منظمة الأغذية والزراعة للأمم المتحدة | 联合国粮食及农业组织 | Food and Agriculture Organization of the United Nations | Organisation des Nations Unies pour l'alimentation et l'agriculture | Organización de las Naciones Unidas para la Agricultura y la Alimentación

E

COMMISSION ON GENETIC RESOURCES FOR FOOD AND AGRICULTURE

POTENTIAL IMPACTS OF GENETIC USE RESTRICTION TECHNOLOGIES (GURTS) ON AGROBIODIVERSITY AND AGRICULTURAL PRODUCTION SYSTEMS

by

Bert Visser [1], Derek Eaton[3], Niels Louwaars[2], Ingrid van der Meer[2], Jules Beekwilder[2], and Frank van Tongeren[3]

1. Centre for Genetic Resources, the Netherlands (CGN), Wageningen
2. Plant Research International B.V., Wageningen
3. Agricultural Economic Research Institute (LEI), The Hague

This study was produced at the request of FAO by Wageningen University Research Centre, The Netherlands; part 5 of the study summarizes a parallel study carried out on the request of FAO by David R. Notter, Department of Animal and Poultry Sciences, Virginia Polytechnic Institute and State University, Blacksburg, VA, United States of America. The study was used by the secretariat in preparing a document on GURTs for the First Meeting of the Inter-governmental Technical Working Group on Plant Genetic Resources for Food and Agriculture of the FAO Commission on Genetic Resources for Food and Agriculture (CGRFA/WG-PGR-1/01/7; Potential impacts of Genetic Use Restriction Technologies (GURTs) on Agricultural Biodiversity and Agricultural Production Systems); A revised version of this document is available to the Ninth Regular Session of the Commission as document CGRFA-9/02/17. This study, and the additional information it contains, is put at the disposal of the Commission. The study is the responsibility of its authors, and does not necessarily represent the views of the FAO, or its Members.

Index

Introduction

This study has been conducted on the request of the Food and Agriculture Organization (FAO) of the United Nations, as an input to a paper that it was preparing on genetic use restriction technologies in food and agriculture. The opinions expressed in this study are those of the authors and are not necessarily those of the FAO or its Members.

In May 2000 FAO received an invitation by the Conference of the Parties (COP) V of the Convention of Biological Diversity. COP V invited the FAO and its Commission on Genetic Resources for Food and Agriculture (CGRFA), in close collaboration with the United Nations Educational, Scientific and Cultural Organization (UNESCO), the United Nations Environment Programme (UNEP) and other member organizations of the Ecosystem Conservation Group to "further study the potential implications of GURTs for the conservation and sustainable use of agricultural biodiversity and the range of agricultural production systems in different countries, and identify relevant policy questions and socio-economic issues that may need to be addressed". This study aimed to contribute to FAO's response to the request.

The study was set up as a cross-sectorial approach to investigate various aspects relating to the applications of Genetic Use Restriction Technologies (GURTs). It distinguishes between the uses of genetic use restriction technologies in terms of (i) an appropriation strategy for business (technological protection of seed or planting material); (ii) a possible tool for containing genetically modified organisms or transgenes, by sterilizing the product of genetically modified seed or planting material; and (iii) possible production advantages. Policy decisions regarding genetic use restriction technologies need to consider these different aspects of genetic use restriction technologies separately: much of the debate so far has been confused, by not analysing these factors separately.

Although the study has focused on crops, it has included an evaluation of the impacts in the other agricultural domains of livestock, trees and fish rearing. The study builds on a previous 'trail-blazing' study by Richardson and co-workers, which was presented to the Subsidiary Body on Scientific, Technical and Technological Advice (SBSTTA) of the CBD in 1999. The report below consists of four parts which each consider some of these aspects in more detail.

Part 1 deals with the expected technical developments regarding the introduction of GURTs over a 10-year time span. An extensive analysis of published patent applications relating to the technology proper as well as to technologies potentially providing components for application in GURT has formed the basis for this part. This analysis, scientific literature, and interviews with experts in molecular breeding allowed an assessment of the future technical developments in molecular biology relevant to GURT as well as the likely potential applications of GURT, including their robustness.

Part 2 deals with the potential impacts of GURT applications on the maintenance of agrobiodiversity and on biosecurity. For this purpose an analysis was made of current gene flows within and between industrial as well as autonomous farming systems. In addition, the potential effects of outcrossing of genetic information from varieties and breeds containing GURTs and the use of inducer compounds to regulate gene expression were studied.

Part 3 has focused on the socio-economic impacts of GURTs at the level of farming systems, in particular regarding food security and household security. The effects on the functioning of seed systems have been investigated in more detail, since seed forms the potential carrier of GURT, and since farming systems often incorporate various seed systems.

Part 4 complements part 3 with a study of the economic impacts for the industry, in particular concerning concentration trends, the relationship with intellectual property right positions, and the effects for various stakeholders at the national level.

In the preparation of these four sections, more extensive documents were prepared, in which major questions are further elaborated. Those documents are available from the authors upon request (contact e-mail: L.Visser@plant.wag-ur.nl).

Part 5 summarizes major issues covered by a study on the implications of GURTs for farm animal genetic resources management, carried out in parallel on the request of FAO. It emphasizes the use which medium- to low-input production systems could make of V-GURTS.

Finally, part 6 wraps up policy-related issues and attempts to link these to existing agreements and regulatory frameworks, in particular, at the international level, to the Global Plan of Action on Plant Genetic Resources, the FAO International Treaty on Plant Genetic Resources for Food and Agriculture, the WTO TRIPS Agreement, the Code of Conduct on Biotechnology of the CGRFA and the Cartagena Protocol on Biosafety of the Convention on Biological Diversity, as well as national legislation regarding intellectual property right protection, seed flows, and the deliberate release of genetically modified organisms (GMOs).

The study has identified several knowledge gaps which might merit further studies, as well as close monitoring of developments following the introduction of GURTs. The study also revealed that predictions on impacts can be made in a qualitative sense only, by lack of data for a more quantitative analysis.

1. Molecular and technical assessment of GURTs and their potential use in agricultural sectors

Technical methods providing specific genetic switch mechanisms which aim to restrict the use of genetic material have been described in a number of patent applications. These methods have been grouped under the collective noun 'Genetic Use Restriction Technologies' (GURTs). The genetic switch can be used to restrict either autonomous use of the germplasm itself or expression of traits associated with that germplasm, or unwanted release of genes from that germplasm into the environment.

The concept of GURT has raised discussions on the impacts of this set of genetic switch mechanisms for biodiversity maintenance, agricultural practices, food security and rural economies, and the organisation of industry. In this part the technical potentials of GURTs, especially for crops, and the technical aspects associated with the use of GURT as an appropriation strategy (technological protection) and as a production technology are elaborated. These are considered separate issues.

1.1 Motives and uses for GURTs

Among the patent applications disclosing GURT concepts, two types of use restriction can be distinguished: use restriction of the entire variety (V-GURTs), by interfering with reproduction, or of a specific trait in a variety (T-GURTs), by regulating its expression (Jefferson et al., 1999).
The application of GURTs can be inspired by different, not mutually exclusive motives. These motives are:

- Appropriation of benefits

Breeding companies wish to safeguard their investments in improved varieties, whether produced by classical breeding or genetic engineering, and to realise a sufficient level of appropriation of the benefits derived from the use of improved germplasm by the use of GURTs as a technological protection of their product through preventing its reproduction. This strategy may complement, or possibly even replace, intellectual property regimes (plant breeders' rights and patent rights). In particular, it may be used to protect investments requiring high-capital inputs and providing low rates of return, such as the genetic engineering of crops in which multi-gene pathways are introduced, resulting in increased nutritional value, improved flavour or fragrance, improved health (functional foods), flower synchronisation, production of high value compounds, and introduction of apomixis (allowing unlimited asexual reproduction). GURTs may offer a better insurance against 'free-riding' on genetic innovations than patents, plant breeder's rights, or licences. For many cross-fertilising crops, protection of germplasm from reproduction by farmers is ensured by hybrid technology, which prevents amplification of elite varieties. For some self-fertilising crops hybrids have been recently created as well. Crop species for which hybrids are not feasible or effective and which represent a substantial potential market may form primary targets for V-GURTs. Such species are in-breeding crops like rice, wheat, soybean and cotton, and horticultural crops, as well as ornamentals for which vegetative multiplication is used. T-GURTs may be applied to virtually all crops.

- Containment of GMOs

GURTs can be used for the environmental containment of transgenic seed (V-GURT) or transgenes (T-GURT). The focus will be most likely on species which may establish themselves in ecological niches, and/or for which wild relatives exist in the local setting. Traits that need containment will be those with putative health risks, or traits that can threaten biodiversity or the environment. Examples are formed by traits involving potentially allergenic, novel compounds expressed from transgenes with highly unpredictable consequences, as well as traits rendering its host more vigorous than its natural counterparts, including insect resistance or traits that improve germination, growth or performance under stress conditions. Alternatively, containment of transgenes to allow for GMO-free food chains might form a public interest.

- Added production value

It can be in the producer's or farmer's interest to restrict the expression of a trait to a specific phase in the development of the plants or animals, or during biotic or abiotic stress. Such traits could include resistance to pathogens, lactoferrin production, production of high value compounds that affect plant growth, the regulation of flowering to boost yields of vegetative parts, and the limitation of seed setting in certain fruits. T-GURTs would enable a producer to restrict expression of a trait at will, provided a producer has access to the appropriate inducer compound. Alternatively, V-GURTs may be used to control the reproduction of farm animals in order to safeguard the integrity of adapted maternal breeds.

Regarding T-GURT applications, its focus will likely follow the thrust of GMO applications in general. Applications may be expected for any crops, trees and breeds in which major investments for genetic improvement by private industry are undertaken.

Regarding V-GURT applications, the situation is more complex. On the one hand V-GURT application is unlikely in those cases in which hybrid technology provides sufficient protection against utilization of the product by third parties, thus diminishing the likely scope for application. On the other hand, environmental concerns may enlarge the demand for applications of V-GURT.

GURT applications for appropriation purposes will be particularly sought for those crops which currently cannot be properly protected by biological hybrid technology protection, meaning that wheat, rice, potato, soybean and cotton will gain particular attention. In contrast, biosafety requirements may be regarded as an impetus for the application of GURT in all crops which may outcross or may have detrimental environmental effects. If the plant as factory gains importance, 'factory' crops might be gradually selected. Although the issue which crops best qualify for such production has not been settled yet, production of specific high-value compounds might be attractive in for example potato tubers and sugar beets, tobacco leaves and rape seeds on the basis of crop familiarity, yield and efficient purification procedures, resulting in novel 'niche' crops which might be protected by GURT.

Regarding traits to which genetic use restriction technologies are likely to be applied as an appropriation strategy, a major distinction can be made between agronomic traits directly influencing field performance, and quality traits with neutral effects on growth behaviour. On the one hand, a shift in general breeding efforts can be expected from agronomic traits towards quality traits, and given the early stage of GURT development and major developments in genomics and genetic modification; a major future application of T-GURTs can be expected for quality traits rather than for agronomic traits. Quality traits may regard taste and texture, as well as shelf life (in particular for horticultural crops) and ease of processing. On the other hand, environmental concerns will in all likelihood focus on agronomic traits, in particular pest and insect resistances. In terms of the containment of GMOs, environmental concerns resulting in demands for V-GURT application are more likely for those crops for which geneflow into relatives and in particular into weedy relatives is high. At a global scale, this is less likely for crops such as maize, potato and soybean, and higher in the case of wheat and rice, but also for example oilseed rape and sorghum.

The use of GURTs may also result in an added production value. For example, sterility would prevent undesirable early germination of seeds or sprouting of tubers (potatoes), and allow extension of the harvesting period. For several plant species (e.g. grasses and trees) a higher yield of the vegetative parts is obtained when flowering is inhibited. For many fruit bearing species seedless fruits would give a higher quality fruit in the market (e.g. grapes, citrus fruits). Regulation of phytate levels would result in proper germination in combination with a high nutritive grain value. In addition, specific traits, in particular resistances against pests and diseases and drought tolerance that are often expressed at a yield cost, could be mobilised selectively during substantial pest and disease pressure only, and thus prevent unnecessary yield reductions. This application may also be attractive in dairy farm animals in which expression of anti-bacterial proteins or other compounds might interfere with milk processing, and may only be selectively activated upon infection. In general, production of specialty compounds may have to be limited to a certain growth stage or developmental phase since its production may interfere with plant growth or health, and be best induced externally rather than upon genetically built-in induction.

Only a very limited number of farm animal species have gained global importance and all of these qualify for the application of GURT, namely cattle, sheep, goats, pigs, chickens and turkey. Based on market size, investments in biotechnology are most likely in cattle, and genetic modification has most advanced in ruminants. Both V-GURT and T-GURT qualify as interesting private breeding strategies, given the substantial investments in hybrid breeds of pigs and chicken. The hybrids developed, however, do not offer a similar level of alternative property protection as in crop breeding, given that yield depression as a result of further breeding with progeny can be circumvented more easily. Sterility of the offspring of local animal breeds and exotic animals would prevent the dilution of the native stock, and this would represent an added production value.

Fish has been a major contribution to the diet of the human population, but growing demands have resulted in a threat to the survival of many fish species, as well as in higher prices for catch fish. This development has resulted in a large increase in aquaculture. Genetic improvement has focused on a limited number of species (e.g. salmon, tilapia, crustaceans; Bartley, 2001), and these all potentially form the target for GURT applications as a containment strategy, which is relatively simple in comparison with the application of the technology in farm animals. Production of GM fish for human consumption might be a reality within the next five years, and application of GURT might follow suit, if the expected benefits would be higher than the expected costs of developing the technology for fish. Chances for eventual escape of farmed fish and other aquatic species are high.

The overall majority of forest trees are wild, undomesticated and outcrossing; tree breeding and selection programmes, even using traditional technologies, have been undertaken on a limited number of valuable, economic species. Forest trees growing in commercial plantations will only be planted once every 10 years, at least. The returns on investments will warrant investments in a limited number of species only. Therefore, only few tree species are commercially planted at sufficient acreage to warrant biotechnology efforts, and these species may thus qualify for GURT application, in particular, *Eucalyptus, Populus, Pinus and Acacia spp*. Possibly, some tropical hardwood species might be included here as well, depending on future wood production policies in tropical countries. (Dale Smith, 2000; contribution to the FAO Biotech electronic conference; http://www.fao.org/biotech/logs/C2/130600.htm). The long life cycle of trees forms another disincentive to invest in technology which may be outdated before the same area can be replanted. V-GURT application may have no interest from an appropriation perspective, given that cuttings are often used for multiplication, rendering protection of sexual reproduction non-effective. Like for fish species, environmental concerns may call for V-GURT applications. For T-GURT applications the cost of applying an inducer may be prohibitively high. Alternative expression control through photoreceptors has been suggested.

Table 1. Traits that qualify for GURTs application

Traits/ products	Interest	Reason/ Motivation
Increased nutritional value Improved flavour/ fragrance Functional Food Production of high value compounds Flower synchronisation Quality improvements in ornamentals Apomixis	Industry	Appropriation of benefits ▪ High capital investments ▪ Currently low rates of return ▪ Knowledge protection
Production of pharmaceutical and industrial products (contained use) Containment of potentially allergenic compounds and compounds with unpredictable effects General containment of spread of transgenes or transgenic organisms	Public	Containment requirements ▪ Putative health risks ▪ Potential disturbance of biodiversity, in particular genetic resources ▪ Ethical objections
Resistance traits Production of antibiotics or medicines against diseases Production of compounds that affect growth of the organism	Producer	Added production value ▪ Trait only necessary under certain circumstances ▪ Trait to be expressed just before farmer will harvest

1.2 Technical aspects of GURTs

At least three general V-GURT strategies can be distinguished. The first strategy makes use of induced activation of a disrupter gene (Delta & PineLand/USDA patents; e.g. US 5.723.765 and US 5.925.808). The plant is provided with a disrupter gene that can inhibit embryo formation. This gene is held inactive by a transcriptional blockade (see fig. 1). So, normally the GURT is dormant, but when the seed to be sold is treated with an inducer chemical, a cascade of events is started, eventually leading to expression of the disrupter in second generation seed. As a result, seeds are fit for consumption, but not fertile.

The second strategy is different from the first in that the breeder applies a chemical in all generations, but stops to do so before selling the seed (e.g. WO9735983/Syngenta and WO 9744465/Monsanto). In this concept a disrupter gene is expressed in the seed by default, resulting in sterile seed. This is prevented by applying the chemical, which provides a restorer protein to safeguard fertility of the seed and reproduction of the variety, when under the control of the breeder/developer of the variety (see fig. 2).

The third strategy focuses on vegetatively reproducing crops like root and tuber crops and ornamentals (e.g. WO 9906578/Syngenta). The described method is not only suitable for investment protection, but also for prevention of growth during storage, which is in the interest of growers and consumers**.** In this concept a gene blocking growth is expressed by default, which can be restored by induction of a second gene. Hormone metabolism and function forms the target of this strategy.

In T-GURT concepts only a trait is switched on or off at will. This can be realised by inducible promoters to regulate the expression of the transgene, by induced gene silencing (e.g. anti-sense suppression) or by excision of the transgene using a recombinase. Applications may involve traits protecting a plant from pathogen attack at a certain yield cost or traits involving compounds toxic to the plant to be produced just before harvest. Government regulators may promote the use of analogous technologies by requiring marker-free transgenic plants. However, such application does not entail use restriction, and should not be regarded as GURT.

Other methods of 'use restriction' that can be compared with V-GURTs to some extent are hybrid technology, triploidisation and male or female sterility (e.g. US 5808034/Syngenta, and US 859341 and US 5432068/Pioneer). An overview is offered via the Internet source http://www.nbiap.vt/edu). In this respect, it is important to stress that hybrids do not merely represent an appropriation technology, but have a direct production value as compared to current open-pollinated varieties, through hybrid vigour, which is the basis for their market potential. Differences between these technologies and V-GURTs are that both for hybrids and male or female sterile plants, the germplasm remains available to farmers and competing breeders, which is not the case if V-GURTs fully function as envisaged by the developer. Also, utilization of triploids for breeding purposes is usually within reach of breeders.

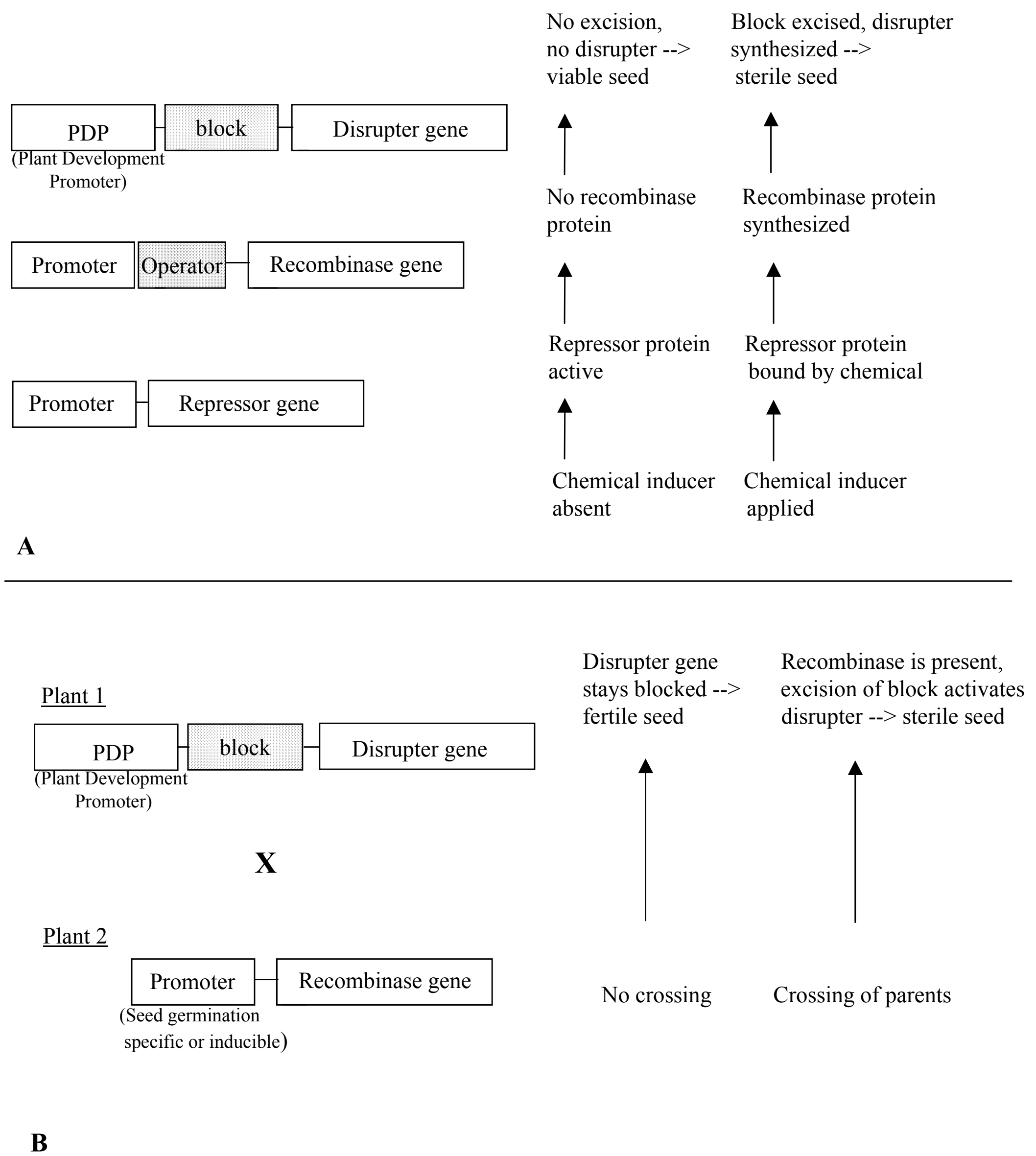

Figure 1. Simplified model of V-GURTs concept using induced activation of disrupter gene. A. Three elements in one-plant system. B. Two elements in two-plant system.

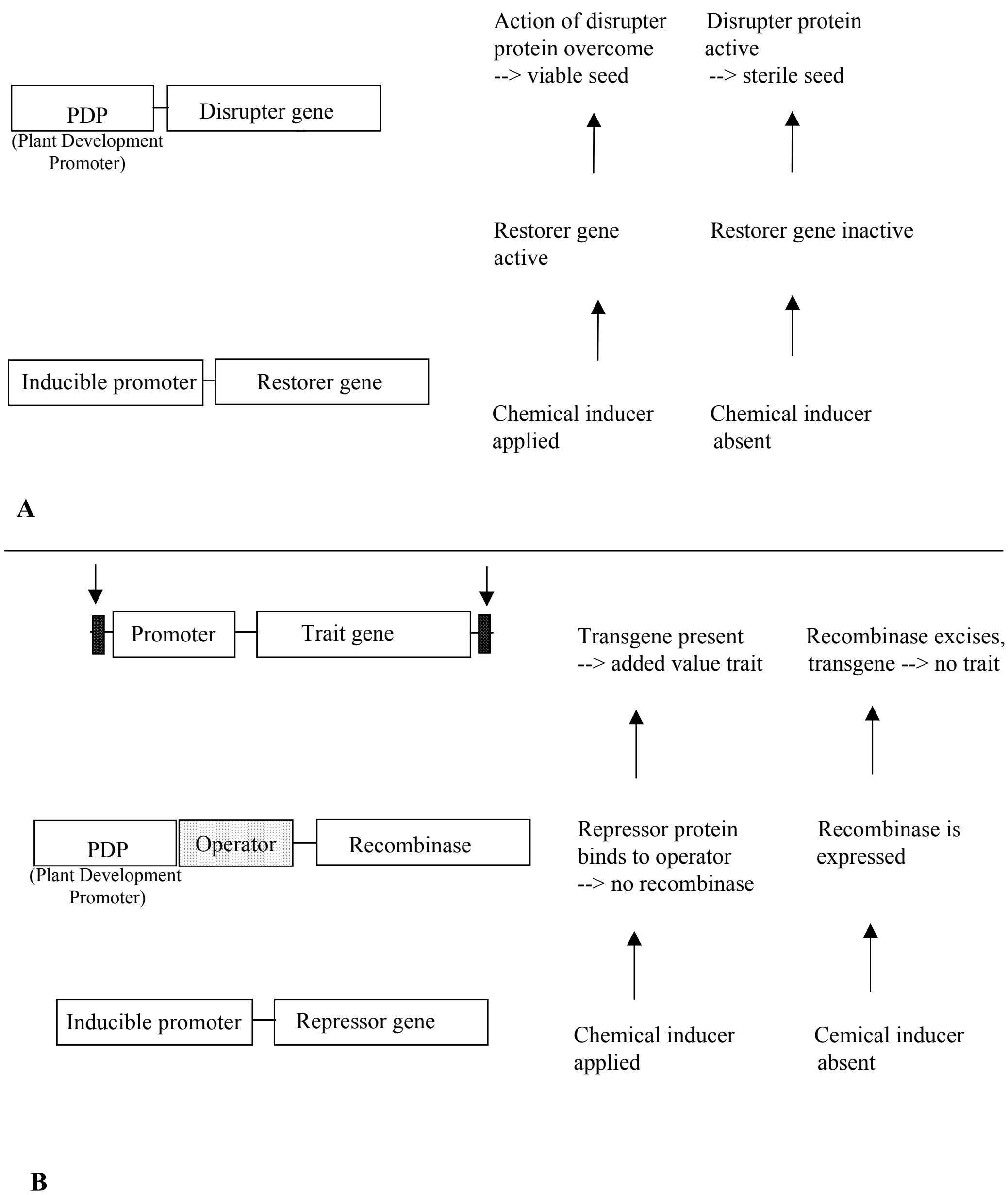

Figure 2 A. Simplified model of V-GURTs concept using induced expression of disrupter-suppressor (Zeneca). B. T-GURTs concept using transgene excision by recombinase (Zeneca).

In other words, V-GURTs can be distinguished from these other technologies in that they protect not only against unlicensed reproduction of the germplasm, but also prevent the use of that germplasm in breeding by third parties.

Whereas GURTs may be used for the environmental containment of transgenic seed (V-GURT) or transgenes (T-GURT), non-GURT method for the containment of transgenes are available or under development. For example, male sterility can be an alternative to GURT when the goal is to avoid the spread of transgenes to the natural environment. For appropriation strategies this method will not be satisfactory, because the germplasm is not fully protected (comparable to hybrid seed production). In employing a plastid transformation strategy, the transgene is introduced into the plastid genome instead of the nuclear plant genome. As the pollen cells of most crops do not contain any plastids (and hence no plastid DNA), any gene introduced by engineering the plant chloroplast is unlikely to be transferred via the pollen to neighbouring crop stands or wild relatives. Until now, chloroplast transformation techniques are only available for tobacco and tomato (progress is reported for potato and Arabidopsis) and not all major crop plants show maternal inheritance of plastids. Furthermore, not all transgenic traits can be incorporated via plastid transformation (e.g. modification of non-plastid located metabolic pathways). Although this method will restrict the dispersal of transgenes via pollen distribution to neighbouring crops or wild relatives, it does not contain transgenic seed dispersal.
A non-GURT, related, genetic switch application that comes close to practice aims to obtain marker-free transformed plants, as increasingly requested by biosafety regulations.

Whereas GURT concepts have been described in patents on plants, analogues of the concept can be developed for farm animals as well. For farm animals, a technically more amenable V-GURT strategy is proposed for some applications, in particular for meat production in mammals, based on modifications of the sex chromosomes. This strategy requires the development of pairs of gene-constructs that induce sex-linked sterility, with compensating elements that can restore fertility in the initial breeding animals. Control of the process to overcome infertility would remain with the organization producing the animals.

From a technical perspective, the concepts elaborated above can be developed for trees and fish and other aquatic species as well. In the case of aquatic species, next to less reliable triploidisation, moose technology offers an alternative to GURT-based protection.

1.3 Technical status of GURT models described in patents

The V-GURT concept from Delta & Pine Land/USDA has not been turned into practice yet, although several components of the concept have been demonstrated to work. Proof is lacking for efficient control of the recombinase, to prevent expression of disrupter genes until desired. Another problem is that inducer chemicals must be efficiently applied to the seed to induce sterility in all treated seeds. In other words, this GURT system will only be effective for successful appropriation of the variety, when all L2 layer cells from the seed are reached by the inducer compound, and the blocking sequence is removed from all disrupter genes. If not, a certain percentage of seed of the second generation will be able to germinate. Furthermore it should be demonstrated that the promoter driving synthesis of the disrupter is under any circumstance restricted to late embryo development. If expressed at a low level before that stage, expression of the disrupter will occur before the seeds have matured and impair plant development or seed filling. This system would therefore be more feasible for crops in which the seed is not the product.

The Zeneca concept has recently been shown to function in the laboratory, but would still need further improvements to render the system applicable in the field. In a related literature report (Kuvshinov et al., 2001) transgenic tobacco plants have been described that only survive if treated with an inducer. The system uses an embryogenesis-specific promoter expressing Barnase as disrupter gene, which is repressed (muzzled) by Barstar protein, expressed from an inducible promoter. When the flowers and seeds are given the inducing treatment, normal levels of germinating seed are made by the plant. When

the inducing treatment is not given, progeny seed is unable to germinate. The described experiments are in some aspects inconclusive (numbers and statistics are lacking).
Potatoes that carry the sprouting-suppression element are reported not to sprout for two years. However, it is still not clear if this is a practical system, because inducible sprouting by the restorer element is not reported.

Whereas some proposed applications add a new trait to the receiving organism, leaving the receiving genome intact, other applications effectively replace a native gene by a transgene, e.g. through gene-silencing of the native gene.

It seems safe to conclude from those examples that T-GURT applications in which the added value trait is removed from the plant genome by recombinase activity for reasons of appropriation is a concept that is coming close to application. Still it remains to be established how well such systems work outside the laboratory as well as in different crops.

Important components in the described V-GURT and T-GURT concepts are: tissue- and stage-specific promoters, disrupter and restorer genes, inducible promoters and their inducers, and recombinases. Many tissue- or stage-specific promoters (including promoters exclusively active in flowers, anthers, pistils, seed, fruit and tubers) have been described that are active in reproductive organs or during embryo formation and germination, but the exclusiveness of their activity is often not 100%, which is necessary for V-GURT applications. Inducible promoters have been reported since long. Early variants have been used to induce herbicide safeners and heat shock proteins, but to their disadvantage many of such promoters can be induced by multiple triggers. In recent patent applications (e.g. US 5464758, WO 9321334, WO 0009704, WO 9938988, US 5880333) more tightly controlled systems have been described, including promoters that can be induced by tetracycline, alcohol, homoserine lacton, oestrogen, glucocorticoids or ecdyson (see also Mandava, 1988; Seigler, 1995; Simon et al., 1996; Aoyama et al., 1997; Zuo and Chua, 2000). Ideally, inducer compounds should not occur in nature and be unique in their ability to activate the promoter. Desirable for appropriation strategies would be that they are difficult to identify, and cannot be replaced by other compounds. Furthermore they should comply with the pesticide regulations, and be water-soluble, non-toxic, not affecting plant development, and stable but bio-degradable. So far, no inducer has been found that fits all these criteria. Tetracycline for instance is not stable, poorly water-soluble, light-sensitive and toxic to the environment. From the described inducers in combination with inducible promoters, alcohol (for biosafety interests) and steroids (for appropriation strategies) probably form the most promising candidates.

The disrupter genes known so far may conceivably function, although counter-acting restorers are not present for all disrupter genes suggested. Disrupter genes can be grouped in two categories: general disrupters and expression-suppressors. The first category comprises pathogenesis factors, metabolic blockers and toxins. The pathogenesis factors are usually of bacterial origin, and include enzymes that mediate pectin breakdown (pectate lyase from Erwinia), or RNA breakdown (Barnase from Bacillus). Metabolic blockers interfere with mitochondrial functioning, such as TURF-13 from male-sterile maize, or UCP from rat. The described toxins are usually quite general toxins, like diphtheria toxin or Bacillus cytA. When general disrupter genes are expressed in seed for consumption, their effect on consumer health should be studied prior to release on the market. The second category of disrupter genes are those that interfere with the expression of late embryogenesis-essential genes. An example is formed by an anti-sense ACOX gene (see WO 9744465). ACOX is a gene that is essential for germination, as it is implicated in lipid mobilization from the seed, to supply the germinating seed with sucrose. Anti-sense ACOX genes form potentially efficient expression –suppressors by silencing the original ACOX gene in the host plant.

Some satisfactory recombinases seem to be available. Important requirements are that they exclusively recombine designed targets, do not cause a phenotype in plants, and work 100 % efficient (see also Kilby et al, 1995). Although most recombinases are from microbial origin, they sometimes recognize non-target sequences in plant DNA. The Gin recombinase is known to cause rearrangements in plant chromosomal DNA. The Cre recombinase is useful in some plants (Zuo et al., 2001), but when expressed to high levels, may cause phenotypes like dwarfing and chlorosis in for instance tomato (Coppoolse in Gilissen and Nap, 1999). In contrast, Flp recombinase, beta-recombinase and R recombinase have not been described to cause such phenotypes. The efficiency of recombinases may differ from species to species, and depends on the setting of the genes. The Flp recombinase, when provided by one of the parents, is reported to function efficiently in rice and *Arabidopsis thaliana*.

Application of GURTs is confined to species that are transformable. Not all elite lines of crops are well transformable (whereas often specific breeding lines are) and introgression of the GURT via a long lasting breeding scheme should be taken into account. Also, stability of transgene expression throughout several generations may form a bottle-neck to GURT applications.

A number of major patent applications related to GURTs can also be found in Table 2 in this document, describing potential effects of outcrossing.

1.4 Impact of future developments in molecular technology on GURTs applications

The pace at which information from genomic research is becoming available will most likely result in several effective GURT prototypes for plants within 5 to 10 years. The availability of a huge number of genes in combination with high throughput screening of their (tissue-specific) expression via DNA micro-array analysis will result in the isolation of a number of candidate promoters that will meet the strict requirement for use in GURT applications. The progress in functional genomics will generate many new disrupter genes taking into account that more than 100 ‘embryo lethal’ mutants have been reported in *Arabidopsis thaliana*. The proper combination of disrupter and restorer gene is challenging, but will be available within a few years. For example, genes causing male sterility will need extensive development. Novel genes are required, which will mainly come from transposon-tagging technology and other reverse-genetics approaches. Engineering technologies will aim to create artificial diversity in promoters, control-proteins and inducer chemicals. For all of these purposes, very powerful technologies are well implemented, such as gene shuffling, molecular modelling and combinatorial chemistry. Using high-throughput screening methods, promoter-inducer combinations will be selected that match the described criteria (Klug, 1999; Zuo and Chua, 2000). In turn, all these technologies are heavily dependent on genomics.

Still, several current bottle-necks in the concepts will prevent the application of GURTs in some crops. A major one is the water-tight regulation of expression of the disrupter and recombinase genes.

The application of GURTs in animals currently experiences much higher technological as well as ethical barriers. Options for introduction of GURTs in tree species are technically similar to those in crops. Applications in aquatic species may also soon emerge, although economic and environmental issues may result in a slower or more restricted development.

It can be envisaged that T-GURTs will be applied more readily because it will prove to be wider acceptable and because the technology appears less demanding. This is elaborated in more detail below.

2. Potential impact of GURT applications on agrobiodiversity and biosecurity

In order to properly assess the potential impact on agrobiodiversity, the social and economic context in which GURTs will be applied, is shortly summarized. As outlined above, a number of technical factors determine for which purposes, on which crops, trees, farm animal and fish breeds, and on which time scale GURTs, will be developed and applied. V-GURT applications require very rigid control mechanisms, whether the default state is expression or suppression of the gene resulting in cell death. If the gene resulting in cell death is not properly expressed in all embryos upon induction, industrial protection of the variety is lost. If the gene resulting in cell death cannot be effectively suppressed in all embryos, this might affect the efficiency of the propagation of the variety for the producer. In most applications, requirements for T-GURT expression will be less rigid, assuming that expression levels may somewhat vary from plant to plant (animal to animal) and cell to cell comparable to normal variation in expression patterns observed for heritable traits not controlled by GURT. Whether an inducer needs to reach the root system, leave tissue, flower organs or germ cells or specific animal tissues and organs determines the choice of available compounds and mode of administration.

Costs to solve technical bottlenecks as well as costs stemming from regulatory requirements will be juxtaposed against expected rates of return in deciding on investments in GURT development. These rates of return depend on markets for a certain crop, tree species or breed, both the total size as well as the market position of the specific party developing an application of the technology, in relation to the degree of improvement conferred by the variety or trait to be protected. GURTs will not be developed if they do not offer an advantage to the breeder, and GURTs will not sell if they do not benefit the

Regulators will balance the perceived economic benefits with the potential negative impacts, and consumers might be mobilised to participate in the debate and through their purchasing choices as well.

Application of GURT in crop breeding can be expected to precede its applications in the breeding of trees, fish and farm animals, as is also reflected in current patent applications. In our search for GURT-related patent applications no applications in the latter domains surfaced. The rapid pace of technical developments as a result of the short lifetime of crops as compared to animals and trees lends further support to this assumption.

Only the private sector has sufficient means to not only develop but also market genetically modified varieties. Genetically modified varieties will be primarily developed and applied for large-scale agro-production systems, purchasing power being largely absent in small-scale agriculture (Pinstrup-Andersen and Cohen, 2000; Anon., 2000a; Anon., 2000b). A major influence of GURT availability might be a redistribution of breeding efforts towards crops and animal breeds with the largest market shares or highest profit margins, since appropriation of breeding investments is no longer dependent on hybrid technology, triploidisation and male or female sterility, which are only available for some species. All these effects are further elaborated in the other chapters and are mentioned here to guide our discussion of the potential impact of GURTs.

2.1 Potential impact on agrobiodiversity

The Convention on Biological Diversity, article 2, (1992) distinguishes three integration levels of biodiversity, including agrobiodiversity, i.e. "the diversity within species, between species and of ecosystems". Genetic resources regard the diversity within species and are defined as genetic material of actual or potential value. Indigenous knowledge on the maintenance and utilization of agrobiodiversity can be added as a fourth major aspect of agrobiodiversity.

Only genetic resources, i.e., the biodiversity at the lowest integration level, can be conserved *ex situ*, at a site distant from the original occurrence of the conserved material. Diversity between species and of ecosystems, as well as the indigenous knowledge relating to agrobiodiversity can only be effectively maintained *in situ*, in the agricultural production context in which these are functional.

The public and private sector, as well as farmers and the civil sector, form stakeholders in our efforts to maintain and utilize genetic resources and agrobiodiversity, both *in situ* and *ex situ*, and each have different roles and interests. In assessing the potential impacts of GURTs on agrobiodiversity and agro-production systems, the organization of agrobiodiversity conservation forms a major determinant. Such impacts can be compared with the general impacts of the industrialization and specialization of agriculture on the conservation and utilization of agrobiodiversity, including genetic resources.

The relationship of breeders with agrobiodiversity is complex. On the one hand, the very industrialisation of agriculture from which the private breeding industry emerged, resulted in well recognized and partially documented genetic erosion in the field (Pistorius and Van Wijjk, 1999); private breeders provide farmers with high yielding varieties and breeds which have replaced traditional farmers' varieties. Since the numbers of private breeders are naturally much smaller than of the former farmer-breeders and their overall access to genetic resources is necessarily more limited than that of the former farmer-breeders, the diversity of genetic resources in the field is much lower than in former times, although arguably from wider origin. In other words, in an individual farming system industrialisation of crop production may not always result in a reduction of total genetic diversity, since farmers' varieties based on a more limited genetic resource base may be traded for commercial varieties which introduce exogenous germplasm. However, in a global perspective the multitude of autonomous farming systems with their own genetic resources are likely to cover a much wider genetic diversity than handled by the commercial sector. In addition, most of the crops and animal breeds have been developed for uniform growing conditions and uniform produce, and this - together with the globalization of agricultural markets - has severely decreased the agrobiodiversity in the field at the higher integration levels.

Farmers in autonomous production systems mainly rely on their own seeds and animals adapted to their particular agro-ecosystems, their farming practices and cultural preferences. This does not mean that there is no utilization of varieties and breeds stemming from the private sector. On the contrary, as far as accessible these varieties and breeds are used by farmers to test under their own conditions, and most of all to recombine with their own germplasm to improve that germplasm and 'breed' new varieties and breeds (Hardon *et al.*, 2000). In addition, the public sector, represented by the national agricultural research systems and international agricultural research institutes (NARS and CGIAR), acts as a channel by which major genetic improvements developed in the private sector, are made available to autonomous farming systems.

On the other hand, for sustained breeding efforts, the breeding industry is dependent on the continuing availability of genetic resources not available in their own genepools, in particular in cases of new diseases and ecosystem changes and in a response to changing consumer demands. Preferably, these genetic resources should then be supplied from well-documented, well-researched and easily accessible *ex situ* collections. Obviously, the maintenance of agrobiodiversity in autonomous farming systems or the survival of wild relatives in natural ecosystems as a much wider source of genetic resources, is only of secondary concern to most private breeders, and often regarded as a mainly public responsibility.

This picture also largely applies to the animal breeding sector. In contrast, genetic improvement of trees and fish has been relatively limited when compared with the crop and animal production sector and such efforts have been largely confined to specialist enterprises. Farmer breeding for tree production and for aquaculture has been mostly limited to genetic selection. Whereas this means that genetic resources maintained by small-scale farmers sectors is more limited than for crops and animals, these sectors are the more dependent on the maintenance of wild relatives in natural ecosystems.

With increasing GURT application, crop development in farmers' seed systems may lag behind crop development in industrial seed systems due to limited or even absent access to novel industrial innovations under GURT control. To safeguard long-term on-farm maintenance of plant genetic resources, increased investments in public plant breeding, including participatory plant breeding, may be needed to correct the increasing gap in absorption of innovations. This issue is discussed in more detail in chapters 3 and 4. Similar assumptions can be made for more distant applications of GURTs in the farm animal sector. Whereas overlaps of germplasm use and exchange between industrial and autonomous farming systems in trees production are more limited, and as a consequence no GURT varieties of interest to the small-scale sector are likely to be offered on the market, negative effects on agrobiodiversity (loss of species and genetic diversity) may remain more limited. However, in aquaculture, some species, in particular tilapia and crustaceans, are grown in small-scale and large-scale systems. Growing dependence of the small-scale sector on seed provided by industry may have a negative effect on the genetic diversity of species maintained in aquaculture.

In this context, it remains to be seen whether the control mechanisms currently developed will become sufficiently tight to absolutely prevent escape of the V-GURT protected variety or of geneflow of the T-GURT protected trait. If not, originally GURT-protected but now uncontrolled traits may eventually show up in its original or in alternative genetic backgrounds. The probability of such events will be determined by the technological protection level and by the acreage under GURT controlled crops and the dominant farming practices. Farmers trained in searching for aberrant phenotypes, may eventually be able to identify plants from which inducer control of a desirable trait has been lost. The net effect would then be a delay in availability of such traits in non-GURT backgrounds, rather than an absolute separation of genepools. Even low-frequency escapes from V-GURT protected varieties may be selected from grain stocks produced in autonomous and mixed farming systems.

The environmental effects on agrobiodiversity residing in wild relatives of geneflow from GURT controlled varieties into wild relatives does not seem to basically differ from those of GMOs in general.

Concerning effects on *ex situ* conservation, varieties controlled by V-GURT are unlikely to be maintained by genebank holders, assuming that in those cases no inducers can be purchased to maintain the variety, since this would run counter to the breeder's interest. Varieties exhibiting T-GURT can be expected to be introduced in genebank collections assuming that these will exhibit additional traits not under T-GURT control which render their introduction valuable. If expression of traits controlled by T-GURT can be accomplished by an inducer which can be obtained in the market, the interest of genebank curators might extend to the trait under T-GURT.

2.2 Potential environmental effects

Cross-fertilising V-GURT containing crops may cause considerable effects in neighbouring crop stands and wild relatives. This negative effect will also occur in case V-GURT strategies would be employed to prevent unwanted geneflow from GMOs into the environment, cultivated or wild, as an approach to contain the effects of a deliberate release of GMOs. Part of the seed of cross-fertilising neighbouring stands might not be viable, and this may impact on farmers saving their own seed. In addition, inadvertent mixing may occur in the seed production chain. The fact that in North-America, where large stands of GMO varieties are now grown, contamination of non-GMO varieties by GMO germplasm has been observed in maize (mixing) and canola seed (gene flow), suggests that this scenario is a realistic probability. The first event refers to inadvertent mixing of Starlink maize with other USA maize varieties in 2000, disrupting exports of food products to Japan and other countries. The incident reveals that such inadvertent contamination of other varieties may occur, that it may involve high liability costs, and that industry may exert pressure on regulatory bodies to adjust rules to cope with such contamination problems.

Table 2. Potential effects of component outcrossing

Component	Potential effect	Probability of outcrossing	Patents describing element
Disrupter genes			
inversed germination-essential gene + promoter	disturbance of normal germination	depending on normal recombination frequencies	*WO 9744465 Monsanto* *WO 990721 BASF*
pathogenesis factors + general or seed-specific promoter	dead seedlings	depending on normal recombination frequencies	*WO 9911807 Purdue*
general toxins + general or seed-specific promoter	dead plants or toxic seeds	depending on normal recombination frequencies	*WO 9911807 Purdue* *US 5723765 Delta & Pine/USDA*
disrupter genes without promoter, but integrated at transcriptionally active position	altered plant	extremely rare	*WO 9744465 Monsanto* *WO 9911807 Purdue* *US 5723765 Delta & Pine/USDA*
germination-essential gene (ACOX, phytate) + repressible promoter	high phytate expression, reducing nutritional value	depending on normal recombination frequencies	*WO 990721 BASF*
Restorer genes			
phytate gene + inducible promoter	no effect if uninduced level is close to zero; when induced reduced nutritional value and improved germination	depending on normal recombination frequencies	*WO 990721 BASF*
POX gene + inducible promoter	no effect, if uninduced level is close to zero; when induced, effect on vigour may occur	depending on normal recombination frequencies	*WO 9744465 Monsanto*
Inducible promoters + gene cassettes			
single-element promoter (safener-induced, Pathogenesis-Related) + gene	expression of trait or disrupter when herbicide safeners or pathogen are encountered	depending on normal recombination frequencies	*US 5689044 Syngenta,* *US 5608143 DuPont,* *WO 9008826 Syngenta*
microbial promoter with expression control gene (tetracycline, alcohol, steroid,	individual elements have no effect, if uninduced level is close to zero; combination of elements may result	depending on normal recombination frequencies for single element; outcrossing of cascade combination depending on element	*US 5654168 BASF,* *WO 9321334 Syngenta,* *US 6147282 Syngenta,* *WO 0009704 Syngenta*

homoserin-lacton)	in switch-on	configuration	
engineered plant promoter with engineered control gene	Individual elements may have effect on endogenous genes	depending on normal recombination frequencies	*WO 9008827 Syngenta*
Recombinase genes			
Cre recombinase gene	some phenotype, depending on regulation	depending on normal recombination frequencies	*US5658772 DuPont* *US 5723765 Delta & Pine/USDA*
Flp recombinase gene	no phenotype expected	depending on normal recombination frequencies	*WO 9925841 Pioneer* *US 6110736 Purdue*
Phic31 recombinase gene	unknown	depending on normal recombination frequencies	*WO 0107572 USDA*
beta recombinase gene	no phenotype expected	depending on normal recombination frequencies	*WO 9918222 Consejo Superior*
Tissue-specific promoter + gene cassettes			
fruit-specific promoters + gene	dependent on regulated trait	depending on normal recombination frequencies	*WO 9738106 Syngenta*
flower-specific promoter + toxin genes	sterility; inhibition of pollen formation;	depending on normal recombination frequencies	*US 5859328 Cornell* *US 5808034 Syngenta*
tuber-specific promoter + toxin genes	inhibition of tuber formation	depending on normal recombination frequencies	*WO 9906578 Syngenta*
seed-specific promoter + toxin genes	inhibition of (viable) seed formation	depending on normal recombination frequencies	*WO 0068388 Rhobio* *WO 9735983 Syngenta* *WO 9911807 Purdue* *US 5723765 Delta & Pine/USDA*
germination-specific promoter + toxin	inhibition of germination	depending on normal recombination frequencies	*WO 9403619 Syngenta*

It should be stressed that the actual effects are dependent on several variables which have to be considered in estimating these effects. These include the crop itself, its mode of cultivation, its propagation, its ability to produce viable pollen, the rate of outcrossing, the topography of the farming system, and the proximity to wild relatives. A follow-up study might pay more attention to such aspects.

Application of V-GURTs in crops, either as an appropriation strategy or an environmental protection strategy, might be assessed for its negative yield effects, in conformity with the precautionary principle.

In trees, the probability of outcrossing events may even be more likely, but negative impact may be low assuming that seeds form no economically important product. A potential positive impact on human health of GURT varieties not producing pollen (alleviating pollen allergy), depending on species and location, may conceivably outweigh the limited negative effects on seed formation in some crops (grasses) and tree species in some exceptional cases. Escapes in fish may be expected to occur and might have a severe negative effect on wild populations.

The impact of outcrossing of T-GURT constructs will be very limited in most cases. It can be expected that most GURT-protected traits will be under positive control of an inducer. If such constructs due to outcrossing would occur in crops in which these are not expected, inducers will not be consciously applied, and thus the constructs will usually remain unnoticed. A first exception is formed by constructs of which the trait is inducible by a range of related compounds or by triggering events occurring naturally (e.g. steroids, pest and disease infestations). A second exception is formed in cases where the receiving organisms already contain a GURT construct in which expression is controlled by related inducers. Unwanted effects are conceivable dependent on the trait which has been inadvertently introduced, e.g. yield drops, production of undesirable compounds etc. A high specificity of the inducing compounds may well be able to avoid such undesirable effects. A third and major exception is formed by the outcrossing of GURT constructs which exhibit negative control of the involved trait. Such outcrossing could affect not only domesticates but also wild relatives conferring properties which are unwanted. The impacts of negative regulation of traits with potential negative effects on yields and quality in a wide sense may need further discussion and policy development.

It is suggested to consider if constructs to be introduced in commercial varieties and to be deliberately released should also be evaluated for the potential effects of outcrossing of individual GURT construct components. Effects of such outcrossing, e.g. in the case of recombinase gene cassettes or if resulting in constitutive expression of the transgene, can be theoretically expected. In many cases, probability and therefore impact will be low to very low, given the recombination events which have necessarily to accompany the outcrossing events. The potential effects of such outcrossing are described in Table 2.

Potential negative environmental effects in the farm animal sector can be easier contained given the high level of domestication and current practices to control reproduction. In contrast, given the low level of domestication and the high probability of escapes of fish varieties containing GURT constructs, introgression of GURT constructs into wild populations might be substantial. The probability of negative effects on local fish populations would warrant further study. Similarly, the probability of impacts of introgression of GURT constructs into tree relatives would require further analysis.

Inducers (e.g. steroids) used on GURTs will also need to be evaluated for their potential effects on the target organisms as well as the environment and human appliers and consumers, particularly as they are likely to be unusual molecules, in order to make unauthorized reproduction more difficult, or to be able to bring them under intellectual property protection. They may be regulated as pesticides and veterinary medicines, depending on the nature of the compound.

2.3 Legislation and regulations

Compensation for the effects of the separation of genepools, and the limitations on access, may need to be sought within relevant forums, such as the FAO Commission on Genetic Resources for Food and Agriculture and, upon entry into force, the Governing Body of the new International Treaty on Plant Genetic Resources for Food and Agriculture. Such compensation could not only contain the identification or establishment of funds from public or private sources, but also the provision of advanced germplasm to local farming systems by private industry, its use being limited to certain applications.

The application of GURTs provides a strategy by which the need for plant variety or patent protection as an appropriation strategy can be avoided. GURTs can function as technological protection, independently of whether or not the GURT technology is itself patented. However, it can be expected that for competition motives industry will wish to protect its GURT strategies and components, as exemplified by the substantial number of filed patents which are either specifically directed at the development of GURTs or provide interesting components for such technology. The options to regulate the use of GURTs through intellectual property rights systems will be discussed in more detail in chapter 4.5.

GMO legislation may form a framework for the regulation of undesirable biosafety effects of GURT introductions, since all GURT containing organisms will be classified as GMOs.
The question of how to prevent the unauthorized production and use of an inducer, in law and in practice, needs some additional attention. One strategy would be to protect the applied inducer by intellectual property rights (patents). However, this strategy will not be available to pre-existing compound, particularly if that compound already has a recognized use, as a commodity, or under intellectual property. Presumably, inducers would have to be new molecules or combinations of molecules, and subject to risk assessment and regulation as such. Existing legislation on pesticide use and on veterinary medicines may be adapted to include applications of inducers described in this study.

Because of their function in switching on valuable traits, small volumes of these compounds unlock substantial commercial benefits. This makes it likely that inducers will become the target of unauthorized production and sale, and of smuggling. Prevention of unauthorized use of inducers could add considerably to a company's legal expenses, and perhaps to the policing costs to be born by governments.

3. Potential socio-economic impacts of GURTs from a farming systems perspective

In analysing the impact of GURTs on crop farming systems, this chapter has focused on seed systems and in particular the various seed sources of farmers and the movement of varieties, and on the levels of intensification of farming systems, distinguishing between farmers' and formal seed systems. The rationale behind this approach is twofold. First, GURTs are carried by seed, and thus the seed system is the most direct determinant in analysing the effects of GURTs on farming systems. Second, almost all farming systems combine farmers' and formal seed systems, blurring an analysis of the impacts of GURTs at the farming system level. The farmers' seed system is based on farmers' selection, multiplication and exchange mechanisms. It is closely integrated in crop production practices and the local knowledge systems surrounding agriculture. The formal seed system is characterised by a chain rather than a cycle of activities, starting with collection and characterisation of genetic resources, and followed by breeding, multiplication and marketing or distribution. Formal seed production and distribution are commonly regulated by national and/or industry regulations. Findings at the seed system level have been integrated in a subsequent analysis from a farming systems perspective.

The transformation of farming from a subsistence activity into commercial agriculture in modern times led to the functional separation of plant breeding and seed production from common farming. However, the resulting specialised seed production has not nullified the importance of farmers' seed production, except for some highly intensive production systems, such as greenhouse horticulture. Thus, in most countries two distinctive, but interacting types of seed delivery systems are encountered: the formal (regulated) seed supply system and the farmers' own seed supply system. At a global scale, farmers themselves by far produce the largest quantities of seed and numbers of animals. Farm-saved and locally exchanged or traded seed significantly reduces the market for commercial seed.

Commercial seed production and plant breeding is only viable when market competition can effectively be reduced. Marketing (branding), legal (intellectual property rights) and biological (hybrids) strategies are used with varying rates of success and transaction costs to contain market competition. Genetic Use Restriction Technologies (GURTs) offer additional biological means to protect the seed market.

3.1 Farmers' seed systems

Local knowledge and cultural traditions surrounding seed are very diverse among and within communities, and often strongest for the most important food crop seeds. Seed selection and storage are women's tasks in most cultures, pointing at the strong gender aspects relating to the functioning of seed systems. The genepool that is used in farmers' seed systems is dynamic. Genetically diverse landraces (also called farmers' varieties) evolve with changing conditions, requiring a regular influx of genes. Farmers value 'new' materials as a source for such influx. Materials may be accessed from neighbours, relatives and immigrants, and from farm supply stores and extension services.
Modern varieties are often reproduced and distributed in farmers' seed systems. This so-called 'lateral spread' has been successfully promoted in relatively uniform areas in developing countries in order to maximise the benefits from formal breeding, the Green Revolution forming a prime example of such developments. Whereas modern varieties rarely perform as well in marginal conditions, their characteristics often do enrich the genetic base of farmers' varieties in the more marginal production systems.

Alternative approaches in plant breeding and seed supply have emerged in the 1990s in response to the limitations of the Green Revolution in more marginalized farming systems. These include breeding for specific adaptation and participatory variety selection and participatory plant breeding, combining scientific and farmers' knowledge and materials. Even more so than in conventional plant breeding, free access to a wide range of plant genetic resources is vital for the success of this approach.
Germplasm development in animal breeding has largely followed analogous patterns. Modern breeds from the private sector are often interbred with local populations, maintained in autonomous farming systems. Tree and fish germplasm maintained in large-scale industrial and small-scale farming systems probably experiences various exchange due to a more limited overlap in cultivated species.

Expected effects of the introduction of GURT on farmers' seed systems include:

Reduced access to genetic resources and technologies

Farmers tend to use all genetic resources available to them for local crop development. Materials that are derived from formal plant breeding serve to introduce important new traits such as new disease resistance alleles. The widespread use of V-GURTS or T-GURTs for such traits would cut off local crop development from formal plant breeding accomplishments. GURT-protected modern varieties would not be available for further introgression and adaptation to local conditions, either or not as part of participatory breeding initiatives. Also, public initiatives to support breeding for the rural poor, such as performed by the CGIAR centres and NARS, may face problems to access new traits (e.g. disease resistances) from commercial breeding programmes.

Risks of reduced seed security

Serious seed security risks can be expected for those already seed insecure poor farmers who are not able to save their own seed for the next season. Risks of crop losses due to absent viability exist when poor farmers access the grain market for their seed (in many areas over 20% of farmers), often at a late moment. Similar risks may follow from food aid consisting of GURT containing seed and distributed to disaster-struck communities, since relief food supplies are often used as seed.

Less diversity

When breeding and marketing of GURT-protected crop varieties proves successful, such varieties are likely to replace a number of farmers' varieties which now constitute the cultivated germplasm. As a consequence total genetic diversity in farmers' fields might further decrease. This has been elaborated in chapter 2.1.

3.2 Formal seed systems

Specialised seed production, whether by public or commercial breeders favours the development of varieties that can be used by as many farmers as possible. Varieties are bred for large, rather uniform ecological areas. Access of public and private breeders to new genetic diversity is vital for the breeding process. Large investments are made in the collection, storage and characterisation of plant genetic resources in national or international (CGIAR) genebanks and the strategic stocks of genetic diversity in breeding companies that are usually not shared with competitors.
Government institutions traditionally dominate the formal seed system in the South as part of policies to increase agricultural outputs. In industrialised countries, the private sector is dominant. Structural adjustment policies have been the basis of privatisation initiatives in the seed sector in many countries. Mixed systems have developed, in which a private seed industry develops seeds for some crops, leaving less profitable seeds to the public sector. In general, it is unlikely that the public sector will develop or access GURT-protected varieties. In other words, development and marketing of GURTs will only affect farmers when making use of seed produced in the private sector.

The following effects of GURTs can be anticipated when water-tight GURTs are introduced. The degree of impact will strongly depend on the extent to which and the number of crops for which GURTs will be developed.

More breeding

GURT offers commercial possibilities in crops that hitherto were not commercially interesting such as cereals, pulses and various vegetatively propagated crops. Thus, the formal seed market may supply a broader product range. The increased expected profits may result in more investment in breeding of such crops. An example is formed by the increased breeding investments by the private sector in rice. These efforts will be directed towards high intensity farming systems mainly.

Cheaper 'hybrid' seed

Apomixis creates opportunities to produce 'hybrid' seed as a self-fertilised seed crop. This reduces the costs of seed production considerably, but creates competition from farm-saved seed. V-GURT-protected apomicts, however, may be seen by industry as providing both cheap seed production and an effective protection.

Dependence on external seed sources

Farmers using GURT protected seed will become completely dependent on seed suppliers. This condition is comparable to that of hybrid seed users, who also depend on seed suppliers. However, in extreme cases the latter farmers have the option to use F2-seed. In areas where local seed production is already risk-prone, an added dependence on purchasing power may further decrease seed security.

Monopolisation of genepools

Breeding depends on the availability of a wide array of parental germplasm for further crop improvement. Commercial varieties are intensively used in further breeding by developers and competitors alike, as allowed under the UPOV plant breeder's rights. Although the company that introduces new traits has a significant commercial advantage because competitors will need several years to introduce such traits in their new varieties, GURTs will offer breeders a biological instrument to protect their materials from immediate use by other breeders and thus offer protection over a much longer period.

Wider acceptance of genetic modification

Four main concerns relate to the introduction of genetically modified organisms in agriculture: environmental safety, food safety, economic concentration and ethical concerns. In those situations in which environmental safety is the overriding concern, availability of GURTs to contain unwanted spread of genetically modified organisms may render the introduction of living modified organisms more acceptable. However, in situations where economic or ethical motives for the major concern, the potential development of GURT-protected varieties will further hamper the introduction of genetically modified crops.

3.3 A farming system analysis

The FAO Global Farming Systems Study identifies 5 levels of intensification of farming systems and their respective drivers (see table 3 below).

Table 3. Levels of intensification of farming systems

	Resources	**Features**	**Drivers**
I. low intensity	Land & labour	Food crops, traditional technologies	Population, technology
II.a medium intensity	Land & technology	Limited improved land management; mixed crop/livestock or diversified	Population, resources, technology
II.b medium intensity	Resource & technology	Low diversity; high market integration	Technology, markets, services
III high intensity	Technology & market	Significant integration	Technology, markets, services
IV.a very high intensity	Technology, market, information	High on-farm integration	Services, information, knowledge
IV.b very high intensity	Market, information	Specialised, vertically integrated	Information, knowledge

The likely effects of GURTs on farming systems will depend to a large extent on their level of intensity.

Very high intensity farming systems

Where T-GURTs can support farmers' management decisions, effects on high intensity farming systems might be positive. When V-GURTs become available, increased breeding investments for these systems can be expected in countries with weak (or expensively controlled) intellectual property rights systems.

High intensity and medium intensity (IIb) farming systems

The introduction of GURT-protected varieties in these farming systems characterized by major food and fibre crops may create new business opportunities for seed suppliers that are absent now. GURTs may support the shift from medium intensity farming systems to high intensity, market-oriented farming systems, as also affected by the introduction of other technologies, such as fertiliser-responsive cereals and hybrid maize and millets. Where GURT is combined with important agronomic traits, it is likely to support a shift to a higher use of other farm inputs and higher market integration.

Medium intensity (IIa) farming systems

Farmers in medium intensity farming systems are most vulnerable in their dependence on suppliers, since often they can not afford yearly purchase of seeds. The large-scale introduction of GURT might force them to spend a larger proportion of their budget on seeds or alternatively it may cut off these farmers from technology development. Often these farmers are also more vulnerable because of climatic conditions. Varieties that were developed for more benign conditions are likely to do well on average in such medium intensity farming systems, but farmers may lack the resources to cope with occasional unfavourable seasons caused by drought or epidemics, and lack the finances to purchase seed for the new season, while simultaneously lacking the option to use farm-saved seed. Furthermore, social implications of the introduction of GURT-protected germplasm may be similar to those of the introduction of Green Revolution varieties, i.e. a shift in responsibilities from women to men, and larger differences between early and late adopters, combined with greater total output and greater environmental problems due to loss of biodiversity.

Low intensity farming systems

It seems unlikely that GURT varieties will be successful in low-intensity farming systems. The poorest farmers in these farming systems, however, who depend on the grain market for their seeds, risk loosing crops when GURT-containing food grain enters such local markets through trade or relief channels.

Food security at the household level is not always positively affected by increased total food production. Even though the introduction of GURTs may increase total agricultural output, their introduction may not positively influence access to food by poor sectors in society.

3.4 Policy considerations

The following considerations are based on the assumption that water-tight GURTs might be developed, patented, and widely used in commercial plant and animal breeding.

- The introduction of GURTs may positively influence the availability of commercial seed developed for high intensity agriculture and simultaneously widen the gap between resource-poor and better-off farmers. This may call for public investments in breeding targeting resource-poor farmers.
- GURTs may obstruct the transfer of technology from the formal sector to local initiatives, and among formal plant breeders. The level of market control that GURT may create could be brought in line with patent protection, which provides only a temporary monopoly to the inventor in exchange for publication.
- Dependence of farmers on formal seed supply through the use of GURTs may result in a food safety risk in poor-infrastructure seed markets in developing countries. Strong anti-trust laws could form an instrument to avoid undesirable and erratic dependence on single or few suppliers.
- GURTs could also increase seed insecurity of resource-poor farmers who can not afford purchase of seed and who depend on the local grain market for their seed needs. It may be considered to promote the use of GURT-protected crops only in closed production chains.
- The possible displacement by GURTs of plant varieties under intellectual property rights would weaken a country's ability to tailor appropriation mechanisms to its policy needs like, for example, by provision of a breeder's exemption, or of a farmers' privilege to resow the product of the harvest under certain conditions.

4. Potential Economic Impacts of GURTs

This section (re)examines the economic rationale for GURTs, potential impacts of GURTs on investment in agricultural R&D and productivity, followed by a discussion of concentration and integration issues, and finishes with a review of the regulatory support and reactions possible for governments.

4.1 Economic rationale for GURTs

GURTs fulfil one of two roles as technological innovations for their developers: (i) productivity improvements (largely T-GURTs), or potential advantages accruing from sterile harvests or sterile progeny animals in certain production systems, and (ii) appropriation of benefits from other innovations (primarily V-GURTs). It is the potential economic impact of the latter role of benefit appropriation that has the most relevance for sectorial, national and international policy, which is considered here. In addition, impacts on breeders and farmers may be substantially different.

There are two general applications of GURTs that can provide a means to restricting the use of breeding improvements by farmers or other breeders. First, V-GURTs could be used to produce seed that ensures that farmers cannot re-use saved seed and that breeders cannot use seeds in their own competing breeding programmes. Second, T-GURTs can ensure that value-added traits of seeds (such as induced flowering) can only be used by farmers that have purchased the seed or necessary inducers from the breeding company, or its agrochemical affiliate.

Economic growth in the agricultural sector has been based on a number of factors, of which technology development, in the form of improved varieties/breeds of cultivated plants and domesticated animals and fish, has played an important and documented role. Given the self-reproducible nature of these innovations, it can be argued that the private sector, in particular breeding companies, is likely to underinvest in R&D in the area of breeding. For this reason, intellectual property protection, for example in the form patents or plant varietal protection (PVP) is granted in most countries and has been included under the WTO TRIPS Agreement (Article 27.3b).

Plant varietal protection (PVP) is the most common form of intellectual property right available to plant breeders. Exclusive rights over the production and sale of the protected variety are generally balanced against provisions that allow other breeders to use a protected variety in their breeding research (breeders' exemption) and/or that allow farmers who plant a protected variety to re-use or possibly sell the seed they then produce themselves (farmers' privilege). Standard requirements for PVP legislation have been agreed upon internationally in the form of the UPOV (Union for the Protection of New Varieties of Plants) treaties of 1978 and 1991.

In many situations, PVP systems operate with only partial enforcement due to the high transaction costs involved. The development of GURTs has thus been partly motivated by a desire by some breeding enterprises to capture a greater proportion of the research benefits where enforcement of intellectual property systems is ineffective or too expensive. But GURTs can also be an attempt to extend the scope of benefits appropriated beyond that granted in IPR legislation, partly through further limiting the farmer's privilege. GURTs can thus be seen as another move in a history of developments leading to greater appropriability of research benefits in the agricultural sector.

From a seed producer's point of view, the use of GURTs as an appropriation strategy will be particularly attractive in markets where legal protection (plant varietal protection or patents) is not possible or not effective. The latter is the case in countries with an inefficient court system, and with high costs of exercising property rights: in (developing) countries with poor infrastructure for information gathering and physical royalty collection, and in countries with an expensive court system, e.g., in the USA.

To maximize the returns and to contain the costs, it is possible that industry will seek regulatory support to defend the use of GURTs as part of an appropriation strategy, once established in practice, by banning for example reverse engineering of inducers, or deactivation of the GURT complex. In this context, strategies to enforce copy protection in the information industry form an example. If the legitimacy of the use of GURTs as an appropriation strategy is accepted, important implications for government policies and regulations regarding reproductive materials result. GURTs are independent of any legal national control, except over whether or not their use as a general category is allowed. Therefore, GURTs do not allow governments a similar flexibility of policy direction as for intellectual property rights.

The various economic benefits and costs from the development and introduction of GURTs are summarized in qualitative terms in Table 4.[1]

Table 4: Summary of Economic Benefits and Costs from GURTS used as an appropriation strategy

	Benefits	**Costs**
Farmers	Increased *productivity* from improved inputs due to increased R&D investment	Increased *input costs* from seed purchase (incl. transaction costs)
Breeders (especially private sector)	Increased *appropriation* of research benefits from new products	Increased cost *for access to gene pools* of other breeders
	Increased *market segmentation*	
Consumers	Lower *food costs*	
Governments	Reduced *investment requirements* in breeding	Alternative *investment requirements* to close the technology gap
	Fewer *enforcement costs* for PVP	Other *regulatory support* required for GURTS
		Less options for *regulatory control* through IPR policies

Governments need to assess the benefits and costs associated with GURT introduction in order to develop the policy response most appropriate for their circumstances. The discussion here aims to offer some initial qualitative expectations based on a cursory review of existing knowledge related to this technological development.

4.2 Potential impacts on R&D and productivity

GURTs are essentially an appropriation mechanism for the breeding sector, providing the opportunity to increase profits by protecting the efforts needed to develop new varieties. A key question is how much the increased appropriation offered by GURTs will lead to increased investment by the private sector and associated productivity improvements. Experience with plant varietal protection and hybridization offers some insights.

PVP systems have been subjected to some study for their economic impacts, particularly in the United States and to some extent in the UK (Butler 1996, Perrin, Hunnings and Ihnen 1983, Lesser 1997,

[1] The formal tools of cost-benefit analysis are not an appropriate tool of analysis for assessing the broad nature of the potential impacts of GURTs but the concept of benefits versus costs provides a useful framework for presenting these impacts across various groups.

Alston and Venner 1998).[2] Economic studies have been somewhat divided but there appears to be a moderate consensus that plant breeders rights do not provide incentive for adequate investment by the private sector in breeding activities (Eaton 2001). Inadequate incentives provided by PVP could be attributed to two aspects: the scope of the protection and the effectiveness of enforcement. While the scope of protection has been increased in many countries, (and as seen in the differences between UPOV 1991 and UPOV 1978), this provides an operational means of increased appropriation only if the enforcement of the property rights granted is effective. Not only are the costs of checking and pursuing potential violators of restrictions on farm-saved seed generally high, involving field checks, possible laboratory analysis and legal proceedings, but the necessary level of institutional development is not present in all countries.

Unlike the use of GURTs as an appropriation mechanism *per se*, the use of hybrids has direct production benefits, which ensure a market for hybrid seeds. However, because the harvested seed results in less productive starting material, hybrids also provide breeders with a way to increase benefit appropriation. This strategy has been effective in a limited number of crops, including maize, sorghum and rice. Hybridization has been associated with increased private sector investments in agricultural R&D.

Limited evidence from the U.S. supports the hypothesis that hybridization of major crops has, by increasing the appropriability of research investments, attracted more private investment into plant breeding (Srinivasan and Thirtle 2000). Table 5 shows that for the hybrid crops maize and sorghum, private plant breeding has accounted for more than 10% of seed sales in the US while the ratios for three non-hybrid crops are 5% or lower (Fuglie *et al*., 1996). Appropriability is seen from the higher percentage of seed purchased for the hybrid versus the non-hybrid crops.

Table 5. Seed Sales, Private Plant Breeding and Trends in Seed Prices and Yields of Major Field Crops in the US (1975-1992)

Crop	**Seed sales**	**Private plant breeding**	**Ratio private breeding to sales**	**Seed cost**	**Share of seed purchased**	**Growth in seed price**	**Annual growth in crop yields**
	US$ million (1989)	US$ million (1989)	%	$/acre	%	%/yr	%/yr
Hybrid seeds							
Maize	1031	112.9	11	21.09	95	4.75	1.33
Sorghum	90	12.6	14	5.13	95	5.08	1.54
Non-hybrid seed							
Wheat	256	13.5	5	8.92	40	0.97	1.13
Soybean	610	24.9	4	12.03	73	1.92	1.23
Cotton	108	4.6	2	14.93	74	4.46	2.23

Source: Reproduced from Fuglie et al. (1996); ratios of private breeding to sales are authors' own calculations.

It is most likely that GURTs will only be applied in new breeds and varieties that offer considerable productivity improvements to farmers, given the considerable costs of GURT development and application. Some of the latest improvements witnessed in GMO crops give reason to expect that the

[2] It is quite plausible that increased investment in breeding need not accompany increased productivity, as such investments might be oriented towards activities, such as brand marketing, or replacement of seed varieties in the market with marginally improved ones, that are largely intended to profit from the "monopoly" powers conferred on the right holder.

rapid advances being made in this area will lead to yet further agronomic improvements that go beyond the rate of increase seen in conventional breeding efforts (James and Krattiger 1999).

T-GURTs, in particular, may provide the protection necessary for breeders to provide differentiated products for the needs of different farmers and maybe also consumers. While trait-specific benefits would probably be achievable without the use restriction, the latter might provide sufficient incentive for the development and commercialization of the innovation.
The existence of net productivity improvements from GURTs as a result of increased private investment depends on whether the increased investment from GURTs is additional in the sense of expanding the overall portfolio of research activity as opposed to displacing publicly-financed activities. Thus the productivity benefits might be indirect, being found in the impacts of another crop that consequently receives higher public breeding investment. Freed public R&D resources for breeding could be directed to more marginal or orphan crops, which could be particularly important in developing countries. But it is important to emphasise that realising these benefits for the agricultural sector depends on continued support for publicly-financed agricultural R&D. In most OECD countries, there is currently a long-term trend of decreasing public agricultural R&D or at least decreasing growth in public spending in this area (Alston et al 1997). In any case, increased private investment implies a stronger need for developing countries, and also the international agricultural research centres, to find new mechanisms for accessing the benefits of research in industrialised countries (Goeschl and Swanson 2000).

To the extent that GURTs do lead to greater investment in agricultural R&D and therefore greater productivity, there will be benefits not only for farmers and breeders but also for consumers. However, there is one important caveat in relation to this conclusion that lies in the fact that the application of GURTs is accomplished through the generation of GMOs. The capital costs of developing GM crops in general, including regulatory costs, legal costs and possible product liabilities, are high, and as such the application of GURTs in minor crops, or crops for limited niches, is unlikely to attract private investment. It has been estimated that $ 30 million or more is required to commercialize a GM crop, not counting perhaps an additional $ 6 million to cope with regulatory costs (Christian Science Monitor, August 30, 2001). By this analysis, it is likely that GURTs would not be applied to minor crops, and this would, if anything, limit the scope of private sector R&D, and thus of perceived benefits not only to breeders, but also to farmers and consumers.

While GURTs may lead to an increase in investment for some crops, the nature of the technology may have a negative effect on the productivity of these breeding efforts over the longer term by resulting in more separated pools of genetic diversity. This could translate into lower potential productivity in the future than would otherwise be possible with open use of genepools. Quantification of such a loss is quite difficult and will certainly take place over a longer time horizon.

An increased productivity lag is a concern for developing countries. With V-GURTs, but also T-GURTs, use of advanced breeding lines would become more difficult or costly, leading to a further productivity lag for developing country farmers. Varying rates of diffusion of GURT-embodied productivity gains at an international level could also lead to shifts in international markets, including the emergence of new "growth clubs" among developing countries (Goeschl and Swanson, 2000).

The most important effect that can be expected from the introduction of GURTs (especially V-GURTs as an appropriation mechanism) is an increase in the seed replacement rate by farmers. This implies the potential to increase the amount of seed purchased i.e. an effective increase in demand, with a transfer of benefits from farmers to seed suppliers. GURTs are likely to form part of a longer term strategy of breeders that allows them to increase slowly (and thus not immediately) the appropriation of benefits from farmers. There is also the potential to generate longer-term lock-in of farmers.

Both V-GURTs and T-GURTs may open up possibilities for market segmentation by breeders and seed suppliers, where essentially the same variety is sold in different market segments at different prices. This could yield efficiency gains and result in the diffusion of new varieties to segments of the market that previously could not afford the newest seed technology.

4.3 Industry structure

GURTs provide possibly a further rationale for a strengthening of vertical integration in the seed breeding and agrochemical sector. Whether it provides further concern for the development of monopoly power in the biotechnology and seed sector depends in part on the extent to which incumbent firms or new entrants can develop their own GURT or non-GURT technologies.

Recent vertical integration in the seed industry can be separated into two waves. First, multinational companies, mainly active in agricultural chemicals and pharmaceuticals, acquired smaller biotechnology start-ups. The second wave involved the acquisition of seed companies by the diversified multinational firms with significant capabilities in discovery and product development (Kalaitzandonakes and Hayenga, 2000). This integration is relevant not only for industrialized countries: with few exceptions, each of the major companies has a significant presence in the developing world (Byerlee and Fischer, 2000). This wave of vertical integration has thus been driven by the desire to reduce transaction costs in accessing and applying biotechnology in integrated product development. Some of the past motives for vertical integration may be reinforced in the context of GURTs. T-GURTs involve the need for complementary and specialized assets in the form of specific chemicals (inducer compounds). T-GURTs also provide possibilities for strategic entry deterrence in either the seed or inducer market. In addition, the need for co-ordinating product development between the seed and the inducers can reinforce the benefits from vertical integration. There may thus be strong reasons to expect that vertically co-ordinated structures are necessary to foster the development of GURTs. Whether this is beneficial or detrimental to consumers depends on the balance between efficiency savings and the tendency to cartelization and restricted entry. This is an empirical matter requiring assessment on a case-by-case basis.

Horizontal concentration (fewer suppliers of the same product) in breeding and agricultural input industries has also been taking place due to increasing economies of scale associated with the application of biotechnology (Brennan et al, 2000, Hayenga 1998; see Table 3). Research and development in the seed industry is also concentrating from the point of view of crops. A few crops are receiving the major share of investments in the industry (Rangnekar, 2000). Along the same lines, concentration of intellectual property rights is also a preoccupying issue, as a few companies have control over most patents (Brennan et al, 2000). Such situation tends to erect barriers to the entry of new firms (Lesser, 1998; Falcon, 2000; Rangnekar, 2000), which in turn reduces the possibilities to increase competition in the industry.

Table 6. North American seed market shares, 1998

Company	Corn	Soybean	Cotton
Pioneer	39	17	-
Monsanto (cotton shares split below)	15	24	
Delta & Pine Land	-	-	71
Stoneville	-	-	16
DeKalb	11	8	-
Asgrow	4	16	-
Novartis	9	5	-
Dow Agrosciences / Mycogen	4	3	-
Golden Harvest	3	-	-
AgrEvo / Cargill	4	-	-
Hoechst / Schering / Advanta	3	-	-
Syine	-	4	-
Others private	20	39	13
and (public)		(10)	

Four firm concentration ratio (combined market share of four largest shares in the market)	67%	49%	>87%

Source: Based on Kalaitzandonakes and Hayenga, 2000

The potential for GURTs to contribute to this increasing concentration is clear. But it remains to be established which type of competitive (or anti-competitive) behaviour is actually emerging. Indications of increasing concentrations of market share are themselves not an indication of misuse of monopoly power. Detailed research is necessary to examine whether excessive pricing is occurring.

National anti-trust laws and regulation ends at the border. There do not yet exist international institutions that may step in to support countries with lacking national institutions. There have been some developments within the WTO to address this issue.

4.4 Intellectual Property Systems

GURTs, in particular V-GURTs, provide increased scope of protection through technological means as opposed to through legal means. The essential question facing governments is whether such increased protection is desirable. Other things being equal, the answer may well be yes, if this leads to increased levels of R&D activity. However, in some developing countries, a major consideration may be the relative inability of GURTs, as compared to legal means, to discriminate between different types of uses of protected material. Such flexibility allows developing countries, which have diverse farming systems to moderate the privileges of other breeders and farmers, as can be recognized in the farmers' privilege. If a government has worked to ensure the maintenance of the farmers' privilege through its approach to PVP and patent legislation, then it may wish to restrict or even prohibit the use of GURTs as a broader appropriation mechanism. Such a perspective may be particularly relevant for a number of developing countries that are seeking to do just this in their actions to meet their TRIPS obligations.

Intellectual property rights are either based on novelty, non-obviousness and industrial application (patents) or distinctness, uniformity, and stability (Plant Breeders' Rights). GURT-based varieties are likely to be protectable in those countries that offer patents and/or plant breeders' rights. There are generally no existing grounds in IPR legislation for disapproval of GURT as a technology.

4.5 Policy Considerations

Very few viable options are currently available for regulating the use of GURTs as an appropriation mechanism, should governments wish to do so.

Biosafety regulations do apply to organisms containing GURTs. However, such regulations cannot simply be used to prohibit the introduction of GURTs, if the organisms containing GURTs would not pose a specific threat to food or environmental safety.

Patent protection is a negative right permitting the patent holder to prevent unauthorized use. It does not, in itself, regulate the commercialization of a patented product, depending on whether such product meets other relevant regulations. A possible basis for exceptions may be formed by a clause in the WTO TRIPs Agreement that mentions 'ordre public' as a ground to regulate patent applications. Article 27.2 enables a Member to exclude from patentability inventions whose use would seriously prejudice the environment. This provision reads as follows: "Members may exclude from patentability inventions, the prevention within their territory of the commercial exploitation of which is necessary to protect ordre public or morality, including to protect human, animal or plant life or health or to avoid serious prejudice to the environment, provided that such exclusion is not made merely because the exploitation is prohibited by their law". The question can therefore be asked whether patent

applications describing GURTs, as a set of technologies which may impact food security, may warrant further discussion on the relation with the ground of 'ordre public' as in this agreement. In addition, it may be considered to request information in the patent application for GURTs on the existence of studies regarding socio-economic and biodiversity-related effects. A precedent for such provision may be formed by the requirement in some patent laws for a disclosure on the origin of the germplasm that forms the subject of the patent application.
Even if a patent right may not be withheld on the basis of the patent application encompassing the use of GURTs, the granting of a patent does not in itself provide a positive right to commercialize the product. Governments may wish to regulate or ban the use of GURTs as a production strategy by mechanisms other than patent legislation. Some types of seed legislation may offer an opportunity for regulation of GURTs. Variety release procedures are often liable to registration procedures and performance testing. Where variety release includes compulsory performance testing, it is possible to regulate market access of V-GURT varieties, even if they include agronomic improvements, on the basis of not producing a viable second generation. This requires having a system of compulsory performance testing as part of a restrictive variety release system. Many countries have, however, dispensed with this type of seed legislation or maintained it only for certain crops.

From their perspective, in future, breeders may request from government authorities new regulations to prevent unintended utilization of GURT-protected varieties and breeds, e.g., by reverse engineering or unauthorized sale of inducers. Adoption and implementation of such new regulations would enlarge the regulatory burden and increase costs for all stakeholders involved. Liability claims against contamination of produce, whether seed or food products, might further add on costs associated with the application of GURTs.

Summarised the following policy considerations can be made:

- In evaluating the impact of GURT technologies, a clear distinction should be made between the use for added production value, the use for genetic containment, and the use as an appropriation technology.
- GURTs, as an appropriation mechanism, may lead to an increase in agricultural productivity for a limited number of large-scale crops that have not yet been hybridized, by stimulating further investment, with long-term benefits for farmers and consumers.
- Although GURTs, as an appropriation mechanism, may stimulate private investment in large-scale crops, this may imply a corresponding strengthening and readjustment of public agricultural research, in order to mitigate potential direct and indirect negative consequences for the welfare of resource-poor farmers and for the agricultural productivity of countries and farming systems that may become more deprived from the benefits of agricultural research.
- Technological protection by GURTs could undercut intellectual property rights, and replace it by technological protection. This would weaken governments' ability to use intellectual property rights systems as a policy instrument.
- GURTs, as an appropriation mechanism, may well reinforce the concentration and integration trends in the breeding sector in such a way as to lead to possibilities for misuse of monopoly power. This issue requires continuous monitoring of the situation on a case-by-case basis, including strengthening of competition and anti-trust institutions in developing countries and at the international level.
- Given the impacts on the welfare of farmers, governments in many developing countries may wish to find ways to regulate the use of GURTs, particularly as an appropriation mechanism. This may require new forms of legislation with compulsory varietal registration and the clause in Art, 27.2 of the WTO TRIPS agreement providing a possibility.

5. Implications of GURTs for farm animal genetic resources management

Research to exploit GURT for livestock systems is likely to develop. Applications in industrial farming systems would most obviously focus on restricting access to genetically modified animals designed to produce therapeutic or nutritionally enhanced foods or other novel products. However, GURT could also have significant direct production value in traditional livestock production systems. In contrast to annual crop species such as wheat, rice, and soybeans, livestock species are long-lived and mobile, and breeding stock for the next generation is commonly derived from the commercial animals of the previous generation.

One of the main challenges in implementation of optimal livestock breeding programs in medium- to low-input production systems, extensive pastoral production, or communal grazing systems is to achieve sufficient control over matings to avoid mongrelization of breeding stock, dilution of adapted local genetic resources through uncontrolled crossbreeding, and loss of hybrid vigour due to *inter se* matings among first-generation crossbreds. In meat production, the most common crossbreeding objective is to improve productivity by mating females of adapted, native breeds to males of breeds with higher growth potential to increase efficiency of lean tissue production in crossbred offspring. Incorporation of GURT into male lines to induce sterility in crossbred offspring would allow optimisation of the crossbreeding system without control over matings and protect the integrity of adapted maternal breeds. Provision to modify the composition of the female line could be retained by maintenance of parallel male lines without the sterility traits used for GURT. Availability of GURTs in dairy production could encourage development of genetically modified animals capable of producing novel milk products. However, such applications of GURTs would have implications for the control over reproduction and breeding programmes, which may shift from farmers to breeders.

Application of GURT is more difficult in dairy or fibre production than in meat production. An effective GURT for dairy or fibre production must preserve the reproductive capacity of the breeding female and the viability of her offspring while regulating future access to the genes she carries. Use of GURT to control access to genes is conceptually easier in egg production than in meat, dairy or fibre production. First, if eggs are the product of interest, the producing female must be fertile but need not produce fertile eggs, so long as the farmer is willing to forego the option of using the line for meat production. Second, in poultry, live birds of the desired genotype are commonly provided to farmers directly from hatcheries, so genetic screening is possible at an individual level to control the sex and genotype of the birds offered for sale.

The development of GURT in animals will likely initially focus on the X-Y and X-O systems of sex determination in mammals and birds, respectively.

In conclusion, GURTs offer direct production values in animal agriculture, but their development will be complex, requiring development of both new knowledge and improved techniques for molecular manipulation of animals.

6. Conclusions

It is important to distinguish between the application of GURTs to increase production value, where farmers may be willing to buy the GURT-containing variety for this production increment, and the application of GURTs as an appropriation mechanism, intended to create technological protection over a product. In addition, the potential advantages of the application of GURTs as a genetic containment mechanism need separate analysis.

Development and application of GURT as an appropriation mechanism may potentially have considerable impact on agriculture, the environment and the food security of rural areas in developing countries. Positive impacts may include increased investments in breeding as a result of increased intellectual property protection. Increased investments may contribute to higher yields and more advanced varieties, and thus to increased food production, a more sustainable production, and better consumer products. Potential negative impacts have been identified as well. These may require further discussion and close attention by regulatory authorities.

Impacts of reduced access to innovations stemming from crop breeding by the application of GURTs as an appropriation mechanism may emerge. It might be considered necessary to compensate such development through a system by which GURT-free variants of GURT-protected varieties or GURT-free germplasm incorporating novel traits, are made available to national and international public agricultural research programmes for use in autonomous farming systems after a limited embargo period or alternative conditions. Such compensation for the effects of the separation of genepools could be considered within relevant forums, such as the FAO Commission on Genetic Resources for Food and Agriculture and, upon entry into force, the Governing Body of the new International Treaty on Plant Genetic Resources for Food and Agriculture.

Related to this issue is the potential increased dependence of farmers on breeding companies, and potentially monopolistic effects stemming from the further development and application of GURTs. Both effects indicate the need for well-developed anti-trust legislation as well as institutions monitoring adherence.

GURTs can function as technological protection, independently of whether or not the GURT technology is itself patented. In principle, the application of GURTs provides a strategy by which the need for patent protection to have farmers refrain from seed reproduction can be avoided. However, it can be expected that for competition motives industry will wish to protect GURT strategies and components themselves against its competitors, as apparent from current patent applications.

Although patent legislation may be theoretically adapted to require conformity to regulations governing the development of GURTs to avoid unwanted effects, no such specialised elements have yet been introduced in patent legislation. It may be considered to investigate the desirability and feasibility of adapting existing patent legislation to avoid undesirable impacts of GURT applications. It can be argued that regulating patent applications on GURTs will discourage appliers and induce them to avoid patent protection. However, if patent protection is not obtained in major markets this would allow adoption of the technology by competitors.

The WTO TRIPS Agreement mentions 'ordre public' as a ground to regulate patent applications. Article 27.2 enables a Member to exclude from patentability inventions whose use would seriously prejudice the environment. This provision reads as follows: "Members may exclude from patentability inventions, the prevention within their territory of the commercial exploitation of which is necessary to protect ordre public or morality, including to protect human, animal or plant life or health or to avoid serious prejudice to the environment, provided that such exclusion is not made merely because the exploitation is prohibited by their law". The question can therefore be asked whether patent applications describing GURTs, as a set of technologies which may impact food security, may warrant further discussion on the relation with the ground of 'ordre public' as in this agreement.

Governments may wish to develop new legislation, e.g. adapted variety registration, to avoid negative impacts of the introduction of GURT-protected germplasm which can not be prevented by existing legislation, including the legislation referred to above. In particular, risks relating to the planting by small-scale farmers of food grain or even emergency relief supplies that may turn out not to germinate due to GURT presence, may justify such regulations.

As a genetic containment mechanism, GURTs may prevent unwanted geneflow into neighbouring crop stands and animal and fish populations and/or their wild relatives. However, cross-fertilising V-GURT containing crops may cause considerable effects in neighbouring crop stands and wild relatives. This negative effect will also occur in case V-GURT strategies would be employed to prevent unwanted geneflow from GMOs into the environment, cultivated or wild. Part of the seed of cross-fertilising neighbouring stands might not be viable, and this may impact on farmers saving their own seed.

Biosafety questions need to be considered separately, whatever the intended use of the GURT technology.

Since all GURT containing organisms will be classified as genetically modified organisms, legislation on the biosafety of genetically modified organisms may form a basis for requirements regarding the environmental and biodiversity-related effects of the release of GURT containing organisms. The Cartagena protocol of the Convention on Biological Biodiversity, and in particular its precautionary principle, forms a crucial framework to reach international consensus on the implementation of such requirements.
Inducers employed in GURT applications deserve further consideration. Presumably, inducers would be under separate patent protection, since they would have to be novel compounds to realise a sufficient level of technological protection. Being used in novel applications, such inducers will be subject to risk assessment and regulation as such. A strong possibility exists that inducers will become the target of unauthorized production and sale, and of smuggling. Prevention of unauthorized use of inducers could therefore add considerably to companies' legal expenses, and perhaps to the policing costs to be born by governments. Adaptation of existing legislation on pesticide use and on veterinary medicines to include the use of inducers related to GURT-protected varieties and breeds and in the framework of applications described in this study may be considered in specific cases, depending on the nature of the compounds involved.

An issue not covered relates to a rights-based approach. Several international declarative instruments mention the right to food and food security as a basic human right. Some applications of GURTs might raise rights issues, in line with the considerations made above. It is currently unclear to which extent such instruments would be applicable to the introduction of GURTs that would potentially increase food insecurity.

In general, a step-by-step and case-by-case approach appears a major principle in dealing with future introductions of GURT-protected germplasm and their impacts on breeders and farmers respectively. Such experience could be preferably first gained with T-GURT applications, if V-GURT applications would be considered to be socially acceptable.

Acknowledgements

The contributions of Zewdie Bishaw, Hans Komen, Andréanne Léger, and Paul Richards to the underlying documents, and the comments of various reviewers of earlier versions of this document, in particular the comments by Clive Stannard of the FAO CGRFA secretariat, are thankfully acknowledged. A short summary of this study has appeared in two issues (no. 48 and 49) of the Biotechnology and Development Monitor, Amsterdam, the Netherlands.

Glossary of molecular terms

Gene	is the segment of DNA involved in producing a polypeptide chain; it includes regions preceding and following the coding sequence as well as intervening sequences between individual coding segments.
Genome	the whole set of genetic information of an organism.
Heterozygote	an individual with different alleles at particular loci on the homologous chromosomes derived from each parent.
Homozygote	an individual with the same allele at corresponding loci on the homologous chromosomes derived from each parent.
Hybrid	the progeny of two genetically different parents
Inducer	a small molecule that triggers gene transcription by binding to a regulatory protein or to a promoter sequence.

Phenotype the appearance or other characteristics of an organism, resulting from the interaction of its genetic constitution with the environment.

Promoter a region of DNA involved in binding of RNA polymerase to initiate transcription. The promoter as such is a DNA sequence located upstream of a gene involved in the regulation and initiation of gene expression.

Ploidy reference to the number of copies of the chromosome set present in a cell; a haploid has one copy, a diploid has two copies, a triploid has three copies, etc.

Recombinase an enzyme catalysing recombination between specific target sequences resulting in inversion or deletion of the fragment flanked by the target sequences.

Transcription the synthesis of RNA on a DNA template.

Transformation reference to the acquisition of a new genetic trait by integration in all cells of added DNA into the genome.

References

Almekinders, C.J.M. and N.P. Louwaars, 1999. Farmers' Seed Production; new approaches and practices. London, Intermediate Technology Publications 291 pp.

Almekinders C and De Boef W. 2000. Encouraging Diversity. The conservation and development of plant genetic resources. Intermediate Technology Publications Ltd., London.

Alston, J.M., P.G. Pardey and V.H. Smith 1997. Financing Agricultural R&D in Rich Countries: What's Happening and Why. IFPRI Environment and Production Technology Division Discussion Paper No. 29, September, Washington.

Alston, J.M. and R.J. Venner. 1998. The Effects of US Plant Variety Protection Act on Wheat Genetic Improvement. Paper presented at the symposium on "Intellectual Property Rights and Agricultural Research Impact" sponsored by NC 208 and CIMMYT Economics Program, El Batan, Mexico, March 5-7, 1998.

Anon. 2000a. The EU – U.S. Biotechnology Consultative Forum. Final report.

Anon. 2000b. Plant Biotechnology: a summary of interviews, prepared for the Rockefeller Foundation. Meridian Institute. Washington D.C., USA.

Anon. 2000c. Biosecurity in Food and Agriculture. COAG/01/08. FAO, Rome, Italy.

Anon. 2000d. One third of farm animal breeds face extinction. FAO. See http://www.fao.org/news/2000/

Aoyama, T. and Chua, N-H. 1997. A glucocorticoid-mediated transcriptional induction system in transgenic plants. Plant J. 11: 605-612

Ashby, J., 1986. Methodology for the Participation of Small Farmers in the Design of On-Farm Trials. Agricultural Administration 22: 1-19

Ashby, J. and L. Sperling, 1995. Institutionalising Participatory, client driven Research and Technology Development in Agriculture. Development And Change 26: 753-770.

Bajracharya, B. 1994. Gender issues in Nepali Agriculture: A review . Research Report No. 25. Katahmandu, Nepal: MOA (HMG)/ Winrock International.

Bartley DM. 2000. Genetics and breeding in aquaculture: current status and trends. FAO, Rome, Italy.

Berthaud, J., J.C.Clément, L. Empiraire, D. Louette, F. Pinton, J. Sanou & G. Second, 2001. The role of local-level geneflow in enhancing and maintaining genetic diversity. In: H.D. Cooper, C. Spillane & T. Hodgekin. Broadening the genetic base of crop production. London CABI and Rome FAO & IPGRI, p. 81 – 103.

Boef, W.de, K. Amanor and K. Wellard, 1993. Cultivating knowledge – genetic diversity, farmer experimentation and crop research. London, Intermediate Technology Publ.

Brennan, M.F., C.E. Pray and A. Courtmanche. 2000. Impact of Industry concentration on innovation in the US plant biotech industry. In Lesser, W. (Ed.) Transitions in Agbiotech: Economics of strategy and policy. Proceedings of NE-165 Conference June 24-25, 1999, Washington, D.C. http://agecon.lib.umn.edu/cgi-bin/pubview.pl?pubid=24

Brush, S.B. (Ed), 2000. Genes in the field. On farm conservation of crop diversity. Boca Raton, lewis Publ, Ottawa, IDRC and Rome, IPGRI.

Bulfield G. 2000. Farm animal biotechnology. Trends Biotechn 18: 10 – 13.

Butler, L.J. 1996. "Plant Breeders' Rights in the U.S.: Update of a 1983 Study." In Van Wijk, J.,Walter Jaffe (eds.) Proceedings of a Seminar on the Impact of Plant Breeders' Rights in Developing Countries held at Santa Fe Bogota, Colombia, March 7-8; University of Amsterdam; Amsterdam, pp. 17--33.

Byerlee, D. and K. Fischer. 2000. Accessing Modern Science: Policy and Institutional Options for Agricultural Biotechnology in Developing Countries. Paper presented at the XXIV International Conference of Agricultural Economists, Berlin, 13-18 August 2000.

Ceccarelli, S., S. Grando, and J. Hamblin. 1992. Relationship between Barley Grain Yield measured in Low- and High Yielding Environments. Euphytica 64: 49-58.

Ceccarelli, S. and S. Grando, 1999. Barley landraces from the Fertile Crescent: a lesson for plant breeders. Pp. 51 - 76 in: Brush, S.B. (ed.). Genes in the Field; On-farm conservation of crop diversity. Rome, IPGRI, Ottawa, IDRC and Boca Raton, Lewis Publ.

Cook J. 1999. Science-based risk assessment for the approval and use of plants in agricultural and other environments. Proceedings of Agrobiotechnology and the poor.. IFPRI, Washington D.C., USA.

Cooper, H.D., C. Spillane and T. Hodgekin, 2001. Broadening the Genetic Base of Crop Production. London CABI & Rome, FAO and IPGRI, 452 p.

Christian Science Monitor, August 30, 2001. No bumper crops of genetically altered plants.

Cromwell, E., E. Friis-Hansen and M. Turner, 1992. The seed sector in developing countries: a framework for performance analysis. ODI Working Paper 65. London, Overseas Development Institute.

Daniell, H. 1999. The next generation of genetically engineered crops for herbicide and insect resistance: containment of gen pollution and resistant insects. http:www.agbiotechnet.com/reveiws/aug99/html/daniell.htm

David, S., 1994. Seed First: developing farmer seed enterprises in Uganda for the production and distribution of bean varieties. Rockefeller Foundadtion Social Science Fellow Workshop, ILCA, Addis Ababa, Ethiopia.

Desplanque B, Boudry P, Broomberg K, Saumitou-Laprade P, Cuguen J, and Van Dijk H. 1999. Genetic diversity and gene flow between wild, cultivated and weedy forms of Beta vulgaris L (Chenopodiaceae), assessed by RFLP and microsatellite markers. Theor Appl Genet 98: 1194 - 1201

Eaton, D. 2001. TRIPS and Plant Varietal Protection: Economic Analysis and Policy Choices. Agricultural Economic Research Institute (LEI) Report, The Hague, The Netherlands.

Falcon, W.P. 2000. Globalizing Germplasm: Barriers, Benefits and Boundaries. Paper presented at the XXIV International Conference of Agricultural Economists, Berlin, 13-18 August 2000.

FAO, 1999. Restoring farmers' seed systems in disaster situations. Proceedings of a workshop in Rome, Italy, 3-5 November 1998. FAO Plant Production and Protection Paper 150. Rome, FAO.

FAO. 2001. FAOSTAT website. http://apps.fao.org/

FIS/ASSINSEL website. 2001. http://www.worldseed.org/statistics.html

Fuglie, K., N. Ballenger, K. Day et al. 1996. *Agricultural Research and Development: Public and Private Investments Under Alternative Markets and Institutions*. AER-735. Economic Research Service, United States Department of Agriculture.

Gilissen, L.J.W.J. and Nap J.P. (1999) Biosafety of site-specific recombination-mediated and homing endonuclease-mediated chromosome modifications in plants. CPRO-DLO, 42 pp.

Goeschl, T. and Swanson, T. 2000. The Impact of Genetic Use Restriction Technologies on Developing Countries: A Forecast. Paper presented at the 4th International Conference on the "Economics of Agricultural Biotechnology". International Consortium on Agricultural Biotechnology Research (ICABR), Ravello, Italy.

Hayenga, M.L. 1998. Structural Change in the Biotech Seed and Chemical Industrial Complex. AgBioForum, 1(2) pp. 43-55 www.agbioforum.org

Hardon J, Engels J and Visser B. 2000. Towards integration of policy frameworks. *In:* Encouraging Diversity. The conservation and development of plant genetic resources, C. Almekinders and W. de Boef (eds.), pp 317 - 322, Intermediate Technology Publications Ltd., London.

IFPRI. 2020 Focus 2. 1999. IFPRI website (http://www.ifpri.org/)

James, C. and A. Krattiger. 1999. Biotechnology for Developing-Country Agriculture: Problems and Opportunities. The Role of the Private Sector. IFPRI Focus 2, Brief 4 of 10. October.

Jefferson, R.A. et al., (1999) CBD Assessment of Genetic Use Restriction Technologies-Expert Paper.

Jordan N. 1999. Escape of pest resistance transgenes to agricultural weeds: relevant facets of weed ecology. Workshop on Ecological effects of pest resistance in managed ecosystems. Behesda. MD, USA.

Joshi and J. Witcombe, 1996. Farmer Participatory Crop Improvement II. Participatory Varietal Selection, a case study in India. Expl. Agric. 32: 461-477.

Jusu, M.S., 1999. Management of genetic variability in rice (Oryza sativa L. and O. glaberrima Steud.) by breeders and farmers in Sierra Leone. PhD Thesis, Wageningen University.

Kalaitzandonakes, N. and B. Bjornson. 1997. Vertical and Horizontal Coordination in the Agro-Biotechnology Industry: Evidence and Implications. *Journal of Applied and Agricultural Economics* 29(1) July 1997, pp. 129-139.

Kalaitzandonakes, N. and M. Hayenga. 2000. Structural change in the biotechnology and seed industrial complex: theory and evidence. In Lesser, W. (Ed.) Transitions in Agbiotech: Economics of strategy and policy. Proceedings of NE-165 Conference June 24-25, 1999, Washington, D.C. http://agecon.lib.umn.edu/cgi-bin/pubview.pl?pubid=24

Kilby, N.J. et al. 1995. FLP recombinase in transgenic plants: constitutive activity in stably transformed tobacco and generation of marked cell clones in Arabidopsis. Plant J. 8: 637-652.

Klug, A. 1999. Zinc finger peptides for the regulation of gene expression. J Mol Biol. 293: 215-218.

Kugbei, S., M. Turner and P. Witthaut (Eds.), 2000. Finance and Management of Smallscale Seed Enterprises. Aleppo, Syria, ICARDA, 191 pp.

Kuvshinov V et al. (2001) Molecular control of transgene escape from genetically modified plants. Plant Sci. 160: 517-522.

LeBuanec, in press. The Rules for International Seed Trade. N.P.Louwaars (Ed.) Seed Policy and Law. New York. Haworth Press.

Levings, C.S. 1990. The Texas cytoplasm of maize: cytoplasmic male sterility and disease susceptibility. Science 250: 942-947.

Lesser, W. 1994. Valuation of Plant Variety Protection Certificates. *Review of Agricultural Economics* 16 (May): 231-238.

Lesser, W. 1997. Assessing the Implications of Intellectual Property Rights on Plant and Animal Agriculture. *American Journal of Agricultural Economics* 79(5): 1584-1591.

Lesser, W. 1998. Intellectual Property Rights and Concentration in Agricultural Biotechnology. AgBioForum 1(2): 56-61. www.agbioforum.org

Lesser, W. 2000. “An economic approach to identifying an ‘effective sui generis system’ for plant variety protection under TRIPS”. In Santaniello, V., R.E. Evenson, D. Zilberman and G.A. Carlson (Editors), *Agriculture and Intellectual Property Rights: Economic, Institutional and Implementation Issues in Biotechnology*. CABI International, Wallingford, U.K.

Louwaars, N.P. and G.A.M. van Marrewijk, 1996. Seed Supply Systems in Developing Countries. Wageninge, CTA, 135 p.

Maeser S and Kahmann R. 1991. The Gin recombinase of phage Mu can catalyse site-specific recombination in plant protoplasts. Mol Gen Genet. 230: 170-176.

Mandava NB. 1988. Plant growth-promoting brassinosteroids. Ann. Rev. Plant Phys. Plant Mol. Biol. 39: 23-52.

Maredia, M., J. Howard and D. Boughton, 1999. Increasing Seed System Efficiency in Africa: Concepts, Strategies and Issues. MSU International Development Working Paper No. 77. East Lansing, Michigan State University, 60 p.

Maurya, 1983. The innovative approach of Indian farmers. In: R. Chambers, A.Pacey & L.A.Thrupp (Eds), Farmer First: farmer innovation and agricultural research. London, Intermediate Technology Publ.

Mc.Guire, S., 2000. Farmers' management of sorghum diversity in eastern Ethiopia. In: C. Almekinders & W. de Boef. Encouraging Diversity; the conservation and development of plant genetic resources. London, Intermediate Technology Publ. p. 43-49.

Mohammed, L., F.H.C. Scott & M.H.C.G. Steeghs, 1985. Seed Availability, Distribution and Use in Machakos District: short rains 1983 – short rains 1984. District Agricultural Office and National DrylandFarming Research Station, Machakos, Kenya (in Louwaars & van Marrewijk, 1996, p. 72-73.

Nap JP et al. (1992) Biosafety of kanamycin resistant transgenic plants. Transgenic Res. 1: 239-249.

OECD, 2001, *The OECD Agricultural Outlook*, Paris: OECD.

Pal, S., R. Tripp & A Janaiah, 2000. Public-private interface and information flow in the rice seed system of andhra Pradesh (India). National Centre for Agricultural Economics and Policy Research Policy Paper 12. New Delhi, NCAP.44 p.

Perrin, R.K., K.A. Hunnings and L.A. Ihnen. 1983. Some effects of the US plant variety protection act of 1970. Economics Research Report No. 46, Dept. of Economics and Business, N.C. State University, Raleigh.

Persley GJ and Doyle JJ. 1999. Biotechnology for developing-country agriculture: problems and opportunities. Overview. Proceedings of Agrobiotechnology and the poor.. IFPRI, Washington D.C., USA.

Pinstrup-Andersen P and Cohen MJ. 2000. Modern Biotechnology fro food and agriculture: risks and opportunities for the poor. IFPRI, Washington D.C., USA.

Pistorius R. 1997. Scientists, plants and politics: a history of the plant genetic resources movement. IPGRI. Rome.

Pistorius R and Van Wijk J. 1999. The exploitation of plant genetic information: political strategies in crop development. CABI Pub., Wallingford, UK.

Rabobank 1996. *The World Seed Market: Developments and Strategies*. Netherlands.

RAFI. 2001. RAFI website. http://www.rafi.org/

Rangnekar, D. 2000. *Intellectual property rights and agriculture: an analysis of the economic impact of plant breeders' rights*. ActionAid, UK.

Rotino et al. (1997) Genetic engineering of parthenocarpic plants. Nat. Biotech. 15 (13): 1398-1401.

Sage GCM. 1999. The role of DNA technologies in crop breeding. In: Gene flow and Agriculture. Relevance for transgenic crops, pp. 23 - 31. Britisch Crop Protection Council, UK. See also: http://www.agbiotechnet.com/reviews/july99/html/hemming.htm

Sampson V. and Lohmann L. 2000. Can't see the trees for the wood. Seedling. GRAIN, Barcelona, Spain.

Santen, C. van, and Heriyanto, 1996. The Source of Farmers' Soybean Seed in Indonesia. In: H. van Amstel, J. Bottema, m. Sidik & C. van Santen (Eds.). Integrating Seed Systems for Annual Food Crops. Bogor, indonesia, CGPRT Centre.

Seigler DS (1995) Plant secondary metabolism, Kluwer (Boston) chapter 23.

Simon R et al. (1996) Activation of floral meristem identity genes in Arabidopsis. Nature 384: 59-62.

Smith NA et al. (2000) Total silencing by intron-spliced hairpin RNAs. Nature 407: 319-20.

Srinivasan, C.S. and C. Thirtle. 2000. Impact of Terminator Technologies in Developing Countries: A Framework for Economic Analysis. Paper presented at the 4th International Conference on the "Economics of Agricultural Biotechnology" organised by the International Consortium on Agricultural Biotechnology Research (ICABR), Ravello, Italy, 24-28 August.

Steenhuijsen Piters, B. de, 1995. Diversity of Fields and Farmers: explaining yield variations in Northern Cameroun. PhD Thesis, Wageningen Agricultural University. 272 p.

Sugita, K. et al. 2000. A transformation vector for the production of marker-free transgenic plants containing a single copy transgene at high frequency. Plant J. 22: 461-469.

Szechtman et al. 1997. Seedless fruit setting in response to NAM treatment of transgeinc tomato expressing iaaH gene speciafically in the ovary. Acta Horticulturae 447: 597-598.

The Economist. 2000. Biotechnology: Dry Season (Nov. 2nd 2000).
1999. Terminator genes: Fertility Rights. October 7th, 1999.
1999 Biotechnology: Big is beautiful. March 25th, 1999.
2000. Life Sciences: Green and Dying. Nov. 16th, 2000.

Thiele, G., G. Gardner, R. Torrez and J. Gabriel 1997. Farmer involvement in selecting new varieties: potatoes in Bolivia. Exp. Agric. 33: 1-16.

Thro AM and Spillane C. 1999. Biotechnology assisted participatory plant breeidng. CGIAR Program on Participatory Research and Gender Analysis, working document 4. Cali, Colombia.

Tripp, R. 1997. New seed and old laws. Regulatory reform and the diversification of national seed systems. London, Intermediate Technology Publ., 259 p.

Turner, M., 1994. India Debates Expanding Seed Legislation. Seed World Dec.1994: 48-50

Turner, M and Z. Bishaw. (in press). Linking Participatory Plant Breeding to Seed Systems. Paper presented in international Symposium of Scientific Basis of Participatory Plant Breeding and Conservation of Genetic Resources held 9-13 October 2000, Oaxtepec, Mexico.

Varoquaux F, Blanvillain R, Delseny M, and Gallois P. 2000. Less is better: new approaches for seedless fruit production. Trends Biotechn 18: 233 - 242

Visser, B. and Engels, J. 2000. The common goal of conservation of genetic resources. In: Encouraging Diversity. The conservation and development of plant genetic resources, C. Almekinders and W. de Boef (eds.), pp 145 – 153, Intermediate Technology Publications Ltd., London.

Visser, B. and Nap JP. 2000. Biotechnology and agrobiodiversity. Encyclopedia of Life Support Systems. UNESCO, Paris, France. In press.

Welcomme, R.L. and Bartley, D.M. 1998. Current approaches to the enhancement of fisheries. Fish Manag Ecol 5: 351 – 382.
Walker, D. J and R. Tripp. 1997. Seed management by small-scale farmers in Ghana and Zambia *In* International workshop on seed security for food security . Proceedings of a workshop in Florence , Italy, 30 November 1 December 1997. Rome, FAO. 207-216

Witcombe, J., K.D. Joshi, R.B. Rana & D.S. Virk, 2000. Participatory Varietal Selection and Genetic Diversity in High-Potential Rice Areas in Nepal and India. Pp 203-207 in: C. Almekinders & W. de Boef. Encouraging Diversity; the conservation and development of plant genetic resources. London, Intermediate Technology Publ.

Woldeamlak, A. and P. Struik, 2000. Farmers' use of landraces in the Hamfez mixed cropping system in Eritrea. Encouraging Diversity; the conservation and development of plant genetic resources. London, Intermediate Technology Publ. p. 49-53..

Woldeselassie, Y. S. 1999. Status and quality of barley seeds used by the northern and central Ethiopian farmers. MSc. Thesis. University of Jordan, Amman, Jordan.

Zuo, J. et al. 2001. Chemical-regulated, site-specific DNA excision in transgenic plants. Nat. Biotech. 19: 157-161.

Zuo, J. and Chua N.H. 2000. Chemical-inducible systems for regulated expression of plant genes. Curr. Op. Biotech. 11: 146-151.