Regulating the dual-use and dual-impact life science research: influenza virus versus biotech crops

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Dual-use research of concern (DURC) is the research that is intended for legitimate benefits, but also carries a risk of being misused. In this article, the work related to regulation of dual-use influenza virus research involving genetic engineering of the subtype H5N1 has been compared with the research involving regulation of biotech crops including Bt cotton and Bt brinjal in India, which the author likes to describe as dual-impact research of concern. The growth of biotech crops globally has been briefly described to highlight that no harmful effects of any biotech crop grown and utilized during the last more than 15 years have been reported. The contrast between the responsible manner in which scientists dealt with the regulation of DURC and the manner in which the civil societies and some NGOs have been spreading misinformation, thus creating obstacles in commercialization of biotech crops meant for public good is revealing indeed. Therefore, major efforts are needed on the part of scientists and the media to develop good communication system involving newspapers, extension workers and TV programmes, which should highlight the merits and safety of biotech crops. Scientists should also work hard to convince the government that there is a need to reduce the burden of regulation for biotech crops, so that the benefit of this technology could reach the masses.

Keywords: *Bacillus thuringiensis*, dual-use and dual-impact, genetically modified crops, recombinant DNA.

DUAL-USE research of concern (DURC) in life sciences has been recently defined as research that is intended for legitimate beneficial purposes, but also carries a risk of being misused for malicious purposes[1]. This definition may be further extended by including research which is intended for beneficial purposes, but is likely to pose a threat to other living systems and the environment, as is perceived in case of biotech crops (also called genetically modified (GM) crops). This may be described as dual-impact research of concern (DIRC), although no such expression seems to have been used in the literature. There are two main areas of research which may fall within the definition of DURC/DIRC: (i) research on human genome, human diseases, pathogens and drug development in the field of medicine and (ii) development of transgenic plants leading to commercialization of the so-called biotech crops developed for food, feed, edible vaccines, molecular farming/pharming, bioremediation, etc. Both these areas of research largely make use of recombinant DNA (rDNA) or genetic engineering (GE) technology, which started during 1970s and has now become routine in all biology laboratories for the purpose of teaching and research. Products of both these areas of research fall within the jurisdiction of Indian regulatory bodies, including the Review Committee for Genetic Manipulation (RCGM) and Genetic Engineering Appraisal Committee (GEAC).

In this article, an attempt has been made to highlight the contrast between the regulation of research involving influenza virus on the one hand, and that involving *Bacillus thuringiensis* (*Bt*)-cotton and *Bt*-brinjal on the other. The results of the much debated research on influenza virus were recently published after a waiting period of eight months, whereas cultivation of *Bt*-cotton even after 10 years of success is being questioned, and *Bt*-brinjal is facing an indefinite moratorium that was imposed in February 2010 by the Ministry of Environment and Forests (MoEF), Government of India. As an introduction to the subject, a brief history of rDNA research and the debate of 1970s about the risks involved in using it will be presented first. This will be followed by a brief account of the recent debate on the publication of the research conducted for genetic manipulation of influenza virus to assess the possibility of its becoming infective and air transmissible among mammals. An account of commercialization of biotech crops globally and at the national level in India, including both *Bt*-cotton and *Bt*-brinjal, is presented next. This will also include an account of the debate on the moratorium on *Bt*-brinjal, which is currently

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in vogue and is being debated. In the end, we compare the regulatory approaches followed in dealing with the genetic manipulation of influenza virus on the one hand and commercialization of biotech crops on the other. There are other areas of research involving ethical and biosafety issues, which are also receiving attention of the scientists, society and the government, but these aspects will not be covered in this article.

History of rDNA and DURC

One may recall that during 1970s, after the discovery of recombinant DNA technology, questions were raised globally whether or not research involving recombinant DNA technique was to be allowed in research laboratories. One may also recall the 'moratorium letter' that was issued during 1974 for putting a halt on research involving rDNA[2], followed by the Asilomar Conference of 1975, where the scientists themselves (not the activists, the stakeholders or the politicians), including the Nobel Laureate Paul Berg discussed the risks involved in undertaking research involving rDNA. At the conference, there were apprehensions that the rDNA technique may be used either by accident or by mischief leading to emergence of pathogens and bioweapons which, according to some, could wipe out the human race from the earth. Despite these apprehensions, the major conclusion of this conference was that the research involving use of rDNA should be continued, provided appropriate safeguards are used in conducting this research. It was also agreed that certain experiments with potential risks of serious nature be not conducted for the time being, although future research may show that these perceived biohazards were really not as serious as suspected at that time[3]. The Asilomar Conference is an example of the responsible manner in which scientists performed in undertaking research, which they conducted. However, following this transition during 1970s, the rDNA technique became popular and is now used for teaching and research, sometimes even at the school level. This has brought about a revolution in the field of life sciences education and research, so that every area of education and research in life sciences now involves a component of rDNA. Had this DURC involving rDNA been disallowed or voluntarily dropped during 1970s due to perceived biosafety risks, we would not have witnessed the revolution that occurred in the area of life sciences during the last few decades.

Influenza virus (A/H5N1) and 'bird flu'

The influenza A virus causing seasonal influenza (generally in the winter months) is a threat to public health and takes away ~ 500,000 human lives globally every year. The virus is known to undergo extensive changes, sometimes giving birth to a form, which can cause global influenza pandemics. Such pandemics actually occurred in the past during 1918, 1957, 1968 and 2009, causing loss to human life[4]. It is also known that a highly pathogenic strain of influenza A virus (genus A; subtype H5N1) that emerged during the last decade[5] often infected human beings causing the so called 'bird flu', particularly among those who are exposed to infected birds (at least 600 cases were reported from 15 countries since 2003, of which 60% succumbed to this infection). In several countries in the East (including India), on poultry farms, this also led to a major activity involving mass culling of chickens, suspected to be infected with this strain of virus (hundreds of millions of domestic birds were culled in Asia, Middle East, Africa and Europe); there was also a panic among humans who, therefore, avoided chickens in their non-vegetarian diet; poultry farms thus suffered major losses. Despite this, the virus could not be wiped out; it persists and continues to be a threat to humans, as humans have no immunity against this virus, although in mammals, including humans, the virus is not transmitted through air.

The influenza viruses, including the strain A/H5N1, derive their name from the type of proteins they carry, which includes the type of haemagglutinin (HA) and the type of another surface glycoprotein called neuraminidase (NA). It is known that the HA of H5N1 viruses preferentially binds sialic acid (Siaα2,3) in receptors located on the surface of avian cells, but cannot bind sialic acid (Siaα2,6) that is found in the human receptors on the surface of cells in the respiratory tract, thus making the avian virus incapable of infecting humans. It is also known that alterations in HA alone are not enough to make H5N1 infective and transmissible among humans, since another transmissible influenza A virus is known, where transmission among humans is attributed to three component proteins, including HA, NA and basic polymerase protein 2; it is possible that other viral proteins also contribute to mammalian transmissibility. This suggested that HA, NA and polymerase proteins, and possibly some other unknown proteins of avian H5N1 need to undergo mutations to acquire the ability to infect and transmit through air among humans. Consequently, experiments were recently conducted to find out if the avian virus can be artificially converted into a strain that infects and can be transmitted through air among mammals (ferrets were used as a model for mammals in these experiments). It was observed that in order to achieve infection and transmissibility through air, one had to alter a number of proteins, including HA, NA and polymerase through mutations, which had to be introduced artificially through genetic manipulation[6].

In June this year, two important papers, one each in *Nature* (21 June 2012) and *Science* (22 June 2012) were published on experimental manipulation of A/H5N1 virus in such a manner that it developed the ability to be transmitted in mammals (ferrets) through respiratory droplets released during cough and sneezing. In one of these two studies, a team led by Yoshihiro Kawaoka at the Univer-

sity of Wisconsin, Madison, and the University of Tokyo successfully produced a hybrid virus by taking one gene for a viral protein called HA from A/H5N1 and seven other genes from another virus H1N1, which is adapted to humans and is known to have created a pandemic in 2009 and 2010. From this stage, four additional mutations in the HA gene resulted in a genotype which was transmissible from one caged ferret to another through air; no such hybrid strain was available in nature[7]. The other study was conducted by a group led by Ron Fouchier of Erasmus Medical Centre in Rotterdam, The Netherlands, who started his work with an actual H5N1 virus strain from Indonesia and successfully introduced several mutations within the receptor binding site available within the HA protein of the virus, which is the first molecule that makes contact with the host cell. Two of the several mutations that were introduced were already known to confer ability on the virus to prefer mammalian cells over bird cells. Another mutation that was introduced altered the polymerase protein complex in such a way that it will facilitate replication of the virus in the cool environment of the upper respiratory tract of mammals rather than a warmer environment of the bird's intestine, where the virus generally resides. However, these mutations in HA and polymerase enzyme were not enough to enable the virus to be transmitted through air from one mammal to another. This was, therefore, followed by passaging the virus through uninfected animals (one ferret to another through inoculation), thus producing additional mutations, which conferred upon the virus the ability to be transmitted through air from one caged ferret to another[8].

In the 22 June 2012 issue of *Science*, the second of the above two papers[8] was part of a special section that was devoted to the issue of whether publication of some of the data produced by research on a controversial subject like influenza virus should have been withheld to disallow free access in public interest[9–15]. This kind of research has been classified as DURC in USA. It is also argued that perhaps there should be an international system for assessing and handling DURC in a way so that only those who need to know should have access to research data, which should not be freely accessible. These studies initiated a debate about whether in the first place such studies should at all have been conducted, and even if conducted should the results be published to become freely accessible. The major basis of disagreement was that firstly, the bioterrorists might use the results to develop bioweapons and secondly, that the genetically engineered virus might escape by accident and cause a pandemic. The arguments in favour of such studies, however, emphasize that such studies increase our knowledge, so that we will be better equipped to recognize and deal with influenza outbreaks, whenever these outbreaks occur in future. The debate on DURC has also been described as Asilomar 2.

The publication of the above two studies involving engineering and transmission of influenza virus to ferrets was withheld for about eight months, and was eventually allowed by the US Government on the recommendation by an independent federal committee called the National Science Advisory Board for Biosecurity (NSABB) after intensive discussion[16]. In this process, the US Government also developed a document described as 'United States Government Policy for Oversight of Life Sciences Dual Use Research of Concern'[12]. This document describes how different federal departments and agencies will assess the risks and benefits involving 15 agents from the select list of ~80 agents, and then take a considered decision whether or not to allow conduct and funding of such research projects, if they fall within the definition of DURC. It was also emphasized in this document that the research falling within the definition of DURC should be allowed and the results published only when the benefits to society at large overweigh the risks/harms to national security and the society.

World-wide growth of biotech crops (including *Bt*-cotton in India)

Biotech crops are the crops that are derived through the use of rDNA technology. Plant breeders would like to avoid using the popular terms 'genetically modified crops' or 'transgenic crops', since all cultivars resulting through plant breeding are genetically modified, and in all cases genes are transferred from one source to another, the only difference being the use of rDNA technology for gene transfer in the case of biotech crops. Perhaps another distinction is that the introgressed gene involved in a biotech crop could not have been transferred by conventional methods of plant breeding. But it is only the rDNA technology, which really makes the distinction, because, even when the gene is transferred from the same species (cisgenic plants), and even when no transgene is carried by the product, it is still classified as a biotech crop, if rDNA technology is involved[17,18].

Biotech crops have shown a remarkable rate of adoption for cultivation during the last 15 years. Starting in 1996 with 2 million hectares (m ha) of land occupied by biotech crops, the global area occupied by biotech crops in 2011 approached 160 m ha (13% increase over the previous year) and involved 16.7 million farmers in 29 countries, although the traits involved for improvement mainly included either herbicide resistance or insect resistance. Almost invariably, the insect resistance was due to one or more *cry* genes derived from *Bt*, which are lethal to certain classes of insects, and the herbicide (glyphosate) resistance was often due to microbial genes that would either modify the herbicide target, or will detoxify the herbicide itself. In some cases (42.2 m ha of the 160 m ha), the traits for insect resistance and herbicide resistance were also stacked together (for more details, see James[19]). It is also known that in USA in 2010, 85% of corn and 90% soybean acreage was planted with biotech corn and biotech soybean respectively[20], suggesting

that in due course of time, corn and soybean crops in USA will be represented exclusively by biotech crops.

Second generation of biotech crops

Only recently, biotech crops carrying genes for resistance against either abiotic stresses or a variety of fungal and bacterial diseases are being developed. However, the progress in this direction is rather slow, the first such biotech crop being Monsanto's drought-resistant biotech maize (MON 87460) that was approved in December 2011 by USDA for commercial cultivation in USA, even though questions have been raised about its performance in the field[21]. These biotech crops are described as the 'second-generation biotech crops', which also include biotech crops to be used for biofuels, industrial chemicals and even for biopharmaceuticals.

For the development of second-generation biotech crops, additional novel biotechnological approaches have also become available, which include the following: use of zinc-finger nucleases (ZFN) and transcription activator-like endonucleases (TALE) for genetic engineering, oligonucleotide-directed mutagenesis (ODM), RNA-dependent DNA methylation (RdDM), grafting on GM rootstocks, reverse breeding (involving silencing of recombination during meiosis), agroinfiltration (transgene is introduced only in some tissues) and MADS box gene-accelerated flowering[22,23]. Several of these new approaches fall within the category of targeted genetic modification (TagMo), so that questions are being asked if these products resulting due to the use of TagMo will fall outside the definition of biotech crops for the purpose of regulation[24]. It is obvious from this shift from first-generation to second-generation biotech crops (sometimes involving the use of newer approaches) that we are entering into a second phase of the development and commercialization of biotech crops, despite the fact that the debate on the first-generation biotech crops is not yet over. This second phase has been described[25] as Agbiotech 2.0 and will be a challenge for both the developers of biotech crops and the regulators, since the civil society advocacy groups in several parts of the world including India will keep on working to block the process of progress in science and technology for crop breeding.

Ten years of successful cultivation of *Bt*-cotton in India

Bt-cotton in India is an extraordinary example, where pressure from the farmers, who illegally grew this crop prior to its approval by the regulatory authorities, facilitated the approval for commercial cultivation of this biotech crop in 2002. Following the regulatory approval, more than 1,000 *Bt*-cotton hybrids were released during the last 10 years, so that a record 11 m ha (> 90%) of the total cotton area of 12.2 m ha was occupied by *Bt*-cotton during the year ending June 2012. It was only due to *Bt*-cotton that the total production of cotton in 2012 reached 35.6 million bales (170 kg/bale), with an average yield of 496 kg/ha (the domestic consumption is only ~ 28 million bales, leaving a surplus of ~ 15 million bales); the average yield was still higher in earlier years, approaching over 550 kg/ha in 2007. Also, the pesticide consumption due to use of *Bt*-cotton has gone down by at least 50%, this fall ranging from 46% in 2002 to 26% in 2006 and 21% in 2009 and 2010. The number of *Bt*-cotton farmers increased from 20,000 in 2001–02 to seven million in 2011–12, representing ~88% of the eight million cotton farmers in 2011–12 (refs 26 and 27). This dramatic change in cotton cultivation has been described by some as 'white gold revolution'.

More recently, the economic impact of *Bt*-cotton in India has also been examined through a systematic study[28]. The authors have shown that *Bt*-cotton caused a 24% increase in cotton yield through reduced pest damage and a 50% gain in cotton profit among farmers with smallholdings. According to them, this led to a positive economic and social development in India and improved the standard of living of the farmers who were growing *Bt*-cotton. Similar results were reported in another independent study. The Council of Social Development (CSD) also conducted a study (involving socio-economic impact of *Bt*-cotton), commissioned by Bharat Krishak Samaj, and reported a decline of 23% in the use of pesticide during 2002–2009, although the level of decline in pesticide consumption has slowed down during the last two years[29]. Also, the cotton area and production may drop in India this year (2012–13) due to global fall in prices, the export policy of the Government of India and the subsidy provided for cotton export in USA, so that farmers may shift to other crops. However, this trend has nothing to do with the merit or demerit of *Bt*-cotton per se, although several civil society advocacy groups, including some NGOs, may like to attribute this to the failure of *Bt*-cotton.

Despite the above success of *Bt*-cotton in India, the controversy about commercial cultivation of biotech crops continues, and more often the negative attitudes dominate, mainly due to several civil society groups, although sometimes even a section of the scientific community also joins them and disagrees with the majority opinion in favour of biotech crops. The negative attitudes have recently been reinforced by the report of Parliamentary Standing Committee placed before the Parliament on 9 September 2012. Earlier, in a meeting during 11–12 June 2012, organized by CSD, Centre for Environment Education (CEE) and Centre for Sustainable Agriculture (CSA) to examine the results of 10 years of *Bt*-cotton in India, mixed opinions were expressed by developers, farmers, NGOs and some scientists; however, in the concluding session, the Minister Jairam Ramesh accepted that *Bt*-cotton in India has been a success (although he also emphasized on the need for further work), though many

advocacy groups still keep on arguing against the benefits accrued to the farmers due to cultivation of *Bt*-cotton[30].

The fate of *Bt*-brinjal in India: an indefinite moratorium

Bt-brinjal was developed by M/s Maharashtra Hybrid Seeds Company Limited (Mahyco) through introgression of the *Bt* gene *cry1Ac* to provide tolerance to the fruit and shoot borer (FSB), a major pest that attacks brinjal crop throughout its life cycle. An appropriate selected biotech event, EE-1 was subjected to field trials and after due consideration of the biosafety data by RCGM, and the report of an 'Expert Committee on *Bt* Brinjal' (called EC-I), large-scale trials (LST) for two seasons were allowed. In order to study the findings of all the studies conducted by that time on *Bt*-brinjal event EE-1 (including LST) and to examine the concerns expressed by several groups, the GEAC again constituted an 'Expert Committee' (called EC-II) to examine all aspects. After due consideration of the report of EC-II, on 14 October 2009, GEAC took a decision in favour of commercialization of *Bt*-brinjal, but chose to send their recommendation to MoEF for a final decision.

The MoEF placed the recommendation of GEAC as above on the web and invited comments. The then minister in the MoEF, Jairam Ramesh, also had seven meetings with the public in different regions of the country to know the acceptability of *Bt*-brinjal by the consumers. He also invited comments from the Chief Ministers of different states and sought opinions of some selected scientists and civil society organizations (CSOs), including some NGOs. After considering the information thus collected from different sources, the minister announced his decision for a moratorium on *Bt*-brinjal on 9 February 2010, a day before the date earlier fixed for the announcement. In order to strengthen the decision and to deal with similar cases in future, the name of GEAC was also changed from 'Genetic Engineering Approval Committee' to 'Genetic Engineering Appraisal Committee', thus in a way withdrawing the powers of approval from this regulatory body.

The moratorium on *Bt*-brinjal announced by MoEF had a mixed reaction, the civil society advocacy groups appreciating this decision, but developers and majority of the scientific community considering it unfortunate. The report of the MoEF, which was the basis of indefinite moratorium on *Bt*-brinjal, was reviewed by Kameswara Rao[31], who believed that the order of MoEF was not based on science, but was politically motivated; this view is shared by majority of the scientific community, although MoEF and many NGOs may disagree. Several commentaries on GM crops in general, and on *Bt*-brinjal in particular (both for and against), have also appeared in the columns of *Current Science*[32–38]. The diverse opinions and views which have been expressed with respect to the utility of *Bt*-brinjal for the farmers and consumers in India, and also with respect to whether or not the moratorium on *Bt*-brinjal should be lifted, have been collated by Yadugiri[39].

In an interview to *Current Science*[40], Jairam Ramesh also admitted that he had a bias against GM crops, and that he would have swallowed his biases, if there was an overwhelming view of the scientists and the states in favour of *Bt*-brinjal. In this interview, he also mentioned three issues, namely safety, acceptability and seed control[40]. As we know, the question of safety was examined by RCGM and EC-II to the satisfaction of GEAC, but their findings seem to have been questioned by the minister, while taking the decision for a moratorium. The process of assessing the acceptability followed by the minister was also not flawless, since the audience to whom the question of acceptability was addressed did not have full knowledge either about the process or the product; they were instead being constantly fed with biased information that was not based on science. The only issue then left pertains to seed control, and for this we need to compare *Bt*-brinjal with *Bt*-cotton, where the seed is now being controlled by a number of Indian seed companies, although a major part is still controlled by Monsanto, which is the most important company controlling the biotech seed market in India. Despite this, it may not be appropriate to deprive Indian farmers and the consumers of the benefit of a technology, just because it is dominated by an MNC. If this were to be so, we would not have seen the kind of economic growth that we witnessed in our country during the last 20 years due to economic liberalization (for example, in the auto industry, we would never have the kind of growth we witnessed, if the government had not allowed entry of foreign companies).

Inter-Academy report on GM crops

After the moratorium imposed on *Bt*-brinjal on 9 February 2010, the Minister Jairam Ramesh and Planning Commission member K. Kasturirangan had asked the six national academies to assess the safety and viability of growing biotech crops in the wake of countrywide protests over the approval for *Bt*-brinjal, which was the first biotech food crop that would have been commercialized. The six academies that were involved in the task included are: Indian Academy of Sciences (IASc), Indian National Science Academy (INSA), National Academy of Agricultural Sciences (NAAS), National Academy of Medical Sciences (NAMS), Indian National Academy of Engineering (INAE) and National Academy of Sciences, India (NASI).

A meeting of some selected fellows/scientists from all the six academies, who were experts on the subject of crop breeding and biotech crops, was convened at the INSA premises on 1 June 2010. As many as 46 scientists, most of them fellows from different academies took part in the meeting (including the author of this write-up), where eight formal presentations were made, followed by detailed discussion. An overwhelming support in favour of commercialization of GM crops was witnessed in this

meeting. There were just a few scientists who spoke against the biotech crops, but the opinion of at least some of these scientists could be politically motivated.

An Inter-Academy report jointly prepared by the six academies was made public in September 2010, without either convening another meeting to discuss this report, or first circulating the report among the fellows present at the meeting on 1 June 2010. This report invited adverse comments from many, including CSOs and the academia, since apparently sections of the report were copied from an article earlier written by a NAAS fellow and himself a developer of biotech crops. Jairam Ramesh dismissed this 25-page report, saying that 'it does not appear to be the product of rigorous scientific evaluation'. Therefore, the Academies withdrew their controversial report, revised it, and released their updated report in January 2011. According to some, the updated report was worse than the original report[41]. The report appears to some as one-sided and in favour of the seed companies, but it certainly reflects the majority opinion of the scientific community having nothing at stake and having nothing to do with the seed companies involved in developing *Bt*-brinjal.

Role of science, society and government in DURC/DIRC

In all research activities falling within the definition of dual-use/effect-research, the relationship between science and society becomes important. The research of this kind is always debated amongst the stakeholders, including scientists, businessmen, general public and politicians. This calls for a role of the government to regulate, but not overregulate such research. The provisions of this regulation differ in USA and Europe; in India, we are somewhere in between, but more like Europe, where the merits of biotech crops have largely been overlooked. Let us examine the issue using the examples of the 1975 Asilomar Conference, the recent research on influenza virus (described by some as Asilomar 2), and the case of *Bt*-brinjal, which is currently facing an indefinite moratorium.

In the case of rDNA discussed at the Asilomar Conference (held in 1975), and also in case of the research conducted on influenza virus A/H5N1 (published in 2012), the debate was initiated by the scientists, who themselves cautioned against the possible risks and decided to postpone research or publication of their results. While drawing a contrast between this situation and that of the biotech crops, one would find that while in the case of the rDNA and influenza virus debate, scientists and the government worked together in a responsible manner, in the case of biotech crops, particularly *Bt*-brinjal in India, the government did not take the scientific community into confidence (instead a group of scientists supporting the minister's biased view were picked up). Also, even after the so-called shoddy Inter-Academy report, the government made no further efforts to know the opinion of the majority of scientists, who did not get a chance to see the report before it was released. The scientists would like to ask the government, that if the Inter-Academy report was not a result of rigorous scientific evaluation (as the minister said), why were further efforts not made to get a report with the desired rigorous evaluation? Instead of doing this, the government constituted a Parliamentary Standing Committee, which once again submitted a report against biotech crops.

It has also been recognized that any overregulation of DURC/DIRC may lead to slow growth of useful research, which may be necessary for the country to avoid disasters that may follow if such research is not conducted; these disasters may involve occurrence of pandemic diseases in the field of human healthcare and lack of food and nutritional security in the field of agriculture. The resolution by the US government to allow recent publication of the results of the two studies on influenza virus[7,8], and the deregulation of a number of GM crops earlier are examples of how the government can take necessary action in the interest of the society.

The government has the responsibility to recognize the benefits and compare these benefits with the perceived unknown risks. However, in many such cases, where research is allowed on the basis of balancing benefits and risks, the issue of 'mitigating the risks' is sometimes overlooked and does not receive due attention which it deserves. The US policy on DURC actually calls for a risk assessment and also for the necessary measures for mitigating these risks in consultation with the institution and the scientists involved in conducting this research. It is also recognized that it is difficult to draw a line between acceptable and unacceptable risks, since these risk assessments are often subjective, and made by individuals with different backgrounds, beliefs and opinions[42]. In the case of *Bt*-brinjal, perhaps no effort has been made so far to examine the balance between benefits and risks, and to see if the benefits outweigh the risks, which could perhaps be mitigated through appropriate action.

One of the major problems in the acceptance of GM technology for commercial cultivation is also the ignorance of public (both educated and uneducated) about the technology. Therefore, there is a need of communication programmes through extension workers, newspapers and television to educate the public. Also, it has not been possible to discuss among scientists, whether we should follow the principle of substantial equivalence (as done in USA) or the precautionary principle, which sometimes becomes almost preventive (as done in Europe). According to some, it is unfortunate that the government in India is taking a promotional approach for biotech research, but is using a precautionary/preventive approach in commercializing the same. Unfortunately, some scientists like Pushpa Bhargava and M. S. Swaminathan, whose views are used by the government to support their action of moratorium on *Bt*-brinjal, also recommend the use of precautionatry principle, although a large section of enlightened plant breeders all over the world agree that there is

hardly any difference between a conventionally bred cultivar and a biotech crop. Also, when some scientists like G. Padmanaban and Mahtab S. Bamji suggest for a limited release of *Bt*-brinjal, others like Pushpa Bhargava see the risks involved citing examples of *Parthenium* and water hyacinth[39], which became noxious weeds, without realizing that there is a difference between a crop and a weed, and that a crop is grown by the supplied seed. We know that this seed supply can certainly be stopped through denotification of the variety under section 5 of the Seed Act, 1996. Hundreds of crop varieties that were released for cultivation have been rejected by the farmers, and are not grown now and no seed for these varieties is produced. Therefore, the argument that 'for a plant there is no such thing as a limited release', does not seem to be valid.

Regulatory burden: can it be reduced?

Regulation is the main burden on the developers in terms of time and cost, partly due to the demands of a section of civil society, which can perhaps never be fulfilled (chronic toxicity tests). According to some estimates, the cost of developing the first biotech variety in a crop could approach close to Rs 50 crores (6.8 million Euros) in Europe[43], and the situation in India may not be very different. As in Europe, rules are often framed, which discriminate against biotech crops, rather than those, which facilitate development of biotech crops in the interest of public good. Also, there is no evidence that the biotech crops pose higher level of risk than the conventionally bred cultivars. In view of this, one could think of making the regulatory system to be less stringent and less expensive, thus encouraging the seed companies and the public institutions to spend more energy and effort towards the development of novel biotech crops to meet the food and nutritional demands of the future.

It seems that no experiments have been conducted to demonstrate the manner in which the transferred gene in a biotech crop could become a hazard, although some efforts have been made to suggest harmful effects of biotech crops on the non-target insects or on rats/mice used as human models. Even in these cases, most experiments conducted were later proved to have had inherent flaws, and the results of these experiments could never be verified.

In view of the experience of more than 15 years, the governments in the developing countries like India should now be able to relax some of the regulatory provisions, if no evidence is available about the risks involving these regulatory provisions. For instance, a number of experiments have demonstrated that although pollen transfer from biotech crops does take place, the consequences of this pollen flow, even if followed by hybridization with related or wild species, could not be alarming. Therefore, one could examine whether or not pollen-flow studies are necessary.

The major environmental risks that are generally perceived to be associated with the commercialization of GM crops include the following: (i) adverse effect on non-target organisms; (ii) weediness and invasiveness of GM crop; (iii) transfer of transgene to wild species due to pollen transfer; (iv) development of resistance in insects against *Bt* endotoxin, and in weeds against herbicides and (v) loss of biodiversity and disruption of ecosystem. There are other issues like allergenicity and toxicity on one hand, and social, ethical and economic issues on the other, which may not fall within the jurisdiction of MoEF. However, substantial evidence is now available to suggest that at least some of the environmental risks have no scientific basis, and therefore regulatory tests involving these risks (e.g. pollen transmission) can be dispensed with. But we know that the civil society advocacy groups will never let this happen.

Role of MoEF and MoA in regulation of GM crops

The regulatory system in India is currently managed by three ministries – Ministry of Agriculture (MoA), Ministry of Science and Technology (MoST) and MoEF. However, the final approval for commercial cultivation of biotech crops rests with MoEF, which collates information from RCGM, MEC and ICAR, and issues permission for field trials and finally for commercial cultivation. This appears unusual, because, release of all crop varieties for commercial cultivation after necessary breeding work is under the jurisdiction of MoA. In USA, the issue of environmental impact of a biotech crop is examined by the Environment Protection Agency (EPA), the toxicity and allergenicity aspects of biotech foods are examined by the Food and Drug Administration (FDA) and approval for commercial cultivation is finally granted by the United States Department of Agriculture (USDA). If this is so, why should the authority for final approval for commercial cultivation of GM crops in India rest with MoEF, which should examine only the regulation for environmental risks.

Conclusions

The regulation of DURC/DIRC is important for the scientists, society and government in any country, and requires immediate attention. The recent developments involving research conducted on genetic engineering of influenza virus to study whether or not the virus strain H5N1 can acquire the ability to infect and to become transmissible among mammals, prompted the author to see a contrast between the approach used in USA in dealing with the regulation of this research and the regulation of biotech crops in Europe and India. The contrast became all the more pronounced, in view of the recent report of the Parliamentary Committee Panel on agriculture, which has opposed the introduction of GM food crops, including *Bt*-brinjal. Fortunately, they also recommend a professional evaluation of these developments, their possible causes and consequences by an expert committee of eminent

scientists. When an evaluation is done, there will be questions regarding how to select these eminent scientists who would conduct the evaluation, because those who think and speak against the GM crops are seen to be biased in favour of the civil society groups, that are inherently opposed to biotech crops, and would not like to see any merit in these crops. In contrast, eminent scientists who favour the commercialization of biotech crops are perceived as supporters of MNCs like Monsanto. The only alternative then is to conduct experiments to show that there is merit in biotech crops and if there is any risk, it should be demonstrated through specially designed experiments. Since during the last 16 years, cultivation of biotech crops in 29 countries did not suggest any risk, we should at least change our attitude from 'risk, if not proved harmless' to 'harmless, if not proved risky'. This is necessary, because, it is almost impossible to prove that a product is harmless, except that you can test a product for some of the known risks. But, we know that even products of conventional plant breeding may prove to be harmful, as shown in the case of some potato varieties with toxins, a celery strain which causes skin rashes and certain improved wheat varieties which were shown to cause the coeliac disease. But using these examples, we cannot start subjecting all plant breeding to the same regulatory system, which is being currently used for biotech crops. Unless the government of India takes difficult decisions and allows GM crops to be commercialized (as done earlier in case of the nuclear deal), future generations will hold the present generation responsible for not having done what was expected of them.

1. Wolinetz, C. D., Implementing the new US dual-use policy. *Science*, 2012, **336**, 1525–1527.
2. Berg, P. *et al.*, Potential biohazards of recombinant DNA molecules. *Sci. New Ser.*, 1974, **185**, 303.
3. Berg, P., Baltimore, D., Brenner, S., Robin III, R. O. and Singer, M. F., Asilomar Conference on recombinant DNA molecules. *Science*, 1975, **188**, 991–994.
4. Morens, D. M., Taubenberger, J. K. and Fauci, A. S., The persistent legacy of the 1918 influenza virus A. S., *N. Engl. J. Med.*, 2009, **361**, 225.
5. Guan, Y. *et al.*, H5N1 influenza: a protean pandemic threat. *Proc. Natl. Acad. Sci. USA*, 2004, **101**, 8156.
6. Yen, H.-L. and Peiris, J. S. M., Virology: bird flu in mammals. *Nature*, 2012, **486**, 332–333.
7. Imai, M. *et al.*, Experimental adaptation of an influenza H5NA confers respiratory droplet transmission to a reassortant H5NA/H1N1 virus in ferrets. *Nature*, 2012, **486**, 420–428.
8. Herfst, S. *et al.*, Airborne transmission of influenza A/H5N1 virus between ferrets. *Science*, 2012, **336**, 1534–1541.
9. Yong, E., Controversial study shows how dangerous forms of avian influenza could evolve in the wild. *Nature*, 2012, **485**, 13–14.
10. Enserink, M., Public at last, H5N1 study offers insight into virus's possible path to pandemic. *Science*, 2012, **336**, 1494–1497.
11. Fauci, A. S. and Collins, F. S., Benefits and risks of influenza research: lessons learned. *Science*, 2012, **336**, 1522–1523.
12. Frankel, M. S., Regulating the boundaries of dual-use research. *Science*, 2012, **336**, 1523–1525.
13. Lipsitch, M., Plotkin, J. B., Simonsen, L. and Bloom, B., Evolution, safety, and highly pathogenic influenza viruses. *Science*, 2012, **336**, 1529–1531.
14. Rappuoli, R. and Dormitzer, P. R., Influenza: options to improve pandemic preparation. *Science*, 2012, **336**, 1531–1533.
15. Russel, C. A. *et al.*, The potential for respiratory droplet–transmissible A/H5N1 influenza virus to evolve in a mammalian host. *Science*, 2012, **336**, 1541–1547.
16. Cohen, J., The limits of avian flu studies in ferrets. *Science*, 2012, **335**, 512.
17. Schouten, H. J., Krens, F. A. and Jacobsen, E., Cisgenic plants are similar to traditionally bred plants. *EMBO Rep.*, 2006, **7**, 750–753.
18. Holme, I. B., Dionisio, G., Brinch-Pedersen, H., Wendt, T., Madsen, C. K., Vincze, E. and Holm, P. B., Cisgenic barley with improved phytase activity. *Plant Biotechnol. J.*, 2012, **10**, 237–247.
19. James, C., *Global Status of Commercialized Biotech/GM Crops*, ISAAA Brief No. 43, ISAAA, Ithaca, NY, 2011.
20. USDA, Adoption of Genetically Engineered Crops in the US, 2010; http://www.ers.usda.gov/Data/BiotechCrops
21. http://www.treehugger.com/green-food/usda-approves-monsantos-drought-tolerant-corn.html
22. Lusser, M., Parisi, C., Plan, D. and Rodríguez-Cerezo, E., JRC Technical Report EUR 24760 EN, European Commission Joint Research Centre, Rome, 2011.
23. Lusser, M., Parisi, C., Plan, D. and Rodrigues-Cerezo, E., Deployment of new biotechnologies in plant breeding. *Nature Biotechnol.*, 2012, **30**, 231–239.
24. Kuzma, J. and Kokotovich, A., Renegotiating GM crop regulation. *EMBO Rep.*, 2012, **12**, 883–888.
25. Gruskin, D., Agbiotech 2.0. *Nature Biotechnol.*, 2012, **30**, 211–214.
26. Brooks, G., and Barfoot, P., Global impact of biotech crops: environmental effects, 1996–2010. *GM Crops*, 2012, **3**, 1–9.
27. Brooks, G. and Barfoot, P., The income and production effects of biotech crops globally 1996–2010, *GM Crops* 2012, **4**; Available on the worldwide web at www.landesbioscience.com/journal/gmcrops (in press).
28. Jonas Kathage, J. and Qaim, M., Economic impacts and impact dynamics of *Bt* (*Bacillus thuringiensis*) cotton in India. *Proc. Natl. Acad. Sci. USA*, 2012, **109**, 11652–11656.
29. Council for Social Development (CSD), Study on socio-economic impact assessment of *Bt*-cotton in India. *Farmers Forum*, 2012.
30. Manjunath, T. M., *Bt*-cotton: It is time to stop the false allegations. *Daily News and Analysis* (*DNA*). Wednesday, 4 April 2012.
31. Kameswara Rao, C., *Moratorium on Bt Brinjal: A Review of the Order of the Minister of Environment and Forests, Government of India*. FBAE, Bangalore, 2010.
32. Chowkshi, A. H., To *Bt* or not? *Curr. Sci.*, 2011, **100**, 624–626.
33. Dharmapalan, B., GM crops are not the only solution. *Curr. Sci.*, 2011, **100**, 1119.
34. Bokolial, D., *Bt* brinjal: need for a consensus. *Curr. Sci.*, 2011, **101**, 136–137.
35. Shanmugam, G., The *Bt* brinjal debate. *Curr. Sci.*, 2011, **100**, 147.
36. Padmanaban, G., GM technology in India – is it a quiet burial? *Curr. Sci.*, 2011, **100**, 157–158.
37. Samuels, J. and Shanmugam, G., The *Bt* brinjal – biodiversity issue. *Curr. Sci.*, 2011, **101**, 985–986.
38. Samuels, J., *Bt* brinjal, wild relatives and biodiversity. *Curr. Sci.*, 2011, **100**, 603–604.
39. Yadugiri, V. T., What shall we do with *Bt* brinjal? A debate among scientists. *Curr. Sci.*, 2011, **101**, 472–476.
40. Malhotra, R., Jairam Ramesh (in conversation). *Curr. Sci.*, 2011, **100**, 1610–1612.
41. Jishnu, L., Scientifically invalid. *Down to Earth*, 31 January 2011.
42. Bouvier, N. M., The science of security versus the security of science. *J. Infect. Dis.*, 2012, **205**, 1632.
43. Anon., Agnostic about agriculture. *Nature Biotechnol.*, 2012, **30**, 197.

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