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Review Paper

Biosafety Concerns and Regulatory Framework for Transgenics

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Abstract

The executive environmental release and cultivation of transgenic crop varieties have aroused tremendous safety concerns such as risk to human health, risk to environment, risk to ecology and socioeconomic concerns. Issue regarding human health, toxicity, allergenicity, development of antibiotic resistance, eating foreign DNA etc. are global debate. Development of antibiotic resistance and eating foreign DNA are merely apprehensions and has no scientific basis. Among the environmental biosafety issue, transgene escape from a transgenic crop variety to its nontransgenic counterpart or wild relatives has aroused tremendous debates worldwide. Public acceptance is one of the major hurdles for adaptation of first wave of products of agricultural biotechnology. The role of credible experts in communicating the issue to the public in a realistic and effective manner is mandatory to make the difference. Comprehensive regulatory mechanisms have been evolved for development of Genetically Modified Organisms and rDNA research work by the regulatory authorities.

Keywords: Transgenic, genetically modified organisms, safety concern, transgene.

Introduction

The commencement of genetically engineered crops into the environment affects the food chain and has become highly debatable. The GM crops has reflected the possibility of covering large proportion of the food crops cultivated by growers in the coming future which has pleased some while making others feel unease to acceptance. However transgenic consumption may result to suffer from uncertain reactions, recent reports from the various organizations e.g. National Academies of Science, and various published research work, throws a light on the safety of these products[1]. The arguments mainly revolve around ethics, which are neither universal nor absolute. Controversies keep revolving around transgenic crops including their proponents and opponents both in the society and scientists being viewed with suspicion by many while others see it ethically sound[2].

The genetic nature of plants has been manipulated by farmers for more than ten thousand years, affecting the genetic consistency of most crops without any knowing what is heredity. Farmers have been the plant breeders as well as genetic engineers[3], although until the rediscovery work of Mendel genetics was not known by the people as a part of biological sciences[4]. But now because of the advent of plant breeding in the form of genetic engineering (GE) is there is no longer confinement to be dependent on making crosses [5]. This is becoming a routine to develop transgenic crops in the present time leading towards more sustainable breeding programmes, while raising considerable ethical concerns simultaneously[2]. People today want to get maximum benefits but are reluctant to accept the changing aspects of technologies being applied unless they find it completely risk free. Thus the degree of risk involved plays a major role in social acceptance of genetic engineering and genetically transformed crops [6]. The so-called 'synthetic biology' continuously keeps focuses on the advantages and disadvantages of GM crops and has become a highly debatable and burning issue[7]. In each aspect the GM technology affects safety, trade-related aspects and ethical aspects of consumers, researchers and environmentalists which automatically explain to necessitate the need for implying regulation of GM products[8]. To exploit the huge theoretical as well as probable potential from modern biotechnology applications while simultaneously safeguarding against potential risks, most of the countries have participated ratifying and signing the Convention on Bio Diversity (CBD), Cartagena Protocol and many other regulatory legislations.

The main features of these steps towards safety concerns are being agreed on taking required necessary and appropriate administrative actions and to implement certain obligations to undesirable consequences which may cause risks to human as well as animal health. These countries are also involved in developing National Biosafety Frameworks (NBFs) so that development and utilization of GM products could not be hampered. There may be the compelling economic, social and political issues intending not to use the technology either from the scientific point of view or the environmental safety point of view. However the best approach is to proceed with caution to enforce legal regime[9]. Genetically modified organisms have been quite fascinating to the people. But many concerns seem to be misplaced to plant researchers. GM crops can be used to promote a specific goal if governmental regulation could ensure food and environmental safety.

Genetically Modified (GM) Plant and Global status

Transgenic organisms, also known as Genetically Modified Organisms (GMO), are generally produced by applying the techniques of genetic engineering or modification of genetic materials of crops in the desired direction [12]. In most cases the main objective is the introduction of a new trait which is not available naturally in the species. For example resistance to insects-pests, biotic and abiotic stress or resistance to chemical treatments (e.g. herbicide), or making available a trait which is of pharmaceutical interest. The modification most commonly includes the transfer of gene or region of genome of interest from a different species (bacteria, animal or plant). Sometimes the transfer of artificially synthesized gene is also done into a target plant. The first successful genetic engineering of plant was reported in 1983 when tobacco and tomato were transformed. Though reliable transformation of cereal crops such as rice and maize were not reported until the late 1980s[13], transformation of wheat and barley came only in the mid 1990s[12]. In 2000, transgenic crops were grown on 44.3 million hectares globally. Of this, 23% was maize that had been genetically modified (GM) to possessing insecticidal δ-endotoxins from the soil bacterium *Bacillus thuringiensis* (*Bt*) conferring resistance against European corn borer (*Ostrinia nubilalis*)[14]. In India, conditional clearance was given to Monsanto and Mahyco for commercial planting of the genetically engineered *Bacillus thuringiensis* (Bt.) cotton in four states of southern and central India[15]. In 2002, 58.7 million hectares of GM crops were grown worldwide with two thirds in the US. The global share of transgenic crops is already considerable; 36% of all soybean, 16% of cotton, 11% of oilseed rape and 7% of maize was transgenic in 2000[14]. Though the industries promoting transgenic food crops and products are required to assess the potential environmental hazards and health consequences of their products, the results seem to be not much effective[16].

Biosafety Concerns and Popular issues

Human hunger and Transgenics: Transgenics have served enormously to overcome human hunger. It is required for a successful adoption of transgenics that what are the probable results arising by the adoption of the technology and how this can contribute to sustainable farming practices[17]. Furthermore, transgenic research is much popular among chemical companies which are mainly profit oriented and conduct research directed towards chemically dependent crop varieties[18] and value-added products rather than staples[19]. For them who can afford the technology believe that the agricultural biotechnology can potentially contribute to sustain food production while for others it promises disaster and is misdirected[20]. While some stand with the perception that in less developed countries GE can banish malnutrition and can cause increased food production[21], whereas some are of the opinion that GE will adversely affect the conventional farming in poorer countries and jeopardise smallholder and marginal farming[22]. Thus the ambiguous and wide ranges of perspective on the probable impact of transgenic crops have significant impact on food production and food security issues[2]. Seeing variety of views from different aspects would bring different results and decisions. In this regard it is quite essential that the production of transgenic food should be more critically analysed because its positive aspects which can potentially prove beneficial to the developing countries cannot be ignored.

Gene flow: The movement of genes between genomes of species or between environments is termed gene flow[23]. However, from the biotechnology point of view gene flow is the possibility that GM crops can hybridize with other related species and their wild relatives which leads to the transfer of the transgenes from the GM crops to their wild counterparts[26]. Engineered genes i.e. "transgenes" from GM crops might escape and be incorporated into wild populations[24] affecting the genetic consequences of advancing generations. Studies with transgenic herbicide-tolerant rapeseed (*Brassica napus*) in the UK, showed that the gene flow rates through cross pollination ranged between 0.0156% and 0.0038% at 200 m and 400 m, respectively[25]. On one hand agro-biotechnology has the potential to introduce the trait of interest, on the other hand it also includes the risks of genetic movement of genes that otherwise would not exist in plants.

New Weeds: Most of the genetic transformation now a day is being done for herbicide tolerance or insect resistance which is beneficial to protect our crops. However gene flow due to cross pollination for the traits involving resistance can result in development of tolerant/resistant weeds that are difficult to eradicate[27]. The development of resistance in organisms naturally is a long term evolutionary process but incorporating resistance gene through cross pollination among the compatible genomes could speed up this process considerably[27]. Transgenes might lead to the "superweed" evolution that confers a competitive benefit to the GM crop species' wild relatives. As a result our aim to develop crops resistant to specific chemical or herbicide or insecticide might disrupt the natural ecosystems. For example, if a transgene that confers pest or herbicide resistance is incorporated into a weedy relative of the GM crop, then the transgene would contribute to the evolution of increased weediness[28].

Threat to Genetic Diversity: A plant acquiring insect or disease resistance genes will have more chances to become popular within a short time because of its enhanced fitness and preferential selection. This selection results in a shift in the original population structure[29]. The selection would affect not only the concerned locus in which the wild-type alleles would be lost but also other loci that are closely linked to the fixed new allele[27] leading to a final danger of "genetic erosion," a situation where the affected gene become quite rare with severe chances of being disappeared from the natural genetic pool of the population[30]. This reduced genetic diversity results in response to the GM organisms when farmers restrict themselves to a few popularly grown varieties/crops[31].

Antibiotic resistant: Horizontal gene transfer (HGT) is quite rare[32], though documentation through evolutionary timescale gives evidences of HGT[33]. However, even its chance occurrence may have significant health and ecological impacts thus a focus of attention for biosafety consideration is the possible consequences of horizontal gene transfer[34, 35]. The possibility of HGT between bacteria and plants in either the soil or gut has been seen as a hazard associated with transgenic plants, particularly when this is related to the possible transfer of genes encoding antibiotic resistance. The thus the level of significance of this concern as a risk depends on the likelihood of horizontal gene transfer and the magnitude of associated adverse outcome[36].

Health concerns: The antibiotic resistance marker genes generally used for the screening purposes of transgenic plants and organisms. But their effect on human health should also be ascertained beforehand to assure the critical level[11]. In a press release, Gay and Gillespe[38] stated: the contribution that recombinant bacteria might make is so small that antibiotic resistance markers do not pose a substantial risk to human health, because the contribution made towards antibiotic resistance by GM plants quite negligible compared to the antibiotic prescription generally given in clinical and pharmaceutical practice[10]. However health benefits can also not be ignored, especially when we talk about reduced pesticide consumption in residual form in the food products. Some of the health benefits have been obtained in the form of biofortification i.e. augmented specific nutrients. One example is Golden rice with increased the availability of vitamin A[6]. But Mannion and Morse have argued that still many gaps exist even at the cellular level because of the incomplete knowledge of how genes govern their expression. Transgenic soybean expressing allergenic seed storage protein from Brazil nut was reported to retain the allergenicity. The issue was so intense that it was withdrawn from release subsequently[49]. Another example includes development of a genetically engineered pea expressing the "α-amylase inhibitor-1" protein from beans. It was also found to contain protein that could invoke an immune response[50]. Hence no guarantees can be provide from scientists and plant researchers that a variety produced using GM process will be of completely free from all the negative impacts on environment or human health. Therefore, the expression of the recombinant protein needs to be critically and carefully assessed by all means and from each aspect including the most important ones like health, allergenicity, toxicity etc[48].

Impact on non-target organisms: It is feared that the toxins produced by genetically engineered resistant plants may adversely influence non-target insect species which either live foraging on the toxin carrying plants or prey on insects that forage on such plants[47]. Another concern on impacts of biotechnology is the probable harm of GM crops and their seeds to other, beneficial non-target organisms[40]. A report on the harmful effects on the monarch butterfly of maize genetically modified to express insecticidal δ-endotoxins from the soil bacterium *Bacillus thuringiensis* (Bt) caused much public interest. However ecological studies conducted subsequently to evaluate the impact of pollen from genetically modified crops to quantify the risks. The results showed that the large-scale commercial cultivation of Bt–maize hybrids did not pose a risk of significant effect to the monarch butterfly population. Further studies also demonstrated that Bt-expressing crops posed little risk to other nontarget insects, including beneficial insects like natural enemies and pollinators.

Traditional Breeding Compared to Transgenic Technology: Conventional breeding programme has been an integrated part of varietal development and has contributed hugely in improvement of crop grain production. Moreover it provides inclusion of all the newly arriving plant improvement techniques and assists new approaches such as transgenic varieties that have the potential introduce traits of interest from different crop variety or different plant species. However traditional plant breeding methods are time consuming to generate improved varieties because of the crossing and re-cross plants over several generations and keeping eye for traits considered advantageous. Once a potential variety is developed the new variety must be evaluated under different environmental conditions to see whether the cross introduced any disadvantageous traits, if any. But the advantage of transgenic technology is that it allows introducing a gene of interest or clustering of genes for required traits and evaluating its effect in early generations. Simultaneously it is also possible to ascertain the presence of undesirable gene introduced at the same time. Thus, transgenic technology can be used to complement the potential of traditional plant breeding to produce quality crops with higher precision. In addition, transgenic technology is not limited to gene transfer from same species but can introduce traits from other species. There are many transgenic crops exhibiting advantage of expressing herbicide or pesticide resistance genes that make the crop tolerant.

Trade Dilemmas: The conservation of agrobiodiversity is worldwide issue for the present era. Any threat associated with biodiversity need to be handled with extra care because of the ease with which plant materials can cross national boundaries, the common example being air-borne pollen. In this regard international agreements about the movement of plant materials are of high relevance to the regulation of agro-biotechnology for the nations[9]. Weak and faulty regulatory systems in developing nations are the drawbacks which allow international agribusinesses and industries to promote genetic engineering technology without considering its impacts[37]. Both the international as well as individual national governmental organizations need to function in a coordinated way so that the challenges for this aspect could be handled with an effective approach because it is an interdisciplinary issue spanning "trade, health, environment, intellectual property and agriculture"[38]. GM crops are not universally accepted throughout the international market. Some organizations such as European Union (EU) have restricted the import of crops with inserted genes, citing concerns about the environment, ecology and human health[39].

Consumer acceptance and regulatory uncertainty: The safety assessment of GMOs is very extensive. It includes the evaluation of substantial differences between GM crops and their non-GM counterparts, molecular characterisation, toxicity and allergenicity studies and the assessment of the environmental impacts and unintended effects[42]. There is reasonable evidence that consumers are more comfortable with the use of genes from within the same species than transgenes originating from organisms such as bacteria[43]. Likewise acceptance by the scientific community will depend on the classification under the GMO legislation. Crops obtained by the new plant breeding techniques not yet commercialised and therefore their economic impact is not known. Therefore, the legal status of the new plant breeding techniques will determine if they will be used only in specific projects or extensively by scientific community[42].

Components involved in risk analysis

Risk assessment: The risks involved or the criticizing concerns need to be carefully analysed before making any use of biotechnological aspects so that the anticipated risks can be minimize. A prior estimation of the degree and rate of transgene escape will help to estimate the risk involved. No technology can make progress unless adopted by the target audience. Thus adequate adoption measures to mitigating the amount of risks involved need to be analysed. The kind of measures to be undertaken will be determined by the severity level to minimise the risk level. Through assessment should be conducted at grower, producer, processing, and marketing including adoption levels [10]. Molecular breeders must ensure that the markers do not code for any toxin of considerable danger to consumer health, for which it is essential to undertake assessment studies to determining gene flow [11].

Risk management : Katia *et al* [44] defined risk management as "the process, distinct from risk assessment, of weighing policy alternatives, in consultation with all interested parties, considering risk assessment and other factors relevant for the health protection of consumers and for the promotion of fair trade practice, and, if needed, selecting appropriate prevention and control options." The Framework principles of risk management should affirm the use of science-based safety assessments and management with the goals of protecting environment, ecology, human and animal health, while contributing to the prosperity and well-being of consumers. The approach should also guide one to create an enabling environment for biotechnology that strikes a balance between the necessary cautions in regulation while still allowing innovation to precede[36].

Risk communication: Risk communication is also considered as part of the overall risk analysis. Risk communication is defined as "the interactive exchange of information and opinions throughout the risk analysis process concerning risks, risk related factors and risk perceptions, among risk assessors, risk managers, consumers, industry, the academic community and other interested parties, including the explanation of risk assessment findings and the basis of risk management decisions[44]." Mayer has stated in his article "it too late to keep the genie in its bottle" [45]. Research into genetic engineering will continue despite its bad or good impacts but still transgenics are being produced in enormously touching every kind of crop, food, drug and industry. Such changes should have reliable communication regarding the sufficient information from researchers, policy makers, industries and the government[2]. One of the strategies to be of effective use could be the increased participation from public in agricultural research and planning of programmes from different perspectives in the future [46]. The regulatory framework should communicate clear and transparent information requirements for the risk assessment to applicants and stakeholders. Clear communication of these requirements will enhance public confidence in the robustness of the risk assessment, assure that applicants have clear expectations, assure equal treatment for all applicants and reduce delays delivering new technologies into the marketplace[36].

Regulatory Framework

The legislative measures being framed now-a-days aim to safeguard the nation's agricultural diversity and ecosystems resources from the unknown consequences associated with genetically engineered crops. Strong enforcement mechanisms can improve implementation of these regulations by implementing a centralized regulatory authority and strengthening the complementary requirements to bridge the regulatory gaps [9]. In this regard many biosafety guidelines to conduct research and apply biotechnology and genetic engineering have been evolved by the Asia-Pacific region. These regulations also take care of the transboundary movement of genetically modified (GM) crops and their products. Harmonization of each and every regulation at the regional, national as well as international level to building capacities are critical for the coordinated implementation and generation of the benefits of biotechnology to farmers, researchers and consumers[51]. There are various organizations which vigilantly take account of the activities related to genetically engineered crops. For example, ICGEB (International Centre for Genetic Engineering and Biotechnology) focuses on training and research in biotechnology and molecular biology. It also ensures developing countries to make safer use of biotechnological aspects. Likewise IFPRI (International Food Policy Research Institute) harmonizes research implications of genetic engineering technologies and policy for to alleviate poverty in countries under development. CAMBIA (Centre for Application of Molecular Biology in International Agriculture) has been commissioned by most of the developing nations to develop a database aiming at indicating the technology ownership, an important issue determining whether scientists have "freedom to operate" in manipulation of certain crops and germplasm[13]. An information initiative of UNIDO (United Nations International Development Organization) named as BINAS (Biotechnology Information Network and Advisory Service) serves as a centre for disseminating information of biotechnology laws and regulations. For the fulfilment of biosafety regulations in the concerned countries, the Global Environment Facility of the United Nations Environment Programme (UNEP-GEF) has supported these nations since 2001 to develop their own National Biosafety Frameworks (NBFs). NBF is a "combination of policy, legal, administrative and technical instruments that are developed to ensure an adequate level of protection in the field of safe transfer, handling and use of LMOs (Living Modified Organisms) resulting from modern biotechnology that may have adverse effect on the conservation and sustainable use of biological diversity taking into account risks to human health" [52]. The Food and Agriculture Organization of the United Nations (FAO) addresses requests for assistance from member governments for strengthening national biosafety systems, including thorough development and implementation of regulations, training of personnel of regulatory bodies in risk assessment and detection of genetically modified organisms (GMOs), upgrading infrastructure, and improving communication and public participation in biosafety decision making[52]. To date, numerous protocols have been developed to deal with the regulatory issue of regulation at different levels. The Cartagena protocol on biosafety is the global treaty that reaffirms and incorporates the handy, safe and precautionary approach to genetic manipulation and biotechnology. It promotes the uptake of GM technology and controlled adoption and has various provisions specifically addressing the safety concerns of consumers and the society. To enhance the benefit exploitation from the modern biotechnology while safeguarding users and consumers against potential risks, most of Asian as well as African countries have ratified and signed the Convention on Biological Diversity as well as the Cartagena Protocol on Biosafety[8]. The continuing need for expert bodies is becoming highly important to account for the regulatory issues to authorities on genetic modification applications for approval of new planting material and genetically engineered foods. The basic need of such regulatory bodies is to include highly skilled experts and independent but effective decisions along with reliable acquaintance of means, laws and authority to conduct vigorous analysis of any issue which according to them should be critically investigated.

Conclusion

Evidences clearly reveal that, the acreage of transgenic crops is increasing day by day and will play a major role in coming future. This technology has vast opportunities to sustain agriculture in terms of food and nutritional security. However the perspectives are quite controversial and require stringent policies to be undertaken by the regulatory authorities and government for the release of transgenic crop varieties, to assure human health and environment safety.

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