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Terminator Technology: Perception and Concerns for Seed Industry

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ABSTRACT

Terminator technology is a genetically switch mechanism that can be triggered off by a specific chemical inducer. As a result, this technology put a ceiling on the illicit use of genetic material either by hampering reproduction or the expression of a particular trait through an inducible molecular mechanism, thus approaching to the rescue of long suffering multinational companies who have been unable to clutch farmers back from their old age practice of brown bagging and breeding seeds. The terminator technology claims to provide various benefits like protection of intellectual property rights, use of newer and more productive varieties, checking of transgene contamination. Despite of these rewards, its cons cannot be put on hold. The potential hazards of terminator technology includes -out crossing threat, reduced choice to farmers in procuring seeds and gag on using last year seeds, control on access and consequent higher costs of research material to breeders, enhanced need for monitoring and regulating GURT technology, undue control and interference of corporate in agriculture. This technology, thus, demands a very thorough investigation and extensive evaluation before terminator technology is given a free ride.

Key words: *terminator technology, intellectual property, seed saving, food security.*

INTRODUCTION

The agricultural research is progressing at a very swift race day by day. The solution for food hunger, ecofriendly agriculture and other related challenges is being pursued by scientists with great vigour. In this regard, the discovery of terminator technology has been very phenomenal.

Terminator technology or genetic use restriction technologies (GURTs) are new technological means invented by biotechnology firms to protect the IPRs of their innovations. Genetic use restriction technologies (GURTs) are the name given to experimental methods, described in a series of recent patent applications and providing specific genetic switch mechanisms that restrict the unauthorized use of genetic material[7] by hampering reproduction (variety-specific V-GURT) or the expression of a trait (trait-specific T-GURT) in a genetically modified plant.

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The biotechnology and seed industry is promoting this technology as a 'biosafety' solution to disguise its true role as a biological means of preventing farmers from saving and re-using proprietary seed. This technology has not yet been commercialized or field tested but tests are currently being conducted in greenhouses in the United States.

TYPES OF GURTS

There are two main classes of GURTs: trait based and variety based GURTs[6,20,25]. Trait based technologies (T-GURTs) regulate the expression of a particular trait; whereas variety based technologies (V-GURTs) restrict the use of an entire variety by blocking its reproduction.

V-GURT:

Variety-GURT (also known as suicide/sterile seed/gene technology, or terminator technology) is designed to control plant fertility or seed development through a genetic process triggered by a chemical inducer that will allow the plant to grow and to form seeds, but will cause the embryo of each of those seeds to produce a cell toxin that will prevent its germination if replanted, thus causing seeds to be sterile and allowing manufacturers to maintain their intellectual property rights and avoid concerns related to GM seed dispersal[17].

T-GURT:

In case of T-GURTs, also considered by some authors as the second generation of V-GURT[9], one or more genes conferring a single trait are switched on or off through application of chemical inducers[20,25]. Therefore, T-GURTs are not intended to affect the viability of seeds, which is in contrast to V-GURTs, which result in sterile seeds. Thus this technology would enable both seed and allied agrochemical corporations to market both proprietary seed variety and component agrochemical inducers that unbolt the value added engineered traits in a proprietary seed. In this way, T-GURTs could enable seed companies to practice price discrimination of a kind.

HISTORY

On March 1998, United States Patent and Trademark Office granted the joint application of United States Department of Agriculture (USDA) and Delta and Pine Land (D&PL) Company of Mississippi and issued the patent for V-GURTs (US Patent 5,723,765) entitled "Control of plant gene expression". Although this patented technology was originally developed for tobacco and cotton, it could potentially be applied to all seed-propagated crops[14]. The patent work was mainly done by Melvin Oliver, a scientist with USDA-ARS in Lubbock, Texas, through cooperative research with D & PL. In accordance with its original intention, in the promotional communications the holders of the patent called this invention 'Technology Protection System' (TPS), whereas in the scientific publications and discussions of international institutions, it was eventually called 'Genetic Use Restriction Technology' with reference to the limitations imposed on its users[17].

Protests were raged worldwide as many saw it as a very disadvantageous and unethical mechanism for poor farmers, especially in developing countries where brown-bagging is a common practice, and as an advantage for multinational companies that would have thus increased the dependence of indigenous and rural communities worldwide on their GM seeds. These objections are borne out by the fact that worldwide, greater than 1 billion people depend on seed saving practice.

In June 1999, as a result of the great opposition to this technology by the public opinion, non governmental organizations and farmers, Zeneca announced that they would not market terminator seeds. In 2000, governments at the UN Convention on a Biodiversity created an "international moratorium" which recommended countries not to approve the technology for field testing or commercial use. As a consequence of the moratorium and of the rising farmers' alarmism, in 2001, the Indian Parliament ratified the 'Protection of plant varieties and farmers' rights act' banning the registration of seeds containing terminator technology. Similarly, in Brazil, prohibited utilization, marketing, registration, patenting and licensing of use restricted genetic technologies[17]. The CBD Moratorium was under attack in January

2006 by 3 governments-Australia, Canada and New Zealand that insisted on "case by case risk assessment" of technology. However due to strong public pressure the case by case risk assessment strategy was rejected and the moratorium was upheld in March, 2006.

RATIONALES BEHIND GURTS

In case of hybrid varieties, there is a built-in protection as the increased vigour is exhibited only in the F_1 seed. Accordingly, farmers are forced to buy hybrid seeds every year. In several self-pollinated crops, on the other hand, there is no such inbuilt protection as the commercially grown cultivars are actually 'pure lines' so that the yield does not decline and harvested seeds can be used for sowing the next crop. In crops for which hybrids are impracticable, the implementation of patents/PBRs is lax particularly in developing countries because of different belief systems, insufficient institutions and legislation, and few incentives for local governments to protect foreign intellectual property rights. Weak enforcement of IPRs has led to a widespread use of farm-saved seeds and emergence of non-licensed seed dealers. The result is that large multinational biotechnology companies are unable to fully capture their innovation rents from the producers who have a "free ride" by using their technologies. In view of these innate difficulties in the implementation of patents/PBRs crops, the termination technology is intended to be used. The utilization of this technology potentially could bring non-hybrid yield increases in line with those of hybrids.

BASIC DESIGN

The general molecular construction, similar for both T- and V-GURTs, provides the use of gene constructs (Figure 1) which code for:

(i) a repressor gene (the gene switch) that is responsive to an external stimulus; (ii) a recombinase gene (the trait activator gene), the expression of which is blocked by the repressor; and (iii) a target gene that produces cell toxin.

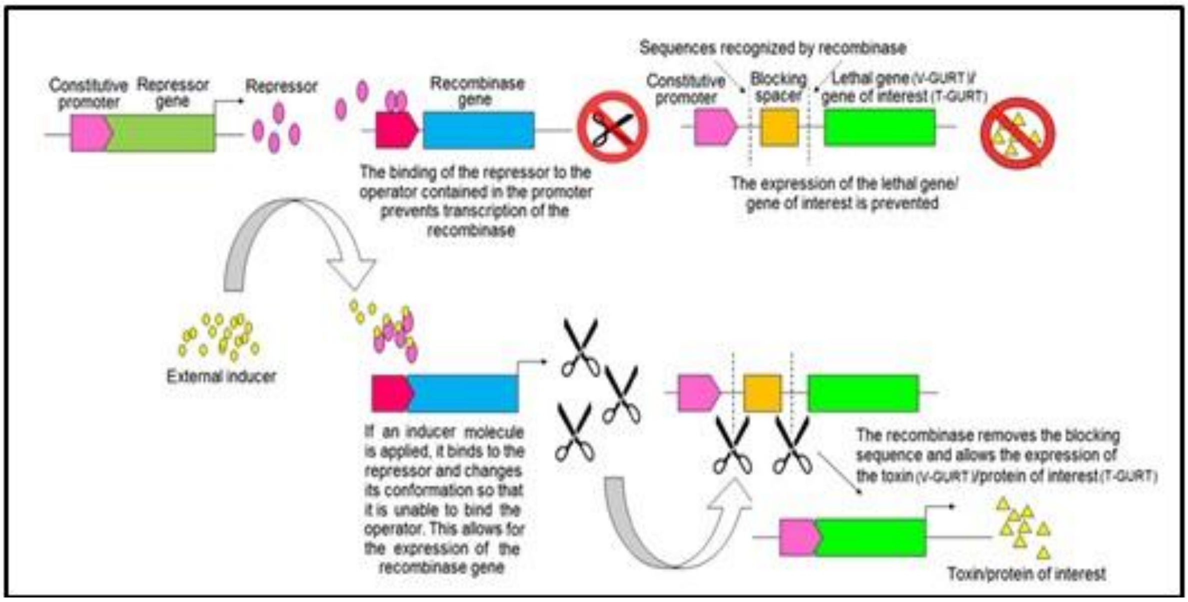

Figure 1: the repressor proteins are normally unable to bind to the pertinent DNA and the inducer is applied to bind the repressor that undergoes a change in its conformation so that it can bind to the DNA and activate transcription. (Lomborda, 2014)

MECHANISM OF V –GURTs

V-GURTs

For V-GURTs, essentially three different restriction mechanisms have been proposed[25]. The first mechanism of action is that described in the patent (U.S. 5,723,765) by the USDA and Delta & Pine Land (nominally the first V-GURT). The patented method is based on a gene that produces a protein that is toxic to the plant and therefore, does not allow the seed to germinate. One such gene indicated in the patent, is ribosomal inactivating protein (RIP) gene, which if expressed, does not allow protein synthesis to take place. The gene is placed under the control of LEA promoter permitting RIP to express only during late embryogenesis, thus affecting only the embryo development. This gene (RIP gene) will not express in the first generation, because its expression is blocked through the use of a spacer or a blocking sequence between the promoter and the lethal RIP gene. On either side of the spacer are placed specific excision sequences that are recognized by a recombinase enzyme (CRE/LOX system from a bacteriophage), whose function is to excise the spacer or the blocking sequence. The 'second' gene encoding recombinase is placed behind another promoter/operator, specific for a repressor encoded by the third gene, which is a repressor gene[11].

Before being sold to the consumer (in most cases, to the farmer), these seeds are exposed to the inducer that inhibits the function of the repressor, which causes transcription of the recombinase gene, which produces Cre that recognizes the Cre blocking sequence in the lox sequence and splices lox from the genome, thus placing the ribosomal inactivating protein under the direct control of the late embryogenesis abundant promoter.. Thus, the seeds purchased by farmers will be able to germinate in the field,. However, the seeds produced in the harvest will be sterile and thus cannot be stored for later cropping. This technology was designed specifically for pure line seed production in self-pollinated crops; the genes introduced into separate transgenic founder lines were then cross-pollinated to provide a genome with the full suite of TPS genes in the target crop[20].

The second mechanism of action of V-GURT is based on a reversed process because it is characterized by the presence of a gene encoding a disrupter protein permanently active in the seed, which makes it sterile. The gene promoter is under the control of a specific operator sequence. A further repressor protein, whose gene is under control of a chemically inducible promoter, can bind to the operator, inhibiting the expression of the disrupter protein. In the absence of the exogenous chemical inducer, no repressor protein is expressed; therefore, the breeder must apply the specific chemical inducer throughout the process of seed multiplication to inactivate the disrupter gene that causes sterility, interrupting the application only at the time of selling the seeds.

The third strategy is applied to vegetatively reproduced species, such as tuber and root crops and ornamental plants, or plants'organs such as the cotyledons, leaves and stem, where growth is prevented during the period in which they are stored to increase the 'shelf life' of the product. This mechanism patented by Zeneca (Syngenta) in 2001 involves a permanently active gene able to block the vegetative growth of the plant, preventing the multiplication of the seeds. This default-expressed blocking gene can eventually be suppressed by application of a chemical activating a second gene allowing the plant to develop.

T-GURT

There are two mechanisms by which T-GURTs work[8]. In the first one, a gene cassette is expressed in the seed and programmed so that the gene responsible for the production of a toxin/disrupter protein is instructed to undo a particular plant trait of interest, without, however, killing the embryo. Thus, a desirable characteristic may be excised selectively by applying or withholding chemical application before being sold to farmers; consequently, the first generation plant is capable of expressing the trait of interest, but the second generation is not (e.g. Zeneca patent WO 9403619 titled 'Improved Plant Germ- plasm'). In the second mechanism of action, the gene encoding the trait of interest is kept silent, but it can be activated by the farmer through the application of a chemical inducer to the plant or seed. In the subsequent fertile generations, the gene is inherited in the inactive state, so that the chemical must be purchased each year that farmer needs the trait to be expressed[22].

POTENTIAL BENEFITS

The main advantage for which GURTs were designed is the technological protection of genetic resources and innovations however, their possible application would be further useful for preventing undesired transgene flow and obtaining specific agronomic/economic benefits. The degree of potential benefits derived from GURTs depends on social group (i.e., private companies, farmers, government or society in general) that will be discussed below:

Transgene containment

Genetic use restriction technologies could be used for the environmental containment of transgenic seeds (V-GURT) or transgenes (T-GURT), thus solving or marginalizing one of the greatest concerns associated with GM crops[4]. Seed lethality is the only strategy at present that prevents transgene movement via seeds; however, GURTs may generally prevent unwanted gene flow from transgenic to nontransgenic varieties (including wild relatives) because it is argued that pollen carries the dominant allele of the lethal/inhibiting protein[5]. Thus, the GURT would most likely be transferred along with the desired trait in the hybrid through cross-pollination[13,16]. Accordingly, GURTs may help the breeding companies to address any legal liabilities if the transgenic crop has the ability to cross with other commercial varieties or introgress into wild relatives[12], thus making it particularly attractive in the case of biopharm crops[20].

Indirectly, as a result of GURTs, the need for buffer zones for gene containment would be removed or reduced and eventuality of volunteer plants would be limited drastically by preventing volunteer seeds from germinating (V-GURTs) or from expressing the GM trait (T-GURTs). Moreover, V-GURTs would be useful to effectively reduce the risk of creating 'superweeds' by reducing the presence of the GM crop in subsequent years[2].

Benefits to farmers

The implementation of GURTs will lead to improved yield as farmers will use new seeds every year. This will result in stiff competition between the public and private sector institutions and eventually the farmers will benefit through this technology.

Furthermore, incentives to breed new varieties may enhance genetic diversity in many important crops, thereby providing further long-term benefits associated with biodiversity (e.g., pest resistance) to farmers[14]. Apart from long-term yield and biodiversity effects, use of GURTs may offer some short-term practicable applications for farmers as well. Terminator technology could effectively eliminate the problem of genetically modified (GM) crop volunteers in farmers' fields[21] and reduce potential for outcrossing with, and increasing the fitness of, weedy relatives[11,25].

Benefits to governments

Governments may benefit from GURTs through reduced investment requirements in breeding and fewer enforcement costs for plant variety protection[6,20]. Governments could, thus, use GURTs as justification to decrease funding to agriculture R&D and biosafety/copyright infringement enforcement programs.. If implementation of GURTs results in yield gains and benefits to farmers, then governments can gain politically with policies that support GURTs

Benefits to breeders:

GURTs represent a novel mechanism for capturing returns from innovation in the plant breeding industry, in a similar manner to more conventional hybridizing techniques. The GURT mechanism greatly improves the plant breeder's capacity for rent capture, potentially increasing private investment into agricultural R&D and, hence, a higher rate of innovation in the plant breeding industry[10]. Breeding companies hope to protect their investments in improved varieties, thus, GURTs may present a better form of insurance (i.e., a biological one) against the free use of genetic innovations than patents, plant breeders' rights or licenses[3] . GURTs would allow better enforcement of property rights[15]. Apart from the sterile seed technology of GURTs, it is also possible that T-GURTs protecting value added traits in newly released commercial varieties could be applied to virtually all crops[25]. Plant breeders and seed companies, thus stand to make substantial intellectual and financial gains through implementation of GURTs.

CONCERNS

One of the most often cited environmental risks associated with GURTs is the risk of transgene escape. Scientists who have studied genetic seed sterilization models believe that Terminator will never be 100% effective or reliable as a gene containment mechanism because it will not achieve 100% seed sterility. Terminator is a system that is made up of many constructs or pieces of genetic material that are genetically engineered into plants. In order to create sterile seeds, the technology relies on all of these constructs to work perfectly, over generations of seed breeding. The chances of failure are high and will increase with each component included in the system.

There are a number of known biological events such as gene silencing and epigenetic changes to trangenes, mutations and loss or reduction of transgene activity, that can interfere with the reliable performance of any one of terminator's components, thus rendering this complex technology incapable of fulfilling its claimed 'biosafety' role. Additionally, segregation of the genetic components that make up the terminator mechanism can occur during reproduction and could disable the Terminator mechanism. Importantly, the main aim of all living organisms is successful reproduction and this strong evolutionary pressure means that everything in the plant itself will be working to counteract and overcome terminator genes and remain fertile[1].

Besides the risk of transgene escape, there are several other concerns associated with this technology that include impacts on biodiversity, increased cost of acquiring genetic resources from private breeders farmers' access to and use of genetic resources through the inability to save seeds. Regarding the impact on agro biodiversity, the first concern is that the introduction of new, uniform, GURT-protected varieties would replace the adapted or selected (possibly less productive) autochthonous cultivars and wild relative species, resulting in the erosion of genetic diversity in fields, adverse effects on local germplasms (or at least the landraces), and effects on the co-evolution of crops at the farm level[25]. While the advent "Green Revolution" has already initiated the erosion of local agroecological capital[24], it is expected that GURTs will exacerbate this situation.

GURTs may be potentially detrimental to farmers, especially poor farmers. Farmers would be unable to maintain commercial varieties from their own seed stock and would be forced to return to the seed provider. This will translate into non availability or lack of seed inputs to the farmers. This will greatly affect the level of agricultural production and the farmer's income thus, undermining food and social security[23].

Breeders will have an increased cost of acquiring genetic resources from private breeders[6]. With increased intellectual property protection and proprietary of materials it will be very difficult to share resources amongst competing companies and institutions. Thus there will be a reduced atmosphere of sharing genetic resources with the implementation of GURTs and other property rights protection.

Genetic use restriction technologies-transformed crops may also produce low quantities of autotoxic compounds with negative impacts on nontarget organisms, induce competition with wild species, and eventually, as food/feed, transfer aller-genicity and antibiotic resistance Similarly, the chemicals used to treat the seeds each year may have negative impacts on the environment where a massive use of antibiotics such as tetracyclines, although harmless to humans and plants, may have a detrimental effect on soil ecology, particularly on microflora and fauna, and increase the prevalence of antibiotic-resistant bacteria[18].

CONCLUSION

Various MNCs for long have been eyeing food business as it is one of the ever sustaining sectors. The ushering of terminator technology has opened this window quite wider and MNCs would not spare any effort to grab this opportunity. It is no surprise that huge chunks of money are being pumped to create a positive perception of terminator technology in public at large. To be pragmatic enough, terminator technology does pose appealing on various fronts like: protection of intellectual property rights, broadening of genetic diversity, checking of transgene contamination.

But the above reasons are not that much versatile that we should shelve its cons. When measured on scale, its cons create an environment of uncertainty. Various potential hazards of terminator technology can be summoned as-out crossing threat, reduced choice to farmers in procuring seeds and gag on using last year seeds, control on access and consequent higher costs of research material to breeders, enhanced need for monitoring and regulating GURT technology, undue control and interference of corporate in agriculture.

The above threats demand a very thorough investigation and extensive evaluation before terminator technology is given a free ride. In Indian context, where about 75% of population is directly or indirectly engaged in agriculture, our approach needs to be caution of higher standard. We need to look at terminator technology through the prism of service rather than business motives. Before any major intervention in this field we need to take on board experts, farmer organizations and chalk a strategy that shields our core agricultural interests. Every effort needs to be made so that terminator technology assures an era of boon rather than bane.

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