ANNEX

GENETIC USE RESTRICTION TECHNOLOGIES

Technical Assessment of the Set of New Technologies which Sterilize or Reduce the Agronomic Value of Second Generation Seed, as Exemplified by U.S. Patent No. 5,723,765, and WO 94/03619

Expert paper, prepared for the Secretariat on 30 April 1999,
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EXECUTIVE SUMMARY POINTS

A. The Technologies and their Uses

a) Genetic Use Restriction Technologies (GURTs) are a set of proposed technological means that rely on genetic transformation of plants to introduce a genetic switch mechanism which prevents unauthorised use of either particular plant germplasm, or trait(s) associated with that germplasm.

b) GURTs are designed to provide a genetic, in-built protection against unauthorized reproduction of the seed or the added-value trait. GURTs thus may be broader, more effective and less limited by time constraints, than the protection conferred by intellectual property rights.

c) Although certain GURT methods and some core technologies underlying them have been patented, no form of GURT has to date been reduced to practice. The main transnational agri-business industries and seed corporations are currently conducting research in this area, nonetheless, it is estimated on the basis of the state of the art today that neither form is likely to be commercialized for at least five years.

d) Because the proposed GURTs are transgenic, they can be envisioned to function in any seed bearing crop species for which suitable transformation technologies are available.

B. Variety-level Genetic Use Restriction Technologies (V-GURTs)

e) GURTs currently under scrutiny operate at the level of the entire variety (Variety-level Genetic Use Restriction Technologies, V-GURTs), in which the plant variety so engineered cannot be propagated by the farmer without seed purchase. One example of the V-GURT has been dubbed •erminator’ and is described in US patent No. 5,723,765.

f) Crop species likely to be targeted for using V-GURTs would likely be those for which hybrids are either not feasible, not readily accessible to the private sector or not highly effective; these will typically be moderate to high value, in-breeding seed crops, e.g. rice, wheat, soybean, cotton, etc.

g) Targeted markets for V-GURTs are likely to be those in which either plant-back of farm saved seed is widely practiced, or those in which increased seed costs associated with added value traits would encourage •irating’ or free-riding.

h) The V-GURT described as •erminator’ in the media has many features that, upon scientific analysis with an awareness of commercial standards, indicate that in our opinion <u>this particular implementation</u> would be unlikely to meet industry requirements for robustness, reliability or cost-effectiveness until new gene expression technology is available.

i) There are many potential V-GURTs, which can be envisioned and which are likely to be developed by the private sector that will, however, increase the commercial viability of the V-GURT concept. Several different prototypes are already under development by the major seed and pesticides multinationals.

C. <u>Trait-specific Genetic Use Restriction Technologies (T-GURTs)</u>

j) Alternative forms of in-built genetic protection, called Trait-specific Genetic Use Restriction Technologies, or T-GURTs, are also possible in which only the •dded value’ transgenic trait is protected by technological means, and indeed could be activated at the will of the farmer / end user.

k) These technological interventions could contribute towards addressing concerns by the private sector to secure return on investment, while substantially increasing choice by those farmers who would have access to such protected seed and would be in charge of the decision to activate the trait. This could arguably encourage a more fair market-driven industry development, using a broader genetic diversity of crop varieties,

l) In contrast to V-GURTs, T-GURTs could eventually provide an empowering mechanism to allow public and private priorities in agriculture to be partially reconciled.

m) Trait-specific Genetic Use Restriction Technologies have a similar time frame to development of Variety-level GURTs.

D. <u>Policy, Regulatory and IPR issues</u>

n) The general phenomenon of V-GURTs, and their appropriateness or desirability should be considered rather than the specifics of one particular patented implementation. Such assessment at policy and technical levels should take into consideration agricultural production, food security, biological diversity as well as socio-economic and ethical perspectives.

o) The greatest potential risks to food security associated with wide adoption of V-GURTs may be the increased dependence on seed production and distribution by a few commercial suppliers and the vulnerability of such supply to disruption, either civil or environmental.

p) Experimental analysis under field conditions of the performance as well as potential direct and indirect effects of these GURTs as and when they emerge from research, and wide publication of the outcomes of these analyses should be encouraged before they become commercially available. Domestic policy, if appropriate, could then have a solid, scientifically sound basis on which to act.

q) The motivations for development of V-GURTs seem clear, essentially economic criteria to facilitate greater market presence and return on investment. However, the arguments for the need for these technologies to foster private sector investment that would result in improvements in agriculture for the greater public good, especially for the rural poor in developing countries need much more substantiation. Where possible, comparisons with investment in alternative sustainable technologies which preclude crop homogenisation should be provided.

r) The role of public sector research and development in providing a viable, competitive alternative for public-good applications should be seriously expanded, if priorities of food security in less developed countries, maintenance of biological diversity and enhancement of environmental health in the medium-to-long-term are to be accommodated.

s) Critical enabling technologies that are necessary to provide such biotechnological alternatives for neglected crops or problems, or for use in developing countries, must be accessible through licensing or through development of alternative methodologies for which freedom to operate can be secured. Where necessary, compulsory licensing of such bottleneck technologies for certain public-good applications may be considered appropriate.

t) It is not yet clear what may be required in terms of explicit global-level regulatory policies, protocols or procedures for these technologies. First, further and more detailed assessments on a case by case basis, will be essential to anticipate potential consequences in specific targeted crops, regions and agricultural systems. On that basis it will be possible to determine whether and, if so, what specific tools and instruments may be required to maximize public-good outcomes of adoption of new technologies and minimize adverse impacts.

u) In many countries, existing domestic regulatory mechanisms could be adapted for restricting or preventing the use of V-GURTs --should that be desired.

v) Patent legislation is an irrelevant mechanism by which to discourage use of these technologies. Invalidating patents on V-GUR Technologies, without simultaneously restricting their use, is likely to have the opposite to the desired effect, and actually could stimulate their use commercially.

E. Genetic Diversity and Environmental Issues

w) Genetic diversity effects from adoption of V-GURTs in general will largely be indirect, and will likely ensue from rapidly changing agricultural use patterns resulting from new market dominance of transgenic varieties. These effects will depend completely on the patterns of commercial uptake and market penetration of the technology users that are correspondingly unpredictable at this time. Therefore, comprehensive analysis by international bodies competent to assess trends in agricultural economics, technology adoption and societal acceptance should be initiated as soon as practicable.

x) In the case of broad adoption of the V-GURT germplasm, the semi-formal farmer/breeder sector in the developing world would likely find substantially less opportunity to continue to alter the genetic makeup of crop species through combining landraces with improved varieties. Hence such traditional and current practices of enhancing genetic diversity could be compromised. Data to clearly indicate the extent and nature of this activity should be made available as well to better anticipate any effects from V-GURT of T-GURT adoption.

y) Gene flow from transgenic plants containing V-GURT is unlikely to present any greater risk than from the added value trait transgene itself. Nonetheless all such transgenic modifications in plants should receive suitable attention to ensure environmental and health safety until the possible consequences are better known, in accordance with the precautionary approach.

z) The arguments that a commercially viable V-GURT could decrease the frequency of transgene spread could have substantial merit, but require substantiation with glasshouse and field data in different environments and farming systems.

INTRODUCTION

1. In March of 1998, a U.S patent was issued jointly to the United States Department of Agriculture and Mississippi•ased Delta and Pine Land Company, a major cotton seed supplier in the USA. This patent, simply titled •ontrol of Plant Gene Expression’ was initially hailed by its inventors as an important breakthrough in agricultural biotechnology.

2. The invention described a technical method of enabling controlled non-viability of second-generation seeds, providing a technological means to ensure that the intellectual property contained in those seeds were protected, thus effecting a form of genetic copy protection. Other patent applications by other companies, including Zeneca, had already been published which disclosed similar concepts and technologies, with a variety of additional uses and scenarios, but did not achieve the same notoriety. This general class of technologies we call Genetic Use Restriction Technologies, or GURTs.

3. Attention was initially drawn to these technologies through an aggressive public awareness campaign initiated by farmer advocacy NGOs, especially the Rural Advancement Foundation International (RAFI). International media attention reached unprecedented levels over the next twelve months, prompting major concern over associated with the development of these technologies by multinational corporations, and their potential impacts on genetic diversity, societies and economies. This concern was manifest in public declarations in international fora such as the United Nations General Assembly, the Convention on Biological Diversity and the Commission on Genetic Resources for Food and Agriculture of the FAO.

4. The attention given to the patent has been of great value in drawing attention to a general class of biotechnology intervention that is now on the horizon, of which the D&PL/USDA implementation is only one prototype. These interventions could take a number of commercially viable, forms, each with different implications for agriculture and society

5. Application of these technologies has some substantial similarities to the use of hybrids in view of the need of farmers to purchase new seed for each planting season. However, the ability to prevent not only true-to-type propagation but in fact, germination, and the ability to introduce this trait into most species of plants irrespective of their breeding system, makes these technologies radically different in mechanism, scope and implications.

6. These interventions could take a number of forms each of which could become very viable commercially, but with very different implications for the development of agricultural industries and the applications of research to agricultural improvements. In this light, the potential consequences on biological diversity may also vary according to the specific application and will depend upon the crop type, the type of farming system and agricultural ecosystem as well as the geographic region in which the technology might be utilised. It is largely to this broader class of biotechnology

interventions that this assessment is focused, as they represent the serious issue requiring attention and a valuable opportunity for policy makers.

BACKGROUND

7. Advances in plant biotechnology and molecular biology over the last decade have been exceptionally rapid and applications of these technologies to commercial and industrialised agriculture have followed closely. In parallel, the public concern about the social and environmental costs of capital-intensive agriculture and the entrenchment of its technological paradigm by modern biotechnology is also rapidly increasing.

8. A dramatic example of the existing technological paradigm of capital-intensive research seems to be at hand with the introduction of novel technologies designed to extract maximum value from chosen innovations in biotechnology in agriculture.

9. In short, these technologies in their most extreme form would eliminate the ability of farmers to plant back seeds they have grown through use of a technological means rather than solely relying on legal or contractual instruments, and thus make seasonal seed purchases obligatory. One form of this was dubbed •erminator’ by its critics, and Technology Protection System by its inventors as described in US patent No.5,723,765.

10. With the increasing prominence of biotechnology and the dominant role of a small number of multinational corporations in world agriculture, it is possible that the application of such Genetic Use Restriction Technologies could have far-reaching effects on agricultural practice. This could have social and economic repercussions which in turn could impact on genetic diversity use and conservation. As with all genetically modified organisms, the potential impact in the short and long term on biological diversity of crop plants, wild relatives, as well as other species and ecosystem functioning requires careful scientific evaluation and application of the precautionary principle.

11. Genetic Use Restriction Technologies are viewed by their proponents as a means of encouraging investment in new science for improved agriculture by the private sector. The logic seems persuasive, but the nature of the corresponding investment, the desired outcomes and the targeted beneficiaries of such research must be closely examined to better determine the validity of the assertion.

12. To evaluate these features will require frameworks for policy making that are rarely present or poorly articulated in most national and regional programs. In brief, it is essential in determining the desirability of these innovations to first determine what type of agriculture and what type of socio-economic development is desired; i.e. some definitions of public good must be made. Some of the questions that will need to be posed within such a framework, and which can only be comprehensively answered once domestic or institutional priorities are established are:

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- Will such investments sufficiently stimulate the application of science for socially equitable, environmentally sound and sustainable innovations in agriculture?

- Will the focus for such investment tend towards short-term recovery of profit at the expense of long-term strategic research and development? Are there complementary mechanisms to ensure otherwise neglected priorities for •ublic good' are adequately addressed?

- Will such technology development allow or stimulate the active participation and innovative potential of small to medium enterprise in the development process, or will it tend towards continued consolidation of power in a few entities ?

- Are these technologies, for whatever reason, unacceptable ethically or socially to the society at large ?

- Will the investments so made impact positively or negatively on farming communities, many of which are developers and custodians of the world's agricultural genetic heritage and natural resource base.

- Will the availability of such a mechanism aimed at return on investment hasten the already striking decline of public funding for agricultural research for the greater public good, however this is defined ?

- Will the urban and rural poor of the world see a net benefit through such investments or will they further widen the poverty gap between subsistence and commercial farmers ?

- What are the potential threats to the conservation of biological diversity at genetic, species and ecosystem levels including crop plants, wild relatives of crop plants and other species. Are there any potential benefits in this regard ?

- Will any threat to conservation of agricultural genetic diversity be adequately offset by new opportunities in plant breeding stimulated by investment ?

1. This assessment is structured as follows:

    - Executive Summary;

    - Introduction and Background;

    - I. The genetic diversity, crop improvement and biotechnology context;

    - II. The technologies under consideration and their potential applications;

    - III. Intellectual property and legal considerations;

- IV. Potential consequences on the conservation and sustainable use of biological diversity: impacts on agriculture, biological and socio-economic implications; and

- V. Conclusions

SECTION I: THE GENETIC DIVERSITY, CROP IMPROVEMENT AND BIOTECHNOLOGY CONTEXT

Plant Domestication, Plant Breeding and Crop Improvement

14. Modern crop plants, in many cases, bear little resemblance to the original plants from which they have evolved. This is due to the considerable activity of generations of cultivators who, initially in the centers of genetic diversity of these plants, chose plants and plant populations carefully for uses and characters well beyond those that had initially made these plants fit enough to survive natural selection. Many generations of farmers have produced our major crop plants through a lengthy domestication process which has left the plants of many of today's crops unable to survive in nature without the care and nurturing provided by the current agricultural setting. This has occurred because farmers retained plants that had •alue,” that is, met their locally determined needs such as food, fiber, fuel, or shelter. These values were often realized by dramatic modifications in the morphology and physiology of the plants obtained through lengthy and iterative processes of plant breeding and adaptation by farming communities through repetitive selection of desirable traits which could result from unexpected mutations or combinations of genotypes. These new combinations were evaluated in new environments, and their robustness and performance in these environments determined their desirability to these farmers.

15. Changes thus achieved were hereditary. Genes that were faithfully copied from generation to generation gave stability to the expression of the desired traits. In turn, such predictability gave security to the farmer who could depend on the realization of a successful harvest using selected seeds planted from the previous crop.

16. Farmers valued their seeds and ensured the continuity of their innovations by transporting the seeds with them through short periods of transhumance culture and long or permanent migrations. As the seeds were moved into new areas, the plants faced new environmental challenges and again farmers saved or selected seeds from plants or plant communities that performed well, and which produced the needed crop products. Thus some genetic changes were •ixed’, while other genetic combinations that did not perform well were discarded and not propagated; the phenomenon, known as genetic adaptation, is the basis for the vast diversity now seen in a single crop species. This genetic diversity is the basis for further adaptations to other environments and to changing environmental conditions including climatic, edaphic and those resulting from changing farming systems and cropping patterns.

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17. Genetic diversity in a crop species is ubiquitous: no crop species has been found that was genetically uniform throughout the range of its use. On the other hand, locally adapted •andraces’ of crops have more modest diversity and have definite characteristics that result from their adaptation to the specific local conditions in which they are grown. Even though agriculture has its origins many centuries ago, there are still local or landrace types of crops grown in many traditional farming systems.

18. The age-long role of farmers as developers and improvers of crop plants has persisted even as more specialized agriculture emerged. One of the specialized agricultural sectors that emerged, tightly coupled with emergence of commerce and trade, has been seed improvement and distribution. Some farmers became the providers of seed to others and in this way seed became an item of trade, moving throughout local market systems with acquired value by virtue of its performance and use by farmers as an item of barter and sale.

19. Agricultural systems evolved along with technologies to improve crop yields and value. Among these technologies was that of plant selection by which farmers and seed merchants sought particular genetic modifications in their plants. The existing genetic diversity was used to create new forms and combinations of traits through the science and art of plant breeding.

20. In the 19th century plant breeding evolved from a plant selection activity to one in which controlled hybridizations were made to capture traits of different types, such as those exhibited by locally adapted landraces, into a new version. The genetic basis for trait expression was discovered and formalized as Mendel• laws of inheritance. This formalization gave a scientific basis for plant breeding and a sophisticated system of hybridization, selection, field-testing, seed multiplication, and seed distribution has evolved.

21. An important feature in the development of private and public seeds industries and their contribution to increased yields by farmers worldwide, has been the ability to assure quality of planting material through suitable attention to production of reliable pure varietal seed free of diseases and weed seeds capable of efficient germination. The discovery that heterosis or hybrid vigor occurs when two highly inbred types are genetically crossed resulted in a major seed industry development, especially for maize. Protection of this germplasm and the investments made in its development was afforded by the fact that the seed produced by the farmer's crop was heterogeneous and that if it were used to plant the next crop the yield would be dramatically reduced. The hybrid vigour or comparative advantage in terms of productivity decreases substantially with each successive planting. Farmers could, nonetheless, still use the seed thus produced for breeding and subsequent improvement strategies.

22. The hybrid approach was limited to a substantial degree by the natural genetic systems of breeding inherent in the crop species. However, with sufficient effort, a number of previously recalcitrant crops have begun to be addressed by evolving hybrids industries, such as the Chinese hybrid rice industry.

23. Plant breeding has also been linked to the development of technologies and approaches to shape crops for agricultural systems associated with capital-intensive, purchased inputs, such as nutrient supplements and pesticides. Such developments ultimately produced the genetic, management and environmental changes that together resulted in the modern agricultural systems of much of the industrialized world. Such agricultural systems, especially those associated with wheat and rice, were subsequently transferred to some farming systems in less developed countries in the form of the •reen Revolution.”

24. The actual craft of plant breeding, however, remained a modest capital undertaking until the last decade. Outside the world of certain high-value fruits and vegetables, ornamentals and hybrid maize, the concept of protection of inventions in the seed sector seemed to be reasonably addressed by Plant Breeders Rights (see section 3). The greatest consolidation of capital in agriculture was thus outside the plant breeding and seed sector and was generally associated with the agricultural industries that developed to provide farm inputs, such as chemical fertilizers, herbicides and pesticide, to maximize the performance of the highly modified crop varieties. It is primarily these industries which have recently heavily invested in biotechnology applications.

Plant Variety and Trait Protection

25. Since the advent of capital-intensive molecular biology and biotechnology for agriculture, the concept of protection and the perceived need for this protection has changed substantially. Initially this change was manifest through the application of patents to plant material, as exemplified by *ex parte* Hibberd, a landmark case that opened plants to general or utility patent protection in the United States. Soon however, patent protection on key enabling technologies and then gene-based patents became ubiquitous in biotechnology, and a major component in business development strategies in agriculture. These increased levels of intellectual property protection did not follow a carefully considered, or clearly articulated public policy; rather they were often the consequence of precedent established by individual case litigation in national jurisdictions.

26. Patent protection is not intended to assure the performance of the material for the farmer, but to ensure a limited monopoly that may facilitate capital flow to the •alue-adder’, such as the plant breeder and biotechnologist, and hence improve the profitability of research and investment and likelihood of commercialization of the product. Patents, while powerful tools in some jurisdictions in which intellectual property law and tradition is well developed, are subject to national laws and valid only in the country of registration. They place the enforcement onus on the patent holder. Enforcing patent rights is a difficult enough task for an inventor of a mechanical invention, for example, a better mousetrap, but extremely challenging for an invention embodied in a self-replicating organism, especially where the substantive component of the invention is at the unseen level of the genes.

27. Inherent in biological materials such as plants, is the ability to replicate and reproduce and to faithfully duplicate their genetic constitution at each generation. In the view of many within the biotechnology-based industry, this feature made the use of legal instruments such as patents, an insufficient means of ensuring protection of the •alue-added technology’. Newly introduced genes are also reproduced and copied, and as seen above, the traditions of seed trade and movement are such that these new transferred genes are also liable – even as passengers in the genomes – to be traded or sold. Monitoring this trade can be extraordinarily difficult and expensive, and in many cases, simply impossible.

28. The extreme cases now being seen in implementation of some commercial agricultural biotechnology innovations involve •echnology use’ contracts with farmers that specifically deny them the right to propagate their grain as seed. These contracts, recently introduced in some countries, have been unpopular; but they have been seen by a part of the private biotechnology community as the only way of ensuring ready return on investment, and have been accepted by many farmers who expect added value for the attendant inconvenience and costs.

29. The other means of ensuring sufficient capital return, ubiquitous since commerce began, is the attempt by individual firms to capture as large a market share as possible. Historically in many fields of commerce, this individual competitive drive has arguably worked to the benefit of consumers through competition among diverse suppliers, ideally leading to better products and lower prices.

30. However, the approach to this goal in agriculture in the last few years does not seem to be following this route, but is rather tending towards growing concentration, and the potential for development of monopolies, with vertical integration of technology suppliers and seed producers and distributors.

31. These large and powerful firms argue that delivery of their technologies requires control of the delivery vehicles of that technology – the seed - and the genetic background in which the technology would act – the improved variety.

32. It is claimed that the principal motivation for such consolidation has been the need to evolve business structures that could cope with the natural copying mechanisms intrinsic to living organisms. In agricultural industries associated with hybrids, these copying mechanisms are largely avoided by the hybrid, non-true-breeding nature of the product. Correspondingly in such industries, for instance the hybrid maize industry there has been well-documented progress in genetic and management schemes associated with high capital investment. This is not to say that alternative approaches, with suitable investment, could not have achieved similar increases in performance.

33. This perceived business need has contributed to the vertical integration described above, but also has evoked the strategy of reducing or eliminating competition by restricted technology access.

34. One of the principal tools of such commercial approaches has been selectively denying competitors access to critical ‘enabling technologies’ through aggressive patenting of inventions, and through acquisitions of rights over other core methodologies by exclusive licensing and by outright purchases of the inventing entities. Some of these entities were also themselves seed companies, furthering both goals of dominating technology and delivery.

35. The consequences of these combined strategies, culturally, socially, financially and environmentally could potentially be very great, but only the financial costs can be readily measured in the short term, and hence these costs have been the major factor in industry development strategies.

36. These financial costs are associated with technology invention and protection, and capital outlays for acquisition of seed companies and competitors, but also with the high costs of meeting regulatory obligations. With these high costs associated with biotechnology innovation, it is no surprise that the highly capitalized chemical input corporations rather than seed and plant breeding companies, have emerged as the dominant players in the field, having acquired or otherwise associated themselves with most of the breeding and seed companies.

37. As the capital invested in the development of new transgenic applications increased, the need to find means to ensure that the stream of capital recovery was maintained and strengthened became more urgent. These means ranged from expansion of the scope of patentability, to crafting new technologies to achieve more profound protection of intellectual property or indeed to supplant intellectual property with an in-built technical protection. The model of hybrids was and is very attractive for ensuring a captive market and a predictable income stream, when used to produce seeds of higher value to the farmer. However, commercial hybrid formation is either very expensive or unavailable for many of the world’s crops that do not lend themselves, by their very biological nature, to ‘outcrossing’.

38. Missing in this outline of the evolution of agricultural biotechnology industries is a substantial role for the public sector operating under clear public policy. The role of such research has been perceived to be to ensure the public good, and to provide a crucial balance to guarantee social equity and fair play, and long term environmental sustainability in those circumstances in which private investment cannot meet these needs. But this role, whether real or wishful, has been diminishing rapidly worldwide.

39. The technologies that are under assessment here are thus the historical and seemingly inexorable consequence of four main factors: (1) the existing technological paradigm in commercial agriculture, which is predicated on the intensive use of many purchased inputs; (2) the capital- and knowledge-intensive nature of biotechnological research; (3) the consolidation of the seed sector with biotechnological and genetic innovators and with agricultural-chemical input suppliers, and (4) the extreme reduction of the role of public-sector funding in research leading to cultivar development.

40. The advent of Genetic Use Restriction Technologies thus presents a very timely opportunity to seriously reflect on the policies associated with their emergence and other trends in the agricultural-inputs and biotechnology

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industries. It is time to place more weight on long term sustainability issues and to formulate clear policy frameworks in which social and environmental implications of technology development and application can be assessed

41. It will then be necessary to articulate clear criteria for responsible approaches that can harness creative science to reconcile business needs with criteria for sustainable and equitable development, including the preservation of genetic diversity in agriculture. These criteria, consistent with the precautionary approach, may be used to determine the acceptable limits of uncertainty in pursuing innovation in agriculture, in accordance with Principle 15 of the Rio Declaration on Environment and Development (UNCED, 1992).

SECTION II: THE TECHNOLOGIES UNDER CONSIDERATION AND THEIR POTENTIAL APPLICATION

How do the Genetic Use Restriction Technologies work?

42. There are basically two levels at which a genetic copy protection or Genetic Use Restriction Technology can act: at the level of an introduced transgene, or at the level of the host variety. One protects an added-value trait, the other protects both the trait and its biological •ost’. We refer to these as Trait-specific Genetic Use Restriction Technologies (T-GURTs) and Variety-level Genetic Use Restriction Technologies (V-GURTs) respectively.

43. These two approaches have enormous differences in their impacts, implications and the business strategies that encompass them. Yet they are very similar in the technical requirements for their development, in terms of the relevant molecular biotechnologies, including externally-inducible genetic control systems and site-specific recombinases.

44. In this section, we will address the questions of how the existing or proposed mechanisms work, and what are the technical requirements. We will also consider the technical constraints to their effective use and the differing forms that these technologies could take.

The Technologies under Examination

45. We will briefly outline the basic technologies contained in the USDA/ Delta & Pine Land (USDA/D&PL) patent, US no. 5,723,765, and use this to illustrate the central features of a Variety-level Genetic Use Restriction Technology (V-GURT). Similar concepts with a number of technical variations are embodied in patents filed by Zeneca, including a clear outline of a Trait-specific Genetic Use Restriction Technology (T-GURT). Both companies have contributed position statements during the course of this assessment (see UNEP/CBD/SBSTTA/4/Inf.3). In addition, the U.S. Department of Agriculture, as well as Zeneca Agrochemicals, have provided statements that are also included in the same information document. As the USDA/D&PL patent has attracted the most attention, we will use this technology to outline the characteristics of this class of intervention.

46. The logic behind this particular technology is surprisingly simple, but its execution is highly complex. While there are two distinct versions of such a technology described in the USDA/D&PL patent, a two-gene and a three-gene system, we will only consider the three-gene system in this analysis. The two gene system would require commercially viable hybridization conditions (e.g. effective male-sterility and cross pollination) to be effective, and as such seem to offer little if any advantage over existing hybrid schemes.

47. Let us consider the basic premise: a desire to inhibit germination of seeds only in the •econd generation’ so that seed can be sold to farmers which will germinate to produce a crop, but the seed (grain) from that crop will be inviable.

The nature of genes, promoters and gene control

48. Genes in all organisms can be considered to have two function components: a control component, or switch, which indicates the •here’, •hen’, and •ow much’ of the gene product to make; and the component that makes the product encoded by the gene – the •oding sequence’. It is quite simple in molecular biology these days to isolate a controlling DNA sequence, for instance a •romoter’, which will only switch on a gene at a particular time and place. One such class of promoters is expressed only in the last stages of embryo development, and is called LEA (Late Embryo Active).

49. In gene fusion technology, such a promoter can be •pliced’ to another gene which, upon introduction to a transgenic plant, can be •xpressed’ in the same manner as the original gene from which the promoter was derived. Thus, one can envision splicing a Late Embryo Active specific promoter to a gene encoding, for instance, a protein that inhibits cell growth or survival - for our purposes, we will call it a •oxin’ gene.

50. Such a gene fusion, or chimeric gene, when introduced into a transgenic plant by genetic engineering techniques would produce a plant that expresses the toxic protein only when the embryo is just about mature – in other words, in the ripening seed.

51. Thus just this simple DNA construction, which almost any graduate student in molecular biology in the world could generate, would cause a •terile’ plant – with a normal looking seed, but which would be unable to germinate because the embryo would be dead.

52. This is the simplest first element of the Varietal Genetic Use Restriction Technology. But of course it is totally useless as such. One would be unable to propagate the plant for plant breeding, let alone for seed production or production of a crop. Thus the next feature necessary to make a commercially useful system is to be able to control this embryo lethality, at will, by suppressing the trait.

53. Suppressing such a trait can be readily imagined by just •nterrupting’ the new gene fusion of the Late Embryo Active promoter and the Toxin gene, with an additional piece of DNA that simply blocks the ability of the Promoter to switch on the Toxin gene. When this new DNA construct is introduced into the plant then the toxin is not expressed, and the embryo is now viable, i.e., it will germinate under usual required conditions of plant growth. This use of a blocking DNA sequence is one of the particular characteristics of the USDA/D&PL patent.

54. However, it is now necessary to selectively remove this •locking’ DNA sequence only when it is desired to produce seed to sell to a farmer. This is now achieved by the two critical technologies of the USDA/D&PL patent. The seed producer/company would like to be able to make these Varietal Use Restricted seeds at their own discretion. So the seed company will need to apply a trigger to allow the •locking’ sequence to be cut out. This trigger could be any controllable external condition, such as a few hours of heat (•eat shock’), or an application of a chemical •nducer’. The latter is greatly preferred, because of course hot days in the field are by no means uncommon, and the seed producer could find his production crop became sterile. The idea of adding a chemical inducer will clearly be attractive especially if the compound is not normally found in a plant, so that the switch will be completely novel and will not thus interfere with plant function or be interfered with by endogenous materials. It is also attractive to the biotechnology and chemical companies who also can manufacture and sell an inducing chemical to the seed producer or seller. The switch described in the USDA/D&PL patent (for reasons outlined below) is only one of a number of possible molecular switch mechanisms.

55. The example used is based around a gene that makes a protein called a repressor that binds very specific pieces of DNA and blocks their action. But this repressor •alls off’ the DNA when a very specific compound – in this case an antibiotic, tetracycline – binds the repressor so inhibiting its function and allowing the expression of the recombinase gene.

56. The repressor is a protein (coded by a gene) that binds to and stops the action of yet another gene, in this case, a gene that causes an enzyme to be made that specifically cuts the •locking’ sequence out of the LEA-Toxin gene fusion, called a site-specific-recombinase. Thus, when all three of these genes are introduced into a stable, genetically engineered plant the following chain of events occurs:

1) The repressor gene is expressed in all the cells making repressor protein.
2) The repressor protein binds to a specific DNA sequence found on the recombinase gene and prevents it from expressing and producing the enzyme.
3) In the absence of recombinase, the blocking DNA sequence that separates the LEA promoter and the Toxin gene remains in place, and the toxin is not produced.
4) The seeds are viable, thus the seed producer can use the plants to conduct plant breeding or to multiply the plants.

57. Now, consider the action of the seed producer when it is time to sell seed to the farmer.

1) The seed producer treats mature harvested seeds which have completed embryo formation with the inducer compound (in this example, tetracycline). The tetracyline diffuses into the embryo cells, and binds to the repressor protein.
2) The repressor protein no longer binds to the specific DNA sequence on the recombinase gene.
3) The recombinase gene is then expressed to make the recombinase enzyme.
4) The recombinase specifically cuts out the DNA sequence that functionally separates the LEA promoter and the Toxin gene.
5) The Toxin gene acquires the potential ability to be expressed during the last stages of embryo development, i.e. in the next generation. The seed is sold to the farmer.
6) The seed germinates normally and the crop develops in the field. But when the plant produces seed, the LEA-promoter switches on the Toxin production gene and the embryo development is not completed, hence the resulting seed will not be able to germinate. The farmer has a crop of grain, but must return to the seed producer to purchase seed for the next season• crop.

58. This train of events, in the first instance the situation in the seed breeding station, the second during the transition to producing a crop, is clearly long, cumbersome and fraught with potential difficulties. To professionals in agricultural biotechnology, the complexity makes it likely that this particular technology, without substantial improvements, may not be the most robust approach to a V-GURT. Let us go through just a few points to discuss why this technology in this form, using the state-of-the-art in plant transformation technology, will be challenged to meet commercial standards.

Current Limitations in Genetic Transformation Technologies

59. Transformation of all crop plants using virtually all technologies available today, results in variable and unpredictable sites of insertion of the new transgene DNA sequences into the recipient plant chromosomes. The integration into the chromosomal DNA does not occur by a mechanism that •eplaces' or substitutes for similar existing DNA, but rather by •dding' new DNA into sites where similar DNA sequence may not have previously been located. This feature of current plant transformation technology imposes some substantial limitations to effective biotechnology intervention.

60. For instance, endogenous, or native traits cannot readily be altered in transgenic plants, except by fairly cumbersome, dominant •nock out' methods, called anti-sense or cosuppression (see below). Precise alterations and insertions are virtually impossible with currently standard technologies. Thus all transgenic traits must be dominant, and the ability to target DNA integration to the original location at which such a gene may have been resident in the chromosome still eludes the industry.

61. This seems to result in transgene locus structures and locations that can produce somewhat variable temporal and spatial expression of the integrated transgene. It is typically necessary - as it is in classical plant breeding - to select from a very large set of •rimary' transgenic lines to find a subset of candidate lines with suitable performance for introgression into elite varieties and analysis or for field analysis and stabilization if already introduced in such varieties.

62. Thus the plant transformation process necessary to produce stably expressing and commercially viable lines, is a very large logistical undertaking. This can greatly restrict the number of varieties that are transformed with a chosen trait, as can the frustrating variability in varietal response to the transformation and regeneration process.

63. While a component of the variation in gene action seen between transgenic lines is genetic, probably related to local effects associated with the sites of insertion, a more troublesome component involves epigenetic mechanisms implicated in such phenomena as •ene silencing' first described as co-suppression by Jorgensen.

64. This co-suppression or gene silencing is now a major issue in assessing the performance of new genes introduced into transgenic plants, and is also a very dynamic and actively studied phenomenon. The robustness, reliability and accuracy of transgene expression seems to be affected by issues that are still somewhat obscure, including the quantity of gene expression, its timing and spatial localization, and the correlation of these features with the site of integration into the genome of the plant.

65. Environmental variation can and does cause genome-wide changes in gene regulation and expression that are not yet fully understood or predictable. That said, when the traits concerned are not critical to the survival of the plant, the consequences of non-performance or altered performance of the transgenic trait will usually most strongly impact the industry that supplies the trait. This caveat may not apply in cases where the germination of the plant relies on very specific gene control by and of transgenic traits.

66. Anticipating the effects of these phenomena for the Variety-level GURTs is not trivial. With current transgenic technology, securing sufficiently reliable control of introduced gene expression to meet the quality-control needs of a seeds industry is a daunting task. When the technology envisioned could, if mis-expressed, result in loss of a crop through insufficient germination, then the criteria for commercial or indeed environmental or social acceptability become very stringent indeed. In this case, the standards imposed by the industry for purely financial reasons would be very high, and in a sense, self-policing.

Anticipated Future Developments in Genetic Transformation Technologies

67. These problems in transgenesis technology may be greatly reduced in the next few years as new technologies emerge which can effect •omologous recombination', •ite-specific integration' and •ite-directed mutagenesis'. These anticipated breakthroughs will provide much more precise means to modify the genetics of plants, which could even be, in many cases non-transgenic.

For instance, site-directed mutagenesis techniques will allow subtle changes in situ to genes within the plant, eliminating much if not all of the problems associated with inserting new genes in inappropriate locations in the chromosome. The same would be true if the ability to exactly replace one gene with a variant of it by •omologous recombination’ becomes routine.

68. The development of these technology breakthroughs is very important to the industry, but the current trends in providing technology access to both public and private sector competitors do not bode well for encouraging diverse competitive choices, if these breakthroughs should be controlled by one or a few large entities.

69. Even the existing technologies for DNA introduction, such as Agrobacterium and particle bombardment, while widely practised in research environments, are not widely available commercially under license to many competitors. As well, most public programs working towards the betterment of agriculture in developing countries are not licensed to use these technologies to produce material that can be grown and sold by farmers in many jurisdictions. These, and related bottlenecks to securing freedom to operate, alluded to in Section I, are very important issues in technology choice and development, and may well be the crux to ensuring a balanced and diverse industry evolve using biotechnology.

Inducible gene control systems

70. Exogenously inducible gene control systems are still in their infancy in plant science, but the pace of research into their development has greatly accelerated in recent years. While patents have been issued on the use of a number of endogenous plant genes whose promoters are induced by proprietary substances such as herbicide •afeners’, there are still very few systems available to accurately and effectively control gene expression in transgenic plants under field conditions.

71. The basic premise of an engineered inducible system is that application of a specific exogenous (typically organic) compound will effect a change in expression of a chimeric gene, typically through altering transcription. However it must be appreciated that in virtually all cases described, the chemical itself does not effect any change on transcription, but rather, by binding to a protein and changing the shape or activity of that protein, an alteration in a promoter• activity can be effected. Thus an •nducible promoter’, if specific for an exogenous compound (i.e. not a normal part of the plant• metabolism) must also have an associated binding protein that can communicate the presence or absence (or concentration) of the chemical to the DNA. In addition the gene encoding this protein must also be introduced into the targeted plant system; thus strictly speaking an exogenously inducible gene control system will usually comprise a multi-factor •ystem’, including the gene(s) for the binding and effecting protein(s) as well as the targeted promoter.

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72. Using natural endogenous plant promoters as inducible switches has some advantages, but many drawbacks. One advantage is that the •achinery’ necessary to transduce the signal - the presence and concentration of the inducing compound - is already in place in the plant and does not need to be engineered to the plant. However, if such a system exists in a plant species, one can anticipate that it is because the compounds recognized also exist in the life cycle of the plant. Thus achieving the degree of control that is usually sought, without background gene expression, would be very problematic.

73. Engineering inducible systems is likely to become very much more straightforward due to the recent explosion in DNA sequencing, including the completion of the DNA sequences of a number of eukaryotic genomes, including those of yeast and <u>Caenorhabditis elegans</u>. •ining’ these genomes for likely candidates, then using new technologies of <u>in vitro</u> evolution to tune the inducing systems to particular compounds seems a productive and rapid means of achieving effective inducibility.

74. Current systems in laboratory use, which are often invoked in patent applications for the purposes only of illustrating to a patent examiner a hypothetical way to make a system function, are without exception greatly limited or completely inappropriate for field-level use in agriculture. For instance, such systems, engineered from genes derived from bacteria, fungi, mammals or insects are inducible by copper, tetracycline, alcohols, glucocorticoids, insect molting hormone (ecdysone) and others. These systems were developed for other purposes, typically laboratory uses in non-plant species - and were rarely seriously considered in themselves for agricultural field uses.

75. The challenges intrinsic to commercial use of exogenously inducible gene control systems are not trivial. The compound must have certain properties; it must be non-toxic to the ecosystem, capable of being formulated for field or seed application; transportable into and within the plant; biodegradable; highly specific to the induction system; affordable and (for many uses) proprietary. The inducer-responsive system must have a very high dynamic range, a low •asal’ level of transcription, sensitivity to low doses of inducer, high specificity for the inducing compound, etc. None of the systems described, to date, in either the patent literature or in the primary scientific literature can meet the necessary criteria to make it commercially viable for the purposes of the V-GURT or T-GURT systems. That said, these methods are often very good research tools, and further, methods to invent inducible gene control systems that do meet these criteria are well developed and are being very actively pursued.

<u>Site-Specific Recombinases</u>

76. The ability to convert an •nalog’ signal (the often variable concentration of, or transient exposure to, an exogenous chemical) to a stable •igital’ signal (the expression or non-expression of a gene) can be afforded by coupling the inducible system to the expression of a site-specific DNA recombinase. These recombinases typically can either cut out or flip the DNA that is located between two precisely defined •lag’

sequences. They may be derived from eukaryotic organisms such as fungi, or indeed from bacteria.

77. There are many such recombinases known, and many more being discovered regularly. Again, with whole genome sequences being published almost weekly, the opportunity for discovering new recombinases with very little research effort is great. The current technologies to precisely engineer and •une’ recombinases are also very powerful. The best described recombinases, dating back to work done more than ten years ago, are still fairly effective for research purposes. But their degree of effectiveness in transgenic plants is variable, and in many cases, one will find only about 90-95% of the target molecules in a population will have experienced a recombination event. In the case of the USDA/D&PL type of V-GURT, this would mean that even if full inducer action were achieved, one might expect a small proportion of the seed would not have excised the •locking’ DNA sequence.

Factors contributing to the effectiveness of the V-GUR technology trait and their influence on genetic outcrossing and gene-flow to sexually related species.

78. A failure of the V-GURT system, as described by USDA/D&PL, would likely confer a commercially unacceptable level of protection, in that any bag of seed produced that had been •erminated’ would have many seeds that would prove fertile, hence breaking the copy protection relied upon by the seed company.

79. Indeed, failure of any number of steps would compromise the effectiveness of the technical protection afforded by the •efault-fertile’ mode of V-GURT. Failure of inducer uptake or action, failure of adequate deactivation of repressor, failure of recombinase – as alluded to above – or failure of expression or activity of the toxin, could all contribute to the ineffectiveness of protection.

80. In the USDA/D&PL V-GURT system, the •efault’ state of the plant in the absence of seed treatment with inducer is fertility. Thus, any plants that escaped the V-GURT germination block would be able to propagate and contribute to outcrossing to the degree that the species would normally be capable. In crops such as rice and wheat, this outcrossing is quite rare (usually well under 1%) but in other crops such as canola, it can be very common. Thus, once the block is bypassed, there would be no technological constraints other than intrinsic natural biological limits, to prevent the spread of the transgene to sexually compatible neighbor plants. That said, with the default-fertile mechanism, the consequences of such spread would more likely be determined by the associated added-value trait, rather than the V-GURT system itself, which would require inducer treatment to be reactivated.

What species and systems will be targeted for these technologies ?

81. As alluded to briefly above, different species, and indeed different varieties within species respond in very different ways to genetic transformation protocols. Sufficient attention commercially can usually break a number of technical barriers, but this is by no means straightforward. Thus one can anticipate that only a limited number of varieties in high-margin, high-value crops will be targeted for V-GURT use in the absence of major breakthroughs in transgenesis technology. Indeed the technical difficulties in transgenesis may currently be among the most substantial bottlenecks to the use of these V-GURTs in diverse germplasm.

82. For a crop to be attractive for commercial protection of added-value traits by V-GURT, it should be a seed-bearing annual (ensuring frequent purchase of seed), typically in-breeding and associated with intensive agriculture practices with sufficient capital pools to justify the seeds industry development.

83. The crops in which GURTs would be used are also very likely to depend on the country, the sector and the societies involved. However, one can anticipate that rice, wheat, cotton and soybean will be amongst the first targeted species, due to the importance and size of the potential markets and the trends in some production systems to be subject to farmer plant-back. Many economic features associated with the viability of a seeds industry, including seeding rate, and cost margins for seed production, as well as the value added by the transgenic trait will each strongly affect the choice of targeted crops and systems.

Forecasting Future Developments of Variety-specific GURTs

84. As described above, we anticipate within three to seven years there will be robust technologies to manipulate endogenous genes through molecular intervention (e.g. site-directed mutagenesis; homologous recombination), and that these must be considered proactively in anticipating trends with these GURTs. We envision these new molecular technologies for genetic manipulation to be more robust and penetrant, but at the same time much harder to detect and police, due to the subtle and potentially non-transgenic nature of the changes made.

85. It is also anticipated that additional and more effective strategies to achieve Variety-level Use Restriction will be developed that are more robust and cost-effective than the initial V-GURT described in the USDA/D&PL patent, including technologies which combine natural mutations affecting germination with transgenic `rescue` of the trait, resulting in default `sterile` mechanism. In such a mechanism, the seed provided would be inviable in the second generation and only application of an inducing compound will restore the ability to germinate.

86. It is very likely that scenarios such as this are under development in a number of laboratories worldwide, and that specifics of the currently well-publicised "terminator" system will be less important in the face of improved commercial systems for achieving the same goal.

87. In considering the pace of research in transgenic biology, it is anticipated that it may well be at least three years before initial field trials of GURT technologies are conducted in any reasonable number, and at least two to three further years before a commercial candidate variety could be ready for release.

Protection of Genotypes Enhanced by Non-transgenic Methods

88. We can anticipate substantial increases in the performance of varieties bred by •onventional’ non-transgenic means, using high-technology molecular markers-based genomics approaches. Some of these may be highly productive and commercially valuable, may represent a very large investment by private or public breeding, and may also be targets for V-GURT technology.

89. Thus, in considering V-GURT applications the use of these when NOT associated with a transgenic added-value trait must be anticipated. However, as the V-GURT mechanism itself would be transgenic, and the development of that V-GURT mechanism and registration of the transgenic line would be high capital investments, it seems likely that many if not most applications of V-GURTs will involve an added-value transgenic trait.

Trait-specific Genetic Use Restriction Technologies (T-GURTs)

90. The basic premise of developing in-built Genetic Use Restriction Technologies is that the intrinsic ability of most seed-bearing plants to reproduce and hence to copy their genetic material by definition also results in copying of any additional genetic materials that have been stably introduced into the plant. This effectively means that plant reproduction copies an introduced transgene. If that transgene-encoded trait constitutes an invention or innovation that has an associated added value, then the very propagation of the plant constitutes a major conundrum for legal and business reasons.

91. Thus, an alternative Trait-specific Genetic Use Restriction technology, called T-GURT could be invoked in which a molecular intervention could delete the gene encoding the added value trait upon germination of the second generation, if not treated with a proprietary compound.

92. This surprisingly simple modification alluded to very clearly in Zeneca• patent, would allow propagation of the host genotype even after such a deletion occurred. It would thus address a number of serious concerns about varietal security, but would still require the development of either a seed production industry, or a sufficiently robust system to allow farm-level suppression of the deletion (excision) event.

Farmer Activated, Facultative Trait-specific GURTs

93. It is not the transgene, per se, that confers the •dded value’ but rather the expression of the trait encoded by the transgene. Thus a further

level of protection could require simply the activation of the trait rather than the physical deletion of the gene encoding the trait. In so doing, the protection mechanism would uncouple the requirement for repeated seed purchase from acquisition of permission to use the trait on a seasonal basis.

94. This way of using the same core technologies could encourage broad, locally chosen, and fairly-compensated use while achieving the goal of stopping unauthorised use of proprietary traits. In so doing, use of such facultative T-GURTs could arguably stimulate broad evaluation and use of proprietary traits in non-proprietary germplasm.

95. Let us •alk-through’ such a farmer-controlled T-GURT method in a manner similar to the V-GURT analysis.

96. The overall goal is to have a variety containing an added value transgenic trait that is activated for (e.g.) one generation by application of a proprietary compound. The activation of the trait would be linked to the use of the compound, and the added-value would be obtained by that activation.

97. In the absence of such activation, the variety would be fully competent to perform at its basal level. For instance, if the farmer chose not to purchase the activator, the crop would produce normal seed and perform at its expected potential in a given environment in the absence of that trait. It would be completely at the discretion of the farmer whether or not to activate the trait. Existing rights and privileges associated with the variety would persist, and compensation for the use of the trait – if any at all – could be obtained.

98. However, if the trait of interest really would add value, in the views of the farmer, the farmer would have the option of purchasing the activator from the technology provider. After application of the activator (e.g. at the seedling level) the transgenic added value trait would be expressed. When the plant sets seed, the trait could be switched off; in a sense, reset and ready to be activated again if it is chosen by the farmer. If the farmer is less than thrilled at the performance of the •dded-value’ trait, he/she can chose to propagate and harvest the crop without such activation, thereby exerting a market force on the technology provider.

99. The activation and resetting can be done by a similar set of molecular technologies to that used in the now classic V-GURT patents of USDA/D&PL. In fact, there are many biological precedents for just such a switch – activated by an external compound, and reset after sexual mating. The baker• yeast, *Saccharomyces cerevisiae*, undergoes an alternation of mating types, induced by an exogenous peptide hormone (an excellent example of a class of natural, yet potentially very specific and proprietary inducers). Examples of this type, widely found in nature, are potentially adaptable technically to provide a binary trait activation capability.

SECTION III: INTELLECTUAL PROPERTY AND LEGAL CONSIDERATIONS

Intellectual Property Considerations:

Nature, Scope and Effects of Genetic Use Restriction Technologies

100. By rendering seeds sterile if replanted a second time, a distinct effect of V-GURT technology is to protect the seed producer against multiplication of the seed by a third party. It may thus prevent the unauthorized copy of a plant variety either conventionally bred or genetically engineered to express a specific trait. The GUR technology thus achieves, by an in-built biological mechanism, a target that under the patent or Plant Breeders Rights (PBR) laws requires monitoring and determination of infringement, and the intervention of courts to enforce the applicable proprietary rights. The technology, in brief, essentially permits to replace a <u>legal</u> means by a <u>biological</u>, <u>in-built</u> mechanism to prevent free riding on plant-related innovations.

101. Patents on genes, seeds or other parts of plants, in countries where they are allowed, generally permit the title-holder to restrict the use of seeds obtained after the first planting of a protected material. In exercising the exclusive rights conferred, a patent may be used to legally prevent farmers from saving seed for further planting. Enforcement requires sometimes lengthy administrative or judicial procedures, and it is not always cost-effective, particularly in the case of small exploitations.

102. The effect of genetically sterilizing seeds is, in terms of anti-copy protection, equivalent to fully enforcing patent rights so as to exclude the saving and reuse of seeds. The use of the V-GURT technology, however, <u>may have a much broader impact than patents.</u>

103. First, a patent is only conferred in respect of inventions which meet certain requirements (novelty inventive step or non-obviousness, and industrial applicability). Therefore, patents can only be obtained when an invention can be claimed. Instead, the V-GURT technology, at least in principle, may be applied to any seed, novel or not.

104. Second, patents have a finite time duration (generally twenty years from the date of application) while the V-GURT technology may be used indefinitely.

105. Third, if effectively implemented, the V-GURT technology would confer an absolute anti-copy protection in the sense that the seed could not be reused by any farmer, either large or small scale. Protection would not be dependent on legal procedures, which often are costly and can not be pursued against all possible infringers.

106. Similar considerations apply to the case of Plant Breeders Rights (PBRs). V-GURT technology would provide a protection much broader and, possibly, more effective than PBRs. On the one hand, the seed producers

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would determine which species and varieties to genetically protect. All species may be subject, in principle, to V-GURT[1].

107. On the other hand, PBRs, as implemented in most countries, allow the saving and re-use of seeds of a protected variety under the so-called "farmers' privilege"[2]. The V-GURT would deprive this "privilege" from any practical applicability, since the seed of a V-GURT variety could not be reproduced even if legally permitted. It is this "privilege" or exception to the exclusive breeders' rights, that will be nullified in practice by the V-GURT[3].

108. With the application of V-GURT technology, the protection of seeds by IPRs, would become largely redundant, since the protection would be embedded in the material itself.

109. The in-built anti-copy protection allowed by V-GURT technology, would directly affect the farmers that plant the seeds; it would make superfluous the recourse to other means of (legal) protection against the final users of the seeds.

110. However, the use of that technology would not prevent by itself the imitation of a certain product by other companies or entities that may possess the technical capabilities to reverse-engineer or otherwise duplicate the "technically protected" seed. Hence, patents, PBRs and trade secrets protection would continue to be important tools to secure control over certain materials in the relationship between the innovator and eventual imitators.

111. In sum, the V-GURT technology offers a tool to restrict the use of seeds of any crop after first plantation. V-GURT is more powerful and broader in scope than IPRs as a means to impede unauthorized use of seeds by farmers, for an unlimited time. It would not substitute, nevertheless, IPRs to prevent eventual imitation by competitors.

Patentability

112. Patents are normally granted if certain requirements are met (absolute novelty, inventive step and industrial applicability). Both the definition and the precise way in which those criteria apply vary from country to country and, therefore, an invention may be deemed patentable in one jurisdiction and not patentable in others. It is outside the scope of this

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[1] Under UPOV 78, member countries were given the possibility to progressively extend protection to the •argest possible number of botanical genera and species” (article 4.2). However, the UPOV Convention, as revised in 1991, applies to all species, and article 27.3. b) of the TRIPS Agreement obliges to protect all plant varieties.

[2] While implicitly admitted under UPOV 78, this exception has been explicitly dealt with in UPOV 1991 (article 15.2 permits member countries to establish it •ithin reasonable limits and subject to safeguarding of the legitimate interests of the breeders”).

[3] The concept of •armers’ privilege” must be differentiated from the notion of •armers Rights” as recognized by FAO Conference Resolution 5/89 approved as an to Annex the International Undertaking on Plant Genetic Resources . The said notion is based on the farmers’ contributions to <u>in situ</u> conservation of plant varieties’. The implementation of such rights is currently under discussion in the framework of the revision of the Undertaking

report to judge the patentability of the GURT inventions, as described above.

113. It should be mentioned, however, that the Trade Related Intellectual Property (TRIPs) Agreement allows World Trade Organisation (WTO) Member countries exceptions that may be relevant in considering the eventual patentability of the V-GUR technology, to the extent that those exceptions are provided for under the applicable national law. They refer to morality and ordre public grounds and to the possible non-patentability of "plants".

Morality and Public Order Considerations

114. Given the potential effects of the V-GURT technology, the question may be posed whether a patent on V-GURT may be refused, or cancelled, on the basis of morality or public order grounds. Many national laws provide for the non-patentability of an invention based on such grounds, Article 27.2 of the TRIPS Agreement also stipulates among the exclusions from patentability that any country may (but is not obliged to) establish in its domestic law, the hypotheses of ordre public or morality. The said article states that:

> *"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 domestic law".*

115. The notions of ordre public and morality are vague and evolutive (Pollaud-Dulian, 1997, p. 166). There is no generally accepted notion of "ordre public": WTO Member countries have, therefore, a considerable flexibility to define which hypotheses are covered, depending upon their own conception of the protection of public values. In some countries, this concept is interpreted as being narrower than "public interest" (for instance, under the Guidelines for Examination of the European Patent Office, it is linked to security reasons, such as riot or public disorder, and inventions that may lead to criminal or other generally offensive behaviour, Part C, chapter IV, 3.1). Article 27.2 of the TRIPs Agreement, however, indicates that the concept is not limited to "security" reasons; it also relates to the protection of "human, animal or plant life or health" and may be applied to inventions that may lead to "serious prejudice to the environment".

116. The concept of "morality" is also relative to the values prevailing in a society. Such values are not the same in different cultures and countries, and change over time. Some important decisions relating to patentability may depend upon the judgement about morality. It may be inadmissible that patent offices grant patents to any kind of invention, without considering ethical issues whatsoever.

117. According to article 27.2 of the TRIPs Agreement, the existence of a legal prohibition will not be sufficient per se to sustain the non-patentability of an invention. Non-patentability may only be established if the commercial exploitation of the invention needs to be prevented to protect the interests referred to above. Since the refusal of a patent does not necessarily lead to the exclusion of commercialization, the decision to prevent the commercialization of a product would generally have to be adopted by other authorities. In the case of V-GURT technologies, such a decision could be based, for instance, on biosafety or seed regulations. If this is the case, to the extent that the commercialization of a V-GURT seed may be deemed to amount to a restriction to trade, consistency with the relevant WTO rules on the matter should be ensured so as to avoid exposure to commercial sanctions, as applicable according to the WTO Dispute Settlement Understanding.

Exception on Plant Inventions

118. Article 27.3.b of the TRIPs Agreement (currently being subject to review by the TRIPs Council) allows Member countries to exclude the patentability of "plants", while obliges to protect micro-organisms and plant varieties, in the latter case on the basis of patents, an "effective sui generis" regime, or a combination of both.

119. The extent to which these exceptions may be applied to exclude the patentability of V-GURT technology would depend on their implementation through national law. The TRIPs Agreement leaves considerable room for manoeuvre in this respect. It seems clear that the exception may apply to claims on plants and seeds, which may be deemed non patentable. The concept of "plants" may be also considered to embrace any part of a plant, including DNA constructs and cells (Correa and Yusuf, 1998), though in the practice of some patent offices the latter are deemed microbiological, and hence patentable, materials.

Effects of non-patentability

120. In the case of the V-GURT, as mentioned, the seed obtained by the farmer using a plant modified with that technology will not germinate. This implies that the farmer will be prevented from saving and replanting seed by a feature built-in in the seed that he/she had acquired. From the point of view of the vendor of the seed, this implies that a legal mechanism based on the enforcement of a patent, is replaced by a technical means that may confer absolute protection against re-use and copy of the original seed.

121. Given the specific effects of the V-GURT, in legal terms the main impact of the existence of a patent on that technology is to create a barrier to competition by other seed producers who, in principle, can not use the method without the title-holder consent. The existence or not of a patent on V-GURT is not a problem that directly affects the farmers: it is the technology itself which prevents the saving and re-use practices, and not the eventual enforcement of patent rights.

122. The V-GURT patent, hence, should be seen as a legal mechanism that mainly regulates the relationship between the title-holder and its eventual competitors. The problem and threat to farmers’ practices of saving seed is not the patent as such, but the existence and diffusion of the technology, patented or not.

123. A patent only confers a <u>negative</u> right on its proprietor to prevent others from using the protected invention for a limited period. The right to positively use or not the invention by the patent holder is, hence, not addressed by the patent law, which is primary an instrument for promoting research by ensuring the possibility of excluding imitation by third parties.

124. Hence, if the V-GURT patent were to be found inviable or invalid on any grounds, the effect of non-protection would be that the relevant method will remain or be put in the public domain. The absence of protection would not automatically lead to stop the eventual adoption and diffusion of the V-GURT technology: on the contrary, such an absence may foster its dissemination.

125. This is not an argument to justify the V-GURT patent. This is to indicate that if a country would envisage to totally or partially prevent the diffusion of that technology (with regard to certain or all species, for a certain proportion of sold seed, etc.) it is not on the basis of the patent law that such a policy may be effectively implemented.

<u>Intellectual Property Implications of a Trait-Specific Genetic Use Restriction Technology</u>

126. The use of the V-GURT technology, as described earlier in this paper, implies that the seed producer may impede the re-planting of the treated seeds, thereby blocking the further exploitation not only of the trait or traits he/she intends to protect, but of the whole associated genome. This would be the case even though the actual interest of the seed producer may be to prevent the unauthorized use of a particular gene or gene construct, rather than of the whole germplasm that carries the added traits.

127. This is an important distinction, in that embodied in transgenic varietal germplasm are many generations of contributions, both in informal plant improvement and in formalized plant breeding, as well as in the biotechnology intervention. And these contributions can have different mechanisms of protection and recognition, ranging from Farmers’ Rights to Plant Breeders Rights to complex patent rights associated with the transgenic trait.

128. Under patent law, the protection of a trait does not necessarily imply the protection of the full genome of the plant that expresses it. A patent on a trait may afford control of the use or commercialization of the plant as long as it expresses the relevant trait. If the trait has been •eleted” so as not to express, there would be no grounds to enforce the patent. This is of course not the case if there are issued claims to a substantive component of the trait, such as a gene or promoter.

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129. The V-GURT technology, therefore, expands the protection from a single element of a plant to its totality, even in cases where the associated germplasm may be non-proprietary.

130. As described in Section II, it is possible to devise a GUR technology specific for a particular trait. This approach, which we call Trait-specific GURT or T-GURT would mean that a transgenic T-GURT seed could be replanted and would germinate, but unless activated by an external inducer, the relevant protected trait would not express in the replanted seed, or would be deleted.

131. This mechanism would restrict the protection achieved to the actual traits where the innovation may lie, while allowing the use of the associated germplasm. Farmers could thus have the option to activate or not the trait through the application of a chemical inducer. If they opt to do so, the seed producer may get a compensation for his/her contribution. If the farmers do not activate the trait, they could use the germplasm without limitation or subject to observance of other applicable rights, such as PBRs.

132. The intellectual property implications of the T-GURT approach are intriguing, as there could be a very substantially re-orientation of the current paradigm of patent control of germplasm and the attendant business structures that have evolved to enforce this. A comprehensive study of the implications and modalities of the use of T-GURTs, particularly with regard to nested forms of IP and technical protection, and apportioning rights and returns would be very helpful in evaluating their potential use.

SECTION IV: POTENTIAL CONSEQUENCES ON THE CONSERVATION AND SUSTAINABLE USE OF BIOLOGICAL DIVERSITY: IMPACTS ON AGRICULTURE, BIOLOGICAL AND SOCIO-ECONOMIC IMPLICATIONS

Potential Impacts of Genetic Use Restriction Technologies

133. Before considering impacts, it is essential to recognize the preliminary nature of such determinations. No working example of a V-GURT or T-GURT is available to study. No data as to its effectiveness or any other features of its biology are available. As this intervention is exclusively in the realm of agriculture, the degree to which GURTs have an impact of any kind is directly related to their success and adoption in agricultural production systems. For this reason, impact assessment in this paper will be necessarily superficial. In this section, we endeavour rather to outline the issues and the context in which GURTs will operate, to help define the scope of subsequent studies.

The Context: Agricultural Systems

134. Three types of agricultural systems are recognized for the purposes of examining potential impacts of genetic use restriction technologies for seed crops, though there are obviously countless variations to these general categories. These are:

1) highly industrialized agriculture, characterized by wide scale use of improved varieties, often extensive use of a limited number of species and varieties, fertilizers, crop-targeted pesticides, chemical seed treatments, irrigation and high degree of mechanization;
2) intermediate agriculture systems, in intensity and nature, including partial adoption of mechanization and external inputs; and
3) traditional subsistence agriculture, with diverse locally adapted varieties, often diverse crop-livestock enterprises, limited external inputs and low adoption of improved varieties, even when available.

135. All three types of agricultural system exist in most developing and developed countries but to different extents and representing different proportions of the farming population and of the agricultural sector.

136. In the first category, highly industrialised agriculture, farmers have been encouraged to use certified seed sources that assure varietal purity and freedom from seeds of other crops and weeds. Commonly used are chemical seed treatments to control seedling and other diseases, and, in the case of legumes, inoculation of seeds with <u>Rhizobium</u> to promote biological nitrogen fixation. These farmers have the option to save seeds from their crops for planting the next year. However, in some countries, where legal plant variety protection applies, they may be required to pay a fee to the holder of the variety protection of any seeds they wish to plant back from their own crop. These farmers generally have access to finances and credit and may have a limited number of enterprises due to the high capital investment for adoption of specialised, mechanised systems.

137. Farmers in this category are receptive to inputs and practices that they believe return greater value to their commodities, including regular, often annual, renewal of seeds of improved varieties. GURTs, for these farmers, may generally be accepted if value-added benefits are reasonably assured in their crops. That said, there is increasing activism amongst this community of farmers against the effects of high-capital farming methods, the use of biotechnology to effect consolidation of private sector control as well as concern regarding their own role in environmental stewardship. Such activism may be a powerful wild-card that makes predicting adoption of such technologies very difficult and tentative.

138. Some farmers with intermediate systems, the second category, have certain characteristics of those in the first category, but many of them would have limited access to external inputs for financial reasons while their soil and water and socio-economic conditions might be less suitable for intensive agricultural systems. As a group, we expect these farmers would be more inclined to save seed from their crops or purchase or trade for seeds with neighbours. Seed conditioning - cleaning, sizing, treating,

and inoculation- would not be done regularly, if at all. Adoption of improved externally produced varieties by these farmers would be quite high if their region and markets were supported by seed and plant improvement programs from either the private or public sectors. It would be low if seed production and distribution systems were not developed and few new varieties were made available to them. A commercial seed industry, including the marketing of varieties produced by private seed companies, would be limited and generally not available to the whole farming community. GURTs would be expected to have mixed acceptance and adoption among these farmers, who, according to their socio-economic situation and need to spread their risks, would decide on the extent to which they would need to maintain local varieties and could afford to adopt new varieties. Landrace varieties and products of traditional breeding programs may be chosen as being most appropriate by many of these farmers. However, T-GURTs, presented in well adapted local varieties could be viewed as an attractive new set of choices by this community, to be activated as and when resources and opportunities to gain added value are presented.

139. The subsistence agricultural sector, the third category, is often characterized by high crop diversity, marginal soil quality, rainfed moisture, and few external inputs, such as mineral fertilizer and pesticides. A formal seed improvement and distribution system is generally lacking and farmers rely on their own, or community sources of seeds. Their access to credit is limited or unstable. Crops of major importance to their food and feed supply are widely grown, but not at sufficient profit to encourage adoption of technological innovations. These farmers would not likely be offered GURT varieties by the developers because of limited ability of the farmers to purchase the seeds, and, more importantly because the intensive plant breeding efforts to produce such varieties would not be directed to meet the environmental conditions of this limited seed market. There is ample evidence for this situation, where farmers have rejected •mproved’ varieties, even in countries having a long tradition of plant breeding and a reasonably viable seed system.

Specific Issues

A: Farmer• Options and Choices of Varieties and Seed Sources

1) Variety-specific GURTs

140. Some proponents of GURTs assert that as long as a farmer has a free choice between technologically protected and non-protected seed, the broad adoption of V-GURT material would be driven by and responsive to only a market need and the perceived value to the farmer of such material. In light of this premise, it is particularly important to consider not only those situations in which such choice is more or less provided by a diverse and effective market system, but also those situations in which other factors may strongly influence or limit choice.

141. If government programs are to control seed distribution, this might include credit schemes that mandate adoption of crop production packages through credit incentives, thus limiting or eliminating farmers’ choice.

There are precedents for such practices that must be considered carefully on a case by case basis. There are no guarantees that public sector (i.e. governmental or non-profit intervention) is benign or acting in the public good, nor conversely any similar guarantees that private sector is acting against the public good. This artificial distinction is not helpful in anticipating impacts nor degrees of choice.

142. The private plant breeding and seed sector has often been a highly effective tool in many parts of the world to transfer innovations to potential beneficiaries. This is most prominently achieved through provision of reliable, clean planting material, as outlined above. If biotechnology does eventually provide dramatically improved performance, as is widely speculated, that performance could be hypothetically transferred to farmers through small to medium-sized breeding companies who should themselves have great latitude in determining which technology to incorporate in their improved non-GURT germplasm. If this scenario were to prevail, it could indeed provide a counteracting choice to farmers, to ensure GURT adoption was determined by fair and open market forces. However the current structure of the biotechnologically sophisticated component of the seeds industry already displays high levels of concentration – either through ownership or through contractual relationships - and the trend seems to be accelerating.

143. If conventionally bred material in the future should not be competitive with biotechnologically enhanced germplasm, and if the access to biotechnology innovations is restricted to a decreasing number of seed companies, then the possibility exists for market dominance by a few suppliers with potentially serious consequences for technology choice and price fixing.

144. Importantly, and especially in the developing world, choice has often been provided by public-sector plant breeding initiatives, even when distributed and marketed through private sector partners or cooperatives. With the extraordinary decrease in publicly funded plant breeding and with the difficulty of public entities to provide commercially useable biotechnology interventions due to IP restrictions which may be imposed by large corporate entities, this mechanism for providing effective alternatives may also be rapidly diminishing. This trend is likely to disadvantage both public and private crop improvement communities, worldwide.

a) Crop Genetic Diversity

145. As has been the case for input-intensive high yielding variety (HYV) adoption, rapidly changing agricultural practices can have a profound impact on use and conservation of land races and locally adapted varieties. This tendency, which has been well documented, has directly affected generally those communities and adopters with sufficient financial capital to purchase the associated inputs, of which seed is only one.

146. This economic self-limitation could well be exacerbated in a circumstance in which few or no additional inputs were required to extract maximal value from an innovation.

147. This very lack of input dependence is being promoted by much of the agricultural biotechnology community to justify the broad adoption of transgenic seed, for instance with in-built pest protection rather than requiring external pesticide application. However, as can be seen, such input-independence could then lower the capital threshold for adoption of novel technology as that technology could conceivably perform well in locally adapted varieties.

148. In developing the Varietal GURT, the only absolutely required input may be the transgenic seed. The challenge is to balance the potential for even more broad-scale abandonment of traditional varieties and their intrinsic genetic diversity that this may cause, with the right of the farming community to good quality and productive planting material and its own local choice of technology. With Variety-level-GURT technology this conundrum is not addressed, whereas with Trait-specific-GURT, it may well be reconciled.

149. The greatest concern is that extensive use of varieties with V-GURT will stop the flow of seeds that might otherwise be used to improve local varieties. When local varieties are thus improved we have in place a process for evolving new landraces. The latter may well preserve and improve plant genetic diversity, but with broad adoption of V-GURT amongst the semi-formal sector, such improved landraces would no longer be developed.

150. We can say from the outset that it is doubtful that new plant varieties bearing V-GURT will be designed for the subsistence sector of agriculture. It is most likely that such varieties will be targeted basically for the most affluent farmers and markets of the most modern agricultural sectors in both developed and developing societies. Therefore, to the extent that there is genetic isolation of the traditional farming systems from the new technology, and maintenance of traditional systems, there will be conservation of plant genetic resources.

151. On the other hand, it is perceived that seed companies are progressively moving from the realms of modern farming towards subsistence agriculture. So, if varieties with V-GURT are indeed targeted increasingly to the traditional subsistence sector, as some companies express that they will, then we can see either ambivalent or negative impacts. In this context, the greatest concern is with the mixed sector of cash and subsistence agriculture, which is likely to adopt earlier than the more traditional sector. The key question here is how to deal with conservation versus improvement of varieties in regions of high plant genetic diversity.

152. It is necessary to also address three further levels of analysis: the farm economy, the national level, and global relations between North and South.

153. At the farm level, a new plant variety containing V-GURT would require to have substantially better performance compared to other varieties if it is to be economically attractive to farmers.

154. This is so because the farmer would have to give up his or her right and privilege to save seeds for next season• planting. Only farmers with very solid financial endowments will be able to make the choice of foregoing the possibility of seed saving, provided that, in their calculation, increased yields will more than offset the extra cost of the new plant variety. This requirement clearly skews adoption toward the most affluent farmers. If they are successful in their adoption of the new technology, even if only temporarily for a few agricultural seasons, this will create a great competitive pressure for their neighbours to adopt, shift cultivation to other crops in which they can be competitive, or get out of farming. This represents the usual •echnological treadmill” that has become so prevalent with input- and capital-intensive agriculture.

155. At the national level, there are several important costs and risks of promoting and adopting new plant varieties with V-GURT. First, few of the targeted self-pollinated crops (such as wheat or rice), especially in less developed countries, have well-established seed industries or distribution infrastructures to assure access to farmers. Therefore, developing a seed industry could involve a high cost and possibly a large infrastructure would have to be developed if high degrees of quality control and product control were required to implement V-GURT. The question then becomes who will bear its cost? Given the structure of the global seed industry, the most likely bearers of the extra cost will be farmers and consumers.

156. If the development of new varieties with V-GURT were to be successful, this could displace more robust varieties that are better buffered against environmental changes. Such displacement would entail an increased vulnerability to unexpected environmental stress and could result in increased food insecurity at farmer or indeed national level.

157. Another important risk at the national level is that increased dependence on plant varieties with V-GURT could involve an undue dependence on seed supply of this kind. Widespread use of such technology could reduce food security by making a nation more dependent on the continued operation of a very small number of global institutions. History shows that institutions are not permanent: war, civil disorder, or natural disasters can cause breakdowns in supply chains.

b) Environmental Effects Resulting from Gene Flow of Variety-specific GURT

158. Environmental effects resulting from gene flow of V-GURT can be direct or indirect. With regard to direct effects, we perceive that risk associated with gene flow of Variety-level GURT trait to wild relatives is unlikely to be as serious an issue as the flow of active genes conferring advantage on the plant, such as herbicide resistance. The inability to •ix’ a trait which causes organismal lethality largely ensures that the trait, per se, would not be established in an out-cross population.

159. The gene complex encoding such a trait, in the event of its transient silencing through epigenetic effects, could conceivably transfer and if associated with a selectively positive trait could be envisioned to be fixed in a recipient population. However in this case, if the trait were reactivated one would anticipate lethality of the individual(s) carrying the gene complex.

160. Thus, while there are possible scenarios in which one could imagine the transfer of an inactive form of the V-GURT, such transfer seems somewhat unlikely to have serious consequences. The probability of transfer of an active, penetrant form would be so remote as to be almost negligible. The issue of affecting the viability or performance of neighbouring crops of non-V-GURT plants through pollen-mediated transfer could arise in out-crossing species (e.g. <u>Brassica</u> spp), but can be anticipated and would likely be of similar scale to herbicide spray drift and other such collateral damage effects.

161. It should be appreciated, however that this is a highly contentious and emotive topic, and deserves to be approached with rigorous scientific analysis; data should be obtained and analysed to confirm or refute these assertions.

162. Arguments have been advanced that the use of a facultative dominant V-GURT mechanism, such as that in the USDA/D&PL patent, could be helpful in achieving a safe transgenic agriculture through restricting gene flow due to out-crossing from a transgenic plant to a neighbouring sexually compatible plant, either another crop plant or an uncultivated relative. In considering V-GURTs as a mechanism for preventing pollen-mediated gene flow, the transgene locus would not be prevented from transferring to any plant that can accept the pollen. However, the effect of the V-GURT mechanism would prevent viability of the resulting cross-progeny assuming the trait is suitably functional in the heterozygous form.

163. Some industry groups have also alluded to the potential benefits in preventing volunteers from growing in unwanted circumstances in some cropping systems.

164. Both of these assertions seem to have substantial merit in certain production systems, but the efficacy of particular GUR Technologies needs to be tested under glasshouse and field conditions, and the results widely published and evaluated before their use for these purposes can be properly assessed.

165. Guessing at the probabilities of such outcomes – whether positive or negative in effect - in the absence of working examples of V-GURTs (or indeed T-GURTs), is not likely to be helpful. Instead, encouraging the design and analysis of suitable experimental systems may allow informed, rigorous determination of the value of these traits in meeting commercially, environmentally and socially desirable goals. Transparency in such an experimental assessment process would be of very great importance.

/…

2) Trait-specific GURTs in Improved Varieties: a Future Trend ?

166. By contrast, arguments can be advanced that the use of Farmer-Activated T-GURTs, could have a very positive effect on conservation and use of genetic diversity by adding •arrier’ or •latform’ value to a wide range of varieties that are bred for local conditions.

167. Additionally, as the cost of activation of the trait need not reflect an actual cost of the activator compound, differing markets could be offered activation at differing prices. In theory, a low income community could be offered a lower priced activation, yielding some modest returns to a Trait Provider, whereas a more affluent community could be charged different prices – basically, responsive to market opportunities.

168. Public sector institutions could be greatly enhanced in value and relevance to private AND public sector trait providers by being allowed or even encouraged to passage and introduce T-GURTs into their varietal background with little intellectual property restriction other than a mutual transfer agreement (MTA). The locally bred and adapted variety could thus harbour a pro-trait that may or may not be activated by the local users/farmers depending on their own market needs and opportunities.

169. Two principal forms of T-GURT will have different considerations. In one form, the farmer• treatment must occur or the added-value trait will •elete’, leaving the parental variety as a form of security with the farmer. Re-acquiring the trait would presumably require re-acquiring the seed from the commercial supplier.

170. In the other form of T-GURT, the trait would be cryptic in the genome of the improved variety, but would be activated – for instance on an annual basis – by application of a proprietary compound. The trait could then reset to an inactive form upon completion of meiosis (pollen and egg formation). This approach would require no new seeds industry, and would allow or even encourage the broad sharing of the pro-trait amongst public and private breeding institutions and initiatives. The return on investment would then be made upon activation of the pro-trait through purchase of the activating compound from the technology provider.

B: Is GURT required or even helpful to encourage investment by the private sector in crops and geographical/social markets that are currently neglected ?

171. Funding for public research aimed at promoting the welfare of traditional subsistence farmers is very low, and has been steadily declining in the past two decades. It seems axiomatic that only a reversal of such a scenario might lead to improved varieties for these neglected production systems and communities that are also consistent with the preservation of genetic resources. Left to market forces alone, technological innovation in agriculture may exacerbate the socio-economic polarization that has been associated with the input- and capital-intensive model of agriculture.

172. Resolving industry• concern for the protection of intellectual property rights by use of V-GURT may indeed promote a substantial investment to develop new plant varieties, or at least old varieties with new traits. However, there are no assurances that the investment so promoted will be particularly helpful in terms of socio-economic equity and environmental sustainability. But in fairness, there are few informed claims that the subsistence agriculture sector would be targeted or even beneficiaries of innovations protected by GURT. Of greater concern is the possibility that in accepting the increased private-sector investment as a substitute for visionary public investment, there will be insufficient attention to the most disadvantaged and vulnerable group of farmers, who ironically have arguably the most important role in maintaining genetic diversity *in situ*.

173. The justification for increased investment begs the issue of what type of investment is required/envisaged and whether there would be any reason to anticipate that marginal communities that have little capital to participate in market systems, would benefit, socially, economically or through long-term sustainability.

174. The role of the publicly funded institutions, national programs and small companies must be re-evaluated, focused and promoted to address shortcomings inherent to research driven only by market forces and capital concentration. The very substantial role of taxpayers in most national programs in providing just such investment needs to be appreciated and seriously factored into the equation.

175. We must also consider the crucial issue associated with the denial of access by the public-sector to core enabling technologies that would be needed to allow the public sector to provide alternative innovations that can be commercialized.

176. If past trends in the production of transgenic crop varieties continue, it is safe to predict that the main targets of GURT incorporation will be higher-value crops, mostly concentrated in the modern commercial sectors of both developed and larger developing countries. In other words, new investments on transgenic varieties are likely to focus on protecting input traits such as herbicide and pest resistance, for the better-off farmers in the most affluent markets.

177. This focus is likely to increase the polarization between commercial and subsistence farmers, as well as between developed and developing regions and societies. While subsistence farmers, mostly concentrated in developing societies, may conserve biological diversity by their focus on landraces, their contribution to such conservation will hardly be compensated within existing legal frameworks. In this regard, attention is drawn to the efforts being made through the negotiations for the revision of the International Undertaking, under the auspices of the Commission on Genetic Resources for Food and Agriculture, to bring it into harmony with the Convention on Biological Diversity, including considerations of access to genetic resources and Farmers Rights'.

C: The role of regulatory mechanisms in preventing adverse outcomes associated with use of GURTs.

178. It is likely that with suitable free and fair competition, there will be a tendency for the private and public sector to self-regulate and to add value to farmers through providing new seeds and systems at acceptable prices. However, this free and fair competition may not be possible in the absence of governmental oversight and regulation, including use of anti-trust legislation. With the extraordinary and unprecedented consolidation of biotechnology intellectual property and the delivery mechanisms of seed companies within a few multinational corporations, it may well be time to explore the option of invoking governmental anti-trust laws. Perhaps the most effective regulatory moves to limit an inappropriate use of GURTs would be to ensure that there is no monopolistic constraint to alternative technologies and materials.

D: Non-Issues and Red Herrings

179. There are many issues that are extremely important to consider regarding the use of Genetic Use Restriction Technologies. Informed and focused public scrutiny can have very positive effects on choice and deployment of new technologies, and can shape public policy where appropriate. However, there is much to be lost by focusing instead on distracting side issues, and allowing the more crucial broad and pervasive matters to be obscured. Some of the side issues indeed are •on-issues' that have surfaced over the past year and should be accorded a brief consideration only.

a) The inducing chemical is toxic (e.g. tetracycline) and will cause environmental harm when used to treat seed.

180. In the first GURT patent issued to the USDA and Delta & Pine Land Co., the antibiotic tetracycline was employed in an example and in dependent claims of the patent as an inducing molecule, in concert with the tetracycline repressor. Patents have a very highly formalized structure and wording and there are certain important ways of achieving broad issued claims that require disclosure of •est mode' – i.e. that use the best methods available at the time of patent filing to demonstrate an invention. The tetracycline repressor system had been the most heavily researched system in controlling gene expression in transgenic organisms using exogenous compounds, and as such it was important to describe the use of that system to •nable' the patent specification. The allowance of patent claims in no way indicates the commercial use or intent of a particular invention. The tetracycline system was NOT developed by the private sector, or even originally by agricultural scientists. The system is a laboratory•evel research tool and its use in the patent was simply an example to indicate to a patent examiner how the system could be made to work – irrespective of the commercial applications.

181. In light of new technologies in functional genomics and in vitro molecular evolution, it is clear that development of appropriate commercial technologies that are field-useable is a high priority for most private sector players in agricultural biotechnology. The use of tetracycline for field work would never be considered by any responsible entity, or any entity – public or private – that could be liable for the huge regulatory burden for its approval and use.

b) Patents are an effective means of controlling the GUR technology

182. As clearly outlined in Section III, patents are only an •xclusionary’ right, which allow the patent holder to restrict others from using that particular invention in the national jurisdiction in which the patent is issued. The GURTs are basically technologies that supplant patent protection in many cases, and their very existence and use will be the issue, not the patents on some of the technologies. Denying patents on these technologies may actually stimulate the uptake and use of GURTs by many parties – there would be no effective means to stop it occurring. If control of GUR Technologies is desired in a particular country, existing domestic legislation based on agricultural policy can be invoked. There are no existing legal mechanisms associated with patent systems that would allow enforcement of non-commercialization after claim rejection. However, in most countries, even those without any patent laws, there are existing and enforceable agriculture quarantine and listing laws that could be used.

c) Proteins that •erminate’ plants will be toxic to animals, including humans.

183. The word toxin was used in the original V-GURT patent, to describe the protein used to inhibit germination. Similarly, in media discussions of Zeneca• and other patents related to V-GURTs, the concept of a pernicious toxin was raised. However, the intent in these patents is to demonstrate a technology that could be an example of how to prevent germination. In a commercial implementation of such a V-GURT, it is highly likely, for regulatory and other reasons, that an enzyme or other protein that simply diverted resources from the germination pathway in a plant-specific manner would be used. Again, the formalities and the technique of crafting patent specifications usually involves the least •ubtle’ mode of action, not the commercially germane mechanism. One can readily envisage that any entity proposing to use such a technique would use, for example, a plant enzyme that sequesters plant amino acids or carbon metabolism into a biochemical dead-end, or that caused the mal-functioning of a photosynthetic pathway that was unique to plants. Thus, examples such as diptheria toxin or other extremely cytotoxic proteins are used only to comply with convention in patent specification.

SECTION V: CONCLUSIONS

184. The advent of GURTs presents a unique opportunity and challenge for the world agricultural community to proactively articulate policy before the technology is applied and any impact is experienced.

185. To do this will require informed and mature dialogue, collaboration, patience and understanding by all concerned parties. It will also require more detailed studies using expertise in molecular genetics, agriculture, sociology, business and economics, including experience of the different ecosystems and farming systems where the proposed technologies will be tested and applied. As well, it will require analysis of technical data from field assessments of prototype systems as they emerge. Finally it will require us to continually evolve methodology to listen to people's concerns and to respond transparently and responsibly to shape industry to human needs.

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