, which limits crop productivity significantly. The most important biotic stress that affects brinjal is an insect-pest viz. Brinjal Shoot and Fruit Borer (BSFB). Resistance to BSFB in brinjal germplasm is not available. Efforts to impart pest resistance to the cultivated varieties have been achieved with only limited success due to sexual incompatibilities with the source species or wild relatives. BSFB causes significant losses of up to 60 to 70% in commercial plantings. Damage starts in the nursery, prior to transplanting, continues to harvest and is then carried-over to the next crop of brinjal. BSFB damages brinjal in two ways. First, it infests young shoots during vegetative phase, which limits the ability of plants to produce healthy fruit bearing shoots, thereby reducing potential yield. Secondly, it bores into fruits during reproductive phase making them unmarketable. Because of the cryptic nature of the pest, the larvae remain hidden within shoots and fruits and insecticide applications become ineffective. Farmers usually spray twice a week, applying 15 to 40 insecticide sprays, or more, in one season depending on the level of infestation. The levels of pesticides and their residues are very high in fruits, which is a matter of serious concern to human health. On an average, 4.6 kg of active ingredient of insecticide per hectare per season is applied on brinjal at a cost of Rs 12,000 (Rs twelve thousand) per hectare. According to a study by Indian Chemical Industry (2007), brinjal is the second largest vegetable crop after Chillies that is sprayed with insecticide.

Thus, in brinjal cultivation, there is an urgent need to reduce dependence on pesticides by using safer alternatives to manage the insect-pests. Many insecticidal proteins and molecules are available in nature, which are effective against agriculturally important pests but innocuous to mammals, beneficial insects and other organisms. Insecticidal proteins present in the soil borne bacterium, *Bacillus thuringiensis* (Bt), which has demonstrated its efficacy as a spray

formulation in agriculture over the past six decades, have been expressed in many crop species with positive results. The Bt proteins are packed in the form of crystals and when ingested by the insect larvae are processed to an active form in the highly alkaline larval gut. The active protein binds to a compatible receptor protein present in the gut cell membranes resulting in perforations of the membrane, cell lysis and death of the larvae. Human beings, other mammals and non-target organisms including certain beneficial insects do not contain receptors to Bt proteins and hence are not susceptible to Bt action. Furthermore, it is known that Bt proteins get degraded in the acidic stomach of the mammal.

Early efforts were made at IARI to develop transgenic brinjal expressing insecticidal protein (Cry1Ab) of Bt way back in mid 1990s. The transgenic lines were field tested in 1996 on IARI farm which demonstrated limited protection against BSFB. A novel codon-optimized gene *cryIFal* was introduced in Pusa Purple Long variety with very promising results in 2004. The 'Event 142' was licensed to four companies under Public Private Partnership. Currently biosafety tests and field trials are in progress. Subsequently, an Indian seed company Mahyco has developed transgenic brinjal expressing Cry1Ac protein of Bt. The best transgenic event 'EE-1' chosen out of several events showed a significantly lower number of BSFB larvae (0-20 larvae) on Bt brinjal, as compared to 3.5-80 larvae on the non-Bt counterpart. Multi-location research trials and Large scale trials (2004-2008) conducted by Mahyco, and independently by the Indian Council for Agricultural Research (ICAR) under the All-India Coordinated Research Program for Vegetable Crops (AICRP-VC), confirmed that insecticide requirement for Bt brinjal hybrids was on average 80% less than that for the non-Bt counterpart, which translated into a 42% reduction in total insecticide usage. The average marketable yield of Bt brinjal increased by 100% over its non-Bt counterpart hybrids. It has been estimated that Bt brinjal farmers would enjoy a net gain of Rs. 30,000-35,000 per hectare compared to those cultivating conventional varieties.

Bt brinjal being a transgenic food crop requires environmental clearance under Rules 8, 9, 10 & 11 of the Rules and Procedures notified by the Ministry of Environment and Forests vide Notification no. 1037 (E) dated 05.12.1989. Prior to the deregulation of transgenic fruit and shoot borer tolerant brinjal, data and information are necessary to be produced to demonstrate that this Bt brinjal is equivalent to currently grown non-Bt brinjal varieties in composition and agronomic performance and that the Bt protein expressed by the inserted gene causes no adverse effect when consumed by domestic or wild animals and beneficial insects. The bio-safety and

environmental issues related to the Bt brinjal were assessed, which includes molecular characterization of introduced gene, biochemical characterization of the expressed protein, estimation of the level of the expressed insect control proteins in brinjal and brinjal products, safety of the expressed proteins to non-target organisms, environmental fate of the Bt protein, and agronomic, compositional and food and feed safety evaluation of Bt brinjal compared to non-Bt brinjal.

Bt brinjal 'Event EE-1' has been subjected to a rigorous biosafety regulatory process encompassing all aspects of toxicity, allergenicity, environmental safety, socio-economic assessment etc. Studies on food and feed safety have been conducted on rats, rabbits, fish, chickens, goats and cows. Similarly, environmental impact assessments to study germination, pollen flow, invasiveness, aggressiveness and weediness, and effect on non-target organisms were also carried out. Public research systems like CSIR, ICAR, SAU and ICMR, in addition to private organizations, have been involved in these studies.

Two expert committees, Expert Committees I and II, constituted by the Genetic Engineering Approval Committee (GEAC) under the aegis of the Ministry of Environment and Forests (MoEF) have analyzed the biosafety data thoroughly and deliberated upon the representations made by various stakeholders including scientists and NGOs. Based on the observations made by the Expert Committees, GEAC has approved the environmental safety of Bt brinjal 'Event EE-1' on October 14, 2009. The 'Event EE-1' has been transferred to brinjal varieties by the scientists of the Agricultural Universities at Dharwad and Coimbatore. Furthermore, Indian Institute of Vegetable Research at Varanasi has also introgressed the event into its varieties. After a critical analysis, the Expert Committee II concluded that all the concerns raised by various persons / experts and organizations before and after the 'Public Consultations' have been adequately addressed. It is possible to add more and more tests for field assessment, but all the data generated so far confirm the safety and utility of Bt brinjal, especially considering the fact that his gene has been in use globally for over 15 years

Summary

From a presumably common origin, different genomes evolved independently to have different traits. In the course of evolution, there has been large scale gene transfer across species and

kingdoms. From the dawn of civilization, in addition to natural selection, there has been conscious selection by humans to produce food crops. In recent times, plant breeders have created new varieties by crossing and selecting for desired traits. In fact, the green revolution, which freed India from “ship-to-mouth” existence, owes much to these efforts. Genetic modification using modern techniques is a natural step forward. Modern genetic modification is more precise and the time taken to implement is short. It can be, and it has been, argued that there are differences between what have evolved through selection over millions of years or millennia and those produced by human beings. These differences are in detail; the processes are fundamentally the same. However, one should be cognizant of these differences and they should be addressed.

Safety aspects and possible health hazards of GM crops have been studied and discussed in detail. The evidences so far suggest that they are no more deleterious than ordinary crops. The US experience on GM corn is a case in point. There is no evidence to suggest that GM food is more allergic than other forms of food. It is unlikely that biodiversity, which has resulted from large-scale vertical and horizontal transfer of genes, can be affected by the insertion of one or a handful of genes in a few genomes. Hybrid maize varieties have been in cultivation for decades. There does not appear to be any evidence to suggest that they have affected biodiversity. The extent of usage of different varieties would of course depend upon the choice by farmers. All the same, safety and health issues should be continuously examined before and after the introduction of each GM crop. The same applies to biodiversity. The interest of the farmer and the consumer and the national interest, particularly in relation to food security, should always be kept in mind.

Recommendations

1. After taking into consideration all available evidences and opinions, the overwhelming view is that transgenic crops, along with traditional breeding, molecular breeding and other innovative alternatives, should be used for sustainable agriculture to meet the increasing food, feed and fiber demand of the growing population of India. GM crops are not a panacea, but they should be an important component of our strategy. Decisions have to be made on a case to case basis.

2. GM crops which are already in use and which are proposed to be introduced, should be continuously studied for environmental and health effects. Post-introduction monitoring is as important as studies prior to introduction. Particularly, in relation to food crops, perceptions are nearly as important as facts. Sometimes, it is difficult to easily distinguish between the two. Therefore, facts as well as perceptions need to be adequately addressed. For instance, while use of antibiotic resistance selection markers in present day transgenics do not seem to compromise biosafety, use of alternative as well as marker free technology should be encouraged.

3. While the role of the private sector in the development of GM crops is important, food security is too critical and strategic an area to be left wholly or predominantly in private hands. The main responsibility for the development of transgenic technology in the country should rest with publicly funded institutions. This calls for massive government investment in the programme. Capacity should be expanded and further strengthened for designing and implementing different biosafety tests of international standards, including those for long term effects, where necessary. Mechanisms should also exist for sharing experience and expertise among different institutions. A PPP model may be considered for commercialisation.

4. The available scientific evidence does not indicate any appreciable effect of GM crops on biodiversity. However, it is necessary to address the perceptions in relation to this issue. In any case, biodiversity is seriously threatened on account of other human activities. Therefore, the effort at collection, conservation and preservation in relation to biodiversity needs to be further strengthened.

5. An independent high-power expert committee, with a strong component of scientists, should be in place to oversee efforts involving transgenics in the country. This committee should be entrusted with the responsibility of strategic planning and establishing priorities in the area. For example, transgenics to improve nutrition and combat abiotic and biotic stresses are a priority for India.

6. The regulatory mechanism in place in India for approval of release of transgenic crops is strong. However, the same is not true about monitoring after release. A specific mechanism should be created for post-release monitoring, which should include provisions for providing effective technical advice to the farmer.

7. The issue of Bt brinjal deserves special attention in terms of its immediate relevance. The overwhelming view is that the available evidence has shown, adequately and beyond reasonable doubt, that Bt brinjal is safe for human consumption and that its environmental effects are negligible. It is appropriate now to release Bt brinjal for cultivation in specific farmers' fields in identified states. Appropriate distance isolation needs to be maintained, although no deleterious environmental effect is anticipated. The performance in the field, in all its aspects, should be monitored by an independent committee which should not include the suppliers or their representatives. The limited release of Bt brinjal need not wait for the establishment of BRAI.

8. Development of resistance to Bt is a real concern. Therefore, in parallel with the introduction of Bt brinjal, efforts for gene stacking should be seriously pursued preferably in publicly funded organizations. Improvements such as the elimination of antibiotic resistance selection markers, should be seriously explored. Efforts should also be made to treat Bt as part of the Integrated Pest Management strategy.

9. Immediate steps should be taken to restore confidence and allay fears that the moratorium would influence research on transgenics and their use on individual merit. Spreading public awareness on Bt brinjal, indeed transgenics in general, is important and mechanisms for doing so should be set up. Transparency should be maintained in methods of testing, different procedures, results and impact assessment.

10. The National Bureau of Plant Genetic Resources (NBPGR) already holds 4350 accessions of brinjal germplasm. In parallel to the limited release of Bt brinjal, NBPGR along with other concerned persons, should work towards ensuring that the collection is as exhaustive as possible.

11. As indicated earlier, there does not seem to exist any reasonable doubt on the biosafety of Bt brinjal. However, particularly to address public concerns as well as to doubly ensure biosafety, a group of experts or/and institutions should be constituted for conducting post market surveillance study of short, medium or long term health hazards, if any, of Bt brinjal and other genetically modified food items. This group should regularly submit its follow up report to the Government/Regulatory Body.

It might be appropriate to end this report with two quotations, one from a joint statement of six major Academies of the world and the other from an article by the acknowledged leader of Green Revolution.

“.....GM technology, coupled with important developments in other areas, should be used to increase the production of main food staples, improve the efficiency of production, reduce the environmental impact of agriculture, and provide access to food for small-scale farmers.” –*the Royal Society of London, the US National Academy of Sciences, the Brazilian Academy of Sciences, the Chinese Academy of Sciences, the Indian National Science Academy, the Mexican Academy of Sciences, and the Third World Academy of Sciences, In **Transgenic Plants and World Agriculture (2000)**, Document made available by the Indian National Science Academy, New Delhi*

“The affluent nations can afford to adopt elitist positions and pay more for food produced by the so-called natural methods; the 1 billion chronically poor and hungry people of this world cannot. New technology will be their salvation, freeing them from obsolete, low-yielding, and more costly production technology.” –*Dr. Norman E. Borlaug (Nobel Prize Laureate for Peace 1970), Plant Physiology (2000). 124, 487-490*