Covering Note

for

INTER-ACADEMY REPORT ON GM CROPS

(Updated)

The Inter-Academy Report on GM crops submitted in September, 2010, elicited a great deal of public discussion, although it was meant only for limited circulation. In retrospect, this was to be expected in view of the nature of the issue. The report has now been updated. The updating involved the rectification of the slip which has been acknowledged and the consequent rewriting of the section containing the narrative on Bt brinjal. That does not materially affect the main conclusions and recommendations. The literature on GM crops is voluminous. More than a hundred appropriate references have been included in the updated report. In other respects, the body of the report remains substantially the same.

As have been mentioned repeatedly, the conclusions and recommendations arose out of the Brainstorming meeting on June 1. The report is not meant to be the result of a new scientific investigation. It is meant to convey opinion on the basis of investigations already conducted. The names of the more than forty distinguished participants of the Brainstorming meeting are given in an Annexure. The introductory presentations at the meeting have been posted on the website, reference to which has been given. The dissenting views of a small minority have been mentioned. The recommendations represent a synthesis of the opinions of an overwhelming majority of participants.

Every attempt has been made to make the recommendations in the report well-balanced. Only one of the 11 recommendations figured prominently in public discourse. Even that is in consonance with what has been described as “a possible compromise route” in the decision of the Minister of Science for Environment & Forests early this year on commercialisation of Bt brinjal (Ref. 76 in the report). Nearly half of the recommendations seek to enunciate a national strategy on GM crops. The rest deals with concerns, surveillance etc.

INTER-ACADEMY REPORT ON GM CROPS

(Updated)

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)

December, 2010

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.

A. K. Sood
The Indian Academy of Sciences

P.S. Goel
The Indian National Academy of Engineering

M. Vijayan
The Indian National Science Academy

Mangala Rai
The National Academy of Agricultural Sciences

K.K. Talwar
The National Academy of Medical Sciences

Asis Datta
The National Academy of Sciences (India)

INTER-ACADEMY REPORT ON GM CROPS

(Updated)

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.

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*Annexure 1

**Presentations are available at www.insaindia.org

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 a stable novel combination of genes. Sometimes, a single gene for a 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 the 1970s, allows the 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.

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 the 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 (26). 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 (49, 116). Recombinant DNA technology allows to clone, modify and multiply a gene (12, 114). 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 the transgenic plant is monitored by molecular methods. The phenotype of the transgenic plant and inheritance of the introduced gene/trait is monitored in subsequent progenies to achieve stable integration of transgene (74, 117).

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 (54). The share of developing countries is 46%. Out of the 25 countries growing transgenic crops, the countries growing transgenic crops in more than one million hectares 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 the 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% of the area planted under transgenic crops). In USA, maize transgenics with eight different genes for pest resistance and herbicide tolerance have been approved. World-wide, the area covered by transgenic soybean, cotton, maize and canola represents 43% of the 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 (117). Recently, transgenic Bt rice and phytase maize were approved by China (56). 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 the 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 (28).

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) are concerned 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 the 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 the 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 (33). This will necessitate 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 (112).

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 will require an increase of more than 50% in agricultural production (100) and calls for judicious use of agricultural biotechnology (101). This has been kept in mind in the approach to the problem enunciated below.

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.

Concerns about transgenics

(i) Fate of transferred DNA

Production of the transgenics involves use of constructs which include the target gene, the reporter marker 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 (92). 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 – 5µg under average situations (41). This DNA is mostly degraded in the digestive system and only small fragments of DNA have been detected in body tissue (93, 94). 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" (38).

(ii) 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 (1). 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 (25).

It has been noted that infection with multiple viruses results in homologous and nonhomologous recombination between viruses, resulting in new viral strains (91). 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 (45, 69), no novel viruses have been reported yet. The likelihood of detecting such an event would be high if the new virus causes an adverse effect. Recently, the use of small sequences by way of RNAi technology for viral resistance has been proposed (18, 115) and it is also likely to reduce the chances of recombination.

(iii) Antibiotic resistance

A concern about transgenics is related to the use of antibiotic resistance genes as selectable marker genes. In 1999, a report to the Food Standards Agency, UK has articulated such concerns and advised against increasing the opportunity of the 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 (27). 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 the 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 needs 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} (47, 80). 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 (84, 88, 118).

(iv) 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 the 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 (35). 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 the 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 environmental risk. Care needs 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 (34). Further, all efforts should be made to minimize the flow of transgene that might affect the environment and the farming community should be made aware of the consequences, if any.

(v) 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 kinds 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 the lack of effect in animals and humans is based on the mechanism of action (57, 99). Exposure to Bt in bacterial spray or transgenics can result in insect resistance in the long run (48, 55, 102, 103). To delay the emergence of resistance, strategies like plantation of refuge non-transgenic crop along with transgenics or deployment of multiple forms of Bt genes have been proposed (103). Nevertheless, the use of Bt genes requires close surveillance and compliance with the use of strategies helpful in suppression and delay of resistance development (22). Despite this, the emergence of field resistance in insects against Bt has been observed (109, 111). 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 (6, 7, 9, 42, 67, 71, 90, 99, 119).

(vi) Effect on non-target organisms

Concurrent with resistance development is the fear of the adverse effect on non-target organisms (79). The famous case of monarch butterflies has been followed by several investigations (67, 70, 95). 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 (32), which is important for pollination of several crops. Similar influence on soil microbes has not been confirmed by several investigators (53, 98, 113). 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 the transfer of herbicide tolerance to non-target species, wild-types and weeds from transgenic crops has also been considered as it had happened with traditionally bred herbicide tolerant crops (20). 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 (10). 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.

(vii) 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 the death of persons. Subsequently, a change in the process of production was found to be responsible for the contaminant producing this effect (73). 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 Savr™ tomato was subjected to such testing and approved as having GRAS status in USA (87) which means that the nature of substance does not raise significant safety issues.

Concerns about the safety of genes and their products have been raised for various reasons (66). 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 (39, 61, 65, 107). Major concerns have been raised regarding safety of food containing the Bt gene or protein. Bt as microbial insecticide has been in use for several decades and no report of harmful effects have been recorded except for a report on immune response and skin sensitization in 2 out of 123 persons after inhalation of spray containing Bt (13). 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 (75). Data on toxicity of Bt in animals have been generated and evaluated in several countries including India. Multi-tiered stepwise assessment for allergenic potential has 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 have also not substantiated the safety concerns that have been raised (8, 14, 24, 37). It may, however, be noted that all Bt are not the same and tests for each Bt protein need to be conducted separately. For example, the Cry9C protein is slow to digest in human and it is also more stable to heat (21, 36). Starlink™ corn was recalled after deregulation for animal consumption to establish non-allergenicity of Cry9C. Although certain studies showed that the product may not have been responsible for the allergenic response, Starlink™ was removed from the market in 2000. Similarly, the 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 (81). 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 and appropriately selected test system with transgenic food items would give the opportunity to eliminate chances of allergenicity or toxicity to a large extent (40, 51, 97, 110). At the same time, transgenics can be generated with the objective of reducing allergens/toxins in certain crops (15, 104).

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 the existing non-GM 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 the limits of 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 has already been 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 the 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.

(viii) 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 the requirement of nutrients in children (83). 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 (29, 72) with the promise of reaching the common people and make health management cost-effective.

(ix) Socioeconomics

Increasing demand for food and nutritional requirements are the major reasons to seek 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 for genetic enhancement of crops. This 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 extents. This is the reason for varied, sometimes extreme, reactions from different social groups, countries and regions of the world to GM crops. This aspect 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 (68, 109). 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 the high cost of transgenic seed or loss of market (31). 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 and in common local varieties. Also the 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 the prevailing conditions (e.g. high infestation) (11, 78). 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 (16).

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 (5). At the same time, suitable humanitarian models for freedom to operate (FTO) could be evolved for the benefit of the society (30). 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 (83, 85). 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 could 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. The 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

1997. PNAS USA 94:2111; 1998. Mol Breed 4:33; 1999. Plant J 17:385; 2002. Theor Appl Genet 106:51, Transgenic Res 11:447, Transgenic Res 11:411; 2003. Plant Biotechnol J 1:231, PNAS USA 100:14672; 2004. Theor Appl Genet 109:1399, J Biotechnol 111:131, PNAS USA 101:6309, J Biol Chem 279:28539; 2005. PNAS USA 102:509; 2006. J Genet 85:157; 2008.

Transgenic Res 17:281, BMC Plant Biol 8:102, Transgenic Res 17:897, Transgenic Res 17:171, Plant Mol Biol 66:445, Plant Cell Rep 27:1635; 2009. Biotechnol Letters 31:239, Plant Biotechnol J 7:512, Plant Cell Rep 28:1827, Transgenic Res 18:529; 2010. PNAS USA 107:2413, PNAS 107:17533, Plant Cell Rep 29:261, Biotech News 5:96, http://igmoris.nic.in/field_trails.asp

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 change in pesticide use pattern and decrease in yield loss which increases over-all yield leading to environmental and socio-economic benefits (11, 58, 59, 78). 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

The family Solanaceae includes more than 3000 species which are well known as vegetable crops and diverse in utility as vegetable, ornamental and medicinal plants. *Solanum lycopersicum* (tomato), *S. melongena* (brinjal or eggplant), and *S. tuberosum* (potato) are major vegetables of the world including India. Brinjal may have indirect ancestry from *Solanum incanum* and has been, apparently, domesticated in India and/or China, from where it might have spread to the Mediterranean (http://solgenomics.net/). Now it is also grown in Southern Europe, Southern United States and other parts of the world. While round and slender fruit types are grouped as *var. esculentum* and *serpentinum*, respectively, dwarf plants are grouped as *var. depressum*. The chromosome number (n) of brinjal is 12. The size of the brinjal genome has been estimated to be 956 Mb and it is expected to code for 35-40,000 genes, like potato and tomato, in addition to possessing repeat elements representing a major part of the genome (44)

Brinjal is grown throughout the year in different parts of India excluding high altitude regions and its fruit (a berry) is used as vegetable for cooking in diverse ways. Allergic reactions to brinjal have also been reported. Out of 741 subjects, 9.2% showed adverse reaction based on case history, skin prick test and allergen-specific IgE (50). This could be due to pharmacologic action or IgE-mediated allergy (0.8%), females being more sensitive to the latter. The major brinjal growing states include Andhra Pradesh, Bihar, Gujarat, Karnataka, Maharashtra, Orissa, Uttar Pradesh and West Bengal. West Bengal leads in brinjal production. The yield of brinjal varies between 15-50 tons per hectare. It is said that more than a million farmers grow brinjal in India.

Although brinjal is a self-pollinated species, cross-pollination in the range of 0.14-48% has been reported by various groups. The higher rate of cross-pollination may depend on the presence of pollinating insects. The hybrid/variety foundation seed production for brinjal requires 300 m isolation distance in India. A low frequency of crossability with certain other species has also been reported. It is said that natural crossing with wild species of brinjal either does not occur or it is not sustainable (77).

The variety development program includes testing through the All India Coordinated Vegetable Improvement Programme (AICVIP) spread over eight zones. The major objectives include high productivity, protection against pests and pathogens, and quality improvement of location specific/preferred cultivars. The number of brinjal accessions in NBPGR germplasm collection is 4350. Insect pests are considered the predominant limiting factor for brinjal productivity. *Leucinodes orbonalis* is the most destructive pest of brinjal resulting in up to 60% loss and it is commonly known as Fruit and Shoot Borer (FSB). Farmers use 25-40 or even more sprays of insecticide depending on affordability and level of infestation. With the view to provide biotechnological intervention, genetic transformation of brinjal/eggplant has been established (43, 89) and transgenics using various Bt genes have been raised (52, 63). In an experimental field study on species assemblages in Bt and non-Bt eggplants, a comparable species assemblage was observed although some taxa required more specific study (4). Transgenic brinjal expressing Bt (Cry1Ab) were field tested in the 1990s at IARI and showed limited protection against SFB (62). A novel codon-optimized gene *cry1Fa1* was introduced in Pusa Purple Long variety in 2004. The 'Event 142' was licensed to four companies under Public Private Partnership (62). The biosafety tests and field trials for the same are in progress. Also, an Indian seed company Mahyco has developed transgenic brinjal expressing Cry1Ac protein of Bt. The transgenic event 'EE-1' is chosen out of several events. Under a MoU, the back crossing of 'EE-1'and integration of *Cry1Ac* have been carried out into four varieties by the Tamil Nadu Agricultural University, Coimbatore and six varieties by the University of Agricultural Sciences, Dharwad.

The event EE-1 of brinjal contains the *Cry1Ac* gene which has been delivered by *Agrobacterium*-mediated genetic plant transformation and sourced from a soil bacterium *Bacillus thuringiensis*. For the purpose of gene expression in plants, it has been endowed with regulatory elements (CaMV35S promoter) functional in a plant. For monitoring the presence of recombinant DNA molecules in bacteria and plant, *aad* and *nptII* genes have been used, respectively. As a result of feeding on Bt brinjal, larvae of FSB ingest Bt protein made in the plant tissue by the *Cry1Ac* gene. The alkaline pH of >9.5 in insect gut helps activate the Bt protein leading to disruption of digestive process and ultimate death of FSB larvae. It has been estimated that Bt brinjal farmers would enjoy a net economic gain per hectare and health benefits compared to those cultivating conventional varieties (60).

The EE1 event has undergone evaluation through the established national regulatory system in India. The GEAC - constituted Expert Committee II reviewed various findings on this issue including those related to the problems of biosafety, large scale trials, food and feed safety, environmental safety, substantial equivalence, and considered comments received from stakeholders and certain objections raised (46, 76). EC-II submittted its recommendations to the GEAC stating that "Bt brinjal event EE-1 is safe for environmental release in India" (76). Further, "after detailed deliberations and taking into consideration the findings of the review by three high level technical committees, namely, the RCGM and two Expert Committees constituted by the GEAC in 2006 and 2009, the GEAC concluded that Bt Brinjal is safe for environmental release. Since this decision of the GEAC will have major policy implications, the GEAC decided to forward the recommendations and report of the Expert Committee on the safety and efficacy of Bt brinjal event EEI to the Government for a final view" (46). The MOS (I/C)E&F, GOI, Shri Jairam Ramesh held several consultations and on 09.02.2010. decided that "…it is my duty to adopt a cautious, precautionary principle-based approach and impose a moratorium on the release of Bt-brinjal, till such time independent scientific studies establish, to the satisfaction of both the public and professionals, the safety of the product from the point of view of its long-term impact on human health and environment, including the rich genetic wealth existing in brinjal in our country" (76).

A large number of views supporting release of Bt brinjal or GM crops as well as reflecting concerns regarding the same due to 'inadequate assessment' have been expressed (2, 3, 17, 23, 46, 62, 64, 76, 82, 86, 96, 105, 106, 108). Some have suggested alternatives like organic farming or integrated pest management. There exists a difference of view about the ‘right thing’ and the ‘due regulatory process’ followed by the GEAC. These parallel views are likely to continue to exist. Thus a balanced approach is required, keeping in view and learning from the evolution of agriculture which sustains human life on earth, the present day knowledge, prevailing crop production practices and the need of food in the future. All stake-holders look forward to appropriate action that will define parameters for assessment, carry out such a process and have suitable independence/infrastructure/human resource to arrive at a decision in a timely manner.

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.

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*As indicated earlier, no unanimity is claimed. Fundamental differences were expressed by a few persons. The views of one of them are reflected in a presentation at www.insaindia.org. The differences expressed by those who dissented include views that random unpredictable insertion of transgene could have position effects; Bt is not a specific toxin to Lepidopetra and it harms species of widely different taxa; Bt is not in harmony with ecoagriculture; and that it would not be favourable to farmers in view of break down of Bt-resistance, gene flow etc. These views were also considered and countered to different extents, but fundamental differences cannot often be reconciled. The recommendations are synthesised from the opinions of an overwhelming majority of participants.

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 seven 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

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Annexure 1

List of participants in the June 1, 2010, Brain Storming Meeting

The three Science Academies invited all those who showed interest for the brain storming meeting on June 1. The other three Academies nominated a few identified Fellows each. All of them were invited. The responses of all those who showed interest and the documents brought to attention by them were made available to the participants listed below.

IP Abrol
Centre for Advancement of Sustainable Agriculture
New Delhi

Mahtab S Bamji
INSA Honorary Scientist
Hyderabad

A Banerji
School of Biotech
Amritapuri Campus
AVV, Kollam Dist

KC Bansal
NRC on Plant Biotechnology
Indian Agricultural Research Institute
New Delhi

CR Bhatia
Formerly Secretary Dept. of Biotechnology
Navi Mumbai

Dipankar Chatterji
Indian Institute of Science
Bangalore

Bharat Bhushan Chattoo
Biotechnology Programme
M S University of Baroda

VS Chauhan
International Centre for Genetic Engineering and Biotechnology
New Delhi

Atul Chokshi
Indian Institute of Science
Bangalore

Malavika Dadlani
Indian Agricultural Research Institute
New Delhi

Bhudev C Das
Dr. B.R. Ambedkar Research Centre for Biomedical Research
University of Delhi
Delhi

Asis Datta
National Institute of Plant Genome Research
New Delhi

KK Datta
National Institute of Cholera & Enteric Diseases
Kolkata

SK Datta
Indian Council of Agricultural Research
New Delhi

Vibha Dhawan
Tata Energy & Resources Institute
New Delhi

SN Gaur
VP Chest Institute
University of Delhi
Delhi

PS Goel
Defence Research & Development Organisation
Delhi

HS Gupta
Indian Agricultural Research Institute
New Delhi

PK Gupta
Meerut University
Meerut

VP Kamboj
Formerly Director
Central Drug Research Institute
Lucknow

PC Kesavan
Distinguished Fellow MSSRF
Chennai

Jayant Modak
Indian Institiute of Science
Bangalore

D Mukhopadhyay
INSA Honorary Scientist
Kolkata

H.Y Mohan Ram
INSA Honorary Scientist
Delhi

Indira Nath
Institute of Pathology, Safdarjung Hospital
New Delhi

Oommen V Oommen
University of Kerala
Trivandrum

G Padmanaban
Indian Institute of Science
Bangalore

R. Rajaraman .
Jawaharlal Nehru University
New Delhi

Prema Ramachandran
Nutrition Foundation of India
New Delhi

Arjula R Reddy
Yogi Vemana Univeristy
Vemanapuram Kadapa

Asha Chandola Saklani
Apeejay Svran Institute of Biosciences & Clinical Research
Gurgaon

P.V. Sane
Formerly Director,
National Botanical Research Institute
Lucknow

B Sesikeran
National Institute of Nutrition
Hyderabad

P.K Seth.
Indian Institute of Toxicology Research
Lucknow

Balram Sharma
Indian Agricultural Research Institute
Delhi

Manju Sharma
Formerly Secretary DBT
New Delhi

N.K Singh.
Indian Agricultural Research Institute
New Delhi

K.K.Talwar
Postgraduate Institute of Medical Education and Research
Chandigarh

P.N.Tandon
National Brain Research Centre Society
Manesar

Akhilesh Tyagi
National Institute of Plant Genome Research
New Delhi

S Varadarajan
Indian National Science Academy
New Delhi

Anupam Varma
Indian Agricultural Research Institute
New Delhi

M.Vijayan
Indian Institute of Science
Bangalore

V.K.Vijayan
V.P Chest Institute
University of Delhi
Delhi

M.P.Yadav
Ex. Vice Chancellor
Gurgaon

S. Yashonath
Indian Institute of Science
Bangalore