The terminator technology for seed production and protection: Why and how?

P. K. Gupta

Although farmers in the developing countries would like to use their own harvested seeds for replantation, despite the provisions of Article 27.3(b) of the Trade-Related Aspects of Intellectual Property Rights (TRIPS) Chapter of World Trade Agreement and those of the 1991 Act of Union International Pour la Protection des Obtentions Vegetables (UPOV), the multinational seed companies (MNCs) would like these farmers to buy seeds for each sowing, so that they may get fair return for the heavy investments they make in developing improved crop varieties. Since the national laws may allow the farmers to use their own seeds for replantation, a terminator technology has now been developed, which will render the harvested seeds inviable, thus forcing the farmers to purchase fresh seeds for every crop season. The patent granted in USA for this technology, the genetic mechanism involved and the defence presented by MNCs while advocating in favour of this technology are discussed in this article.

PLANT breeding in India has largely been the concern of the public sector (agricultural universities, agriculture institutes, etc.) for more than a century and no patents or plant breeders' rights (PBRs) were ever available to protect the cultivars developed through plant breeding. This was needed to encourage a free flow of seeds for the resource-poor small farmers. Only recently, considerable activity for seeking patents/PBRs has been witnessed in the private sector, particularly in the post-GAAT period. Under article 27.3(b) of the Trade-Related Aspects of Intellectual Property Rights (TRIPS) chapter of World Trade Agreement, it is mandatory for all signatories, to allow some kind of protection of the rights on plant varieties. Further, at the global level, patents on living organisms have been allowed in many countries through amendments in their patent laws. This has become necessary in crop plants also, due to the advent of transgenic plants, which are entering the farmers' fields in a big way, the area occupied by them at the end of 1997 being 31.5 million acres[1]. These developments necessitated the provision of patents/PBRs to allow fair return of heavy investments made by private companies. The 1991 Act of International Union for the Protection of New Plant Varieties (UPOV) also diluted the provision of the farmers privilege, which earlier allowed them to save seeds from their harvest for replantation. The rights of corporate plant breeders are thus further strengthened and the rights of farmers to save seeds for re-use are curtailed and will now depend only on the national plant protection laws. However, enforcement of laws for the protection of these rights of seed companies is considered difficult, particularly in the developing world, where the major part of seed requirement is fulfilled by seeds saved by the farmers. Further, the national laws (at least in India) may not incorporate in full the provisions of the 1991 Act of UPOV, so that the farmers' privilege to re-use the seed harvested from their own fields may be allowed in countries like India. Although desirable, this will be against the interest of private multinational companies like Monsanto. In view of this, multinational seed companies have been trying to develop new strategies to protect their rights over their own varieties, so that the farmers may not be able to re-use their own seeds even if the national laws permit them to do so. The terminator technology, patented in March this year, provides for one such technology, which will protect the rights of corporate plant breeders. However, according to many, this will be done at the expense of biodiversity and against the interest of poor farmers. The details of this technology and related issues are discussed in this article.

The patent and its possible uses

On 3 March 1998, a patent under the title *Control of plant gene expression*, dubbed as *terminator technology* in the media, was issued in USA, jointly to Delta & Pine Land Company (D & PL) and the US Department of Agriculture (USDA)[2]. It is claimed that the genetic system described in the patent has worked well with tobacco and cotton, although not completely proven yet. It is also believed that the tobacco system should become workable in a year and cotton system will be ready

P. K. Gupta is at the Department of Agricultural Botany, Ch. Charan Singh University, Meerut 250 005, India.

within two years[3]. Further, the first commercial crop (cotton) utilizing this technology is expected to be marketed by the year 2004 (ref. 4). The patent work was mainly done by Melvin Oliver, a scientist with USDA-ARS in Lubbock, Texas, through cooperative research with D & PL. The patent claims a very broad protection and is valid for plant cells, tissues, seeds and whole plants of any species (both transgenic and conventional crop varieties) containing the combination of genes described in the patent. The inventors of terminator technology have already applied for patents in at least 78 countries. USDA and D & PL also announced that they will make this technology ideally available to many seed companies through licensing agreements. D & PL predicts that the technology could be applied over 400 million hectares (one billion acres) and will be targetted for use in countries like China, India and Pakistan[5]. According to them, this will provide competition between the different seed suppliers. The patent technique has been described as *gene protection technology* by Monsanto and its main future application, as advocated by D & PL, will be the development of *technology protection system*. However, Rural Advancement Foundation International (RAFI), a Canada based, non-governmental organization (NGO) dubbed the technology as *terminator technology*, since they believed that it will terminate the farmers' independence and threaten the food security of over a billion resource-poor farmers in developing countries, where farmers' saved seed accounts for 80% of the total seed requirement[6–8]. In India, all this could have been prevented, if we had the enabling legislation to deal with such problems. In the words of M. S. Swaminathan 'We need to have a National Biodiversity Act, a Plant Variety Act, Farmer's Rights Act and a Geographic Appellation Act and also plug loopholes in the Indian Patent Act' to deal with these problems. Such legislation has not been in place yet, due to lack of will of politicians and bureaucracy in our country. In view of the above, while referring to the slow pace of progress in enactment of relevant legislation in India, Swaminathan further states that 'the terminator can be terminated, but we need to terminate our lethargy first'. It is in this background that the Indian Government has banned the entry into the country of any seed material that may carry the 'terminator gene' and has also decided not to grant a patent to D & PL for the terminator technology. The implementation of these decisions apparently seem to be difficult, although efforts are being made to develop molecular probes to detect terminator genes in the seed, entering the country from outside.

According to Sally Miller Hayes, another scientist from USDA, the above technology was developed for the study of gene expression. For instance, the technology may be used for any trait desired to be expressed in one situation, but not in the other. Such possible traits include male sterility, drought or insect resistance, time of seed germination or flower development. The other possible uses of the 'gene protection technology' advocated by Monsanto[9] are: (i) minimization of outcrossing with related species; (ii) increased choice of seed varieties for the farmers; (iii) help in protecting farmers' rights; (iv) provision for consistently high quality seeds; (v) development of best variety seeds by yearly improvement; (vi) maintenance of desirable characteristics in varieties that are grown for more than one year. The scientists at D & PL, however, believe that its main future application will be in the development of so called 'technology protection system' against free use of technology. Therefore, one major application will be to protect the rights of seed producers/breeders to disallow the farmers to use their own harvested seeds for replantation.

Hybrid varieties vs terminator technology and IPRs

In order to get a fair return on their investment, individual seed companies developing new varieties have been interested in biological protection of their varieties to prevent re-use of seeds harvested by farmers. At present, they intend to achieve this through the grant of patents and plant breeders rights, which have been revised in 1991 under the umbrella of UPOV to provide better control of the breeder/seed companies over the protected seed material. In case of hybrid varieties (e.g. maize, sunflower, etc.), there is a built-in protection, which forces the farmers to purchase hybrid seeds every year, because the increased yield is exhibited only in the F_1 seed that is sold to the farmers and the performance declines in F_2 and subsequent generations. This discourages the farmers to harvest and re-use the harvested seed of hybrid varieties for sowing the next crop. In several self-pollinated crops like wheat, rice, barley, beans, etc., on the other hand, 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. For these inbreds, the patents/PBRs are available, but their implementation seems to be really difficult (if re-use of seed is not allowed), particularly in the developing world having millions of small resource-poor farmers. In countries like USA also, private companies have to hire investigators and detectives to root out farmers, who are saving seeds from these companies for re-plantation. In view of these inherent difficulties in the implementation of patents/PBRs in these self-pollinated crops, the termination technology is intended to be used.

Mechanism involved in terminator technology

The patented method for terminator technology 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 a the third gene, which is a repressor gene. The genetic elements, as above, differ for pure lines and hybrid seed production systems (see below).

Technology for pure lines seed production

In self-pollinated crops, where pure lines are used as cultivars, the promoter for the above recombinase gene is repressor specific and is used by a specific repressor protein encoded by the third gene, which is a repressor gene. The repressor gene can be switched off using a stimulus in the form of a chemical, a heat shock, etc. Due to the stimulus, the repressor gene is switched off and CRE/LOX (recombinase gene) is switched on. This will lead to the production of recombinase enzyme,

Figure 1. Genetic basis of terminator technology envisaged for pure line seed production in self-pollinated crops

which will excise the blocking sequence or the spacer which blocked the expression of the terminator gene (e.g. RIP). Due to excision of the blocking sequence, the promoter will come to lie adjacent to the terminator gene, which will now be expressed and will kill the developing embryos.

In actual commercial production and sale of seeds of pure lines as above, the crop for commercial seed production will be grown by the breeder or seed company without chemical treatment. The harvested seeds from this crop, will be treated with the chemical, before it is sold to the farmer, so that in crops grown by the farmer, the toxic substance is produced at the time of embryo development, and the embryos die or fail to develop (Figure 1). A seed thus produced will carry the endosperm, but not the embryo, so that it can be used or sold as grain, but cannot be used for sowing. Tetracycline is one such chemical trigger that can be used for treatment of the seeds before selling them in the market.

Technology for hybrid seed production

In case of hybrid seed production, a different strategy, utilizing only two genes (terminator and recombinase), one in each of the two parents of the hybrid are used and no repressor gene is needed. One of the parental lines contains the recombinase gene, which becomes active only after germination, and the other parent contains the lethal (terminator) gene separated from its promoter by a spacer (blocking sequence). The hybrid progeny, which is the technology protected hybrid seed bought and planted by the farmer, thus contains both the elements of the system in every cell. The recombinase, expressed right after germination, excises the spacer blocking sequence bringing the promoter and lethal gene together. Since the promoter is embryo specific, the lethal gene does not express till seed development starts. During seed development, the lethal gene expresses during late embryogenesis and kills the embyo (Figure 2). Thus the seeds harvested from the first generation hybrid crop will be normal in all essential respects, except that they will not germinate if sown as a crop.

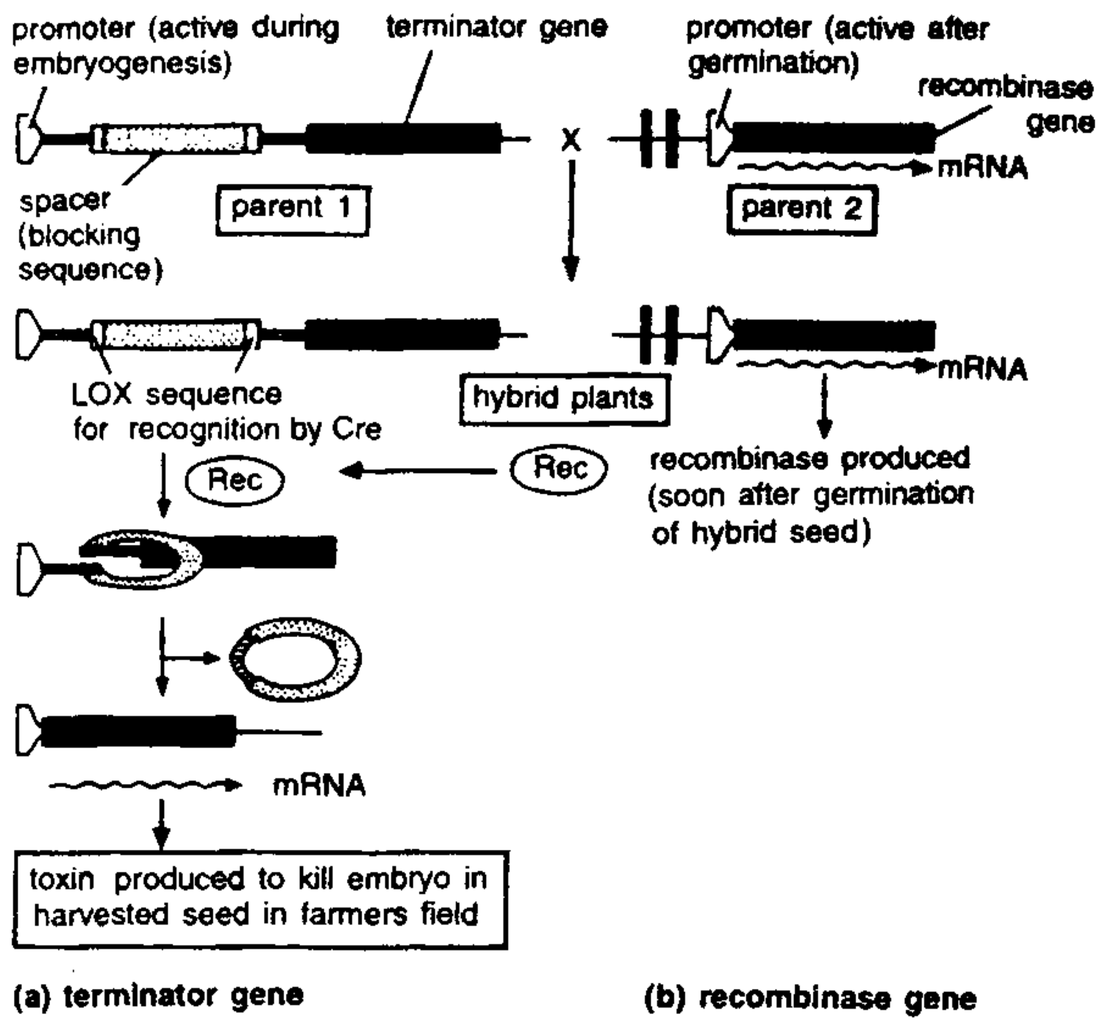

Figure 2. Genetic basis of terminator technology envisaged for hybrid seed production both in cross-pollinated and self-pollinated crops.

'Verminator', an alternative to 'terminator'

More recently, Zeneca of UK indicated that it will seek patents in more than 50 countries for its *improved plant germplasm* invention. This technology will prevent plant growth, rather than killing the seed. The technology makes use of a gene from the fat tissue of a rat, which will block the normal plant growth, unless the blocking process is deactivated by a chemical. The technique has been dubbed as 'verminator' by RAFI and appears to be wider and more flexible than the 'terminator', though intended to serve the same purpose[10].

Defence by D & PL/Monsanto

Harry B. Collins of D & PL argues that the farmers will still have the option to use the traditional varieties, having no protection system, and that the new technology will encourage plant breeders to invest and develop new varieties of crop. D & PL also claims that the technology will help the food security system in the following ways. First, the new technology will stimulate investment and interest by breeders for development of new varieties of self-pollinated crops for which hybrids are not feasible (e.g. wheat, rice, barley, beans, etc.); second, it will provide the farmers access to continuous development of new improved cultivars; third, the incentives for development of new varieties will enhance genetic diversity in many important crops; and fourth, the escape of transgenic to other wild and non-targetted plants will be impossible since unwanted pollination will give seeds that will be non-viable. A list of other uses of this technology listed earlier in this article, have also been discussed by Monsanto/USDA. Several NGOs including RAFI and GRAIN in Europe do not buy these arguments and believe that terminator technology will do more harm than good. At least the following two arguments of these NGOs seem to be valid. First, when a farmer grows a traditional variety, next to a sterile seeds variety, the pollen from the latter may reach the former, thus producing seeds, whose germination on replantation may be greatly reduced, thus harming such poor farmers; and second, the role of farmers in generat-