Transgenics for productive and sustainable agriculture: Some considerations for the development of a policy framework

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Agriculture is of great importance to India. Although the overall contribution of agriculture to India's GDP is gradually declining, agriculture and its related activities continue to contribute in a significant manner to the overall growth of the Indian economy. Time to time, various thinkers have predicted catastrophic consequences of population growth[1–3]. However, predictions of widespread famines proved wrong as major breakthroughs were achieved in agricultural productivity by the deployment of dwarf wheat and rice, and slow incremental improvements were made in other major crops. The world used about 1.4 billion hectares of land for crops in 1961 and only used 1.5 billion hectares in 1998 to get twice the amount of grain and oilseeds[4]. In the absence of improvement in productivity brought about by breakthroughs in breeding varieties that are more productive and more stable, predictions of mass starvation might have come true.

The introduction of dwarf rice and wheat in India and many other developing countries brought about food self-sufficiency, at least in cereal crops. These developments in the 1960s and early 1970s have been popularly called the 'Green Revolution'. The impact of the Green Revolution, extensively studied and analysed, is generally positive. However, in the aftermath of the Green Revolution some negative impacts have become obvious. The cultivation of dwarf varieties requires high inputs, both in terms of fertilizer and irrigation. These inputs are heavily subsidized in India and elsewhere. Higher productivity in wheat and rice coupled with an assured pricing mechanism has led to an over reliance on these crops[5]. Varieties developed by the utilization of dwarfing genes have a narrow genetic base and intensive cultivation of these is leading to a build-up of pests and pathogens. In the last ten years the productivity of the two crops has plateaued while the population continues to increase, and will not stabilize till 2030. The average growth rate of the total food grain production in India during 1994–95 to 2000–2001 has been a dismal 0.8% (ref. 6).

Currently, the food situation in developed countries is very comfortable. Agriculture is heavily subsidized (the US alone provides every year around 50 billion dollar subsidy), but the amount is affordable. Food security has ceased to be a major concern. Organically-grown food has become fashionable. Some land has been reverted to forestry and food surplus is being used to cover the deficit in Asia and Sub Saharan Africa. However, in comparison, the food situation in most of the developing countries remains precarious. Around 800 million people worldwide are food-insecure[7]. In India alone, around 200 million people are undernourished[8]. Many specialists in agriculture have called for a new outlook in agricultural development. Swaminathan has called for an 'Evergreen Revolution'[9] and Conway has called for a 'Doubly Green Revolution'[10]. Many others have simply called for a movement towards more sustainable agriculture[11,12]. The thrust, at least in thinking, is towards creating agricultural systems which will be frugal in their requirement of inputs, involve diverse crop for proper crop rotation, and be based on genetically divergent cultivars within each crop. While reducing the overall exploitation of non-renewable natural resources, such systems should concomitantly provide yield enhancement and stability to feed a growing population.

The wish list of those who want a second revolution in agriculture, which is both productive and sustainable, is very long. It is pertinent to assess the possible contribution of transgenic technologies to sustainable agriculture. In July 2000, a report[13] prepared under the auspices of the Royal Society of London, the US National Academy of Sciences, the Brazilian Academy of Sciences, the Mexican Academy of Sciences, the Chinese Academy of Sciences, the Indian Science Academy and the Third World Academy of Sciences, had the following to say: 'We conclude that steps must be taken to meet the urgent need for sustainable practices in world agriculture, if the demand for an expanding world population is to be met without destroying the environment or natural resource base. In particular, 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'. In this article I will assess the requirements of

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sustainable agriculture, possible role of transgenic (GM) technologies in achieving higher productivity without compromising on sustainability, and the need to develop a policy framework both at the national and global levels for the proper utilization of transgenic technologies.

Sustainable agriculture would require efficient utilization of water resources, crop rotation and crop diversification and in-built resistance to pests and pathogens

One of the biggest challenges facing India and many other developing countries, including China is scarcity of water[11]. In most parts of India, rains are seasonal. As a consequence, ground or stored water has to be used for irrigation, industrial and domestic use. Pressure on water resources is bound to increase in the future due to population growth, urbanization, increased industrial requirement and higher living standards. To enhance the productivity of dryland agriculture, some protective irrigation will have to be provided in the areas which receive low rainfall. The water-table in many parts of India is receding and overexploitation of groundwater resources is a major threat to survival of future generations. Transgenic technologies have little to contribute towards alleviating the problems created by the overexploitation of water resources. However, if transgenic technologies can contribute towards enhancing productivity and yield stability of crops adapted to a low water requirement, the overall dependence on groundwater for irrigation will be reduced.

As discussed by Chand and Pal[5], Indian agriculture, both due to policies on grain procurement and subsidies on power and irrigation and fertilizers, is biased in favour of cultivation of wheat and rice. Rice is historically a crop of eastern India where rainfall is copious, and also of river basins in south India where irrigation has been readily available. Due to its high productivity potential, rice is now grown under irrigation in large parts of the country which traditionally grew other crops. Irrigated tracts give the highest per acre yield of rice, albeit at the expense of groundwater resources and high energy costs. Wheat is mostly grown under irrigation in north India during the winter season. Parts of north India receive some rain during winters, but wheat cultivation even in these areas is supported by six to seven irrigations. In the north, high-yielding wheat and rice varieties are grown in a continuous wheat–rice cycle, year after year[14]. In the irrigated areas of south and east, multiple crops of rice are grown on the same piece of land. This is leading to the depletion of sub-soil water and in the absence of proper rotation of crops, tremendously increasing the pressure of pests and pathogens. Over reliance on rice and wheat has also led to overproduction of these two cereal crops. Currently, the country holds around 60 million tonnes of wheat and rice in reserve[15]. Concurrently, there is a huge shortage of grain legumes and oilseeds. The more input-frugal crops are not grown in the irrigated, high-intensity agricultural areas as their overall productivity is low, while susceptibility to pests and pathogens is even higher than that of wheat and rice[16]. If we have to approach the goal of sustainable agriculture even remotely, it will require proper crop rotation which, in turn, will require proper pricing policies[5] and possibility of high yields from the replacement crops.

Perhaps the most challenging goal before Indian agriculture is to reduce the water requirement of rice and wheat while maintaining their high productivity. Variability is available in the two crops for water requirement, but most varieties that have lower levels of water requirement, such as upland varieties of rice, have low productivity. There could be three broad strategies for reducing the water requirements of the two major cereal crops: (i) development of transgenics with single or few genes[17], which may provide tolerance to abiotic stresses without compromising the overall yield; (ii) characterization and mobilization of QTLs (quantitative trait loci) for conferring resistance to abiotic stresses in the overall genetic background of high-yielding varieties; and (iii) transfer of the highly heritable traits contributing to the yield, from high-yielding materials into the overall genetic background of low-irrigation requiring genotypes.

Most traits related to abiotic stresses (such as tolerance to drought and salinity) have been shown in field-breeding experiments to be quantitative traits. However, a large number of transgenics in which single or few genes have been introduced and modifications have been made only in the quantity or timing of expression (constitutive expression instead of induced), have been shown to confer resistance to the targeted abiotic stresses[17]. If simple overexpression could have contributed to conferring resistance to biotic stresses, genetics of stress tolerance or characteristics such as less water requirement would have been simpler and Nature would have 'discovered' and utilized single gene changes for resistance to abiotic stresses, over and over again. It seems that traits like water requirement and abiotic stress tolerance are predominantly quantitative in nature. Transgenic technologies, in all probability, have little potential for reducing water requirement of crops like rice and wheat. Marker-assisted breeding could be more pertinent for addressing the issue. Most of the QTLs for resistance to abiotic stresses or traits like lower water requirement, however, cannot be so readily marked due to their low heritability. In comparison, the yield-enhancing loci, many of which have high heritability, will be more amenable to mapping, and subsequently, these traits could be mobilized into diverse genetic backgrounds, including varieties that are frugal in their requirement of water. A priori, it cannot be guaranteed that the last-mentioned approach would work. However, if such work is undertaken, it would at least allow diversification of QTLs for yield in a large number of diverse genotypes. If this approach works, as envisaged, we may have varieties with high yield and low water requirement. Tagging of QTLs related to yield and the transfer of the tagged loci would require multidisciplinary teams and a funding commitment of ten to fifteen years. Both requirements, trained manpower and long-term research backing, are currently missing in the Indian research agenda on agriculture.

Transgenic technologies can make the most profound contribution to yield stability and sustainability by developing varieties that are resistant to pests and pathogens

A survey published in this volume[16] clearly shows that a large number of field crops grown in India suffer from major pests and pathogens. A number of articles in this volume have discussed the molecular methodologies and transgenic approaches that could be used for tackling the problems posed by pests and pathogens[18–20]. Providing resistance through genetic means would reduce input costs in terms of agrochemicals and in the long run, would protect the ecosystem from accumulation of chemicals currently being used for controlling pests and pathogens.

The development of disease and pest-resistant varieties has been a major activity in plant breeding. The economic returns of this activity are very high but remain underestimated, as the lag periods between initiation of the research activity and returns are rather long, ten to fifteen years. Options available to plant breeders for developing resistant varieties can be best explained through the concept of gene pools (Figure 1). Identification of resistance within the primary gene pool and its

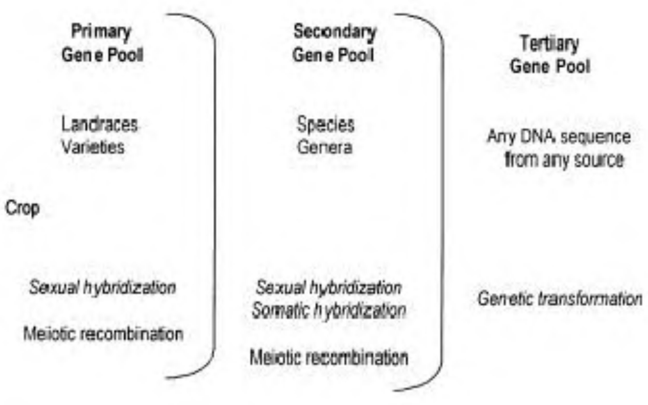

Figure 1. Concept of gene pools was given by Harlan and de Wet[60] in the pre-recombinant DNA era. In the light of the new developments, I propose a modified scheme in which besides evolutionary distance, methods of gene transfer (given in italics) are also taken into consideration. The tertiary gene pool would increasingly become the most important donor of gene sequences for the improvement of crop plants. However, the primary gene pool would remain important for pure line and heterosis breeding, and the secondary gene pool would be of value for the broadening of the genetic base of crop species.

incorporation into a high-yielding variety is the most straightforward option. However, variability within the primary gene pool for resistance has been almost exhausted. In the last twenty years the secondary gene pool, comprising species and genera related to the crop species, has provided a large number of resistance-conferring genes[21,22]. Transfer of genes from wild relatives to crop plants through hybridization suffers from many difficulties. As the evolutionary divergence increases, sexual crosses become increasingly difficult and eventually impossible. Embryo abortion is common, but can be circumvented by embryo rescue. The most excruciating difficulty in transfers is lack of chromosome pairing. If genetic exchanges do occur, the problem of linkage-drag (the gene of interest is linked to a deleterious or yield-reducing gene) could become the limiting step in successful gene introgression. Such tight linkages are difficult to break.

Techniques of molecular biology and genetic transformation have now vastly expanded the scope of plant breeding as these allow mobilization of genes from disparate, sexually incompatible genomes to crop species[23]. Most of the transgenics in the field today[24] are first generation transgenics which were developed with genes from very distant organisms, mostly prokaryotes. Being haploid organisms with small genomes, gene identification is easier in prokaryotes compared to the large-genome, diploid eukaryotic organisms. Two interesting examples of the use of genes from prokaryotes are transgenics for insect resistance in cotton and maize using insecticidal protein genes of *Bacillus thuringiensis*[18]. Conferring resistance to viral pathogens through sequences taken from the pathogen itself is another area where success has been achieved[20]. Being small, viral genomes are easy to sequence. Unfortunately, little work has been done in India on variability in the genomes of major viruses affecting crops in India. I propose that a major effort be launched on studying genomic variability in viruses causing huge economic losses on crops of high economic value. Development of effective PDR (pathogen-derived resistance) strategies will depend upon the availability of information on genomic sequences, transformation protocols and proper testing facilities. Unfortunately, research in this area in India is sluggish, below threshold and therefore inconsequential in terms of providing any benefits to the farming communities.

With the development of high throughput technologies in sequencing, it should be possible now to mine genes of high agronomic value from the near and distant relatives of crop plants and to introduce these into recipient crop varieties through the techniques of genetic transformation. The use of *R* genes for conferring resistance to crop species has been discussed in this volume[19]. Genomes of two higher plants, *Arabidopsis*[25] and rice[26–29] have already been sequenced, and information from these genomes would allow characterization of resistance-conferring genes in related plant species and genera. Many interesting direct approaches have also been taken to isolate resistance-conferring genes from resistant germplasm[30]. For example, a large number of graminaceous species which are sympatric to cultivated rice in northeast India or for that matter anywhere else and are not affected by the diseases prevalent on cultivated rice in that area may contain all the genes for conferring resistance which can be transferred to rice. Unlike in humans where lesion and susceptibility loci are important, in plants, genes from the wild relatives are going to be the most important contribution of the science of genomics. It is hoped that sequencing of the rice genome will be followed by sequencing of some of the wild relatives which have relatively small genomes for allele mining for resistance to diseases and insect pests. However, the current thought process in setting research agendas both at the national and at the Consultative Group on International Agricultural Research (CGIAR) institutes does not seem to be emphasizing this point. Given the national and international needs in agriculture, identification of resistance-conferring genes in the wild relatives of crop plants and their subsequent transfer to high-yield rice varieties through transgenic technologies should be a major thrust area for using genomics and transgenic technologies for sustainable agriculture.

If success is achieved with model crop rice, mining of alleles for resistance to diseases and pests could be taken up in crops which are well adapted to dryland agriculture, i.e. sorghum, millets, mustard, groundnut, safflower, pigeonpea, chickpea, but suffer from a large number of biotic stresses. Little involved work is being undertaken on these crops at the international level, and it would be a major challenge for the developing countries to address these problems through genomics and transgenics, by developing linkages with the CGIAR institutes and laboratories in the developed countries. For a large number of crop plants that are adapted to dryland agriculture, particularly grain legumes, transformation protocols are not available[31]. A major effort will be required to develop efficient methodologies for genetic transformation in these crops.

Transgenics for nutritional enhancement and senescence retardation can contribute to productivity without compromising sustainability

Two other important areas which have been only covered in passing in the articles in this issue are nutritional enhancement and senescence retardation. Research and development in both these areas can have a great impact on developing countries. In the area of nutritional enhancement, an oft-cited example is that of golden rice[32]. There is a lot of argument on how much of golden rice would have to be consumed to fulfil the daily requirement of vitamin A. The issue of golden rice has also been over-exploited by the transnationals to show a humane face so as to gain opportunities to deploy transgenics in developed and developing countries[33]. Nevertheless, golden rice is an interesting development which could open the way for improving nutritional standards in rice-eating cultures. In a similar way, work done in India on the introduction of balanced amino acid–protein-encoding gene *ama1*, from *Amaranthus* into potato holds promise for enhancing nutritional value of a low-protein food[34,35]. Transgenic potatoes with *ama1* genes are undergoing field trials. The results on nutritional benefits of potatoes carrying this gene are eagerly awaited. Critics of nutritional enhancement research feel that the supplementation of one vitamin in golden rice and some nutritional enhancement in potato will not be sufficient by themselves to balance the nutritional requirement. This point is appropriate, but a summary dismissal of these technologies will be, to put it mildly, myopic.

Interesting work is also being done on changing the fatty-acid composition of different oilseeds to enrich these with oil fractions which are healthier for human consumption[36]. Work is also under way to use transgenic approaches to improve the iron content in seed or the other edible parts, and also to accumulate it in a more usable form for the human digestive system to tackle a widespread problem of iron deficiency in the developing countries[8].

A major increase in production of vegetable and fruit crops will be required in the coming two decades[5] as consumption of these will increase due to improved income levels and increasing awareness about health and nutrition. Balanced food requires a fair amount of vegetables and fruit. However, these crops are highly perishable. Hence, farmers who are not well connected to big cities are reluctant to grow these crops. Farmers also have to indulge in distress sales of fruit and vegetables as, at times, there is too much produce and there is no concomitant off-take by consumers. It has been shown that senescence can be slowed by down-regulating some of the genes involved with ethylene biosynthesis[37]. There are other pathways also which can be manipulated to slow down senescence in highly perishable crops. Unfortunately, no such transgenics have been produced in India and studied for their viability. Addressing the issues of post-harvest losses and nutrition could contribute to the earnings of the small farmers and provide enhanced nutritional status to the poor without increasing the pressure on the natural resources.

Transgenic technologies can facilitate hybrid seed production in some of the major crops grown in India

Even in the high-yield crops of wheat and rice, further advances in productivity have been achieved through involved ideotype breeding (rice in China and at International Rice Research Institute (IRRI), wheat at International Maize and Wheat Improvement Centre (CIMMYT) and in rice through heterosis breeding in China and to some extent in South and South East Asia. Projections from various studies show that it will be difficult to increase the cropping area in India. Therefore, productivity enhancement even in wheat and rice would be required, despite the buffer stock availability at present[6,38–40]. In fact, it will be necessary to reduce the area under these crops while taking care of the grain needs of a still expanding population. This can be achieved through reducing losses to pests and pathogens in the two major cereal crops and also by making efforts to enhance productivity, as has been done in China for rice through ideotype breeding and through hybrids[41]. However, breeding for higher productivity in other major crops (minor cereals, legumes and oilseeds) and stabilization of yields in these crops is an absolutely essential requisite for nutritional security and agricultural sustainability. Besides the incorporation of resistance factors, it will be useful to develop technologies for heterosis breeding in crops like pigeon pea, safflower, sesame, rice and wheat. In India, hybrids have performed better than pure lines in the rainfed areas, as hybrid vigour allows plants to establish quickly under limiting conditions.

Heterosis breeding is currently a major method of developing productive materials in maize, sorghum, millet, sunflower and many of the vegetable crops. Essentially, heterosis breeding requires a stable pollination control mechanism and combiners (parents) that would give high productivity hybrids. The efficiency of hybrid seed production also depends upon the pollination behaviour of a crop. The development of hybrid seed is easy in cross-pollinated crops like maize, millet and sunflower. It is readily possible in crops which are pre-dominantly self-pollinated, but have significant levels of cross-pollination, i.e. mustard, pigeon pea, cotton and rather poor in crops like rice and wheat which tend to be mostly self-pollinated. A major impediment in hybrid seed production of rice is lack of opening of the florets for cross-pollination. For crops which are mostly self-pollinated like rice, wheat and soybean, besides the necessity of robust pollination-control mechanisms, changes will also be required through breeding in the floral structures to allow high frequency of cross-pollination for large-scale hybrid seed production. The development of combiners and the modification of breeding behaviour can be done predominantly through conventional breeding methodologies. Transgenic technologies may have little to contribute. However, in the area of pollination-control mechanisms, transgenic technologies provide a lot of scope[42]. In many crops, the genetic male sterility (GMS) systems and cytoplasm male sterility (CMS) systems have proved to be inadequate as these are either labour-intensive or impose yield penalties. Some of the CMS systems tend to become susceptible to diseases. The genetic engineering-based technologies for producing male sterile and restorer lines need to be explored for hybrid seed production in dryland crops like pigeonpea, cotton and safflower.

IPRs, as they exist in the developed countries, if extended to the developing countries will create major impediments for the proper utilization of transgenic technologies

In developed countries, much of the resistance to the deployment of transgenics stems for health and environment-related concerns. Some of these concerns are genuine, others are imaginary. The threat of IPR regimes to the effective use of transgenic technologies worldwide has been overlooked in the developed countries. However, some of the NGOs in the West, despite overall apathy to the issue due to lack of general awareness, have time and again forewarned developing countries on patents which could have a detrimental effect on their agriculture. An illustrative example is 'Terminator Technology', which has been briefly discussed in this volume[43].

In the early days of recombinant DNA technology and genetic engineering, it was felt that breakthroughs would be achieved at breakneck speed, and that their implementation could effectively occur through the well-organized global reach of the transnationals, provided trade and economic policies were effectively liberalized in the developing countries. This optimism perhaps never took into consideration social realities and also the excruciatingly slow pace of agricultural research. The latter facet has been discussed in two thorough research reports by the International Food Policy Research Institute (IFPRI)[44,45].

Unlike the development of antibiotics, chemical molecules and materials which are stand-alone commodities – promoters, vectors, genes and even varieties on their own, are grossly insufficient. It is the combinations of these elements and subsequent stacking of gene constructs in adapted varieties bred through recombination breeding that viable products useful to the farmers can be developed. New molecules can be manufactured and traded in an organized way and their production can be located in any part of the world. No special location-specific inputs are required. Agricultural developments on the other hand, are location-specific. A new variety developed in USA or in Europe may not be of any direct benefit in India. A disease resistance-conferring gene may have to be tested extensively against prevalent races of a pathogen in diverse agroclimatic conditions.

As reported by Grover and Pental[16], almost all the major crops grown in India require multiple character inputs. Important genes that are required to be introduced into each crop will run into tens, if not hundreds. Each gene sequence will require a promoter, a vector and a transformation protocol. All these components which will be necessary for the development of a transgenic for a specific character could be under independent IPR regimes. As an example, the much applauded and cited development in crop biotechnology, 'golden rice', in which provitamin A synthesis ability has been introduced into rice through transgenic technologies, incorporated intellectual property based on at least 70 patents with 32 owners[4]. Pardey and Beintema[45] rightly point out – 'as patenting becomes more prevalent, the number of separate rights needed to produce new innovation proliferates. If ownership of these rights is diffuse and uncertain, the multilateral bargaining problem can become difficult to resolve. Instead of over-exploitation of a common property with low entry cost, there is under-exploitation of a pool of intellectual property due to high costs of access – a manifestation of the so-called 'tragedy of the anticommons' which occurs when too many individuals have rights of exclusion to a common resource'.

There have been two sets of responses to IPRs in crop biotechnology. One has been extensive litigations which have cost millions of dollars. The development and commercialization of the *Bt* gene in corn and cotton illustrates this. Around 81 separate research organizations (59 private and 22 public) owned a total of 388 patents for the *Bt* gene and its use in various crops. The litigations around this technology led to settlements totalling more than US $ 175 million and, by some estimates, destroyed more than $ 1 billion of shareholder value[46]. The difficulties in negotiating the rights to use patents and the high costs of piecemeal acquisition of patent rights have encouraged the second response, takeovers and mergers of agriculture-related industries dealing with seeds, pesticides, herbicides creating behemoths that may end up monopolizing entire sets of technologies required for the production of transgenic plants[47]. Majority of the plant DNA patents are held by around 14 transnationals, the biggest stakeholders being Monsanto, Zeneca and Novartis[48]. Merger or takeover of companies and consolidation of patent rights are continuing unabated.

Most of the genetic transformation technologies, particularly the development of *Agrobacterium*-based vectors (for details see Veluthambi *et al.*[23]) were developed with the support of public funding. However, when used for specific crops, transformation protocols were granted patent protection. The generalized patents and patent protection to gene sequences, the latter being the result of millions of years of organic evolution, could become the most impeding factor in the utilization of transgenic technologies for sustainable agriculture. It can also be argued that findings on naturally-evolved gene sequences are merely discoveries and not inventions and, therefore, these do not come in the preview of patents. If the gene discoveries are through the use of complex and resource-intensive technologies, then for this reason alone, discoveries should not be termed as inventions. However, sequences that have been modified by human intervention or have been searched for in conjunction with some proprietary molecules, i.e. herbicides, could be reasonable cases for patent protection.

In the pre-recombinant DNA era, establishment of genotype–phenotype relationship was not protected by patents. A large amount of germplasm collected from all over the world, particularly from germplasm-rich developing regions of the world, was freely used by breeders in both the public and private sectors to develop resistant or high-yielding varieties or hybrids. Just as germplasm effectively resolved many problems related to crop plants and will probably provide us with the necessary genes for breeding through the use of transgenic technologies in the future, discovered genes must also be freely available for deployment in varieties to meet the requirements of different agro-climatic regions of the globe.

The Indian Plant Variety Protection Act 2002 is a creative solution to IPR-related problems

Proprietary claims started in 1980 when the US Supreme Court ruled in favour of utility patenting for life forms. In 1985, the US Board of Patent Appeals allowed patent protection for asexually, sexually or *in vitro* propagated plants. Prior to this, protection was only available for asexually propagated plants. However, the biggest assault on the free exchange of biological materials came from Bayh-Dole Act in 1980 in USA. This Act gave researchers the right to retain title to materials and products that they invented using the federal (US govt) funding. This has led to profitable privatization of biotechnologies developed at the universities and public institutions. The change was tantamount to using public money for profits through the mediation of industry. Proprietary claims, for example in the US, cover all kinds of biotechnologies which include germplasm, genes, sequences, promoters, transformation technologies, marker vectors, etc. Another landmark development was the agreement in 1994 on Trade-Related Aspects of Intellectual Property Rights (TRIPS) as a part of the Uruguay-round of multilateral trade negotiations. TRIPS now forms a part of the legal obligations of countries that are members of the WTO. Box 1 gives the major features of TRIPS agreement on patents.

In the TRIPS agreement, plants and animals were left out of compulsions of strict patent regimes (Box 1). However, the developing countries, in which no IPR for plants exists, were required to enact a *sui generis* (one of its kind) system for the protection of new plant varieties. In response to this, the supreme law-making body of the country, the Parliament, enacted a Plant Variety Protection (PVP) Act. This has been thoroughly discussed in this issue by Sahai[43]. This author has argued for some changes in the Act to provide the farmers more rights. I believe, clauses related to germplasm usage by private companies would be tedious to implement and are self-defeating. Private industry, if it is to provide superior varieties to farmers, would need free and unhindered access to germplasm. I would urge that no attempts should be made to either dilute the PVP Act towards farmers' benefit or to further strengthen it towards breeders' interest without extensive discussions within the country. It is

Box 1. TRIPS agreement on Patents

Section 5: Patents
Article 27: Patentable Subject Matter

1. Subject to the provisions of paragraphs 2 and 3, patents shall be available for any inventions, whether products or processes, in all fields of technology, provided that they are new, involve an inventive step and are capable of industrial applications. Subject to paragraph 4 of Article 65, paragraph 8 of Article 70 and paragraph 3 of this Article, patents shall be available and patent rights enjoyable without discrimination as to the place of invention, the field of technology and whether products are imported or locally produced.

2. Members may exclude from patentability inventions, the prevention within their territory of the commercial exploitation of which is necessary to protect ordre public or morality, including to protect human, animal or plant life or health or to avoid serious prejudice to the environment, provided that such exclusion is not made merely because the exploitation is prohibited by their law.

3. Members may also exclude from patentability:

a. diagnostics, therapeutic and surgical methods for the treatment of humans or animals;
b. plants and animals other than micro-organisms, and essentially biological processes for the production of plants or animals other than non-biological and microbiological processes. However, members shall provide for the protection of plant varieties either by patents or by an effective *sui generis* system or by any combination thereof. The provisions of this subparagraph shall be reviewed four years after the date of entry into force of the WTO Agreement.

unfortunate that the Government of India has decided to implement UPOV1991 (International Union for the Protection of New Varieties of Plants) when the Parliament had cleared the PVP Act after an extensive and broad-based dialogue. It is certainly a case of bad advice to the government by the 'specialists'.

The PVP Act has taken into consideration some of the provisions of CBD (Convention on Biological Diversity). An extensive study of TRIPS related to agriculture and the contradiction between TRIPS agreement and CBD have been discussed by Watal[49]. Essentially, CBD is more sympathetic towards the rights of gene (germplasm)-rich countries of the developing world.

In developing countries (and fortunately now in developed countries also), there is an emerging consensus amongst experts with liberal leanings that overzealous patenting is not favourable to the future of world agriculture. The British government in 2001 set-up a panel of experts for 'Integrating Intellectual Property Rights and Development Policy'. The report of this Commission on Intellectual Property Rights (CIPR)[50] was published in September 2002. The main recommendations of CIPR on agriculture and genetic resources are given in Box 2. These recommendations come much closer to the PVP Act passed by the Indian Parliament[43] and clearly show more sensitivity towards the needs of agricultural research and development in the developing regions of the globe. This emerging consensus on IPR in agriculture needs to be widely disseminated and discussed. The threat to agricultural research from monopolies and the 'tragedy of anti-commons' is real and must be addressed through appropriate laws and free exchange of materials and methodologies.

The PVP Act can be used in a creative manner to allow protection for both the public and the private sectors. All crop species can be broadly grouped on the basis of their pollination mechanism into three groups: strictly out-crossing, both self-and out-crossing and strictly selfing. In India, hybrid seed is being produced and sold for a large number of cross-pollinated crops (e.g. maize, jowar, bajra, forages, etc. and for a few self-pollinated crops, (e.g. tomato). The seed industry in India has been active in the area of hybrid seed production for many years[51]. If farmers keep the seed of hybrids (F1 generation), characters will segregate in the next generation (F2) and yields would be lower. Consequently, for many vegetable crops, maize, sorghum, millet, cotton, there is an extensive market for hybrid seed and farmers repeatedly go to the seed companies for hybrids. Under the PVP Act, inbred lines and hybrids could be registered, and further protection would be available. For many self-/cross-pollinated crops, both pure line breeding and hybrids are possible. Hybrids, in general, out-yield pure line varieties. While the public system can concentrate on pure line breeding, the private sector could produce more productive materials through hybrids. Transgenes can be stacked in hybrids and there will not only be in-built protection available to hybrids but also protection by the newly-enacted PVP Act. This level of protection should provide enough incentive to private companies to invest in hybrid seeds.

Even for the self-pollinated crops like rice and wheat, hybrids are a distinct possibility. China has achieved notable success in hybrid rice. Again the private sector can be active in this area of R&D. However, for the two major cereal crops, rice and wheat, and many of the other strictly selfing legume crops like soybean and groundnut, there will be little incentive for the private sector to invest in pure-line breeding, as the farmers under the PVP Act would be able to keep their own seeds for fresh

Box 2. Recommendations of the Commission on Intellectual Property Rights* for the area of agriculture and genetic resources

- Because of the restrictions patents may place on use of seed by farmers and researchers, developing countries should generally not provide patent protection for plants and animals, as is allowed under TRIPS. Rather, they should consider different forms of *sui generis* systems for plant varieties.
- Because they are unlikely to benefit from the incentives to research offered by the patent system, but will have to bear the costs, developing countries with limited technological capacity should restrict the application of patenting in agricultural biotechnology in ways that are consistent with TRIPS. For similar reasons, they should adopt a restrictive definition of the term 'microorganism'.
- However, countries that have, or wish to develop biotechnology-related industries may wish to provide certain types of patent protection in this area. If they do so, specific exceptions to the exclusive rights, for plant breeding and research, should be established. The extent to which patent rights apply to the harvested crop also needs to be carefully examined. It is important that a clear exception to the patent right is included in legislation to allow for farmers' reuse of seed.
- The review of the relevant provisions in TRIPS which is currently taking place in the TRIPS Council, should preserve the right of countries not to grant patents for plants and animals, including genes and genetically modified plants and animals. It should also permit countries to develop *sui generis* regimes for the protection of plant varieties that suit their agricultural systems. Such regimes should permit access to the protected varieties for further research and breeding, and provide for the right of farmers to save and plant-back seed, including the possibility of informal sale and exchange.
- Because of the growing concentration in the seed industry, it is important that public sector research on agriculture, and its international component, should be strengthened and better funded. The objective should be to ensure that research is oriented to the needs of poor farmers, that public sector varieties are available to provide competition for private sector varieties, and that the world's plant genetic resource heritage is maintained. In addition, this is an area in which nations should consider the use of competition law to respond to the high level of concentration in the private sector.
- Developed and developing countries should accelerate the process of ratifying the FAO Treaty on Plant Genetic Resources for Food and Agriculture and should, in particular, implement the Treaty's provisions relating to not granting IPR protection on genetic material in the form received from gene banks protected by the Treaty. They should also implement at national level, measures to promote Farmer's Rights. These include the protection of traditional knowledge relevant to plant genetic resources; the right to participate in sharing equitably benefits arising from the utilization of plant genetic resources for food and agriculture and the rights to participate in making decisions, at the national level, on matters related to the conservation and sustainable use of plant genetic resources.

*The Commission on Intellectual Property Rights was set-up in May 2001 by the British government. The report was submitted in September 2002 and can be accessed on www.iprcommission.org. The members of the Commission were John Barton, Daniel Alexander, Carlos Correa, Ramesh Mashelkar, Gill Samuels and Sandy Thomas.

plantation. Consequently, the public system will have to provide breakthroughs in these crops for enhanced and stable yields through the development of new pure-line varieties or transgenics from the existing varieties.

I propose that the PVP Act, if implemented properly, will allow both the private and public sectors to contribute towards agricultural progress. The private sector can invest in hybrids, while the public sector could provide leadership in the development of pure lines.

Public-funded agricultural research in India is becoming ineffective and requires major changes in managerial practices to contribute to productive and sustainable agriculture

The major funding for biotechnology research in India has come from the government[5,52]. However, the impact of this public-funded research could have been far greater. First, India has not recognized any patents either on genes or on plants. Patents are territorial, and scientists in India can use any of the sequences or technologies described in the literature or patents. That we have failed to produce a large number of transgenics based on existing knowledge in itself shows weakness in R&D in the public sector. The Indian Council of Agricultural Research (ICAR) system as it exists presently is extensive (Table 1)[38] but unfortunately over-bureaucratized. The quantum of funding for specific projects remains below threshold. The lack of adequate trained manpower is another dampner, as new recruitments are sparse and the existing scientific staff (although large in number) is unable to cope with the new methodologies of markers, genetic transformation and gene cloning. It is ironic that many of the senior administrators in the ICAR system, both in the past and at present, have observed agricultural research at the global level, particularly in the CGIAR system; yet no effort has been made to develop multi-disciplinary teams for trait-specific breeding as has been done in the CGIAR institutes. Although there is a dedicated institute for every major crop in the ICAR system, no spectacular examples of teamwork exist. A major effort is required in searching for competent research leaders and establishment of teams that work in a time-bound and goal-specific manner. The bureaucratic strangleholds on the execution of projects must be removed if the public system is to contribute towards the development and

Table 1. Institutions under the National Agricultural Research System in India

Institution	1974	1985	Current
Indian Council of Agricultural Research			
Institutes	23	39	49
National Research Centres	–	11	30
Project Directorates	–	5	10
All-India Co-ordinated Research Projects/Network Projects	69	63	80
Central Agricultural Universities	–	–	1
Others	–	8	14
Total	92	126	184
Agricultural Unisversities	17	23	29

Source: Ref. 38.

evaluation of transgenics. If current practices are to continue, R&D in the public sector is definitely moribund.

It is of critical importance to the country that in the next two years, trait-specific programmes of crop improvement are identified and research on these is implemented jointly by Department of Biotechnology (DBT) and ICAR. Although the two departments belong to two different ministries, ways and means must be found to develop coordinated systems of research and to involve both agricultural and non-agricultural laboratories in the R&D programmes.

The current decline of CGIAR system is not in the interest of sustainable agriculture

A major threat to the use of transgenic and other new technologies for sustainable agriculture stems from the decline of the CGIAR centres. The CGIAR system grew out of the initial support by the Ford and the Rockefeller Foundation in the 1950s, to support joint venture programmes in agriculture. IRRI was established to work on rice in 1960 at Los Banos in the Philippines. CIMMYT was set-up at El Botan in Mexico in 1967. The CGIAR system at present has 16 international centres. The overall achievement of the CGIAR system and the contributions of individual centres can be readily accessed[53] and hence will not be described. However, it is pertinent to point out that the CGIAR centres have made immense contribution towards breeding materials for both developed and developing countries. Dwarf wheat and rice varieties bred at CIMMYT and IRRI have been responsible for major yield increase in the developing countries through 'Green Revolution', and these developments have been referred to extensively in this special section. However, contribution of the CGIAR centre to agriculture of the developed countries remains largely unknown. In the early 1990s, one-fifth of the total US wheat land was being sown with varieties derived wholly or in part from material developed at CIMMYT. For the California Spring wheat, this figure was estimated to be 100% (ref. 10).

It is, therefore, quite inexplicable why the overall financial support to CGIAR institutes is decreasing (Japan in 2002 has cut support to IRRI by half)[54] and why there is no attempt in global fora to make these institutions central to the themes of sustainable agriculture. The total budget of the CGIAR system has remained stagnant for the past ten years and as some new institutions have been started, budgetary support for established centres has actually declined[45]. Even centres like IRRI and CIMMYT, despite their well-recognized contributions, are at a receiving end. Many of these centres are doing contractual work with transnationals on which there would be IPR fetters at the end of the day[33].

Throughout the world, particularly in the developed countries, since the advent of recombinant DNA techniques, genetic engineering methodologies and high throughput instrumentation, expenditure on biological research has grown manifold. The CGIAR centres, either due to a design or out of a false sense of food security, are seeing their actual budgets shrink. This should be unacceptable to the world community. A major effort should be made by the Indian government, in partnership with the developing countries of Asia, Africa and Latin America, to seek in the next three years at least 20–25% annual increase in the research budgets of CGIAR institutes.

Effective use of transgenic technologies would require complete transparency in evaluation and release of genetically engineered material

It is clear from the article by James[24] that the two American continents have been most enthusiastic towards transgenic crops. China, by all accounts, is another country which has taken up R&D on transgenics as a major priority[55]. Many of the developed countries in Europe and Japan are rather lukewarm. Currently, no transgenics are being grown in these countries. Transgenics are perceived to give genetically modified food. Hence, the name GM is far more in use in the popular lexicon than the more scientific and esoteric term, transgenics. Most of the food we eat is genetically modified through selection and controlled breeding. This selection occurred throughout the human evolution, mostly in an inadvertent manner, but in the last century has been through controlled methods and elaborate selection strategies. As a consequence all food carries some genetic modification.

Transgenic research has expanded the scope of genetic modification (Figure 1) and brought higher levels of precision to breeding work. However, there are ecological fears about transgenics which should not be dismissed and require careful analysis[56–59]. One major fear is regarding the use of antibiotic resistance-conferring marker genes which are used for the *in vitro* selection of transgenics. Technologies are now available for the removal of the marker genes[23]. The other major fear is on the spread of the transgenes. It is thought that related species which are sympatric with the crop, and some of these at times invade the crop fields as weeds, may receive the transgenes and thereby become super weeds. The fear of super weeds is mostly imaginary. But increasingly, scientific work shows that transmission of transgenes from crops to closely related species is possible. In cross-pollinated species, transmission could be extensive. Also, once transgenics are put in the farmers' field, keeping the transgenic material distinct from the non-transgenic material will become impossible, given that the land holdings in India are very small and farmers tend to keep their own seed, particularly in the self-pollinated crops. Therefore, the possibility of 'GM' food getting mixed-up with 'non GM' food is real and cannot be wished away. Although research published on the movement of transgenes from transgenic corn to land races of corn in Mexico has been shown to be incorrect, once large-scale cultivation of transgenics is undertaken, the possibility of genetic exchange between land races and transgenic material exists as much as it exists for exchange between transgenic varieties and non-transgenic varieties growing in the farmers' field. The best way of avoiding genetic contamination of land races is to secure germplasm in the gene banks of the world.

As transgenic material can cross with non-transgenic varieties and also with the wild relatives, transgenic material must be put through rigorous tests for toxicity and allergenicity. Only material which pass through the most rigorous and well-established tests should be sent to the farmers' field. Fortunately, as discussed by Sharma *et al.*[52] in this volume, the Government of India is already implementing very strict and thorough evaluation criteria for transgenics. The norms for food safety should be stringent and penalties for rogue release of transgenic material should be high.

It is important that till society at large is convinced about the benefits of transgenics, all the trials on such material should be done in a transparent manner. The public system can contribute to the process by setting up trials at institutes and agricultural universities. These trials should be supported by ICAR and DBT. ICAR has the world's most extensive coordinated trial system for the release of new crop varieties. This strength must be utilized to set-up proper trials on yield potential of transgenics and to gain experience on the field behaviour of transgenic crops. The nutritional, toxicological and allergenicity tests should be conducted by ICMR institutes or by those duly certified by ICMR to carry out such tests. Trials conducted under the tutelage of the two organizations would carry more conviction with the public at large.

The current process of Institutional Biosafety Committee (IBSC), Review Committee on Genetic Manipulation (RCGM) and Genetic Engineering Approved Committee (GEAC) should be maintained (discussed by Sharma *et al.*[52] and figure 1 in that article). I propose that to improve the evaluation process, RCGM should be given the powers to receive reports from ICAR on yield and field behaviour, and Indian Council of Medical Research (ICMR) on nutrition, toxicology and allergenicity. However, this may be easier said than done. The involved organizations are under different ministries. An inter-ministerial panel with secretaries of all the concerned departments, viz. Agriculture, Health, Science and Technology, Environment could be created to reach an understanding on all the steps of evaluation and release. Special cells should be created in ICAR and ICMR to direct the process of evaluation. Results from all the studies should be hosted on the web for scrutiny by the public.

A policy framework for supporting crop breeding and concluding remarks

Development of a productive but sustainable agricultural system would require initiatives on many fronts. Transgenic technologies can contribute in a limited but significant way to the lofty goal of sustainable agriculture. This contribution, however, can be realized only if a proper policy framework is created and I propose one on the basis of arguments made in this article.

1. Transgenic technologies are not a substitute for conventional methods of plant breeding. Pure line breeding to diversify varieties and to select transgressive segregants for important traits must continue. Component breeding through marker-aided selection must be provided adequate funding. The development of heterotic pools in some of the important crops like wheat and rice has so far been given little attention. This needs to be rectified as it is essential for enhancing productivity.
2. The most important contribution of transgenic technologies will be in the areas of developing varieties resistant to pests and pathogens. A major effort should be launched to develop transgenics that contain resistance to pests and pathogens.
3. For pests, discovery of new insecticidal proteins encoding genes both from microbes and plants should be given high priority. Currently, there is no work on search for new *Bt* Cry proteins or VIPS. At least three laboratories should be given the charge of collecting new strains from different ecological regions of the country so as to identify new insecticidal proteins. Already described and new genes should be tested on the most devastating insect pests of crops grown in India. *Heliothis armigera*, that effects at least three major crops should receive high priority.
4. Variability at the molecular level needs to be studied for viral pathogens; otherwise strategies based on patho-

gen-derived resistance would be ineffective. Work on variability analysis should be initiated at the earliest.

5. Some of the major bacterial and fungal pathogens need to be more intensively studied, both for variability at the molecular levels and through differentials.
6. Participation of laboratories from India in structural and functional genomics work through international collaborations should be encouraged. India did well to participate in the international rice genome sequencing effort. Such participations should continue on sequencing genomes of model legume species and some of the important pathogens of crop plants.
7. In functional genomics, top priority should be given to identification and isolation of genes conferring resistance to pest and pathogens. India should sequence the genome of a wild relative of rice for allele mining. The choice of the wild relative should be based on genome size and resistance of the wild species to major pests and pathogens of rice. Sequencing of only transcriptionally active areas may suffice. As an alternative, chromosome addition lines with resistance can be sequenced to mine alleles present on the additional chromosome.
8. Development of transgenics for resistance to pests and pathogens would require either strong multidisciplinary groups or collaboration among laboratories specializing in genome sequencing, plant pathology, breeding and genetic transformation. Such groups can be assembled in a crop-wise manner. These groups should be developed only in a few institutes in the country, as general infrastructure in many institutes is insufficient for experimental work in genomics, genetic transformation and molecular breeding.
9. As each crop requires inputs of a number of genes, there should be a crop-wise strategy for gene stacking. Technologies for the removal of marker genes should be used so that transgenics could be protected from homology-based silencing and do not contain a surfeit of marker genes.
10. In India, transformation protocols are available only for a few crops. There is great urgency in developing routine transformation protocols for crops like pigeonpea, chickpea, safflower, mungbean and wheat. Some new and innovative approaches will have to be supported as little success has been achieved to-date with some of these crops.
11. Heterosis breeding would require development of elite heterotic pools and sterility/fertility restoration systems. Groups working in the area of developing heterotic pools will have to be assigned the task of finding and properly recording the heterotic parental lines. Such lines must be deposited with the National Bureau of Plant Genetic Resources. In many cases, data on heterosis are on a limited population size and, therefore, are not reliable.
12. Development of transgenics for reducing post-harvest losses should be given high priority. Basic work on senescence retardation will have to be supported.
13. For each crop, a thorough study needs to be undertaken on technological options that are available to meet the identified breeding goals. In areas where knowledge is not adequate or new strategies are required, basic research work should be funded.
14. A major effort needs to be made in training and retaining scientists who are competent to handle genomics and gene discovery work. Efforts should be made to attract scientists trained abroad in the key areas of genomics, gene discovery and molecular plant pathology. The recruitment of scientists through ARS should be abandoned. Scientists should be hired directly in the institutes according to the need.
15. A major initiative will be required to attract talented students to agricultural biotechnology. At the undergraduate and postgraduate levels, curricula are outdated. These need to be changed.
16. The PVP Act should be followed for the next 15 years. If any modifications are required, these should be made through proper deliberations and assessment of the long-term consequences. The PVP Act should be used creatively to encourage the private industry to invest in hybrid seeds. Patents on gene sequences as they exist in nature should be avoided.
17. India should take a lead in strengthening the CGIAR system. The CGIAR institutes can provide valuable pre-breeding material which can be used for region-specific breeding. The Indian government, to halt the decline of these institutions, could take a proactive role and increase its own contribution to the CGIAR system.
18. Seed industry could be helped by putting up trials on transgenic material through agricultural universities and the coordinated trial system of ICAR. There is sufficient expertise in the universities and ICAR institutes to do proper trials. Seed industry should be also provided germplasm without any fetters.
19. Indian fertilizer industry should be given incentives to enter the business of producing and delivering quality seed of both hybrids and pure lines to the farmers. With their strong distributional networks and ties with the farmers, the fertilizer companies may be able to bring about a rapid turnaround in the seed sector.
20. The current process of clearance through IBSC, RCGM and GEAC should continue. However, the RCGM should be given the powers to receive reports from ICAR on yield and field behaviour, and ICMR on nutrition, toxicology and allergenicity. Special cells should be created in ICAR and ICMR for organizing these studies.
21. It would be difficult to label GM and non-GM foods in India as land holdings are very small and food is

processed predominantly by the small-scale industry. Therefore, transgenics should be released after proper testing and evaluation.

22. All information on trials under RCGM should be put on websites so that the community at large is informed about the performance and the merits/demerits of the transgenic material.

The recommendations given in this article will need to be critically examined and may have to be modified and expanded upon. It is hoped that this article and the other articles in this special section will at least serve the purpose of initiating an earnest debate on how to enhance the productivity and sustainability of Indian agriculture through the judicious use of transgenic technologies.

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