Genetically Modified Cereal Crops Regulation Policies

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Abstract

The history of crop genetic manipulation through conventional breeding (artificial selection and selective breeding) dates back to more than 10,000 years. To feed the intense growing population, conventional breeding is unsuitable due to time, money consumption, and lack of desirable traits in plant genetic pool. The introduction of biotechnology in the late twentieth century and the start of the twenty-first century revolutionized modern agriculture by introducing the unavailable desired traits from other sources. The adaptation of genetically modified (GM) crops may create many socio-economic, food, and sustainability opportunities for both farmer ecosystem and farmers. In the last two decades GM crop adaptation increased due to its ability to multiply the quality agricultural productivity. Worldwide during 2017, 30% of canola, 80% of cotton, 32% of maize, and 77% of GM soybean were cultivated. Globally, 26 countries (21 developing and 5 industrialized countries) planted 191.7 million hectares of biotech crops. Furthermore, 43 other countries have formally cultivated GM crops to measure the utilization of GM crops. Despite the above facts a huge gap exists in both rapid acceptance of GM crops by farmers in many countries and for food, feeds, and limited acceptance by consumers in global market. These facts also characterized the various opinions of consumers. The significant factors influencing consumer's attitudes are the awareness of benefit and risk, knowledge and trust, and personal values. GM crops have sparked tremendous public outrage, particularly on the rising concerns over GM food labelling, prompting the government to withdraw Bt brinjal from India. The increasing GM crop

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cultivation has augmented a wide range of distresses with respect to environmental, socio-economic, and food safety issues. In this chapter, we explained the present status of GM crops research, regulatory framework, and challenges involved in GM research globally.

Keywords

Cereal crops · Genetic modification · Food policy · Transgene

13.1 Introduction

Plants are the most important resource for life as they provide about 90 and 80 percent of calories and protein, respectively, to the global human population. Furthermore, the plants also provide foods directly or indirectly to animals. About 3000 plant species were being cultivated for food purposes by human, but presently total global population mainly relies upon 20 species of crop for nutritional requirements of which 50 percent is shared by eight crop species (Krishna et al. 2019). Minerals and vitamins are obtained from 30 species (fruit and vegetables). As per estimation, the earth can feed 15 billion strict vegetarians or 5 billion mixed diet population but the world total population by 2050 will reach nearly 10 billion. Hence global agriculture is a major challenge to feed and nourish the increasing global population. The world food security status, i.e., the equilibrium between increasing food requirement of the world population and worldwide agricultural output, associated with inconsistencies between supply and demand at the regional, national, and local scales is disturbing (Ingram 2011). It has perceptibly compounded during the ongoing decades, finishing as of late in the 2008 nourishment emergency. It is basic to take note that in mid-2011, nourishment costs were back to their statures of the center of the 2008 emergency (FAO 2011). This is because of abiotic (drought, heat, salt, water logging, etc.) and biotic (virus, bacteria, fungi, insect, and weeds) stresses which potentially hampers the agricultural productivity and quality in natural ecosystem. As conventional breeding procedures were unable to overcome these biotic and abiotic stresses, genetic modifications of crops were initiated (Krishna et al. 2019). Twenty-first century is the era of biotechnology, which deals with the genetic modification (GM) of genetic materials in living organisms, thereby achieving specific functions (Raman 2017; Zhang et al. 2016). Roughly 10,000 years ago, most basic theory of adaptation for domestication and consumption of plants was reported, where our predecessors often selected superior parents to manipulate the genetic material in living organisms, enabling them to perform specific functions which were collectively termed as “selective breeding” and “artificial selection” by Darwin. Although recombinant DNA technology first emerged in the 1960s, the basic principle of recombination was discovered many years earlier. After this discovery of transferable nature of the genetic material between different species in 1946, double helical structure of DNA and the concept of central dogma by Watson and Crick were reported in 1954. Consequently, Boyer and Cohen in 1973 made the world's first genetically modified organism using restriction endonucleases and DNA ligase, commonly referred to as "molecular scissors and glue" that allowed the direct modification of the genome. These advances allowed scientist to manipulate the genetic material of the organism and induce different effects. Rudolf Jaenisch in 1974 created the first genetically modified animal (mouse), while in 1983 first genetically modified plant (antibiotic resistant tobacco) was produced. In 1992, transgenic tobacco for virus resistance was first commercialized in China. Later in 1994, first genetically modified food, Flavr Savr tomato (Calgene, USA) was approved for human consumption. Antisense technology was used in the modification allowing the tomato to delay ripening after picking as the polygalacturonase enzyme production got hampered. Subsequently, few transgenic crops like canola with modified oil composition (Calgene), *Bacillus thuringiensis* (*Bt*) corn (Ciba-Geigy), bromoxynil resistant cotton (Calgene), *Bt* cotton (Monsanto), *Bt* potatoes (Monsanto), glyphosate resistant soybeans (Monsanto), virus-resistant squash (Asgrow), and delayed ripening tomatoes (DNAP, Zeneca/Peto, and Monsanto) received marketing approval in 1995 (James 2011). Up till 1996, nearly 35 approvals were granted for commercial production of 8 transgenic crops and one flower crop (carnation) with 8 different traits in 6 countries (James 1996). After two decades of commercialization of biotech crops, nearly 70 countries covering 191.7 million hectares area have adopted this technology by 2018, thereby making it fastest adopted crop technology in the history of modern agriculture (ISAAA 2018). As of 2019, the USA leads the list of countries for commercial production of genetically modified crops. Presently, GM crops like canola, corn, carrots, cantaloupe, cotton, tomatoes, potatoes, brinjal, soybean, strawberries, lettuce, etc. are easily available in the market. Furthermore, the GM products like medicines, vaccines, foods, feeds, and fibers are currently in the pipeline (Bawa and Anilakumar 2013; Zhang et al. 2016). With the advent of biotech crops, global food crop production has increased by >370 million tonnes from a relatively smaller acreage (Zhang et al. 2016). Furthermore, GM crops have been beneficial to both economy and the environment. As referenced before, these biotech crops pose less impact on the environment, bringing about expansion in species diversity. Therefore, it is obvious that GM crops have been recommended by various agricultural scientists, growers, and most environmentalists worldwide. However, questions related to safety and efficacy have been raised during their advancements. More precisely, the GM seed industry has been plagued with several issues related to human health and insect resistance which truly dilute their beneficial effects. Besides, lack of clear understanding and knowledge of GM technologies, safety studies, and mistrust regarding GMOs have only aggravated the problems. As the result, many countries, particularly the European Union and Middle East have either imposed partial or full restrictions on GM crops. Hence, GM crops are still being one of the hottest topics of debate at public and policymaking levels. Despite the mistrust regarding GMOs still prevails in society, why do scientists often recommend incorporation of transgenic crops into conventional agriculture?

13.2 Need of Transgenic Food Crops

Agriculture sector alone contributes a large share of the GDP which is estimated at US$ 3.2 trillion worldwide and also generates employment in both developing and underdeveloped nations (World Bank 2017). For example: agriculture contributes only 1.4% to the GDP and engages nearly 1.62% of the workforce in USA, whereas it is 18.6% of the GDP involving 50% of the workforce in the developing countries of South Asia (Nayar 2011). Although agriculture industry has contributed much towards the GDP and employment generation with 19% of the world's population, it is projected to suffer significant setbacks by 2050 due to the burgeoning population, pest resistance, and depletion of natural resources. The details of which are elaborated further in this section.

13.2.1 Population Explosion

According to United Nations report, the current world population of 7.6 billion is expected to reach 9.8 billion in 2050 and further to an estimated 11.2 billion in 2100 (www.un.org). In comparison to 2013, nearly 50% increase in the population is expected by 2050; henceforth, the present agricultural practices alone cannot sustain this burgeoning population and eradicate malnutrition on a global scale. In a recent report by FAO, nearly 653 million people will remain undernourished in 2030, regardless of the significant reduction in global hunger (FAO 2017). Besides, previous studies revealed that the top four global crops (soybean, maize, wheat, and rice) are increasing at 1.0%, 0.9%, 1.6%, and 1.3% each year, respectively, which is less than the required growth rate of 2.4%/year needed to sustain the global population by 2050 (Ray et al. 2013). Further, problems like improved nutritional standards of lower-middle class population and estimated decline in arable land (from 0.242 ha/person in 2016 to 0.18 ha/person in 2050) owing to degradation and accelerated urbanization, rapid population explosion will increase the demand for food resources.

13.2.2 Biotic Stresses in Plants (Pests and Diseases)

Biotic stresses pose major economic losses in agriculture every year. Annually about 20–40% of global crop loss is due to pest alone. In order to combat these crop pest and diseases, an expenditure of approximately $290 m annually is incurred by the agriculture industry (FAO 2017). It is estimated that disease and pest of crop occurrence become more frequent and are expanding 2.7 km per year towards the poles (Bebber et al. 2014), which is noted in Central America as wheat rust and coffee leaf rust outbreaks. This phenomenon is attributed to globalization which has tremendously increased the movement of plant materials, associated pest and disease, vectors, and climate change (FAO 2017). However, integrated pest and disease management techniques had tried to manage crop losses due to these biotic stresses to some extent but are incapable to solve the transboundary crop-demics. For example, Tropical Race-4 (TR4) strains of *Fusarium oxysporum* f.sp. *cubense* (Foc) have significantly crippled the global banana industry by causing Panama disease (or Panama wilt) during early-mid 1990s (Ordonez et al. 2015). Later in 2013 nearly 5900 hectares of bananas in Philippines and >20% of total banana plantations from Mozambique in 2015 were abandoned due to TR4 infestation. Moreover, in terms of economic value, this strain had also caused nearly US$ 388.4 m loss in countries like Taiwan, Malaysia, and Indonesia (ProMusa Organization 2017). Hence, increasing transboundary crop and pest diseases movement has environmental, social, and economic impacts on farmers and threatens food security.

13.2.3 Burden on Natural Resources

The FAO's 2050 estimations propose an estimated shortage of natural resources crop care (FAO 2017). In spite of full agricultural efficiency, unsustainable competition has strengthened because of population growth, industrialization, urbanization, and climate change. Agriculture alone accounts for 80% of all global deforestation. Deforestation is still common for agriculture in tropical and subtropical regions and responsible for seven million hectares loss of natural forests per year during 2000–2010 (FAO 2017). Furthermore, excessive groundwater exploitation for agricultural practices alone accounted for 70% of total water exploitation, which severely depletes naturally occurring water resources in many countries. This has been especially reported in the region of low rainfall, like Central Asia, North Africa, and Middle East where 80–90% of total water exploitation is used for agriculture (FAO 2017). The same trends are estimated to be continuing for the twenty-first century and therefore increase the pressure on natural resources globally.

13.3 GM Crops: The Way out

Globally genetically modified crops provide numerous benefits to the farmers and also are potential enough to cope with major challenges faced by agriculture. Benefit from the global farm income alone is estimated to be $117.6 billion from 1996 to 2013. Wherein the yearly global net income has increased by 34.3% in 2010–2012 (Zhang et al. 2016; Chen and Lin 2013; Brookes and Barfoot 2012). Although GM crops increase the global yield by 22%, it has also drastically reduced the usage of pesticide by 37% and its impact on the environment by 18% (Sibhatu and Qaim 2018; Klümper and Qaim 2014). In order to attain the same yield standards through growing conventional crops, >300 million acres of arable land need to be engaged in the cultivation process which may add to the current environmental and socio-economic problems in agriculture (Zhang et al. 2016). Further the impact of GM crops on the economy can be better understood through the success stories from Australia (GM canola) and India (GM cotton) (Brookes and Barfoot 2014).

13.4 GM Cereal Crops and Food Security

The world's population is expected to increase from 7.7 billion to 9.7 billion in 2050, owing to 34% hike during the next 30 years as per the United Nations report 2019. Due to urbanization, population explosion will occur mainly in developing countries, wherein 70% of the world's population will be urban as compared to present day urban population of 49%. Against the background of diminishing natural resource, the immediate priority in global agriculture is to increase the productivity to ensure sufficient availability of food and other raw materials for a growing population (Von Braun 2007). Though burgeoning population has always instilled pressure on food production, our agricultural systems have been strengthened to mitigate food insufficiency through various technological interventions. Cereals are the basic source of food energy (56%) and protein consumed (50%) on earth (Krishna et al. 2019; Zhang et al. 2016). In order to meet the requirements of massive population, global food production must increase by 70% indicating two-fold increase in cereal production from the same available resources (Raman 2017). In modern-day agriculture, transgenic plants play an integral part in ensuing difficulty in differentiating the transgenics from its counterparts in some regions. The genetic transformation of crop plants based on recombinant DNA technology during the early 1980s has enabled breeders to transfer novel gene(s) across species boundaries, unlike conventional breeding. Genetically modified (GM) traits can be distinguished into three categories: (1) First-generation GM crops involve improved agronomic traits (resistance to pests and diseases); (2) Second-generation GM crops involve enhanced quality traits (higher nutrient contents of food products); and (3) Third-generation GM crops involve plants designed to produce special substances for pharmaceutical or industrial purposes. At present, only a few first-generation technologies have been commercialized, of which the dominant being herbicide tolerance (HT) in soybeans, which made up 81% of the global GM crop area in 2010. Since the inception biotech crops, about 148 million ha of GM crops have been grown in 29 countries, signifying 10% of 1.5 billion hectares of cropland in the world (https://www.isaaa.org/resources/publications/briefs/55/default.asp). As far as the area of GM crops is concerned, there is an unprecedented 100-fold increase from 1.7 million hectares in 1996 to 170 million hectares in 2012 (Osmond and Colombo 2019; Bawa and Anilakumar 2013), thus making it the fastest adopted agricultural technology of the recent past.

The concept of integrated pest management (IPM) appeared in the 1970s, when the negative impact on the environment and human health was evident due to injudicious use of chemical pesticides. The indirect (preventive) crop protection practices act as the basis of IPM module, which mainly rely on understanding the ecosystem including the crop, pest, and natural enemy biology and use of optimized farming practices to manage pests. Host plant resistance, either developed through conventional breeding or genetic engineering is the keystone of IPM and also complements the other pest management practices. Most GM crops provide tolerance to herbicides (like glyphosate, dicamba, or 2–4 D), insect pests (like moths, flies, or beetles), or a combination of both traits. *Bt* crop cultivation reduces the use of chemical insecticides and thus provides environmental and economic benefits leading to sustainable agricultural production. The concept of using *Bt* genes was not novel as *Bt* formulations (like Dipel, Foil) were already been commercially exploited for more than four decades to control insect pest in particular Lepidoptera (Cannon 1996). *Bt* toxins exhibit high level of species-specificity against insect pests belonging to the order Lepidoptera, Diptera, and Coleoptera, without affecting predators and other beneficial insects (World Bank 2017; Nayar et al. 2012).

Genetically engineered crops against insect pests were first commercialized during mid-1990s with the introduction of GM maize, potato, and cotton plants expressing genes encoding the entomocidal δ-endotoxin (including Cry and Cyt toxins) from a Gram positive, spore-forming soil bacterium, *Bacillus thuringiensis* (*Bt*). Bt Cry and Cyt toxins belong to a class of bacterial toxins known as pore-forming toxins (PFT) that are secreted as water-soluble proteins which undergo conformational changes in order to insert into or to translocate across the cell membranes of their host. These PFTs are broadly classified into two main groups: (i) α-helical toxins that include the Cry proteins containing three domains (forms the trans-membrane pore) and (ii) β-barrel toxins that include Cyt proteins (aid in insertion into the membrane) (Parker and Feil 2005; Bravo et al. 2007). The Cry genes are located on plasmids of large molecular weight. Currently, more than 70 classes of Cry genes are described (cry1 the cry70). These endotoxins have been classified as Cry1-Cry69 and Cyt1-Cyt3 and different subgroups depending on their amino acid sequence (http://www.lifesci.sussex.ac.uk/home/Neil_Crickmore/Bt/). In most commercial crop varieties, these Cry proteins are usually expressed in their active forms, whereas in biopesticide formulations these Cry proteins are present as protoxins. The relevance of Cry proteins is due to their toxic properties produced after ingestion by insects, which clearly indicated that the plants are to be fed by the insects to get the desired control and their spray forms cannot kill the insects.

13.4.1 Genetically Engineered Cereal Crops against Biotic Stress

Biotic stress is one of the major constraints for plants to release their potential yield. One way to increase the crop yield is to reduce damages caused by biotic stresses such as insects, diseases, and weeds. Pathogens can cause about 10–16% loss of the global harvest (Chakraborty and Newton 2011), whereas insect pest can cause about 14–25% of the total production (DeVilliers and Hoisington 2011). Naturally available gene pool lacks resistance source to biotic stress which limits the plant breeders either to create resistance or introgress this trait into new varieties. Therefore, it is necessary to search for alternative sources of genes in other completely unrelated species of plants or in microbial organisms. Besides, traditional methods are resource- and time-consuming and germplasm dependent (Bidhan et al. 2011). Genetic engineering has transformed plants with foreign genes to enhance their resistance or tolerance against different biotic stresses.

13.4.2 GM Cereals against Insect Pests

Globally, there are very few commercially released GM cereals, including maize and rice being particularly effective against insect pests. The first transgenic cereal crop released commercially was *Bt* maize during 1996 in the USA. Thereafter several countries like Canada, Argentina, Philippines, South Africa, Spain, and France have adopted its commercial cultivation. The area under *Bt* maize has extended to 60.9 million hectares globally, which is 31% of the global maize production in 2019 (https://www.isaaa.org/resources/publications/briefs/55/default.asp). Besides cultivation of *Bt* maize provides both economic and environmental benefits as it decreases the load of active ingredient (*a.i.*) of insecticides by 35% globally (Brooke sand Barfoot, 2010). Reduction in the pesticide load is attributed to coleopteran active *Bt* maize against *Diabroticaspp* which otherwise would have contributed to 25–30% of the global total in maize (James 2003). *Bt* maize has been transformed with either cry1Ab, cry1Ac, or cry9C against *Ostrinia nubilalis* and *Sesamia nonagrioides*, or with cry1F against *Spodoptera frugiperda*, and with cry3Bb, cry34Ab, and cry35Ab against rootworms of the genus *Diabrotica* (James 2012). Similarly, rice (*Oryza sativa* L.) is the staple food crop in several countries all over the world including India, which feeds more than half of the global population. The crop suffers severe yield loss mainly due to the infestation of stem borers and estimated to be 5–10% (Hammond et al. 2004). Use of chemical pesticide is the major method to control insect pests in rice crop. The excessive use of these insecticides not only increased production cost but also pollutes environment and threatens human health. Developing resistant varieties through conventional breeding approaches were not found successful due to the non-availability of resistant source against the pests like striped stem borer (*Chilo suppressalis*), Yellow stem borer (*Scirpophaga incertulas*), and leaf folder (*Cnaphalocrocis medinalis*). However, transgenic crops expressing *Bt* toxins were found to be effective in controlling the pests and have shown some yield advantage too.

Early commercial varieties of insect tolerant GM crops expressed single Cry proteins against lepidopteran pests, for example, *Bt* cotton expressing Cry1Ac (Bollgard I; developed by Monsanto) and *Bt* maize expressing Cry1Ab (developed by Syngenta). Later on, other lepidopteran-active Bt toxins, such as Cry1F and Cry2Ab2, were also introduced and pyramided into a single variety. For instance, Widestrike cotton expresses both Cry1F + Cry1Ac (developed by Dow Agrosciences) and Bollgard II cotton expressing Cry1Ac + Cry2Ab2 (developed by Monsanto). Likewise, Yieldgard maize expressing Cry3Bb1 (developed by Monsanto) was used against coleopteran pests (chrysomelid rootworms). With regard to GM crops, the success story of GM cereals is less perceptible than other economically important crops. Development of transgenics in cereals took a longer period due to lack of techniques for stable transgene production, horizontal gene transfer, and issues regarding its acceptability.

13.4.3 GM Cereals Against Plant Diseases

At the early stages of infection, fungal pathogens usually secrete polygalacturonases (PGs) to degrade pectin, while during the course of evolution, plants have developed strategies to combat it through the production of polygalacturonase-inhibiting proteins (PGIPs) (Oelfose et al. 2006). In cereal crops like wheat, diseases in particular fusarium head blight (FHB) caused by *Fusarium graminearum* result in significant yield loss and mycotoxin (trichothecene and deoxynivalenol-DON) contamination worldwide. Food contamination with DON is a risk for human and animal health. Recently, transgenic wheat expressing a L3 gene (N-terminal fragment of yeast ribosomal protein) showed resistance to Fusarium disease and improved level of DON in transgenic wheat kernel (Di et al. 2010). Likewise, GM wheat with bean PvPGIP2 in their flowers also showed reduced *F. graminearum* infection (Ferrari et al. 2012). Moreover, transgenic wheat and Barley plants expressing bovine lactoferrin gene (a broad-spectrum antimicrobial gene) conferred resistance to head blight (Han et al. 2012). Likewise, in rice diseases such as blast (*Magnaporthe grisea*), bacterial leaf blight (*Xanthomonas oryzae pv. oryzae*) and sheath blight (*Rhizoctonia solani*) are some major constraints for high productivity. GM rice plants expressing wheat puroindoline genes PinA and/or PinB produce puroindolines which reduced the growth of *M. grisea* and *R. solani* by 35–50% in vitro conditions, thereby conferring resistance (Krishnamurthy et al. 2001). Likewise, genes encoding chitinase or 1, 3-glucanase from plants and microbes have been used in developing transgenic rice resistant to fungal pathogens (Fujikawa et al. 2012). In other study, GM rice expressing AtNPR1 showed increased disease resistance against *M. grisea* and *Xanthomonas oryzae pv. oryzae* by priming the expression of salicylic acid-responsive endogenous genes PR1b, PR5, PR10, and PBZ1 (Li et al. 2020; Fitzgerald et al. 2004). Genome sequencing of rice has revealed five NR1-like genes of which three genes, namely OsNPR1, OsNPR2, and OsNPR3 were induced by the infection of *Xanthomonas oryzae* pv. *oryzae* and *M. grisea*. OsNPR1 is the rice orthologue of *Arabidopsis* NPR1 gene; whose overexpression conferred disease resistance to bacterial blight, however enhanced herbivore susceptibility (Chern et al. 2005; Yuan et al. 2007). Another strategy to confer resistance to plants against disease is through activating phytoalexins (part of plant defense mechanisms in some species). Stilbene synthase gene (STS) of Vst1 (a key enzyme phytoalexin biosynthesis in grape) could improve resistance in rice against *Pyricularia oryzae* (Coutos-Thévenot et al. 2001) and in barley against powdery mildew (Liang et al. 2000). More recently, mitogen-activated protein kinase (MAPK) cascade (especially OsMKK6) regulates genes responsible for phytoalexin synthesis in rice in response to UV and blast infestation (Wankhede et al. 2013). Moreover, transgenic rice lines containing OsMKK6 gene showed overexpression of phytoalexins under UV stress.

13.4.4 Genetically Engineered Cereal Crops against Herbicide

In the agroecosystem, weeds reduce crop yield because they compete with the crop for nutrients, water, and light. They occasionally produce allelopathic substances that are toxic to plants and also act as reservoirs for disease inoculum and insect pests during the off-seasons. Yield losses in crops due to weeds were estimated to be approximately AUD 3.3 billion in Australia (Llewellyn et al. 2016), whereas in India it costs over USD 11 billion annually (Gharde et al. 2018). When left unattended, weeds can cause up to 100% yield loss. Several herbicides are available in the market for weed management; however, its efficacy depends on selective or nonselective mode of action. Globally, two nonselective herbicides glyphosate and glufosinate are most widely used. Glyphosate is the nonselective post-emergence herbicide which acts as an analog of enolpyruvate that binds and inhibits the enzyme 5-enolpyruvylshikimate-3-phosphate synthase (EPSPS) involved in shikimate pathway leading to the synthesis of chorismate-derived metabolites including the aromatic amino acids. Inactivating this enzyme by glyphosate would interfere with the growth and kill the weedy plants due to the absence of aromatic amino acids such as tryptophan, tyrosine, and phenylalanine (Steinrücken and Amrhein 1980). Roundup ready was the first transgenic glyphosate resistant corn developed by Monsanto in 1998 (USDA 1997). Subsequently, many commercial cultivars with tolerance to other herbicides were developed such as Liberty Link Corn against glufosinate. Likewise, GM maize against dicamba at pre- and post-emergence crop stages showed tolerance due to dicamba monooxygenase (DMO) enzyme which is linked with chloroplast peptide (CTP) (Cao et al. 2011). Recently, an imidazolinone resistance (IR) XA17 gene was introduced into maize which showed resistance to imazaquin and nicosulfuron herbicides (Menkir et al. 2010). Another mechanism that deactivates glyphosate into a non-toxic N-acetyl glyphosate is by introducing the glyphosate N-acetyltransferase (GAT gene) from *Bacillus licheniformis* to maize (Castle et al. 2004).

Furthermore, stacking of genes in a single cultivar was preferred over GM crops with a single gene for improved insect pest and weed management. For example, GM maize developed by pioneer expressing two Cry genes (Cry34Ab1, Cry35Ab1) pyramided with PAT (phosphinothricin acetyl transferase) genes was found tolerant to insect pests as well as herbicides (Cao et al. 2011). Commercially herbicide tolerant rice plants were developed by targeting either of these three pathways, such as (1) shikimate pathway (Roundup Ready® rice), (2) glutamine biosynthesis pathway (Liberty Link®), and (3) branched chain amino acid synthesis (Clearfield®). Clearfield rice is non-transgenic, whereas Roundup ready and Liberty Link rice are transgenic (Rodenburg and Demont 2009). Likewise, transgenic rice plants with enhanced melatonin levels were developed recently to provide protection against oxidative stress due to herbicide application (Park et al. 2013).

13.4.5 Genetically Engineered Cereal Crops Against Abiotic Stress

Transgenic cereal crops potentially improved the yield under abiotic stresses like drought, salt, cold, and heat. The transgenes from the different sources are transferred to cereal crops aiming to regulate different molecular pathways. Genes responsible for regulating signaling cascade and transcription like *ABF/ABRE* (ABA-responsive element binding factor/ABA-responsive element) *CBF/DREB* (C-repeat-binding factor/dehydration responsive element binding protein), *HSF* (heat shock factor), *MAP* (mitogen-activated protein), phospholipases, and salt oversensitive kinases (Hussain et al. 2011; Shou et al. 2004; Thiery et al. 2004; Qiu et al. 2002) have been transferred in cereals crop and studied thoroughly. DREB genes have been used in transformation of cereal crops especially rice and wheat to increase drought tolerance (Chen et al. 2008). Recently, overexpression of OsDREB2A significantly enhanced drought and salt tolerance of transgenic rice plants (Cui et al. 2011) and overexpression of *ZmDREB2A* with *CaMV35S* or *rd28A* promoter resulted in better tolerance to drought in maize (Qin et al. 2007). The *WRKY* superfamily of plant transcription factors (TFs) has a conserved sequence (*WRKYGQK*) at their N-terminal end (Wu et al. 2008). Transgenic rice expressing OsWRKY11 under control of heat shock protein promoter (HSP101) was shown to survive longer and retain water under a short severe drought treatment than wild type plants (Wu et al. 2009). Regardless of the concerns raised above, the area under commercial cultivation of GM cereal crops is expanding year by year. Seeing the GM cereals production pattern, it may be expected for commercialization of abiotic stress tolerance GM cereal crops in near future.

13.5 Regulation of GM Cereal Crops

The introduction of GM cereal crops sparked debate and piqued public interest in agriculture. As GM cereal crops are consumed as food, feed, and fodder in many countries, multiple regulatory approaches to regulate GM crops have been devised and implemented. However, the key scientific risk element remains same for all regulatory approaches, but the risks and advantage vary significantly by the policy decisions that are influenced by the political and cultural scenario (Smyth and Phillips 2014; McHughen and Smyth 2012). The decision of policymakers is influenced by different factors like tradition of the culture, condition of environment and society, and risk tolerance (Shukla et al. 2018). The policymakers may face pressure from food safety and environmentalist groups, natural crop producers, farmers (large scale), animal husbandry group, animal consumers, global agricultural companies, and other things engage in the chain of complex global food production and distribution (Hicks 2017).

There are many countries which have approved a “process-based” method to regulate GM crops in which modified crops through specific genetic engineering approach are subjected to premarket safety review for environmental and food safety. Some regulation systems for GM crops are beyond the safety of food and environmental protection to tackle economical and social issues, like protection of non-GM crop production, labeling products for consumer information and considering the concern of society and economy. In GM crop regulatory system, a committee first examines the international agreements which have importance to GM crop regulation and then gives illustrations of three countries and European Union (EU) to reveal various methods which may consider for the commercialization of GM crops by national or regional governments (Morris and Spillane 2010).

13.5.1 International Cereal Crop Regulation Frameworks

Internationally, there are limits on international trade agreements due to national product regulation policies of the countries which are parties of the agreements. The WTO (World Trade Organization) agreements and Cartagena Protocol for biosafety protocol are especially followed for the GM crop and food regulation. The GM crop and food safety assessment regulation system of the member countries must be uniform to the WTO principles set in the WTO Agreement on the Application of SPS (Sanitary and Phytosanitary Measures) Agreement (National Academies of Sciences, Engineering, and Medicine 2016). The SPS Agreement regulates measurement of GM crops to protect animals, human health, plant life as well as food safety. The SPS measures scientific fact based evidence except those for which scientific information is not available, in such cases, country may regulate by resolving scientific uncertainty. To encourage similarity in measurement, the SPS Agreement accepts global standards and guidelines set up by CAC (Codex Alimentarius Commission) and other different international organizations. Generally, the guidelines and principles of Codex direct GM foods developer to give information which facilitates regulators to evaluate various risks related to food safety:

- GM plant description (involved crop and genetic modification nature).
- Host plant description and its utilization as food along with cultivation, breeding, and known allergenicity or toxicity problems.
- Gene donor organism’s description including allergenicity or toxicity problems related to them.
- Genetic modifications description consisting of transformation method details, utilized DNA and vector, and any other intermediate host utilized in the process.
- Genetic modification characterization, including inserted DNA copy number, left and right regions of border, DNA sequences expression and impact on host gene expression.
- Assessment of safety, consisting:
  - Substances expressed: Toxicity analysis expressed products from individual genetic events and an ensuring evaluation for toxic compound from donor organisms for accidental transformation. In case of protein, the allergenicity should be analyzed for amino acid sequences.

- Key components composition analysis: An analysis of the host plant key component with GM plants under field trial and natural conditions is closely resembled for large-scale production.
- Metabolite analysis: GM plants metabolite analysis is dissimilar to the original host. If any metabolite is identified, its potential impact on human health must be evaluated.
- Processing of food: Analysis of food processing treatment impacts on metabolites of GM crops. It is needed to assess the potential toxicity of a modified metabolite or protein expressed in GM crops vs non-GM crops.
- Analysis of nutrients: Similar to the compositional evaluation, except that when DNA is inserted, the key nutritional compound is expected to change. In such circumstances, more testing may be required to determine the level of the questioned nutrient and its effects on human health, taking into account typical consumption trends and trait stability in variable environments.

13.5.1.1 USDA Regulation of Pharma Crops

The U.S. Department of Agriculture's Animal and Plant Health Inspection Services (APHIS) is the regulating authority of GM crops established under Plant Protection Act of 2000 (PPA). According to the act "plant pests" are the organisms which cause disease, damage, or injury to plant parts or products, including viruses, bacteria, fungi, and parasitic plants. The generated GM plants are legalized under the (PPA) if they were generated by gene transfer using *Agrobacterium tumefaciens*, which is supposed to be a pest of plant, or DNA transfer from a pest of plant (like terminator gene). USDA controls GM plants either by permission or a notification procedure. Like for the regular Bt crop field trials, viz. Bt cotton and Bt corn, notification procedure is utilized, which are normal formalities. The institution, organization, company, or universities give a notice of APHIS trial and give consent to follow specific rules and regulation set by USDA, and USDA normally signs off. In case of field trial of GM crops having higher risk, like those which are extremely outcrossing or which persist in ground or water for a long period need a permit. The GM crops field trial which produces industrial or pharmaceutical chemicals, a permit is for all time needed. The process of permission may be more or less extensive, needing either an Environmental Impact Statement or an Environmental Assessment.

When an institution, organization, company, or universities decides its desire to commercialize a GM crop and seed of the same for the farmer's cultivation purpose, it can appeal APHIS for deregulated class. This procedure needs submission of risk-assessment details (data) for demonstrating that the crop does not have a plant-pest risk. The appropriate data must be disclosed in public and contain disease susceptibility and insect pests, effects on non-target organisms and beneficial organisms, weediness, and the gene flow risk to wild or weedy relatives. After the incident of ProdiGene 2000, USDA implemented a higher level of scrutiny for the GM crops having higher risk of inherent. As a consequence, GM crops for industrial and pharmaceutical purposes are not suitable for deregulation and must remain under permit even after commercialization. Nevertheless, numerous gaps continue. The present USDA regulatory system does not ensure an in-depth assessment of the environmental impact prior to the planting of pharmaceutical crops. As an alternative, USDA's policy of gene-confinement measures is planned to "minimize" rather than prevention of non-GM crops contamination. In general, USDA is too short-handed to work out sufficient supervision and mostly leaves biotech companies to control themselves. Furthermore, USDA holds the locations of all test fields secret from neighboring farmers and the public, without disclosing the drug or chemical identity being produced, and overlooks biotech companies' pharma crop plantation practices anonymously, without identification.

13.5.1.2 U.S. Regulation of Genetically Modified Crops

The regulation of genetically modified crops in USA is regulated by three different regulatory agencies: viz. EPA (Environmental Protection Agency), FDA (Food and Drug Administration), and USDA (U.S. Department of Agriculture). These three agencies regulate the genetically modified crops from a different point of view with each other (Smyth and Phillips 2014; McHughen and Smyth 2012). EPA is responsible for the regulation of biopesticides like Bt toxins under the FIFRA (Federal Insecticide, Fungicide, and Rodenticide Act) (Ledford 2013). In case of crop developed against insect pest with foreign gene, EPA needs the developing organization to verify the toxin to be expressed in crop for environmental safety and also food safety to insure non-allergic nature of expressed protein1. FDA regulates the safety of GM crops consumed by humans or animals as food and feed. As per the policy in 1992, most GM crops were treated as "substantially equivalent" to non-GM crops by FDA; wherein these GM crops were generally recognized as "Safe" under the FFDCA (Federal Food, Drug, and Cosmetic Act) and does not need prior-market approval. If the expressed protein in edible transgenic crops differs significantly from natural plant proteins in terms of structure, function, or quality and is harmful to humans, the FDA has the authority to impose more stringent standards of Federal Food, Drug, and Cosmetic Act (FFDCA) mandating the premarket approval of biotechnological products.

13.5.1.3 The FDA Consultative Process for GM Crops

FDA set up a willful consultation process in 1997 in collaboration with the developer of GM crops for reviewing the purpose of "substantial equivalence" prior to crop marketing, like assessment of transgene product and plant toxicity and allergenicity. If the results in the food-safety assessment are satisfactory, the FDA notifies the developer that the crop can be marketed (Bonetta 2001).

13.5.2 Regulation of GM Crops in India

In India, Ministry of Environment, Forest and Climate Change (MoEFCC) regulates the GMO experiments, trials, and release under the environment protection act (EPA) 1986. This act has made several rules to solve the environmental issues arising due to hazardous chemicals, hazardous wastes, solid wastes, biomedical wastes, etc. To address the problems associated with microbes and genetic engineering MoEFCC notified the “Rules for manufacture, use/import/export and storage of hazardous microorganisms/genetically engineered organisms or cells, 1989” as per Sections 8 and 25 of EPA, 1986 (Shukla et al. 2018). Sections 8 and 25 deal with the regulation of genetic engineering and gene technology in India (http://geacindia.gov.in/acts-and-rules.aspx). These rules are referred as Rules 1989, which covers all the activities involving GMOs and products thereof including new gene technologies (Kandasamy and Padmavati 2014; Chimata and Bharti 2019). Rules, 1989 defined the term gene technology and genetic engineering as follows: “Gene Technology” means the application of the gene technique called genetic engineering, including self-cloning and deletion as well as cell hybridization. “Genetic engineering” means the technique by which heritable material, which does not usually occur or will not occur naturally in the organism or cell concerned, generated outside the organism or the cell is inserted into said cell or organism. It shall also mean the formation of new combinations of genetic material by incorporation of a cell into a host cell, where they occur naturally (self-cloning) as well as modification of an organism or in a cell by deletion and removal of parts of the heritable material.

These rules were enforced by MoEFCC, Department of Biotechnology (DBT) and state governments through six competent authorities: rDNA Advisory Committee (RDAC), Institutional Biosafety Committee (IBSC), Review Committee on Genetic Manipulation (RCGM), Genetic Engineering Appraisal Committee (GEAC), State Biotechnology Coordination Committee (SBCC), and District Level Committee (DLC). RDAC is constituted by DBT and acts as advisory body on emerging issues on DNA technology. IBSC is set up in each institute included in recombinant DNA research and responsible for following RDNA guidelines in transgenic experiments. RCGM is regulatory body under DBT which involves scientific risk assessment and development of guidelines for GMO research. GEAC is the apex regulatory committee under the MoEFCC and is responsible for final approval for environmental release of GMOs. SBCC and DLC are for monitoring purpose and act as nodal point at state and district level for coordinating GMO related activities (Fig. 13.1). Apart from the Rules of 1989, the following acts are engaged in the regulation of GMOs in India: Plant Quarantine Order, 2003, Biological Diversity Act, 2002, and Food Safety and Standards Act, 2006 (http://in.biosafetyclearinghouse.net/phase2/publications.shtml).

13.5.2.1 Biosafety Assessment Guidelines

GMO regulatory authorities periodically established several guidelines to evaluate the impact of recombinant DNA technology development in the nation (http://geacindia.gov.in/guidelines-and-protocols.aspx). Recombinant DNA Safety Guidelines and Regulations, 1990, categorized recombinant DNA (RDNA) into three categories based on risks and provided guidelines for the measurement of containment in accordance with each risk category. Later, as DNA technology developed in the country, the rules were periodically updated to address the issues that emerged. For instance, updated guidelines for transgenic plant research from 1998, guidelines and standard operating procedures for conducting confined field

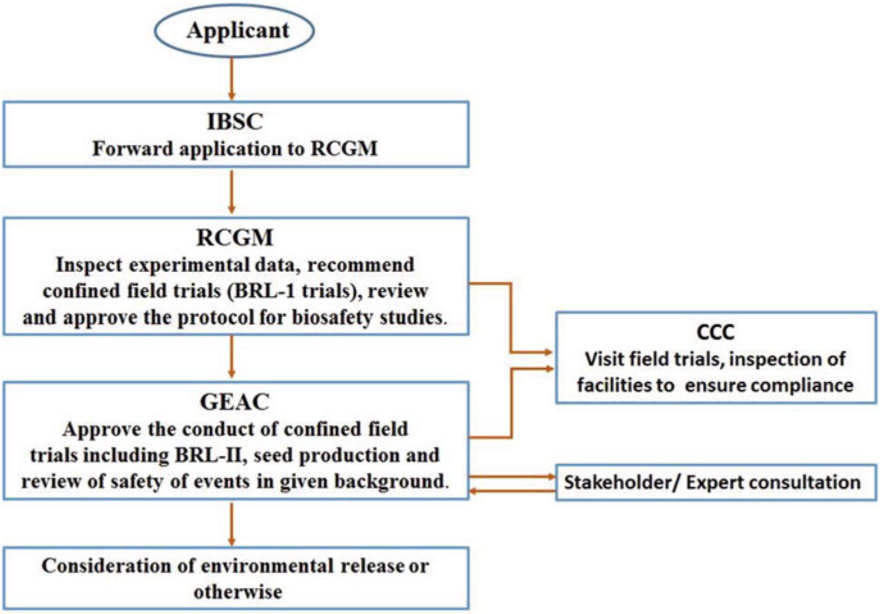

Fig. 13.1 Procedure for approval of confined field trials and environmental release of genetically engineered plants

trials of regulated GE plants from 2008, guidelines for the safety assessment of foods derived from GE plants from 2008, guidelines and a handbook for IBSCs from 2011, and guidelines for the environmental risk of GE plants from 2016 are just a few examples.

Biosafety assessment data has to be generated at various stages of transgenic plant development such as laboratory research, greenhouse studies, field testing, and at environmental release. These data broadly include effect of genetic modification and protein characterization, food and feed safety, environmental safety (http://geacindia.gov.in/resource-documents/biosafety-regulations/guidelinesandprotocols/RiskAnalysisFrameworkforWeb).

13.6 Conclusion

Cereal crops (wheat, paddy, maize, etc.) are globally considered as staple crop. Urbanization and the demand to feed the ever-increasing global population are exerting pressure on the agricultural resources (land, water, and soil nutrients), which have become increasingly scarce. The excessive exploitation of groundwater for irrigation resulted in depletion of groundwater which is also a threat for drinking water in some parts of the world. In contrast, overuse of pesticides and herbicides not only disrupts the agricultural ecosystem but also increases the input required for agriculture, which eventually lowers profits and has a negative impact on public health. In the twenty-first century, biotechnology made it possible to genetically modify cereal crops to have specific traits such biotic and abiotic stress tolerance, and herbicide resistance. In cereal crops many genetically modified plants have been developed and released for commercial cultivation in some countries. Future food security and sustainable agriculture will require the adaption of GM crops with various traits. The acceptance of GM cereal crops around the world is in doubt due to genetic manipulation and the issues it raises. In spite of the fact that most regulatory systems around the world are comparable to one another, synchronising them is still necessary to enable the commercial cultivation and trading of genetically modified crops for the benefit of sustainable agriculture and global food security.

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