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## COMMISSION ON GENETIC RESOURCES FOR FOOD AND AGRICULTURE

### RECENT DEVELOPMENTS IN BIOTECHNOLOGY AS THEY RELATE TO PLANT GENETIC RESOURCES FOR FOOD AND AGRICULTURE

by Charles Spillane

Reports on developments in biotechnology of relevance to the work of the Commission on the Draft Code of Conduct for Plant Biotechnology have been provided to the Commission in its previous sessions: CPGR-6/95/15, CPGR/93/9, CPGR/91/12.

At its Sixth Session, the Commission “agreed to postpone any further development of the draft Code until after the current negotiations for the revision of the International Undertaking were over”. This document is provided for information of the Commission in the interim period, in view of the very rapid developments in this sector. The study is the responsibility of the author, and does not necessarily represent the views of the FAO or its Member States.

Dr. Charles Spillane is a biotechnologist with a particular interest on the potentials and possible impacts of modern biotechnologies in developing countries, and large experience in international cooperation.

For reasons of economy, the paper is available only in the language in which it was prepared.

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## **RECENT DEVELOPMENTS IN BIOTECHNOLOGY AS THEY RELATE TO PLANT GENETIC RESOURCES FOR FOOD AND AGRICULTURE**

### **1. Introduction**

In the early 1990's the FAO Commission on Genetic Resources for Food and Agriculture requested the preparation by FAO of a draft Code of Conduct for Plant Biotechnology, which was discussed by the Commission's members in 1993. Approximately 400 scientists and policy makers were consulted in the preparation of the first draft of this Code. The Commission then decided to postpone further elaboration of the draft Code until after the finalization of the negotiations for the revision of the International Undertaking on Genetic Resources for Food and Agriculture.

The stated overall objectives of the draft Code are to maximize the positive effects and minimize the possible negative effects of plant biotechnologies.. The existing draft of the Code includes aspects such as; the promotion of appropriate biotechnologies (Article 5); national action and international cooperation (Articles 6 and 7); the mitigation of possible negative effects (Article 8); access to plant genetic resources and related biotechnologies, and intellectual property rights (Article 9); information exchange (Article 10) and biosafety and other environmental concerns (Articles 11-16).

Since 1993, the regular sessions of the Commission have received progress reports on international developments in plant biotechnology, the last of which was document CPGR-6/95/15. Document CPGR-6/95/15 was submitted to the Conference of the parties to the convention on Biological Diversity by FAO as an input to the negotiations of the draft Protocol on Biosafety. In January 1999, the FAO Committee on Agriculture considered a document on Biotechnology<sup>1</sup> and recommended that FAO strengthen its capacity in the agricultural biotechnology area to ensure that FAO can better help its members to apply agricultural biotechnologies to the needs of the poor<sup>2</sup>. More recently, FAO has developed an information document which outlines in detail FAO's future role in providing biosafety related advice regarding agricultural biotechnologies to its member nations<sup>3</sup>.

The draft FAO Code of Conduct concentrated on a number of issues that were perceived in the early 1990s by the sample survey group to be issues that might warrant the development of a Code of Conduct for Plant Biotechnology. However few membership based organizations representing farmers, biotechnologists or agricultural researchers were involved in the earlier survey which informed the drafting of the draft Code. Looking at the draft FAO Code of Conduct almost a decade later it is likely that some of the perceived fears regarding the impact of plant biotechnologies that motivated its development may have been exaggerated in the near term e.g. regarding biodiversity loss or economic substitution effects due to plant biotechnology. In essence, the priorities identified in the draft Code may now be outdated with respect to actively promoting plant biotechnology research which can better meet the needs of developing countries, and in particular the livelihood security needs of poorer farmers and consumers.

Indeed, many scientists, research institutions, universities, companies, and scientific NGOs in both developed and developing countries are likely to perceive a "Code of Conduct" as a negative, paternalistic and coercive policy instrument, and to contest the view that current plant biotechnology research in itself is somehow actively involved in 'misconduct'. There may however be a more positive role for public policy instruments, guidelines or adjustments which can help to more actively promote a pro-poor or equity bias in current agricultural biotechnology research, in order to ensure that the needs of poorer farmers and consumers are better met.

This paper reviews a range of recent developments agricultural biotechnology, primarily focussing on the issue of how access to some agricultural biotechnologies might benefit poorer farmers. The paper focuses mainly on the plant biotechnology sector with some reference to the animal and microbial biotechnology sectors.

## **2. Agricultural biotechnology and poorer farmers**

### **2.1 Can the benefits of agricultural biotechnology research reach poorer farmers?**

Over the past decade there has been some advocacy of a need for a pro-poor bias in the development and dissemination of modern biotechnologies<sup>4</sup>. However, whether any benefits of current plant biotechnology research will actually reach poorer farmers and consumers without major public sector intervention is an open question. There are many such poorer people. Over 1100 million farmers, in many different farming systems and environments, are economically active in agricultural production globally (about 50 million farmers in the developed countries and 1050 million in the developing countries). The vast majority of the world's farmers are known to have a limited level of access to external inputs or other productive resources. Resource poor farmers, by definition, are unlikely to have easy financial access to agricultural inputs such as pesticides, fertilizers or irrigation. Moreover, it is now thought that an increasing majority of the world's resource poor farmers are women. For instance, over 70% of the people in developing countries living below the poverty line are women, the majority of whom live in rural areas<sup>5</sup>.

While such resource-poor farmers practice approximately 60% of global agriculture, they produce 15-20% of the world's food<sup>6</sup>. However, when looked at another way the small-scale resource poor farming sector is responsible for 80% of agricultural production in developing countries and is key to future food security<sup>7</sup>. The low productivity of resource poor farmers tends to perpetuate rural poverty to the extent that of the more than 2,500 billion people in developing countries who live in rural areas, approximately 1000 million live below the poverty line: 633 million in Asia; 204 million in Africa; 27 million in the Near East and North Africa; and 76 million in Latin America<sup>8</sup>.

Science alone is unlikely to provide a 'technical fix' for alleviating such poverty. There are many processes, factors and socio-economic structures underlying rural peoples poverty such as; lack of access to land and other productive resources, low purchasing power, political powerlessness, fragile environments, peripherality from markets, etc<sup>9</sup>. In this milieu, agricultural (or indeed plant biotechnology) research is but one factor which could have differential impacts on rural poverty. Indeed, the potential contribution of biotechnology to developing country agriculture or to poverty alleviation is considered to have been overstated, in the short term at least<sup>10</sup>. Yet over the longer term there is little doubt that some biotechnological approaches to crop improvement could generate social, economic and environmental benefits if specifically targeted at specific needs, especially those of poorer groups. Such needs might for instance include the reduction in pesticide use via insect/disease resistant crops, improved nutritional composition of crops, elimination of toxic substances or allergens, developing early maturing varieties, reducing post-harvest storage losses, abiotic stress tolerant crops or reducing labour demands at appropriate times during the cropping cycle<sup>11</sup>.

For commercial reasons, richer farmers are likely to be the main target market for most privately funded plant biotechnology research. The many resource poor farmers in developing countries who depend on an income of less than a \$1 per day are not likely to be a near term target market for most of the agricultural biotechnology companies<sup>12</sup>. If plant biotechnology research is to be better targeted to addressing the needs of poorer farmers, it will be necessary for relevant public sector institutions to more transparently identify which farmers needs are of concern to their research or funding agenda. Yet, even in the face of increasing population pressure and such large numbers of resource poor farmers in developing countries, internationally there are only a handful of underfunded plant biotechnology initiatives (public or private sector) with an explicit focus on poorer farmers as their primary clients/markets (e.g. Cassava Biotechnology Network<sup>13</sup>). This may reflect to overall current bias in agricultural biotechnology research to commercial rather than social markets.

### **2.2 Can public sector plant biotechnology research be more demand-driven?**

The major agricultural biotechnology companies are concentrating on the development of two broad types of proprietary traits; (i) input traits such as herbicide tolerance, insect or disease resistance etc and (ii) output traits which improve the nutritional contents of foods or exhibit unique properties for very specific end uses or markets<sup>14</sup>. Such input and output traits will be incorporated into existing elite varieties to provide higher value seed with further added value, which may offer to the farmer lower costs or higher yield, and increased value of the end product<sup>15</sup>. Initially, it is likely that biotechnology generated varieties brought to the market will focus on input traits. However, the long-term commercial potential of plant biotechnology is considered to be in the development of value-added output traits that will address a wide range of specific needs or market niches<sup>16</sup>.

To assess the level of demand for particular types traits or products, the marketing departments of most agricultural biotechnology companies typically conduct surveys of farmers with different income levels to determine what commercial products might be developed by their technologists to meet the needs of customers who can express their demand in financial terms. Because demand driven companies are likely to make more money, most marketing departments in companies are responsive to customer concerns and demands. However, within many public sector research organizations, there is often an absence of demand driven biotechnology research agendas, especially in relation to the agronomic or socioeconomic needs of poorer farmers or developing countries<sup>17</sup>. Some publicly funded plant biotechnology research could in effect be competing with the private sector for the same customers or clients.

For the private sector, poorer farmers and consumers are by definition not a lucrative market and are unlikely to exert any effective 'demand pull' on the private sector research agenda. In theory, the onus would therefore fall on the public sector to fund and perform any research required to meet the differential needs of poorer farmers or consumers. Yet, in most public sector institutions or funding bodies there are currently few priority setting or needs assessment mechanisms (analogous to the functions of private sector marketing departments) in place to help guide the direction of publicly funded plant biotechnology or crop improvement research towards meeting the immediate needs of poorer farmers.

In some instances plant biotechnology may represent one of a number of competing technological approaches to addressing a particular agronomic problem. For instance, a particular pest problem might equally be addressed through conventional plant breeding, through a transgenic approach, or through an integrated pest management (IPM) approach or any combination of these. Within the broader agricultural research community there is often a lack of priority setting mechanisms and relative cost-benefit analyses to determine which available technological approaches may be the most suitable within particular timeframes for addressing prioritized agronomic needs or the needs of particular groups of farmers<sup>18</sup>.

### **2.3 How are the products of agricultural biotechnology to reach poorer farmers?**

Farmers interface with the products of biotechnology or agricultural research through a range of intermediary service providers, usually through public extension or private marketing agents. Agricultural extension is the public sector equivalent of agricultural sales or marketing or sales agents in the private sector. The distribution channels by which products reach farmers fields are now undergoing major structural changes. There are now a wide range of public, private and NGO organizations with differing objectives attempting to deliver appropriate products to different groups of farmers. This has significant implications regarding the nature of the technology disseminating organizations that plant biotechnologists interact with in identifying what priority technologies are needed, what farmers are the resultant client group and what types of farmers and consumers will ultimately reap the benefits of plant biotechnology research and development.

Agricultural extension is now in a process of reform and transition world-wide<sup>19</sup>. Pressures towards cost-recovery and privatization have led to rapid slimming and of public sector extension services in Europe, the USA and Australasia over the last decade<sup>20</sup>. In parallel, public sector agricultural extension services in developing countries are achieving only limited impact but face unsustainably high recurrent costs<sup>21</sup>. In many countries, governments are withdrawing NARs from extension services and now expects other institutions (private or NGO e.g. farmers organizations) to provide and/or finance such activities<sup>22</sup>. Financial pressures have led to the search for ways of reducing public sector costs by e.g. privatizing parts of the extension service, having farmers pay government for some services, and cost-sharing arrangements between government and NGOs or farmers' organizations. The most efficient public sector extension services of the future are likely to focus on spheres (geographical; thematic, social) inadequately serviced by the private commercial sector<sup>23</sup>. As a result novel extension approaches are emerging which are approaches which are participatory, institutionally pluralistic and geared towards cost-sharing<sup>24</sup>. For example, a range of approaches for farmer-led approaches to agricultural extension have been presented<sup>25</sup>.

It is unclear how plant biotechnology research could better interface with such changes, especially in relation to NGO or farmer-led approaches to agricultural research and extension. It cannot be assumed that even useful agricultural biotechnologies which are wholly in the public domain will actually reach the fields of poorer farmers in the short term through existing state extension channels. The Gatsby Charitable Foundation has recognized this in developing a 'research-managed extension' (RME) model for more effective transfer of agricultural biotechnologies to poorer farmers in developing countries<sup>26</sup>. The RME model relies on a reward system based upon the intensity of contact between extensionists and farmers. Also, the Netherlands Ministry of Foreign Affairs has a Special Programme on Biotechnology and Development Cooperation which has been exploring pilot projects on 'appropriate biotechnologies' which might better meet the needs of small-scale farmers in developing countries. A key feature of such approaches have been farmer participatory needs assessments to determine research priorities prior to initiation of research and development<sup>27</sup>. However, most plant biotechnology research is conducted far 'upstream' of such 'downstream' structural changes in the agricultural extension and marketing sectors.

There has been a lack of biotechnology research which would enable key agricultural 'processes' at the on farm level which could improve or 'empower' farmers livelihoods. Yet in theory at least plant biotechnology research could be applied towards such goals, especially if there were better linkages between farmer participatory researchers/extensionists and plant biotechnologists<sup>28</sup>. The CGIAR's Systemwide Programme on Participatory Research and Gender Analysis (SWP-PRGA) is currently exploring whether some biotechnologies might have utility in 'empowerment'-oriented farmer participatory plant breeding. The Centre for the Application of Molecular Biology to International Agriculture (CAMBIA) in Australia has for some years been trying to develop plant biotechnology tools which could empower low technology approaches to crop improvement in developing countries<sup>29</sup>.

#### **2.4 Plant biotechnology transfer to developing countries.**

Some developing countries have had considerable success in establishing significant capacity in biotechnologies such as plant tissue culture and micropropagation and disease diagnostics, and in meeting farmers needs with such technologies. However, the strengthening of capacity in the plant molecular biotechnology research has proved more difficult to achieve in the short term, especially in a manner which is targeted to meeting country specific needs. In most instances, the existence of a conventional plant breeding programme which is operational is a necessary prerequisite for any rational application of advanced plant molecular biotechnology techniques such as marker assisted selection or transgenesis.

Despite some successes, there is a growing consensus that many international project based initiatives to transfer biotechnology capacity to developing countries have not been as successful as



originally envisaged. The majority of developing countries have limited practical access to the tools and germplasm necessary to apply high technology biotechnology research to their national needs. The barriers to such access are many and mainly include lack of financial, scientific and infrastructural resources.

Cross-country reviews of the state of agricultural biotechnologies in some developing countries have been performed by ISNAR-IBS and OECD. These concluded that there are major differences between countries in their agricultural biotechnology capacity which would preclude any generalizations regarding the appropriateness (or not) of some biotechnologies for developing countries as a generic group. For instance, a number of developing countries in Asia and Latin America such as Brazil, China, India, Malaysia, Thailand, Philippines, and Indonesia have a relatively high level of plant biotechnology capacity, especially in early generation biotechnology areas such as plant micropropagation, transgenics, and marker assisted breeding<sup>30</sup>. In Africa, a significant number of countries (e.g. Burkina Faso, Cameroon, Cote d'Ivoire, Gabon, Ghana, Senegal, Ethiopia, Uganda, Madagascar, Malawi, and Zambia) have some limited biotechnology capacity in the areas of plant tissues culture and micropropagation. In some African countries, basic infrastructure and facilities for even the simplest plant tissue culture or micropropagation are not available. However, other African countries such as Morocco, Tunisia, Nigeria, Kenya, and Zimbabwe have some additional but limited capacity in plant molecular biology<sup>31</sup>. While countries such as South Africa, Nigeria and Egypt have the capacity to generate transgenic plants, mechanisms to ensure that the plants can reach the end user i.e. the farmer are in many instances lacking<sup>32</sup>.

The OECD's Development Centre has published an excellent study on the incentives, constraints and country experiences for integrating biotechnology in agriculture in different developing country situations<sup>33</sup>. ISNAR's Intermediary Biotechnology Service has also produced a series of research reports which provide useful frameworks for decision making regarding national biotechnology priorities, planning and policies, based on the experience selected developing countries have had to date with the integration of biotechnologies into their agricultural research systems<sup>34</sup>.

The OECD study concluded *inter alia* that biotechnology research has not been closely integrated with the problems and constraints confronting the agriculture sector, nor with the obstacles to widespread diffusion of useful new biotechnologies, particularly to low income farmers. A lack of clear priorities and focus was identified. The OECD study called for reflection on the part of developing countries, scientists, NGOs, donors and the CGIAR on the development of innovative public/private mechanisms for the transfer of "public good" biotechnologies in developing country agriculture. The OECD study also stressed the importance of long term public sector funding if the benefits of agricultural biotechnology research are to be realized by the poorer strata of society.

A 1994 survey of 45 organizations involved in the transfer of agricultural biotechnology revealed that most initiatives concentrate on the few developing countries with relatively advanced scientific and technological capabilities, and that developing country scientists and administrators are not always directly involved in their planning and design<sup>35</sup>. Also, a 'brain drain' exists for many developing countries and regions (e.g. China, India, Africa) whereby many of their scientists have moved to work/train in advanced biotechnology laboratories in the USA, Europe, Australia and Japan. If such scientists return to situations where there is no/little conventional plant breeding activity or infrastructure, the comparative advantage that they have learnt in plant biotechnology cannot easily be applied to the improvement of agriculture in their own countries. There are currently few financial or other incentives for such scientists to return to their countries of origin<sup>36</sup>. In the absence of public sector funding for such scientists upon return, it is likely that many such scientists will become technology adapters, and/or marketing agents for imported proprietary products/germplasm developed by non-domestic companies.

In all countries, there is also a need to more actively involve end-users such as farmers and producers organizations in priority setting regarding the objectives of publicly funded agricultural biotechnology. At the international level, the International Federation of Agricultural Producers (IFAP) - an organization which represents a large proportion of the world's farmers - recently made a significant policy statement on 'Farmers and Biotechnology' at the 1998 World Farmers Congress [See <http://www.ifap.org/biotech.htm>]. The IFAP policy statement raised issues regarding; (a) the potential benefits of GMOs to different stakeholders, (b) concerns of different stakeholders regarding GMOs; (c) promoting freedom of farmers to operate (d) promoting safety and accurate information (e) increasing public sector research investment (f) intellectual property rights (g) addressing the needs of developing countries and (h) maintaining biodiversity.

### **3. Scientific and technological developments in agricultural biotechnology**

Agricultural biotechnology research is now generating a wealth of information of utility to crop improvement strategies. Plant biotechnology research is most powerful when it is integrated with conventional breeding or crop improvement approaches. In many countries, plant biotechnology research is being integrated with conventional plant breeding approaches wherever the technical and financial resources are available for such integration. Among the scientific community it is often highlighted that plant biotechnologies could also generate environmental benefits, especially where renewable genetic inputs can be effectively used to substitute for agro-chemical inputs.

A vast range of approaches for the improvement of agronomic traits are either under study or in early development phases. These include the improvement of important agronomic traits such as; yield; pest and pathogen resistance; tolerance to abiotic stresses such as acid soils, drought, salinity and cold; herbicide tolerance; shade and high density planting tolerance; water and nutrient use efficiency; reduced mycotoxin contamination; crop reproductive biology; and enhanced nutritional and product quality through influencing quantity and quality of oil, protein, carbohydrates, nutrients, and novel substances. An in depth review of the scale of ongoing research into a multitude of traits and crops is beyond the scope of this paper.

#### **3.1 The emerging importance of agricultural genomics.**

Genomics is a new term that is used to describe the development and application of large scale, high throughput and parallel processing approaches to the functional analysis of entire genomes (or genetic systems)<sup>37</sup>. Genomics technologies can allow the identity and function of tens of thousands of different genes to be analyzed simultaneously or in parallel. The science of genomics has arisen because the speed and scale with which the genomes of economically important organisms can be sequenced and functionally analyzed is increasing at a rapid pace. It is claimed that with current state of the art technologies a consortium of the leading sequencing institutions could now feasibly sequence the human genome from start to finish within three years<sup>38</sup>. Technology spillovers from such human genome sequencing programmes will result in high throughput DNA sequencing being increasingly applied to the genomes of commercially important organisms such as human pathogens or crops. Agricultural genomics research is currently underway for a range of important agricultural species<sup>39</sup>. Large scale DNA sequencing of some crop and plant genomes is now at an advanced stage, especially for *Arabidopsis* and rice<sup>40</sup>.

Expressed sequence tags (ESTs) are small fragments of genes that have been sequenced and which can act as unique 'bar-codes' for each particular gene in an organism. Large scale EST projects can rapidly generate unique ESTs for 90%+ of all the genes in an organism in a very rapid and cost efficient manner. For instance, ESTs which each uniquely identify more than 95% of the estimated 120,000 human genes are available on public databases on the Internet. Publically funded research has now identified ESTs representing the majority of genes in the *Arabidopsis* (International

Arabidopsis Genome Initiative) and rice genomes (Rice Genome Project in Japan). The majority of such ESTs have been placed in the public domain via their publication in publically accessible EST databases on the Internet. It is also known that there are several large-scale commercially funded EST projects for crops such as maize, and soybean. However, to date most of this EST data is not publically available<sup>41</sup>.

Agricultural genomics initiatives are both generating genetic markers and also identifying genes that can be used either for marker assisted breeding or the development of transgenics with improved agronomic properties<sup>42</sup>. The application of molecular markers to genetic linkage maps of a wide range of crops is allowing the identification of the chromosomal (physical) locations of genes for improving yield and other complex traits important to agriculture<sup>43</sup>. The underlying genetics of a wide range of quantitative agronomic traits are being unravelled through the identification of quantitative trait loci (QTLs) using a combination of molecular markers and advanced statistical breeding procedures. An idea of the wide range of agronomic traits and corresponding QTLs currently under investigation or improvement can be obtained from browsing through the abstracts of the annual Plant and Animal Genome Conferences [<http://probe.nalusda.gov:8000/otherdocs/pg/pg6/pag6.html>].

Powerful 'functional genomics' systems to explore the function of genes through 'knockout' and 'monitoring' strategies have also been developed using existing transposon mutagenesis systems, such as those which have traditionally been widely used for the genetic analysis of maize<sup>44</sup>. The development of DNA 'chip' technology is also set to revolutionize the scale at which genetic experiments can be done and can potentially allow simultaneous and rapid analysis of all (e.g. 10,000 - 100,000) of the genes in any organism at any particular point in time or environment<sup>45</sup>. If this technology becomes cost effective in the same manner which has led semiconductor technology to become widespread it will have a very significant impact on how genetic improvement of crops is conducted. There are some large scale publically funded efforts to develop 'genomics' technologies and tools which would be made available to the academic plant biology community with "no strings attached" regarding intellectual property. In the US the Arabidopsis Functional Genetics consortium is adopting this approach<sup>46</sup>.

The potential value of agricultural genomics has been recognized by the private sector judging by its current level of investment. High levels of public sector funding has also been approved for agricultural genomics initiatives in a few countries. For instance, the US government has approved \$40 million to fund genomics initiatives for crops of national importance<sup>47</sup>, and the Japanese government has earmarked substantial financial support for a national Rice Genome Project<sup>48</sup>. Some analysts consider that the USA's research capacity in agricultural genomics now outstrips that of all other countries or regions and that the technology gap is widening in this area<sup>49</sup>. It is thought that the promotion of the French GenoPlante agricultural genomics consortium is one national initiative which is trying to bridge such gaps between regions<sup>50</sup>. The Indian government is currently assessing proposals to strengthen India's capacity to conduct agricultural genomics research<sup>51</sup>.

Scientists participating in some of the plant genomics initiatives have stated that publicly available research tools and data are a priority for any such initiatives if broader scientific, social and economic spillovers are to be promoted. It is felt by many in the scientific community that international cooperation is critical to such large scale genome projects, both because genome projects are typically too large for any one country and the information forthcoming should be of benefit to the world and not just the countries that do the work<sup>52</sup>. International cooperation is hence seen to be essential to ensure that overly protectionist proprietary positions are not taken which would inhibit the availability of potentially useful public domain information.

### **3.2 Comparative genomics: Unifying crop gene pools.**

A major discovery which is accelerating genetic mapping research has been the discovery that the genomes of distantly related crop species may in fact be quite similar to each other in terms of gene order and structure<sup>53</sup>. For instance, a gene on the chromosome of one grass species can be anticipated to be present in a predicted location on a specific chromosome of other grass family species. For this reason, many cereal geneticists now view the grass family as a single genetic system whereby genomic information from one cereal species can be used to understand much of the genetics of other cereal species<sup>54</sup>.

Because it is cheaper and easier to determine the DNA sequence of species with smaller genomes a number of species (e.g. rice, *Arabidopsis*) are emerging as the 'anchor genomes' which are expected to act as the 'Rosetta Stones' for understanding the larger genomes of other related species<sup>55</sup>. Hence, a number of major multi-partner efforts are underway to determine the sequence and structure of major cereal crop genomes which will provide valuable information for understanding the genomes of other cereals. Examples include the International Grass Genome Initiative, International Triticeae Mapping Initiative, the International Rice Genome Initiative, the Rice Genome Project<sup>56</sup> (Japan) and the National Corn Genome Initiative<sup>57</sup> (USA). The entire *Arabidopsis* genome will be sequenced and publically available by the year 2004. and is already providing valuable information regarding the genetics of economically important crops both within the Brassicaceae and within many other tribes<sup>58</sup>.

### **3.3 Biotechnologies to increase the accessibility and use of wild relative gene pools.**

The crop wild relatives stored in the world's genebanks are valued as a unique source of genetic variation, but they have rarely been used for the genetic improvement of quantitative traits. Indeed it is widely acknowledged that exotic germplasm such as crop wild relatives is infrequently used by breeders<sup>59</sup>. A development of major significance has been the recent development of a powerful molecular marker based methodology whereby quantitative trait loci (QTLs) conferring complex traits such as yield and organ size can now be effectively transferred from wild relatives into crop varieties<sup>60</sup>. This powerful technique has now been demonstrated for rice<sup>61</sup> and tomato<sup>62</sup> and is being rapidly applied to other crop species for which suitable molecular maps are available. This discovery suggests that the innovative use of molecular maps and markers will increase the accessibility and realisable value of wild and exotic germplasm.

### **3.4 The utility of plant tissue culture and micropropagation.**

The rapid propagation of many desirable plant varietal genotypes using plant micropropagation technology is a relatively low technology 'appropriate' biotechnology which is now delivering tangible benefits to many farmers in both developed and developing countries<sup>63</sup>. In addition to its rapid propagation advantages, such tissue culture can also be used to generate disease free planting materials. There are numerous examples of micropropagation initiatives which are delivering disease free planting materials to poorer farmers. These include local level micropropagation work on taro in Samoa<sup>64</sup>, *Musa* spp and multipurpose trees in Kenya<sup>65</sup>, potato in Vietnam<sup>66</sup> and cassava in Colombia<sup>67</sup>. In some instances there have been efforts to involve farmers organizations in the design and running of such micropropagation. This is recently the case for CIAT's proposed small scale cassava micropropagation work with the Colombian farmers' organization FIDAR and for ongoing potato micropropagation in Dalat province in Vietnam.

Micropropagation techniques have now been developed for a wide range of crops. for instance, China now has developed micropropagation technology for more than 100 crop species<sup>68</sup>. In the Guangdong province, 3-4 million micropropagated banana plantlets are produced annually and 1 million exported. Micropropagated bananas are reported to have been successfully adopted by poorer farmers in Guangxi and Guangdong in China. In 1994 it was estimated that the farmers in Guangxi received an extra income of about \$723,000 as a result of adoption of approx. 600,000 disease free plantlets. Similarly, ten percent of the area of China planted to potatoes was derived

from micropropagated virus free material in the early 1990s and yields are reported to have increased by up to 100-200%. As part of the FAO FARM project for farmers in rain-fed areas, China has developed micropropagation systems for multiplication of disease free bananas, potatoes, citrus and apple varieties, which are shown to be benefiting the target farmers.

Micropropagation of both food and export crops is also now routine in many Latin American and Caribbean countries<sup>69</sup>. Large scale micropropagation is conducted for crops such as coffee, banana, plantain, taro, cocoa, cocoyam, sweet potato, apple, blueberry, raspberry, pineapple, citrus, grapes, papaya, mango, guava, potato, kiwi, cherry, pear, ornamentals, yams. The existing and potential benefits of adoption of such micropropagated plants by farmers have been substantial as testified by the following selected examples<sup>70</sup>:

- In Mexico about 2.6 million people are dependant on coffee cultivation and production. However coffee rust affects 90% of coffee plantations. The Mexican government is facilitating the distribution of disease free plantlets both to protect labour in this area and export earnings.
- Costa Rica is the world's second largest banana producer. The national banana corporation, Corbana, a semi-public company is undertaking large scale micropropagation of nematode-free plantlets. The combination of a fallow period with nematode-free plantlets has eliminated the need for the use of nematicides in Corbana's plantations since 1987.
- At the Federal University of Rio de Janeiro, Brazil meristem culture of sweet potato cultivars to eliminate viruses and pathogens, followed by field trials around Rio de Janeiro resulted the raising of yields from 9 to 19 tonnes .
- In Argentina, a company called Tecnoplant SA provides a service whereby it will 'clean' varieties delivered by customers from viruses and other pathogens, through tissue culture methods. It does this under contract for large-scale producers and planters. With appropriate subsidies such initiatives could be extended to producing disease free planting material of the locally adapted varieties of low income farmers.
- At the Biotechnology Institute, Santa Clara, Cuba clonal propagation of banana following in vitro micropropagation produces about 5 million plantlets annually. This is done using relatively low tech facilities at 25-30°C with the result that yield from tissue culture derived plantlets was 30% higher than from conventional planting material.

Micropropagation capacity is less well developed in most African countries, yet it represents a technology which if better integrated with ongoing efforts in seed/planting material production and supply, could yield significant agronomic benefits to farmers. In particular, there are few links between genetic resources conservation initiatives and micropropagation initiatives for the more rapid supply of a wide range of healthy planting materials to farmers. There is no doubt that a strengthening of plant tissue culture and micropropagation capacity if effectively coupled to local seed/planting material delivery channels could generate massive benefits for many resource poor farmers. The application of such biotechnologies to local varieties and landraces of root and tuber crops could generate disease free plantlets while helping to both boost yields and also limit 'genetic erosion'.

### 3.5 The development of apomixis technology.

Apomixis is a naturally occurring phenomenon whereby some plant species can produce seeds without fertilization. While apomixis has been described in over 400 different plant species it is only found in a few crop species. The harnessing of apomixis genetics for heterosis breeding and general crop improvement could have significant implications for agricultural research. One potential benefit is that it may be possible to develop true breeding hybrids which retain their yield advantages over generations. Indeed, the long lists of potential agronomic benefits that could be derived from apomictic systems which are easy to use in crop improvement suggests that apomixis may be one of the most important targets for concerted international research efforts<sup>71</sup>. Such benefits include:

- use of hybrid vigour in almost every crop species, including the numerous crops that that never had hybrid technology available.
- survival, and immediate fixation of genetic combinations - including those made by widecrosses - that are unfit under sexual reproduction, greatly expanding the diversity of utilized genetic resources.
- propagation through seed of crops that are currently vegetatively propagated such as cassava, potato, sweet potato and yams.
- plant breeding to become more simple - no need for inbred line production , nor use of male sterility, restorer lines, isolation plots - and therefore more responsive to environmental, economic and social changes.
- use of hybrid vigor technology at the level of the individual farmer. Without changing his/her traditional practices , i.e. leaving farmers to select the best ears specifically adapted to their particular farming conditions to make the seed for the next cycle, large leaps in crop production might be achieved.

In theory apomixis could allow both plant breeders (and possibly farmers) to genetically adapt plants to specific micro-environments, rather than the current practice of adapting the overall cultivation environment to the crop plants requirements. Hence, through the use of apomixis plant breeding could become extremely rapid and responsive to specific micro-environments, cropping conditions and markets. This in turn could stimulate diverse strategies for more sustainable agro-ecosystem management and could have profound implications for biological resource management within agricultural systems.

The development of apomictic technology is one biotechnology that could provide major food and livelihood security benefits to farmers in developing countries. Considerable strides have been made in application of biotechnology for the development of apomictic crops and a number of promising research approaches are now underway. If any of the existing research approaches are successful, it is thought that apomictic crops may be developed within the next decade. However broad social benefits are only likely to occur if apomixis technology can be made accessible to developing countries and in particular resource poor scientists and farmers. Reflecting this concern, a consortium of the world's leading public sector laboratories (including CSHL, CAMBIA, CPRO, CIMMYT, CSIRO and CIAT) which are attempting to develop apomictic technologies have expressed some concern that current IPR trends could hinder access to apomictic and other enabling biotechnologies for developing countries and poorer market sectors<sup>72</sup>. This concern was expressed in the 'Bellagio Apomixis Declaration' which urged widespread adoption of the principle of broad and equitable access to plant biotechnologies, especially apomixis technology, and we encouraged the development of novel approaches for technology generation, patenting, and licensing that can achieve this goal. The Declaration can be found on the internet at: <http://billie.harvard.edu/apomixis/> and requests the support of individuals, institutions or governments for its principles.

### 3.6 Generating new options for pest and disease resistance.

Breeding for resistance to pests and diseases is a major ongoing activity for the vast majority of crops. There are a vast range of pests and pathogens for which conventional breeding has failed to produce crop varieties with durable resistance. There are also serious pests and pathogens which integrated pest management (IPM) approaches have not yet managed to address. A significant proportion of plant biotechnology is targeted at trying to develop options for control of pests and diseases for which there are currently few control options, although most such work is concentrated on pests and diseases of major commercial crops.

There have been many significant developments in elucidating the genetics of pest and disease resistance. The genetic basis of gene for gene interactions in plant pathogen interactions is being rapidly elucidated. Plant biotechnology research is identifying and isolating a vast range of genes and QTLs conditioning resistance against a wide range of pests and pathogens<sup>73</sup>. Powerful techniques have been developed for 'scanning' crop genomes for related resistance genes and subsequent cloning of such genes<sup>74</sup>. The effective transfer of resistance genes from one crop species to another has been demonstrated as a new option open to resistance breeding. Some transgenic approaches have demonstrating higher levels of broad spectrum resistance against pathogenic viruses<sup>75</sup>, bacteria<sup>76</sup> and fungi<sup>77</sup>.

Plant biotechnology could potentially have significant substitution effects in the global insecticide market. The global insecticide market is estimated to be approximately US\$ 8100 million per annum<sup>78</sup>. The development of genes (conditioning resistance against insect pests) which can substitute for some of this need for application of insecticides could have a significant impact both on the environment and insecticide sales. The source of many such genes has been the bacterium *Bacillus thuriangiensis* (Bt) although many other organisms are now being screened for useful genes. Bt has been used for decades as an insecticide spray but has had limited use outside of 'organic agriculture' and Canadian forestry, in total accounting for less than 1% of the insecticide market. It is now estimated that US\$ 2700 million of chemical insecticide applications could be replaced with Bt biotechnology applications, either as improved sprays or through expression in transgenic crops<sup>79</sup>. Bt transgenic crops are expected to be planted on an estimated 20 millions acres in the USA In 1997.

Interestingly, it has required the advent of transgenic single gene resistance approaches to warrant legal requirements on farmers to engage in large scale resistance gene 'deployment' or 'recycling'<sup>80</sup>. The planting of large contiguous crop areas to varieties which are relying on monogenes to condition resistance to important pathogens has long been recognized to be unwise because some monogenes can exert a selection pressure for resistance breaking strains of the pathogen to evolve<sup>81</sup>. However there have been few public policy instruments developed to encourage that low selection pressures on pathogen populations are maintained in agricultural production systems.

The first generation of transgenic plants expressing the insecticidal *Bacillus thuriangiensis* (Bt) protein now require a resistance gene 'deployment' strategy to limit selection for an insect population that is insensitive to the particular Bt protein. Because Bt transgenic seed is proprietary it can be sold with a legal requirement that a certain % of the cropping area (i.e. refugia or mixed plantings) be planted to varieties which lack Bt transgenes to limit selection for Bt insensitive pests. Also Bt gene 'recycling' strategies are being established whereby a range of transgenic varieties each containing a different type of BT protein are released over time or geography to combat the potential ability of the insect pest to overcome any particular Bt resistance gene, and hence minimize the conventional 'boom-bust' cycles in variety-pathogen co-evolution.

Unless consideration is given to how monogenic resistance genes (whether transgenic or not) are spatially and temporally deployed against important plant pests and pathogens (especially airborne fungi) it is likely that the familiar 'boom-bust' cycle will be perpetuated and valuable genetic

resources will have been wasted. It is suggested that multiline and mixture strategies for resistance (trans)gene deployment may become more feasible because of the increasing number of resistance genes being isolated and the ease with which transgenic crops can be established.

It is also being suggested that past failures with multiline and mixture strategies may have been partly due to a lack of control by breeders over the accurate deployment of resistance genes by farmers and that stronger property rights (IPRs or user contracts) over varieties or resistance genes would allow a requirement to be placed on the variety user to ensure that optimal gene deployment or recycling practices are followed<sup>82</sup>. Less coercive resistance gene deployment strategies are reportedly under development or in use in some IPM programmes, including the FAO's Farmer Field School Approach<sup>83</sup>. However, the lack of fruitful interaction between farmer participatory IPM approaches and transgenic or biotechnological approaches to pest/disease management has been noted<sup>84</sup>. It is suggested that there is a need for more collaborative interaction between experimenting farmers and scientists, especially regarding pest and disease problems that cannot be solved by local level research alone<sup>85</sup>.

The Third CGIAR System Review has proposed that the CGIAR centres promote a global initiative for integrated gene management which would *inter alia* promote more sustainable use of useful genetic resources<sup>86</sup>.

### **3.7 Labour saving approaches to weed management for resource poor farmers?**

While dangerous pesticides have been over-used in many developing countries, herbicide use has been very low even though most herbicides are far less toxic than pesticides. Yet weed control is a major time, labour and resource consuming task for most farmers, and in particular for resource poor farmers with limited access to inputs such as affordable herbicides etc. It is estimated that more than 60% of developing country farmers time is spent in weeding. Much of this weeding is often done by women and children and is often unpaid work<sup>87</sup>. There is a very convincing case to be made that herbicide resistant crops could in the near term offer significant, economically accessible, advantages to many farmers in developing countries, in particular poorer farmers with limited labour availability<sup>88</sup>.

In particular, there are many weed problems faced by farmers in developing countries for which no effective control measures have been developed, with or without herbicides. These include the parasitic broomrapes and witchweeds (*Striga* spp). The areas infested with such weeds are vast and expanding. For example, a survey of 180,00 square kilometres in Nigeria found that 70% of fields were infested with witchweed seeds<sup>89</sup>. In the seven agro-ecological zones of sub-Saharan Africa witchweeds are generally listed as the worst pests affecting agriculture<sup>90</sup>. Witchweeds infest the grain crops of more than 100 million people in sub-Saharan Africa and Asia, reducing yields by 50%, and by more in drought years. Labour intensive weeding is largely ineffective against such weeds. Crop yields could potentially be doubled if such weeds could be controlled. In addition labour spent in weeding could be released for other more productive activities, such as increasing literacy and schooling for children.

It was recently found that it is possible to control *Striga* spp using imadizoline resistant maize<sup>91</sup>. One such strategy of potential utility to developing country farmers is being developed whereby only the transgenic seed is treated with high levels of a systemic imadizoline with a resultant excellent control of *Striga*.. Using \$5 of herbicide gave \$100 of increased maize yield per hectare in *Striga* - infested areas in Kenya<sup>92</sup>. Such strategies would require resistance management measures to ensure that *Striga* resistance to the herbicide would not evolve<sup>93</sup>. Herbicide resistant crops could form part of integrated weed management systems, where resistance management strategies are used to ensure that herbicide tolerance does not develop in the weed flora. However it would seem that current biosafety regulations will limit African farmers access to herbicide tolerant crops in the near term, even for crops such as maize which have no weedy wild relatives in Africa. The FAO held a



workshop on regulating herbicide tolerant crops in 1998 and is reported to be in the process of publishing Guidelines for the Regulation of Herbicide Tolerant Crops<sup>94</sup>.

### 3.8 Other notable improvements in desirable crop traits.

Hidden hunger, such as protein and micronutrient deficiencies, is a widespread and endemic problem for the world's poorest people, especially women and children. A range of transgenic approaches have now been developed to nutritionally improve the amino acid profile of crop protein, either by transferring genes encoding more nutritious proteins from other species<sup>95</sup>, or by manipulation of crop biosynthetic pathways to increase the nutritional profile of endogenous proteins<sup>96</sup>. Where transformation protocols have been developed, many important legumes (whether landraces or modern varieties) such as peanut, beans, clover etc could feasibly be nutritionally improved through the transfer of methionine-rich protein genes from species such as sunflower<sup>97</sup>. Sunflower was chosen as the gene source because, unlike Brazil nut, the seed is not known to cause any allergic reactions.

Insufficient intake of dietary vitamin A is implicated in the death of approximately 1-2 million children annually<sup>98</sup>. In South-East Asia, every year an estimated 5 million children develop the eye disease xerthalmia<sup>99</sup>. Unfortunately, many staple crops such as rice are deficient in dietary vitamin A. In addition, the vitamin A containing tissues of rice (embryo, aleurone layer) are removed during milling of rice<sup>100</sup>. Genetic engineering has now developed milled rice which accumulates vitamin A to provide one means of facilitating increased dietary intake of vitamin A from staple foods<sup>101</sup>. If technology transfer of such vitamin A rich crops can reach its intended clients, it is likely that the transgenes used to increase vitamin A production could be applied to other crop species or varieties in locations where vitamin A deficiency is a medical problem. Similar approaches to combating micronutrient deficiencies by increasing the both content and availability of iron in transgenic rice are showing much promise<sup>102</sup>.

The biosynthetic pathways which produce commercially interesting compounds in plants and other species can now be manipulated by 'metabolic engineering' of the pathway so that higher levels of desirable compounds may be obtained. For example, seed oil content has been increased using this strategy<sup>103</sup>. Such strategies are currently the focus of much commercial biotechnology interest<sup>104</sup>. It is now becoming possible to tailor the specifications for the modification of vegetable oils in transgenic plants that more specifically meet end user needs<sup>105</sup>. One example is the production of higher levels of laurate in rapeseed (*Brassica napus*)<sup>106</sup>. Metabolic engineering approaches are also being explored for the transfer of the key biochemical components of C4 photosynthesis to those crops which rely on the less energy efficient C3 photosynthesis<sup>107</sup>.

Similar antisense or gene-suppression technologies approaches can be used to 'switch off' or control the timing of the production of undesirable (or desirable) compounds<sup>108</sup>. For instance, the Flavr Savr tomato developed by Calgene uses anti-sense technology to suppress one of the genes responsible for ripening, so that tomatoes remain on the vine longer and become sweeter without going soft. The introduction of genes which delay ripening or spoilage could help to reduce the post-harvest losses of some perishable vegetables and fruits, especially in situations where poor farm-to-market roads, inadequate transportation, and inadequate storage facilities exacerbate post-harvest losses. Similar types of transgenic approaches are being extended from tobacco<sup>109</sup> to other crops such as cassava in order to inhibit leaf senescence.

A number of transgenic methods have been developed for changing the molecular structure of plant structural or storage compounds so that the crops are more digestible for either humans or domestic animals<sup>110</sup>. For instance, lignin is a plant compound that adversely affects pulp and paper production processes and which also lowers the nutritional value of animal feeds. Mutant lines of maize, sorghum and pearl millet have been described that have a reduced lignin content and improved

digestibility<sup>111</sup>. A number of transgenic strategies for the manipulation of lignin quantity and quality have now emerged<sup>112</sup>.

Human disease is a major constraining factor to labour availability in many agricultural projects and to socio-economic development general in developing countries. Lack of effective cold storage facilities limits the efficacy of linear supply chains for many vaccines. Production of effective oral vaccines against major tropical diseases in transgenic plants may be an extremely appropriate and low technology means of decentralizing both vaccine production and distribution in developing countries. The potential feasibility of producing oral vaccines in transgenic plants has now been demonstrated for diseases such as cholera - toxin B<sup>113</sup> and hepatitis B<sup>114</sup>. If they are made widely accessible, such transgenic plants may be of major utility to hospitals and medical centres in providing a reliable and cost effective supply of heat-stable vaccines and other protein based pharmaceuticals.

### 3.9 Animal biotechnologies.

Genetic marker technologies, such as marker-assisted selection, parentage identification, and gene introgression can equally be applied to livestock selection programs<sup>115</sup>. Highly saturated genetic maps are now available for cattle, swine, and sheep to provide the genetic framework for developing marker assisted selection (MAS) programs. Clonal propagation of genotypes of crops such as potato and cassava is the norm for such crops, and somatic embryogenesis in plants was first demonstrated in the 1950s. In the animal arena, the advent of the cloning of farm mammals such as the sheep named 'Dolly' has only now become at least a technical possibility within domestic animal breeding programmes<sup>116</sup>. Partly because the vast majority of agronomic traits in livestock improvement are quantitative, transgenic technologies are currently not widely used in animal improvement programmes for agricultural purposes. Transgenic animals have mainly been developed for 'niche' markets such as production of high value pharmaceutical proteins where transgenic plants cannot fulfil the same function. Vaccines against brucellosis, encephalitis, liverfluke, hepatitis etc have been developed for domestic farm animals and poultry. It is likely that some of these vaccines can also be produced in transgenic plants using the same processes as developed for human vaccines. A wide range of new vaccines have been or are under development for animals diseases of importance to commercial animal production. There have also been notable successes with DNA vaccines, which if continued may represent a more cost effective means of both developing and distributing vaccines in many resource poor situations<sup>117</sup>.

### 3.10 Microbial biotechnologies.

Microorganisms are essential components of agricultural ecosystems. For instance, beneficial soil microorganisms such as rhizobia and ectomycorrhizae contribute greatly to agricultural productivity. Conversely, the majority of crop and animal diseases are caused by pathogenic microorganisms. Microbial biotechnology is proceeding at a more rapid pace than other biotechnology sectors simply because the genomes of many scientifically or commercially important microorganisms are typically smaller in size and hence can be easier to analyze. Because of their importance and the relatively higher levels of funding for medical biotechnology research, most of the microbial genomes currently being sequenced are human pathogens<sup>118</sup>. In 1995, *Haemophilus influenzae* became the first free-living organism to have its entire genome sequence published<sup>119</sup>. By 1999, the sequence of the genomes of twenty different microbial organisms had been completed and it is known that the sequencing of an additional 69 different microbial genomes is at an advanced stage in both public and private sector research institutions ([http: www.tigr.org/tdb/mdb/mdb.html](http://www.tigr.org/tdb/mdb/mdb.html)). In 1996 the cyanobacterium *Synechocystis* became the first completely sequenced photosynthetic organism, of critical importance to plant biology for functional and evolutionary comparisons<sup>120</sup>. To date no microbial genomes of direct importance to agricultural productivity are being completely sequenced. However important advances are being made regarding the underlying biology of symbioses between nitrogen fixing bacteria and leguminous crop species<sup>121</sup>.

#### **4. Transgenic biotechnologies and biosafety regulations: Some issues and developments.**

##### **4.1 The origins of a need for transgenic approaches to crop improvement.**

It is important to note that many discussions of the merits or demerits of modern plant biotechnologies for potentially meeting the needs of poorer farmers rarely disaggregate the vast range of technologies which come under the rubric of “modern plant biotechnologies”. Generalizations regarding the utility (or not) of biotechnologies as a generic category to different groups of farmers are usually not informative.

For instance, from a public funding and regulatory (biosafety) perspective it is important to consider that not all biotechnologies generate transgenic or so called ‘genetically modified’ organisms (GMOs). Modern biotechnologies such as molecular genetic mapping, marker assisted breeding and plant tissue culture are also highly useful technologies which can be applied within any particular crop’s gene pool to generate improved varieties which are not transgenic and hence outside the onerous restrictions of current biosafety legislation.

Conventional plant breeding has been extremely successful and increased financial support for plant breeding will be necessary if plant breeding is to both maintain and improve crop yields. However, there are some limitations inherent in conventional plant breeding such as lack of practical access to useful germplasm due to sexual incompatibility barriers or undesirable linkage block and concomitant time lags in incorporating useful genes into existing varieties. Indeed, many transgenic approaches to crop improvement arise from a lack of suitable conventional approaches to dealing with a particular agronomic problem or need (e.g. rice sheath blight, cassava mosaic virus, potato leaf roll virus, black sigatoga in plantains etc.).

For many pests and pathogens which seriously limit agricultural productivity, transgenic approaches may provide new options where current options are lacking in their efficacy or existence. Transgenic approaches can therefore be of use for a broad range of crops and areas where there are limited options available through conventional breeding e.g. nuclear male sterility, improved heterosis breeding, reducing toxic compounds, herbicide tolerance, generating novel resistance genes.

Transgenic approaches have considerably broadened the range of gene pools which are now accessible for crop improvement purposes<sup>122</sup>. For instance, the application of useful gene transfer from microorganisms through genetic engineering techniques range from the introduction of vaccine antigen genes<sup>123</sup> to aluminium tolerance genes<sup>124</sup> to food plants. Isolated plant genes (such as those conferring resistance against pests and pathogens) can now be usefully transferred between sexually incompatible crop plant species<sup>125</sup>.

In the context of ongoing debates regarding transgenic crops, public funding agencies should not forget that modern biotechnologies such as plant tissue culture, molecular genetic mapping and marker assisted selection could still have a major impact on any conventional crop improvement approaches which decide to limit themselves to the genetic variation accessible within the primary to secondary gene pools.

##### **4.2 Ongoing debate regarding biosafety and transgenic crops.**

Biosafety assessment requires that risks, benefits and needs be given a balanced assessment in relation to transgenic organisms. Many opponents of plant biotechnology cite biosafety as the key

risk based issue for the more stringent regulation of transgenic plants<sup>126</sup>. At one end of the extreme, environmental groups are now calling for a moratorium in some European countries on the planting of 'genetically modified foods'. The other end of the extreme would be no regulations regarding transgenic organisms. Much controversy and public scaremongering has been generated by anti-biotechnology groups over the 'safety' of transgenic plants in relation to their perceived negative impacts on human health or the environment.

A new development has been that many of the anti-biotechnology groups have conceded that there are benefits to be had from the application of genetic engineering for addressing human medical problems. However, it is the application of genetic engineering to agriculture that is now the key focus of attention of the anti-biotechnology interest groups. Indeed, civil society perceptions of agricultural biotechnologies in many countries are now distorted because of highly polarised lobbyist campaigns between the biotechnology -industry on the one hand and anti-biotechnology groups on the other. The independent presence of public sector agricultural biotechnologists and scientists has often been lacking from this ongoing polarised debate<sup>127</sup>. Similarly, many membership based organizations which are more broadly representative of civil society such as trade unions, producers organizations and farmers organizations have also not been involved in these debates.

Switzerland is unique in having conducted a referendum to democratically assess public opinion regarding a number of genetic engineering issues. On June 7 1998 40% of the Swiss population voted in a referendum which called for a moratorium on the cultivation of genetically modified crops, bans on research on transgenic animals and on patenting of genetically modified organisms. Almost 1,250,326 voted against the ban, while 625, 227 voters favoured it.

#### **4.3 Biosafety regulations and equitable access to transgenic biotechnologies for poorer farmers.**

The socio-economic cost of non-access to some transgenic crops which may be of utility to farmers is rarely factored into risk-assessment procedures. Assessment of the immediate needs of different groups of farmers and consumers could feasibly become an integral component of biosafety risk-assessment procedures, where costs and benefits could be seen in more social, rather than solely environmental terms exported from countries where food surpluses are a normality.

The issue of who decides what level of risk farmers/consumers should be exposed to is also an important consideration for any countries development of biosafety regulations. This is an area where promoting the greater participation of organizations who actually represent the needs of different groups of farmers and/or consumers could be most appropriate. Many of the most vocal environmentalist or consumer organizations may not actually be very representative of farmers or consumers needs. Membership based NGOs may provide a better reflection of farmers and consumer views than single interest lobbyist NGOs.

The absence of a functional biosafety review system may negatively affects the local development and importation of new biotechnology products, and therefore farmers' access to potentially useful germplasm and technologies. On the other hand, a very stringent biosafety review system can also delay or prevent farmers' access. Indeed, the cost of a regulatory system for biosafety within any one country is an important factor which has implications for determining which farmers will ultimately have access to biotechnology products. High regulatory costs will also have an affect on what transgenic traits are ultimately to reach farmers and will further bias research towards wide rather than specific adaptation<sup>128</sup>. High regulatory costs will select for only those traits which represent the greatest commercial gain to the developer of the variety. Such regulatory costs can be high - In the USA it can cost US\$1 million to get a plant biotechnology product through the regulatory system. If such expensive regulatory systems are used in developing countries the cost will either bias all transgenic research towards meeting the needs of the wealthier sectors of society or plant biotechnology will remain primarily at the research stage<sup>129</sup>.

Also, over-stringent biosafety regulations are likely to disproportionately benefit larger companies over smaller companies or public sector bodies by acting as significant ‘barriers to entry’ to certain markets. The higher the regulatory hurdles the higher the chance that competition will be stifled between companies and that any benefits of biotechnologies will not reach poorer farmers. For example, efforts by the US Environmental Protection Agency (EPA) to regulate some transgenic crop varieties as ‘pesticidal plants’ were opposed by 11 scientific societies representing 80,000 biologists and food professionals. Interestingly, an alliance between the Biotechnology Industry Organization (BIO) and anti-biotechnology groups such as the Environmental Defense Fund were in favour of such types of regulation for differing reasons<sup>130</sup>. In determining whether low income farmers will have equitable access to certain types of transgenic crops (e.g. herbicide tolerant crops or disease resistant crops), is of relevance therefore that FAO has recently indicated that any LMO that can be considered a pest of plants falls within the scope of the International Plant Protection Convention (IPPC) and will be subject to the provisions of the Convention<sup>131</sup>.

Indeed, the broader issue of whether future or anticipated socio-economic impacts of biotechnologies should be considered under the draft Biosafety protocol to the CBD is also currently a matter of debate. In this context there has been much focus on the potential substitution effects of plant biotechnologies on commodity production and exports of developing countries. However, there are many unanswered questions regarding how future beneficial or detrimental impacts could practically be assessed and whether such impact assessment should also be legally applied to other technologies<sup>132</sup>.

#### **4.4 Are some conventional crops transgenic?**

Many conventionally bred crops are by any biological definition transgenic as they contain genes or segments of chromosomes from totally different crop species. For instance most of the bread wheat currently under cultivation contains a large segment of a rye chromosome. Triticale is a conventionally bred transgenic crop containing full copies of both the rye and wheat genomes that was developed 60 years ago and is now grown on more than a million hectares in Canada, Mexico and eastern Europe<sup>133</sup>. Similarly most of not all crop varieties of sugarcane, tomato, potato, rice, maize, oat, sugarbeet, black currant, plum and many other highly bred crops contain genes or chromosome segments derived from different wild relative species. Wide crossing and embryo rescue technologies have been used by breeders for longer than genetic transformation as a means of transferring useful genes across plant species barriers. In a biological sense at least the inter species genetic modification of foods is not inherently new.

In the context of biotechnology risk assessment, there is a widely held scientific consensus that risk is primarily a function of the characteristics of a product (whether it is a purified chemical or a living organism to be field tested) and is not per se a function of the method of genetic modification<sup>134</sup>. For instance, the US National Academy of Sciences concluded that assessment of the risks of introducing recombinant DNA-engineered organisms into the environment should be based on the nature of the organism and the environment into which the organism is introduced and not on the method by which it was produced<sup>135</sup>. However, the current legal definitions of GMOs upon which most biosafety legislation is being constructed are largely ‘process’ rather than ‘product’ based in order to suggest that there is some fundamental distinction between the process of gene transfer resulting from sexual recombination and gene transfer resulting from genetic engineering. However, the same plant gene might feasibly be transferred by either conventional plant breeding (e.g. backcrossing) or by genetic transformation and while the products of both processes for gene transfer could in theory both be genetically or phenotypically identical, one would be labelled a GMO and the other would not. For instance, there is little difference between mutagenesis-derived sulfonylurea or imidazolinone-resistant soybean, maize and oilseed rape and others crops with the same herbicide resistance genes transgenically introduced. Both transgenes and endogenous genes are, depending on their positions in the genome, likely to have similar rates or patterns of

hybridisation<sup>136</sup>. Indeed, if precision gene swapping or knockout mutation approaches through homologous genetic recombination are perfected for plants in the same manner that they have been for mammals it is likely that such approaches will be applied to crop improvement<sup>137</sup>. In instances where exactly the same genotype could be produced by either conventional mutagenesis or by genetic engineering, the 'process' based definition of a GMO will be increasingly difficult to sustain by any biological definition at least.

Many of the biological phenomena which are often cited as unique biosafety issues for transgenic crops actually also occur in conventional plant breeding or other biological processes involving non-transgenic GMOs and in wild species<sup>138</sup>. These include gene-silencing, paramutation, segregation distortion, evolution of neo-virulent pest/pathogen, evolution of fungicide or herbicide tolerance, gene-flow to wild relatives, allergenicity, etc. It is sometimes contended that transgenes may display novel 'emergent properties' when transferred to a novel genetic context. However, conventional plant breeding and indeed agriculture itself also display emergent properties many of which have been beneficial to humanity. Standard plant breeding and selection procedures are equally applicable to the selection of the best transgenic lines from the range of lines generated through genetic transformation. The yield benefits derived from dwarfing genes which were a major factor in the Green Revolution are an example of beneficial emergent properties from conventional breeding that were selected for by plant breeders.

#### **4.5 Relative acreages under conventional and transgenic crops.**

At a global level the agricultural area which is currently planted with transgenic crops as developed by genetic engineering techniques is small relative to the areas under conventional crop varieties and landraces. However it is increasing as some farmers adopt transgenic varieties. The total acreage of cultivated land in the world stands at over 1.4 billion hectares which is predominantly under conventional crop varieties. However for a few crops in a few countries (USA, China, Canada, Argentina) there are significant areas planted to transgenic varieties. In those countries where transgenic crops have been given regulatory approval, the proportion of crop area devoted to transgenic crops is increasing<sup>139</sup>. In 1997 the global area under transgenic crops was 12.8 million hectares - a 4.5 fold increase from the 2.8 million hectares planted in 1996. In 1998 it is estimated that 30 million ha of transgenic crops were planted globally<sup>140</sup>. The large increases in areas planted are currently limited to a few commercially important crops. For instance, transgenic soybean, maize, cotton and canola represented 85% of the global transgenic area in 1997, of which 75% was grown in North America.

#### **4.6 The improvement of transgenic technologies.**

The 'black box' approaches to conventional breeding based upon the generation of genetic variation followed by selection for useful phenotypes is in some ways more imprecise than single gene transfer through genetic engineering approaches. In crosses between weedy wild relatives and their crops, tens of thousands of genes are typically recombined in the progeny plants the exact phenotypic results of which are extremely difficult to predict.

Radiation induced mutation breeding has been applied in plant breeding for decades with at least 20,000 known field tests of gamma radiation treated germplasm conducted in open field trials without any weedy or toxic mutants generated<sup>141</sup>. The FAO/IAEA Division has been instrumental in technology transfer of radiation breeding approaches to developing countries. In spite of any uncertainties inherent in conventional or mutation breeding, such plant breeding has served society well without warranting the level of restrictions that are currently being perceived as necessary for all transgenic crops.

The technologies to routinely make transgenic plants have only been in existence for over a decade or so - which is of the same order of magnitude as the time required to conventionally breed a new

plant variety. Much progress has been made regarding the technologies for generating transgenic crops through genetic transformation and these technologies are constantly being improved. Although some crop varieties and species may be more difficult to transform than others (e.g. cassava, sorghum), few crop species are now considered to be ultimately untransformable and a significant number of (monocot) cereal varieties can now be routinely transformed<sup>142</sup>.

In recognition of biosafety related concern over the use of antibiotic selection markers in the process for generating transgenic plants, improved transformation systems have been developed which allow the generation of marker free transgenic plants<sup>143</sup>. Other biosafety related improvements include systems which can limit any potential pollen mediated gene flow from transgenic crops<sup>144</sup>. Such systems could for instance be used to ensure that transgenic traits do not introgress into weedy wild relatives in situations where they might confer a selective advantage on the weed species in question<sup>145</sup>.

#### **4.7 Biodiversity and plant biotechnology.**

Contrary to current opinion<sup>146</sup>, there is currently no concrete evidence either way to suggest that transgenic crops or biotechnology per se would either decrease or increase biodiversity in agricultural or 'natural' ecosystems. Indeed, any tendency towards monocultures was well established before any transgenic varieties existed, and was also well in evidence before the era of the 'Green Revolution' varieties<sup>147</sup>. Within agricultural systems, plant biotechnology research could be applied to either increasing or decreasing genetic diversity depending on the research objectives. The recent advances in agricultural genomics, marker assisted breeding and transgenesis suggest that useful genetic diversity is actually becoming more accessible to crop researchers with the potential that aggregate increases in genetic diversity within crop gene pools could now practically be achieved through increased use of genes from wild relatives and other species<sup>148</sup>.

Plant micropropagation can generate many clones of a particular variety in an analogous manner to vegetative propagation of root and tuber crops. While plant tissue culture and micropropagation might (contingent on its objectives) possibly increase the propensity for monocultures such techniques may also be used to generate and multiply healthy plantlets of diseased locally adapted varieties which without such intervention are likely to be abandoned by farmers. Reductions in broad spectrum pesticide applications through the substitution effects of resistance genes conferring specific resistances against agronomic pests are likely to contribute to an increase in beneficial insect biodiversity in agricultural systems. If growing food demand due to population pressure is to be met without requiring an expansion of agriculture into natural areas containing high levels of biodiversity (e.g. tropical forests etc) this will require that yields in high potential areas be significantly increased. FAO has estimated that two thirds of the growth in agricultural lands will have to occur through intensified use of lands already under cultivation. Plant biotechnology is likely to be one source of the potential yield increases required for high potential agricultural areas.

It is also worth considering that the wild relatives of crops, although a major genetic resource, are actually rarely used in the breeding of plant varieties, because of practical difficulties in using such exotic germplasm in breeding programmes. With modern biotechnological methods the use of such resources may increase<sup>149</sup>. Crop wild relatives only account for a small proportion of the world's genebank accessions and it is generally agreed that the *in situ* conservation of such resources is preferable to the many difficulties in maintaining them under long term ex situ conditions. Any slight risk potential of mono-transgene gene flow contributing to the genetic erosion of sympatric wild relatives should be assessed relative to other factors which are known to contribute to genetic erosion of wild relatives.

Invasive exotic species (such as zebra mussels, kudzu, water hyacinth, etc) are major and well known environmental and agricultural problems world-wide<sup>150</sup>. In the context of biodiversity, the severe environmental and economic damage that can be caused by such 'genetically unmodified'

exotic species introductions are likely to pose a much greater threat to biodiversity and ecosystems than transgenic crops *per se*<sup>151</sup>. Yet, transboundary movements of exotic species which on rare occasions result in the emergence of an invasive pest are unlikely under current phytosanitary legislation to be subjected to the same level of scrutiny or biosafety regulation as transgenic organisms<sup>152</sup>.

Concern has been voiced about the perceived risks of transgene 'escape' to wild relatives of crops with the potential for creation of novel or herbicide tolerant weeds<sup>153</sup>. For any crop, the risk of any such gene flow will differ considerably according to a range of factors such as whether the crop is cultivated in a region where there are sympatric weedy wild relatives<sup>154</sup>. Any such risk assessment has to be region or country specific and will differ widely according to the reproductive and agricultural harvesting biology of the crop in question<sup>155</sup>. It will also be contingent on whether the transgene in question can confer any selective advantage on the wild relative, either within or outside of agricultural ecosystems<sup>156</sup>. In considering what would happen if gene flow of a transgene to weedy wild relatives there are many additional issues to be considered before any level of risk can be assessed. For instance any long term effects will be contingent on whether the transgene can confer a selective advantage and on the likelihood of persistence and spread of the transgene in weedy or natural populations<sup>157</sup>. A detailed risk analysis methodology for assessing the risks of gene flow from herbicide tolerant crops to their weedy wild relatives has concluded that no generalizations can be made as to whether genetic engineering would either exacerbate or alleviate herbicide resistance<sup>158</sup>.

Nonetheless, it is obviously essential to limit any potential for herbicide resistant transgene flow into weedy wild relatives. However, any such risk assessment should be done based on what is known about weed biology and be assessed relative to the risks and problems encountered with conventional herbicide tolerant weeds. The evolution of herbicide tolerance in weeds which are related to crop plants is very well documented<sup>159</sup>. The more than 10 million hectares of herbicide-resistant weeds that have appeared in the past 30 years all result from selection of naturally occurring herbicide resistant mutants among weed populations. This has occurred for legume weeds in soybean, Abutilon in cotton and bromes in wheat, and is still occurring for major crops such as rice and wheat<sup>160</sup>. In most instances, the use of genetic isolating mechanisms such as male sterility and/or maternally inherited expression systems<sup>161</sup> will substantially reduce any risks of transgene flow into sympatric weedy wild relatives. However some scientists question whether such risk minimization strategies will be sufficient to appease those who are *per se* opposed to transgenic crops<sup>162</sup>.

In general, any risks of transgenic crops to biodiversity should ideally be assessed relative to other non-transgenic related factors, such as urbanisation, agriculture and land use changes, exotic plant introductions, conventional weeds etc which are more likely to more drastically reduce the geographic ranges of useful crop wild relatives or biodiversity in general. Many risk assessment studies regarding GMOs fail to do comparative studies to assess each particular risk comparative to the levels of risk from other factors.



#### **4.8 Human health and transgenic foods.**

There is currently no scientifically accepted evidence to suggest that transgenic crops per se are any more or less toxic or allergenic than their conventionally bred counterparts<sup>163</sup>. Indeed, genetic engineering approaches and other research approaches are underway to develop 'functional foods' or "nutraceuticals" which would contain lower levels of allergens and toxins, or higher levels of beneficial compounds, than conventional foods<sup>164</sup>. There has been much misinformation circulated in the popular media regarding perceived dangers to human health from use of transgenic crops or other GMOs. The recent public hysteria generated in the UK regarding transgenic foods stemmed from a non scientifically reviewed research report on feeding trials of rats with transgenic potatoes containing a lectin with known insecticidal properties [See: <http://www.rri.sari.ac.uk>]. In this case, while the researchers report was subjected to 'political' peer review it has not yet been subjected to peer review in scientific journals and hence all of the conflicting conclusions to date regarding the raw data are considered premature<sup>165</sup>.

Many naturally occurring plant proteins and compounds can be anti-nutrients, toxic or allergenic. Indeed a significant number of crop species are toxic if not cooked or prepared properly to reduce or inactivate such compounds. In most instances, standard procedures for assessing toxicity (LD50) and allergenicity (in vitro test, skin prick tests) can equally be applied to conventional and transgenic varieties to identify those transgenics which are substantially equivalent to conventional varieties<sup>166</sup>. Such standard testing procedures were sufficient to identify that a methionine-rich 2S albumin from the Brazil nut (*Bethollletia excelsa*) was allergenic<sup>167</sup> to some people and hence was not as good a candidate as a non allergenic methionine rich sunflower seed albumin gene for gene transfer to improve the nutritional content of legumes<sup>168</sup>.

Selectable marker genes (e.g. antibiotic resistance or herbicide tolerance genes) are used in constructing transgenic plants containing an associated transgene of interest, but are usually not required once the transgenic plants are produced. Existing biosafety regulations have been stringent enough to disallow corn-borer tolerant maize in Europe because of the extremely low risk of antibiotic tolerance spreading in bacteria in the rumen of cattle<sup>169</sup>. Even though most selection markers in constructing transgenics are likely to pose little danger either to humans or the environment because of perceived consumer hysteria it is likely that future generations of final product transgenic plants will not contain selectable marker genes<sup>170</sup>. This is because a number of quite efficient systems have now been developed for the development of 'marker free' transgenics<sup>171</sup>. More acceptable marker systems which are not based on antibiotic or herbicide resistance genes are also being developed (e.g. mannose-6-phosphate isomerase). Hence it is possible that biosafety considerations regarding such genes may gradually become less of an issue as improved 'marker free' transformation systems become available.

#### **4.9 Consumer rights and labelling of transgenic food.**

Consumers have a definite right to information and hence choice regarding which foods they purchase or eat. However, consumer information is based on the premise that the information provided to the consumer is of utility to the consumer in making an informed choice. For instance, knowledge of the biological or species composition of foods will be of use to those who suffer from allergies to particular foods or compounds. The USA requires labelling of transgenic foods that are substantially different from their unmodified counterparts, including foods that could contain a potentially allergenic compound such as a peanut protein or glutenins<sup>172</sup>. Indeed, it is questionable whether the label 'genetically modified' conveys any information of utility to the typical consumer in terms of making an informed choice based on what is currently known about transgenic food<sup>173</sup>. Nonetheless, such labelling is increasingly perceived as necessary by both the biotechnology industry and some governments<sup>174</sup>.

An increasing number of the OECD countries (e.g. European Union countries, Australia, New Zealand, Japan) are implementing provisions that require the labelling of genetically modified foods. For instance, the European Union has recently approved two directives (CE 258/97, CE 1139/98) which state that labelling must be applied to novel foods and their ingredients produced through the process of genetic engineering<sup>175</sup>. However, directive CE 1139/98 is currently technically unimplementable because there is no validated diagnostic method available to routinely and quantitatively assess levels of transgenic DNA and protein present at threshold levels in foodstuffs, comparative to non-transgenic DNA and protein. Because of the commercial potential in diagnostic services for segregating transgenic and non-transgenic foodstuffs, major research efforts are now underway to develop such diagnostic methods<sup>176</sup>.

Indeed, the labelling of transgenic foods and products is likely to be welcomed by some companies as a means of unequivocally capturing added value. Corporate strategy will require that any of the biotechnologically generated value-added traits for food and feed, and even for industrial markets, will be stacked with a variety of input traits in a variety of combinations that will need to be segregated and identity-preserved to capture the enhanced value of the end products. This will lead to contract production and marketing systems for the resultant grains, oilseeds and their derivative products<sup>177</sup>.

There are now differences between international trading blocs over requirements (or not) to label products developed using genetic engineering processes (i.e. GMOs as legally defined). While the USA does not require labelling of GMOs, the European Union and Japan, amongst others, have opted for labelling of food products or components produced by genetic engineering. It is likely that such requirements for GMO labelling will become a multilateral or bilateral trade negotiation issue (e.g. in the WTO) over whether such labelling constitutes a trade barrier.

Indeed, because of consumer concern over transgenic foods in Europe there may be substitution effects generated in both directions regarding non-transgenic and transgenic foods. For instance, countries which do not have access to technologies to produce transgenic crops and whose exports are perceived to be threatened with substitution may find that the export of labelled non-GMO derived products may be a short term strategy to maintain markets while they devise a means of diversifying their exports in the face of competition from GMO derived products.

#### **4.10 Ongoing scientific and policy developments regarding biosafety.**

Since the advent of transgenic organisms there has been a vast body of scientific research undertaken on risk assessment regarding the use of different types of transgenic organisms. Scientific risk assessment procedures regarding transgenic organisms are now an active and specialised area of scientific research. UNIDO maintains a roster of scientists who have recognized expertise in biosafety related risk assessment regarding GMOs.

On a crop by crop basis, many studies have now been done of pollen dispersal of transgenic crops and gene transfer from transgenic crops to wild relatives. Such 'transgene independent' plant based studies have shown that the likelihood of gene-flow from the cultigen can be estimated for any particular plant species at any particular location. Hence, while gene flow from transgenic potatoes to its wild relatives is virtually impossible in most of Europe it is more probable in the centres of diversity of the potato in the Andean region.

The scientific consensus emerging from the vast range of biosafety studies of transgenic plants is that each case should ideally be evaluated on a case -by case basis. Hence biosafety decisions might differ according to the particular type of transgene, crop, environment and end-use involved. Useful analysis tools for such evaluations can be the general concepts of 'substantial equivalence'<sup>178</sup> and 'familiarity'<sup>179</sup>. Risk assessment procedures can vary widely between countries. In some cases, the competent authorities who conduct the actual regulation find it difficult to agree on factors that

might be considered in a risk assessment and what potential effects might be grounds for a refusal to approve release of a transgenic organism. As a result there are instances where it is thought that regulators have been forced to erect their own normative standards and may in effect be making value judgements in formulating decisions on GMOs<sup>180</sup>.

At the international policy level there are approximately 171 countries which are Parties to the Convention on Biological Diversity (CBD). Article 19.3 of the CBD requests Parties to consider a legally binding international Protocol for Biosafety, recognising the potential risks posed to biodiversity by living modified organisms (LMOs) resulting from biotechnology. The proposed Biosafety Protocol was intended to specify obligations for international transfer of LMOs and set out means of risk assessment, risk management, advance informed agreement, technology transfer and capacity building regarding biosafety. The intergovernmental negotiations of the draft Biosafety protocol reached deadlock in Cartagena, Colombia in early 1999 and have now been postponed<sup>181</sup>.

The WTO's Agreement on Sanitary and Phytosanitary (SPS) Measures is likely to be of increasing importance regarding explicit requirements for transparent, science-based risk assessment of material for import. In the case of beef hormones the USA alleged an infringement of the SPS by the EU<sup>182</sup> and the subsequent WTO Dispute Panel finding stated that risk assessment should not involve social value judgements made by political bodies<sup>183</sup>. Upon appeal by the EU, the Appellate Body supported the Panel's decision and stated further that the precautionary principle did not override the requirements of the SPS Agreement to take into account relevant scientific evidence<sup>184</sup>.

In the context of labelling of transgenic foods the WHO/FAO Codex Alimentarius Commission (CAC) is likely to be of increasing international importance. Its current membership is 163 countries. Since 1962, the Codex Alimentarius Commission has been responsible for developing standards, guidelines and other recommendations on the quality and safety of food to protect the health of consumers and to ensure fair practices in food trade<sup>185</sup>. Codex standards, guidelines and recommendations are based on current scientific knowledge including assessments of risk to human health. The risk assessments are carried out by FAO/WHO expert panels of independent scientists selected on a world-wide basis.

Codex standards, guidelines and other recommendations are not binding on Member States, but are a point of reference in international law (General Assembly Resolution 39/248; Agreement on the Application of Sanitary and Phytosanitary Measures; Agreement on Technical Barriers to Trade). The CAC is presently developing Recommendations for the Labelling of Foods Obtained through Biotechnology<sup>186</sup>. The CAC is also considering the development of a general standard which would apply basic food safety and food control disciplines to foods which are derived from biotechnology. The advice of prior FAO/WHO expert consultations on biotechnology and food safety will be used as guidance for the conditions required for foods prepared from biotechnology. The FAO states that foremost among these are consideration of potential allergenicity, possible gene transfer from LMOs, pathogenicity deriving from the organism used, nutritional considerations and labelling<sup>187</sup>.

At the national level many countries are now establishing national biosafety committees and biosafety regulations regarding the use of GMOs. There are also initiatives to harmonise biosafety regulations at the regional level. For instance, the South Asian Association for Regional Cooperation recently developed an agreement between seven countries on germplasm exchange and the future development of biosafety regulations<sup>188</sup>. The Biosafety Information Network and Advisory Service (BINAS) is a service of UNIDO which monitors global developments in regulatory issues in biotechnology [See: <http://binas.unido.org/binas/>]. The BINAS maintains an on-line database of the state of development of national biosafety legislation world-wide.

It would seem that current debates regarding biosafety and GMOs are unlikely to be easily resolvable in the near term, due to the increasingly entrenched nature of the debate<sup>189</sup>. In Europe, surveys have shown that large percentages of the general public may believe that the view of

environmental and consumer organizations on biotechnology are more trustworthy and believable than politicians, industry or universities<sup>190</sup>. In such contexts, the claims and counter-claims surrounding current public and policy debate make it increasingly difficult for both policy makers and the public to distinguish scientific information from either inaccurate- or mis-information regarding biosafety risks<sup>191</sup>.

## **5. Commercial and socio-economic developments in agricultural biotechnology.**

There is little doubt that if plant biotechnology research was applied to well defined social or economic objectives that it could benefit poorer farmers. However different groups of farmers will have different needs regarding agricultural biotechnologies<sup>192</sup> and hence any meaningful priority setting regarding research objectives are likely to be specific to particular countries, crops or groups of farmers<sup>193</sup>. However, there remains the valid concern that the needs of poorer farmers or nations are unlikely to be a factor which favourably steers the research objectives of biotechnology research which is wholly dependent on private investment. Long term public sector investment in agricultural (biotechnology) research will be essential to address the needs of poorer farmers and consumers who do not constitute a significant enough commercial market for private sector biotechnology research and development<sup>194</sup>.

### **5.1 Private and public sector investment in agricultural biotechnology.**

The global market for agricultural biotechnology products was less than US\$500 million in 1996, but is projected to increase to US\$20 billion by 2010<sup>195</sup>. The world market for crop seed is valued at approximately \$45 billion which can be roughly divided into three main categories of equal size - commercial seed, farm-saved seed and seed provided from government institutions. Of the \$15 billion global market in commercial seed at present, hybrids account for approximately 40% of sales and reportedly most of the profit margins<sup>196</sup>. The value of the global transgenic crop market is projected at approx. \$2 billion for the year 2000, increasing to \$6 billion in 2005<sup>197</sup>. It is also projected that biotechnology based solutions to weed, fungal and insect problems will soon comprise 10-20% of the global \$45 billion crop protection market<sup>198</sup>.

The past decade has seen a major increase in private sector investment in agricultural biotechnology. Private sector agricultural research in OECD countries is now in excess of \$7 billion and accounts for half the world's entire agricultural research investment. An increasing proportion of this agricultural research investment is in modern biotechnologies. In some of the countries where such private investments have been highest there has also been significant public sector investment in agricultural biotechnology research. At the international level, a number of public sector institutions are now assigning a higher priority to agricultural biotechnology. The World Bank has lent \$100 million in support of biotechnology initiatives, whilst the Rockefeller Foundation and various bilateral donor agencies (e.g. USA, UK, Netherlands) have invested \$200 million in agricultural biotechnology over the past decade<sup>199</sup>.

The CGIAR estimate that their biotechnology expenditures are currently \$22.4 million per year, of which only \$10 million is spent on crop biotechnology spread across eight different IARCs. Considering the number of mandate crops of the CGIAR and their global importance in social terms, the CGIAR's expenditure in crop biotechnology is extremely small relative to some other large public or private sector agricultural research organizations. For instance, the USDA's 1995 expenditure on agricultural biotechnology research was \$2 billion. In 1998 the CGIAR's Third External Review Panel concluded that there was a need for the CGIAR to better harness for the public good the advances taking place in agricultural biotechnology, in particular to ensure that the needs of the poor in developing countries are met<sup>200</sup>. Whether such harnessing will be possible

without increased public sector funding for CGIAR research on a crop by crop basis is an open question.

Biotechnology is really an umbrella term that covers a wide spectrum of scientific tools based on molecular biology. As a result it is difficult to clearly define as entity called the 'biotechnology industry'. Rather, biotechnology is a broad, enabling technology that impacts on productivity in a wide range of sectors<sup>201</sup>. The agricultural biotechnology community includes dedicated biotechnology firms, established corporations with a biotechnology division, university departments, national and international research institutes, venture capital firms, regional associations, regulatory authorities and suppliers involved directly or indirectly in biotechnology, amongst others.

Many of the larger agri-business and life sciences companies have substantial resources and hence are now key players in global agricultural research. For instance, Monsanto has approximately 22,000 employees, has annual R & D investments of around \$200 million per year, and generates over \$7.5 billion annually in sales. Pioneer HiBred had an annual turnover of US\$1.7 billion and invested approximately US\$136 million annually in research and development<sup>202</sup>. The Mexico based Empresas de la Moderna's agrobiotechnology division had estimated sales of \$572 million in 1995. Private sector investment in specific technologies such as agricultural genomics may outstrip that of most governments. For instance, Novartis is providing a total of \$600 million in funding over 10 years to establish an Institute for Functional Genomics in California, USA<sup>203</sup>.

Who funds agricultural research can have major implications regarding the types of technologies that are produced<sup>204</sup>. Private-public sector co-funding of research initiatives can be a cost efficient means for technology development, provided that the roles and benefits accruing to each partner are balanced and transparent. However, it is thought that industry funding of cash starved public sector institutions such as universities or NARs can in some cases bias research towards the development of input-intensive or other commodity oriented technology development because input-intensive technologies or products tend to be the most profitable markets for industry<sup>205</sup>. There are consumers and crops which do not currently represent a viable market for many companies. Increased long term public sector funding for agricultural biotechnology which is explicitly targeted at the needs and crops of poorer people will be essential if such people are to benefit from current scientific advances.

## **5.2 Capital concentration in agricultural biotechnology: mergers and acquisitions.**

The past decade has seen a wave of corporate activity in mergers, acquisitions and the creation of new companies in the agricultural biotechnology sector<sup>206</sup>. Seed in the form of elite proprietary varieties has proved to be the delivery mechanism of choice for capturing value from the new input and output traits developed by plant biotechnology research<sup>207</sup>. This has led to high values being placed by agricultural biotechnology companies on 'downstream' seed companies which have high value portfolios of proprietary varieties and good seed distribution networks. Food processing and distribution companies which are even further 'downstream' may also be rational targets for mutually attractive mergers, acquisitions and strategic alliances with the more 'upstream' agricultural biotechnology and seed companies<sup>208</sup>. Such mutual attraction may reflect the fact that agricultural inputs only accounted for 8% of the total food industry value in 1992, whereas food manufacturing and retailing accounted for 56%<sup>209</sup>.

On the other hand, time lags from biotechnology research to product delivery has led to some agrochemical companies (e.g. Shell, Sanofi, Upjohn) divesting themselves of their seed and biotechnology businesses in the 1990s. Nonetheless, most of the recent mergers and acquisitions form part of a broader strategy towards vertical integration of research and development inputs, seed production and distribution channels within commercial crop markets. Some analysts propose that the current restructuring of the global crop seed industry is to some extent based around

intellectual property rights portfolios<sup>210</sup>. However, others contend that patents have only provided weak protection for biotechnology companies with the result that the companies have been forced to engage in vertical mergers and acquisitions in order to better capture value from and protect their technological investments<sup>211</sup>.

As a result of recent mergers and acquisitions several major players in the agricultural biotechnology sector are now emerging<sup>212</sup>. There are now fewer small agricultural biotechnology companies which have not been bought by the largest ten agricultural biotechnology companies<sup>213</sup>. These mergers and acquisitions have contributed to a restructuring of the seed industry<sup>214</sup>. For instance, having previously owned a 20% stake in Pioneer HiBred, on March 15 1999 DuPont became the complete owner of Pioneer HiBred in a US\$7.7 billion stock and cash acquisition<sup>215</sup>. Another large merger has been the establishment of Novartis from a merger of Ciba-Geigy and Sandoz. Other agricultural biotechnology mergers and acquisitions include those by; Monsanto (has bought into Agracetus, Agrocerec (Brazil), Ecogen, Calgene, Cargill Seeds, Asgrow, DeKalb Genetics, Holdens); AgrEvo (has bought into Plant Genetic Systems); Empresas La Moderna (has bought into DNA Plant Technology); Zeneca (has bought into Mogen International); and Dow Agrosciences (has bought into Mycogen, Illinois Foundation Seeds)<sup>216</sup>.

Another feature of commercial strategies over the past decade has been the development of strategic 'partnership' research alliances between agricultural biotechnology companies, especially those with complimentary patent portfolios. Research synergies can also be achieved through such alliances whereby research capabilities and technology are shared across multiple product lines. Such synergies result in cost reductions and greater potential for new product development<sup>217</sup>. For instance, Monsanto has established an exclusive research alliance with Millennium<sup>218</sup> and also with the Mexican based multinational Empresas de la Moderna<sup>219</sup>. Similarly, Pioneer HiBred and DuPont had established a speciality joint research venture<sup>220</sup>. There are also examples where the larger agricultural biotechnology companies are becoming integrated at the shareholder level. Monsanto's acquisitions of 49.9% of Calgene, 45% of Dekalb and 100% of Agracetus involved strategic proprietary technology alliances. Acquisitions of smaller companies such as Plant Genetic Systems, DNA Plant Technology, Mycogen by larger agrochemical companies such as AgrEvo, Empresas de la Moderna and Dow Elanco are considered to have been predicated on obtaining reciprocal access to proprietary biotechnologies (REF). While many of the larger companies are involved in major legal disputes between each other over patent rights and technology contracts, the ongoing legal negotiations to resolve such disputes can in some cases co-exist with strategic research alliances between the disputing parties<sup>221</sup>.

Some of the larger agricultural biotechnology companies are also now establishing international joint ventures with both private and public sector institutions in some developing countries. Successful seed companies in developing countries which have well established seed or planting material distribution systems are also likely to be targets for future mergers and acquisitions. For instance, Monsanto recently bought an approximately 30% controlling share in Maharashtra Hybrid Seeds (India). Micropropagation companies which provide quality planting materials to farmers on a commercial basis are also likely to be logical targets for further mergers and acquisitions.

In some countries, antitrust enforcement policies are sometimes required for consumer protection when competition between industries is stifled because particular companies have monopolistic or oligopolistic control of a market. For instance, in some cases of mergers in the pharmaceutical biotechnology industry (e.g. Hoechst AG's acquisition of Marion Merrell Dow Inc.) the US Federal Trade Commission has intervened in order to preserve competition in the research and development of drugs used to treat medical conditions such as tuberculosis or Crohn's disease. The recent level of amalgamation of the agricultural biotechnology industry has led to antitrust considerations of certain agricultural biotechnology markets (e.g. cotton seed and glyphosate herbicide markets) within the USA<sup>222</sup>, because it is thought that competition between companies spurs innovation<sup>223</sup>.

In both developed and developing countries, the current prospects for independent survival for small companies in agricultural biotechnology are bleak because of tortuous regulatory processes<sup>224</sup> and the high risk of incurring patent litigation costs. Many small companies involved in agricultural biotechnology are now assuming the role of service contractors to the larger companies. Indeed, high levels of regulations are increasingly thought to favour the larger companies which have the financial and legal wherewithal necessary to get useful biotechnology derived products (especially of a transgenic nature) through the tortuous regulatory systems now being constructed<sup>225</sup>. High levels of regulation of the biotechnology sector will favour the larger companies and may be intended to act as barriers to entry for smaller companies<sup>226</sup>. Indeed, the same barriers to entry may exist for (m)any biotechnology products or technologies developed by the public sector or delivered by public sector mechanisms such as agricultural extension services. In the context of food security, it is therefore worth considering that increased regulations will automatically select for commercial products entering the regulatory systems which are targeted only at the most affluent farmers or markets. Non-disaggregated over-regulation of all agricultural biotechnology could actually widen both the technology and income gaps between richer and poorer farmers (or consumers).

### **5.3 Private - public sector research collaborations.**

A significant level of plant biotechnology research is typically performed in public (e.g. NARs) or semi-public (e.g. universities) institutions and is largely funded by public funds. The broader objectives of publically funded scientific research differ according to the political economy of different countries. It is commonly accepted that market failures in agricultural research and development lead to underinvestment in research if left solely to the private sector; i.e. research opportunities that would be socially profitable go unexploited. The solutions or arrangements proposed for solving the underinvestment problem will largely depend on the type of market failure to be rectified<sup>227</sup>. For instance, public sector scientific research has often focussed on either basic research or on pre-commercial research activities. However, many public sector agricultural research institutions such as NARs, universities and the CGIAR play a vital role in conducting applied agricultural research to meet the needs of poorer groups of society, who do not represent a lucrative commercial market for most companies.

In the plant biotechnology sector, publically funded research may become more commercially oriented as a result of shortfalls in public funding, changing incentive structures (e.g. IPRs and government funding criteria) and increasing research integration between the private and public plant biotechnology sectors. Some public sector plant biotechnology labs now conduct research on particular technology modules on a 'contract' basis for private sector agricultural biotechnology companies. Many leading public sector research institutions are establishing research collaborations with private sector companies. For instance, Novartis has entered into a \$25million deal to fund plant and microbial biology with the University of California at Berkeley, USA<sup>228</sup>. In this instance, Novartis will not have exclusive rights to research findings at the university. Similarly, Zeneca has entered into a \$82.5 million research deal with the John Innes Centre (UK) to develop improved strains of wheat over a 10 year period. In India, Monsanto has established a \$5 million R & D centre on the Indian Institute of Science campus in Bangalore. The centre will receive \$3 million annually from Monsanto, which reportedly equates to about 10% of India's total budget on agricultural biotechnology<sup>229</sup>.

Public funding for plant biotechnology research can often be contingent upon having commercial research partners and research success is often partly measured on the basis of what proprietary technologies are developed. For instance, in the USA the 1980 Bayh-Dole Act and the Stevenson-Wydler Technology Innovation Act encourage non-profit organizations such as universities and research institutes to retain certain patent rights in government-sponsored research and encourage the funded entity to commercially transfer the technology to third parties. The Stevenson-Wydler

Act required agencies to establish Offices of Research and Technology Applications at their federal laboratories, and to devote a percentage of their research and development budgets to technology transfer. As a result some publically funded US research institutions cannot accept any research materials or technologies which have restrictive patent exclusion clauses. Access to certain types of EU funding for plant biotechnology research can also be contingent on having commercial collaborators<sup>230</sup>. Indeed, in some countries patents are increasingly being considered to be a better indicator of public sector research performance than the more traditional route of peer-reviewed publications<sup>231</sup>.

The generation of employment through the privatization of publically funded research is encouraged in the university biotechnology sector through the establishment of spin off or start-up companies<sup>232</sup>. Many of the more successful plant biotechnology campus derived companies have now been acquired by the larger agricultural biotechnology companies. Technology transfer accomplishments from publically funded research to private companies is now increasingly incorporated into the reward and promotion systems of public sector institutions<sup>233</sup>. It is difficult to discern distinctions between institutional incentives which promote short term commercial gain and those that promote broader social and economic impacts of research, especially in relation to food or livelihood security. Indeed, when it comes to the needs of poorer farmers and consumers, very few public sector agricultural research institutes or funding mechanisms have incentive systems which rewards those who meet the needs of clients and hence makes research staff more accountable to their clients<sup>234</sup>. For the majority of public sector scientists involved in plant biotechnology research their reward system is largely dependent upon publications. Yet, when it comes to questions of research for food security related objectives additional indicators of research success could also be factored into public funding mechanisms. For instance, adoption rates of plant varieties by farmers and other types of indicators of client satisfaction with the products of crop improvement research may be valid but under-utilised research variables<sup>235</sup>. Technology adoption rates and adoption quality could be used in much more innovative ways to construct reward systems for both public and private sector scientists<sup>236</sup>.

An increasing number of universities in the OECD countries now manage patent portfolio's based on their research from which they try to generate revenue through licensing. Licensing revenues are typically re-invested in research activities. Licensing of patents generated from public funds can be either on the basis of exclusivity or non-exclusivity. While exclusive rights to a patent are likely to be more expensive and hence generate more revenue for public sector institutions, significant revenues can also be generated from non-exclusive licenses provided to wider range of licensees at minimal fees. In the biotechnology sector, one example of successful non-exclusive licensing is the \$38.5 million generated in 1997 for the US universities which hold key patents on genetic engineering technology<sup>237</sup>. If patents on research which is entirely publically funded were limited to non-exclusive licensing provisions (e.g. as a pre-condition of funding) this would be likely to increase competition between companies and other research entities, and could help to ensure broader access to useful biotechnologies generated as a result of public funding.

A number of problems are typical of public sector involvement in IPR protection. These include; overeagerness of university technology transfer managers to file patent applications, their overestimation of the value of their intellectual property and the underestimation of the additional investment required to turn a research discovery into a product, and their readiness to grant exclusive, rather than nonexclusive, licenses. There is hence a need for governments to make their criteria for provision of public funding for agricultural biotechnology research more specific and transparent regarding IPRs, and also to more clearly identify whom the primary clients of such research are.

Technology transfer lawyers in research institutions operate primarily within the boundaries of their respective national laws. Hence, national legislation or conditionalities regarding public funding of agricultural research can be used as a policy instrument to ensure that broader social



and economic goals are met through publically funded biotechnology research. In addition, the encouragement of research institutions to develop clear mission statements and correspondingly transparent IPR policies could help to broaden access of poorer groups and countries to useful biotechnologies. For instance, consideration of the provisions of the Convention on Biological Diversity on biotechnology transfer to developing countries are rarely considered by many public sector agricultural biotechnology research institutions. However there are a number of provisions of the Convention on Biological Diversity which are relevant to the transfer of biotechnologies between research institutions in different countries. *Inter alia*, these include potential rights of the biological resource donor country's institutions to;

- participation in research, Article 15(6)
- sharing in the results of research and proceeds of commercial exploitation, Article 15(7)
- access to and transfer of the derived technology, Article 16(1)

Some types of public sector institutions (e.g. universities) lack the capacity to both research and develop a product to its final stage. Public sector plant biotechnology research in the OECD countries has become increasingly 'atomised' whereby each laboratory may develop and patent a vital modular component of a product but is rarely directly involved in developing the final technology package embodied in novel plant biotechnology products. The final products of plant biotechnology research in the OECD countries are typically distributed by the private sector. However, there are numerous examples of publically funded breeding programmes, seed production and agricultural extension in developing countries that also try to develop and provide finished products (i.e. varieties) to poorer farmers and consumers. It is therefore relevant that an increasing number of biotechnology products can be composed of a range of proprietary modular components that are often owned by a number of different parties. As a result, public sector institutions (e.g. NARs, CGIAR) which are involved in providing finished products (e.g. seed, varieties) to farmers and which wish to incorporate useful proprietary traits in their varieties will increasingly have to negotiate terms of legal access to such inventions with the patent owners. The Third CGIAR System Review recognized this and recommended that the CGIAR establish a legal entity which could hold patents, and develop rules of engagement (involving both the public and private sector) based on the premise that access to the means of food production is as much a human right as access to food<sup>238</sup>.

Public sector funding bodies could also play a stronger role in specifically targeting plant biotechnology research towards longer term social and economic objectives rather than short term commercial objectives. In this respect, it will be very useful if the private sector transparently identifies those public goods in the agricultural biotechnology arena which it cannot provide or fund in the short to medium term. At present, the International Seed Trade Federation (FIS) states that up to now, fundamental research done by the State Institutes has in a great number of countries largely contributed to and stimulated the work done by private companies. It is felt by FIS that there will be an increasing need for fundamental research. However, FIS is convinced that farmers will benefit best if the results of this basic research are developed, increased and distributed by private companies<sup>239</sup>.

The needs, constraints and objectives facing biotechnology researchers in the public and private sectors can differ widely. Yet, public sector scientists who conduct plant biotechnology have not been well represented or very actively involved in policy formulation at the national or international level. In most instances, the views of the private sector plant biotechnology industry on the one hand, and environmental organizations concerned about aspects of agricultural biotechnology on the other hand, have had the most impact on the formulation of national and international biotechnology related policy. Both of these interest groups are not necessarily representative of publically funded plant biotechnologists or agricultural researchers in general. Hence there has been a significant lack of policy input from public sector scientists as a group. For instance, there has not been much involvement in inter-governmental fora (FAO Commission on

Genetic Resources, Convention on Biological Diversity meetings, etc) of membership based international or regional scientific NGOs (e.g. International Society for Plant Molecular Biology, International Association for Plant Tissue Culture, African Biosciences and Plant Biotechnology Networks, The International Society for Tropical Root Crops, Cassava Biotechnology Network, the African Association for Biological Nitrogen Fixation etc) which mainly represent public sector biotechnologists and agricultural research scientists.

#### **5.4 Orphan crops and Orphan Drug Acts.**

Plant biotechnology to date has been biased towards some crops relative to others<sup>240</sup>. Privately funded plant biotechnology research is heavily biased towards major commercial (often export) crops such as maize, soybean, canola, cotton, tobacco, tomato, potato, squash, and papaya which are the main species for which commercial transgenics have been promoted on a large scale. This has been driven by the cost of developing biotechnology-derived crops and the potential large markets for a relatively small number of commodities such as maize and soybean. Similar crop biases are also evident in the crop focus of public sector plant biotechnology research in many OECD countries.

By comparison plant biotechnology research on many of the 'orphan' crops of poorer peoples such as millets, yams, plantains, cassava, sweet potato etc is very limited both in terms of its research intensity and levels of public sector funding. A similar situation exists for the many so-called 'Cinderella' trees and shrubs of major importance to poor peoples livelihoods which have been overlooked by agricultural researchers. The private sector has little interest in investing in the improvement of such crops, unless there is scope for increasing sales of such crops in global commodity markets such as starches, oils or animal feed. Even within particular crops, there may also be a level of varietal bias in current plant biotechnological research. There may be important differences between varieties regarding their response to tissue culture or whether they are easily genetically transformed. A significant effort is often needed to develop regeneration and transformation protocols for specific varieties with a concomitant bias towards commercial or export varieties. For instance, there is a current need for the development of transformation protocols for the different rice varieties which are associated with different rice agro-ecosystems<sup>241</sup>.

In the area of biomedical research the lack of commercial incentive for companies to develop therapeutics for diseases with small number of sufferers (e.g. rare diseases) or with large numbers of financially poor sufferers (e.g. shistosomiasis, malaria) has been recognized for many years. Government legislative intervention in the form of 'Orphan Drug Acts' have been established in the USA (1983)<sup>242</sup>, Japan (1985) and are proposed for the European Union<sup>243</sup> to provide incentives for private sector research into therapeutics for rare diseases<sup>244</sup>. Incentives under such orphan drug acts can take many forms such as:

- limited period market exclusivity,
- grants,
- tax credits,
- regulatory assistance,
- clinical trials assistance,
- subsidies,
- preferential access to public sector research funding
- 'fast track' regulatory trials

However some existing Orphan Drug Acts have been criticised on a number of issues<sup>245</sup>. It is questioned whether the existing Acts can function to promote research on the development of unprofitable drugs, for instance where the end-users are too poor to warrant any private investment. It has also been suggested that the market exclusivity provisions in Orphan Drug Acts, which can be broader in scope than patent protection, can be used to create barriers to entry by

other competitors. More rigid criteria for designation of orphan drugs, targeted incentives for research and greater public accountability are considered to be remedies for the better functioning of Orphan Drug Acts<sup>246</sup>.

Orphan drug acts are in essence limited period joint ventures between the public and private sectors to meet some public goods. Similar arguments can be made for public/private sector co-financing of research on orphan crops of smallholders, in the same way state/commercial interests coincide in Orphan Drugs Act which promotes research in drug development for groups of sufferers who do not represent a large enough commercial market for total private sector interest. For some crops, there may be a need at both national and international level for the development of analogous Orphan Crop Acts to stimulate research and development for locally consumed orphan crops such as cassava, yams, millets, etc. It is likely that most export crops will continue to attract sufficient private sector investment.

Because the basic biotechnology research tools for commercial crops such as maize, wheat, soybean, cotton etc could equally be applied to orphan crops, public sector incentives could tip the balance towards increased public and private sector investment in research to meet the needs of consumers of orphan crops. However this would require the adequate definition of what an orphan crop is and what conditions limit private sector investment in research on the crop in question. In this respect the development of Orphan Crop Acts could learn from the experiences gained in the development of Orphan Drug Acts. Countries who wish to stimulate private sector investment in orphan crops could consider that 'Orphan Crop Acts' with limited duration exclusivity and sales caps may be one means of stimulating research on crops of importance to national food security. Such sales caps might easily be determined from international export figures. This may provide a strategy for the CGIAR and some NARs to get preferential access to proprietary technology for some of its mandate orphan crops which are not internationally traded in a significant commercial sense<sup>247</sup>.

## 6. Intellectual Property Rights and related developments

Intellectual property rights (IPRs) represent a very useful means by which private investment in research and development can be promoted. IPRs provide commercial incentives for research and development activities by prohibiting direct copying without permission (e.g. the payment of a royalty). The concept is that the inventor or other creator cannot compete with a copier who shares none of the development costs. In return for the risk of such investment, the IPR owner obtains for a limited period (e.g. 20 years) the right to use the intellectual property exclusively, assign ownership, license it, or not use it at all. The IPR owner can enforce these property rights if others misappropriate or otherwise infringe the protected intellectual property. In a social sense intellectual property rights represent a means to promote commercially relevant innovation, and are not an end in themselves<sup>248</sup>.

When considering the incentive effects, it is important to recognize what privileges IPR do and do not provide. They do not assure a return; indeed only up to 15 percent of patents are ever commercialized. Hence predicting the level of future use from the simple act of filing a patent is a difficult if not impossible exercise. IPRs do not necessarily permit the use/practice of the creation as this is often controlled by other regulations (e.g. biosafety) or even other patents. Primarily they allow is the right to exclude others from use, what can be called negative rights. All financial rewards must typically come from market sales although social rewards might accrue from licensing at lower rates to non-commercial users. For most IPRs, key factors such as the breadth (scope) of protection are critical in determining the commercial value of the IPR. IPR legislation is national law, applying only in those countries where it is available and has been granted.

It is not yet clear whether IPRs are suitable incentives for public sector biotechnology research for food security and other public goods. For IPRs generated both by the public and private sectors, this will depend on whether such IPRs are practiced for narrow commercial objectives, or whether broader social or economic objectives are factored into promoting the licensing and use of IPR protected biotechnologies. In any market driven system with strong forms of IPRs, it is to be expected that investments will be targeted at projects with the greatest commercial rate of return. While IPRs are excellent incentives to stimulate private sector innovation for commercial gain, they can potentially have a distorting effect on the research objectives and directions of public and semi-public sector institutions. The application of IPRs as research incentives for publically funded research may tend to re-orient research towards short term commercial objectives rather than longer term economic gain for the 'public good'. In essence, the same IPR incentive structures can lead to competition between the research objectives of the private and public sectors for the same commercial markets. In such instances, the needs of resource poor farmers who are not a viable commercial market for the private sector are likely to continue to be unmet.

In the agricultural research arena, both scientific knowledge, and its commercial applications are increasingly becoming proprietary. Proprietary rights over agricultural biotechnology products and processes are being claimed by both private firms and an increasing number of public institutions. Such rights include trade secrets, patent rights, plant varietal protection (PVP), and contractual rights arising from the use of material transfer agreements (MTAs)<sup>249</sup>. How regulations, policies and incentives regarding public sector funding of agricultural biotechnology research are framed by governments will have a major impact on whether agricultural biotechnologies can have a beneficial impact upon global food and livelihood security. In particular, it will be increasingly important for governments to more specifically identify whom the primary beneficiaries of public funding are, what the purposes of such funding are and what stakeholders will have real access to any useful biotechnologies generated from public funds. In this respect, a clarification of the complementary roles and objectives of the domestic private and public sector institutions will inform the development of better incentive structures to promote both commercial and economic

development. While IPRs may be the best incentives for private sector institutions, alternative or modified incentive structures (e.g. limitations on exclusive licensing) may be more appropriate for public sector research institutions (or for publically funded research).

At the international level, the Uruguay Round of the General Agreement on Tariffs and Trade (GATT) has created a subsidiary agreement on Trade Related Aspects of Intellectual Property Rights (TRIPs). Any country ratifying GATT accepts the obligation to establish minimum standards of intellectual property. The TRIPs Agreement is to be reviewed in 1999. The ongoing revision of the WTO's TRIPs Agreement is therefore of key importance to future trends and research directions in agricultural biotechnology research. The current coexistence of different models of IPR law between different countries and regions (see below) will probably lead to negotiations for international harmonization of IPRs within the WTO.

The majority of patents and PVP certificates currently filed are filed by companies predominantly from the OECD countries. It is unclear at present what impact the harmonization of IPR systems will have on the relative roles of foreign and domestic innovation in the agricultural biotechnology sector in developing countries. Indeed, this will to a certain extent depend upon what IPR models result from any international harmonization of IPRs. As part of the Transatlantic Economic Partnership, the European Commission and the USA have recently reopened negotiations on the harmonization of US patent law with that of other countries<sup>250</sup>. The CGIAR's Third System Review has stated that negotiations regarding agriculture and intellectual property rights within the WTO will have major bearings on global food security and in shaping the context within which public sector research institutes will have to operate.

## 6.1 Patents

National patent laws provide protection of inventions demonstrating the key characteristics of novelty, non-obviousness, utility and sufficient disclosure. A patent confers a right on the patent owner to prevent others from freely exploiting what is claimed in the patent. The patent system applies generically to stimulate private sector investment in research and development in many sectors, of which agriculture is but one.

There are significant differences between the patent procedures of different countries and regions regarding agricultural biotechnology<sup>251</sup>. For instance, while most of the world's patents laws operate on the 'first to file' basis, there are some countries such as the USA which operate on the 'first to invent' basis. The US patent system allows prior publication for up to a year before filing while most other countries regard prior publication as prior disclosure. Most patent regimes require that biological material involved in the patent be deposited in a germplasm collection either before filing (e.g. most countries) or after issuance (e.g. USA). The options for intellectual property rights protection for plants also differ considerably between the US and EU<sup>252</sup>. In the US utility patents and plant patents can be taken out on the entire genotype of some types of plant varieties (e.g. mutants, asexually reproducing plants), whereas Article 53(b) of the European Patent Convention states that a plant variety or biological process for the production of the plant variety is unpatentable.

Another difference between the European patent system and US patent law is that the term "invention" means invention or discovery in the US system. In European law "discovery" is distinguished from "invention" and is considered unpatentable. However, the distinction is not easy to define. A discovery involves new knowledge whereas an invention is a practical application of knowledge. Naturally occurring substances present as components of complex mixtures of natural origin, can in principle be patented where they are isolated from their natural surroundings, identified and made available for the first time and a process is developed for producing them so that they can be put to a useful purpose. This applies to inanimate substances as well as to living materials. In some circumstances such substances are not ruled out as mere discoveries but are

considered as inventions. Microorganism patents are granted by the US, European and Japanese patent offices.

While patent regimes differ internationally, a certain level of international harmonization of IPR law is underway under the WTO Trade Related Intellectual Property Rights (TRIPs) Agreement. In addition there are a range of international agreements regarding patents. The Patent Cooperation Treaty and the Paris Convention for the Protection of Industrial property are two relevant examples of such international policy. If an exported patent is filed in a country that subscribes to the Paris Convention (most countries) the foreign filed application will be treated as if it had been filed simultaneously with the original application. Hence, the expiry date for a single patent should be the same if filed at different times in multiple countries. The International Patent Cooperation Treaty offers a centralised system for filing patent applications for its member nations. Membership is open to any countries that are signatories to the Paris Convention. As of January 15, 1998 there were 95 member nations which were signatories to the Paris Convention. The World Intellectual Property Organization (WIPO) is the United Nations body which is responsible for international aspects of IPRs and was established under the Convention establishing the WIPO. There are also a range of regional patent treaties such as the African Intellectual Property Organization (OAPI), the African Regional Intellectual Property Organization (ARIPO), the Eurasian Patent Convention and the European Patent Convention (EPC).

In apparent contrast to many other types of industries, patents are considered as key assets in the agricultural biotechnology industry. Studies of widely different types of businesses have reported that for some businesses patents were not a very important means of securing competitive advantages from new products<sup>253</sup>. However, within the same study it was found that the pharmaceutical, chemistry, and plastic materials industries did consider patents to be an effective means of protecting new products. In the biotechnology industry a patent can be viewed as a means of protecting the large, up-front investments necessary to the research and development of new drugs and biotechnologies.

## 6.2 Plant Varietal Protection (PVP) and other IPR systems.

Plant Breeders' Rights (PBR) or Plant Varietal Protections (PVP) systems are synonymous terms to describe specialized (*sui generis*) IPR systems for cultivated plants. PBRs were first systematized under the International Union for the Protection of New Varieties of Plants (UPOV)<sup>254</sup>. UPOV is an intergovernmental organization which was established under the 1961 UPOV Convention signed by its member governments. The purpose of the UPOV Convention is to ensure that the member states acknowledge the achievements of breeders of new plant varieties, by making available to them an exclusive property right, on the basis of a set of uniform and defined principles. The UPOV Convention entered into force in 1968 and was revised in 1972, 1978 and 1991. The 1991 Act of the UPOV Convention entered into force on April 24, 1998. Membership of UPOV among other steps requires that signatories adopt national legislation along the lines of the 1978 (e.g. China) or 1991 (e.g. USA) UPOV Conventions. As of March 23, 1999 39 governments had become member states of UPOV<sup>255</sup>. As of January 22, 1999 eleven out of 38 member states had developed legislation in line with the UPOV 1991 Convention while the remainder had legislation in line with the UPOV 1978 Convention<sup>256</sup>.

In place of the novelty, nonobviousness, and utility requirements of patent law, PBR uses the requirements of novelty, distinctness, sufficient uniformity, and stability (DUS). Uniformity and stability are measures of reproducibility true-to-form, respectively among specimens within a planting and inter-generationally. The principal test then is distinctness to determine novelty, i.e. that the variety be "clearly distinguishable from all" known varieties. PBRs differ from patents in a number of key respects and it is generally not useful in discussions of IPRs to confuse or conflate these two different IPR systems.

It is worth noting also that both trademarks and trade secrets are widely used intellectual property rights in the agricultural biotechnology sector. For instance, trademarks can be associated with a particular company's name (e.g. Pioneer Hi-Bred), or individual products like the FlavrSavr tomato. Note that the FlavrSavr tomato genotype may also be patented so the two forms of IPR can be complementary. Within agriculture, the parent inbred lines used to generate F-1 hybrids may be considered a form of trade secrets. So long as the crosses and/or the inbred lines are protected, the product is difficult to copy. However, the self-reproducible nature of most living organisms precludes a major role for trade secrets as IPR protection systems for agricultural products. In other technological areas, trade secrets may substitute for or complement patents. When a product or process is difficult to copy, then trade secrets can be a substitute for patents.

The vast majority of patents in plant biotechnology research are taken out by private or public sector institutions in OECD countries (e.g. USA, Japan, EU countries, Australia). The same trend is evident for plant varietal protection or plant breeders' rights certificates. It would seem that domestic innovation in plant biotechnology research in the majority of non-OECD countries has to date yielded few IPR-protected technologies or products.

### **6.3 Technology use fees and contracts.**

Intellectual property rights (IPR's) are not the only legal means that can be used to ensure that proprietary technologies are not mis-appropriated. There is an emerging trend for some companies to also use bilateral legal contracts with growers to ensure that their products are grown in a particular manner and to ensure that value is captured from such downstream end-users<sup>257</sup>. Agricultural biotechnology which focuses on output traits will result to some extent in a shift from agricultural production of commodities towards more specialised production for lucrative niche markets.

Agribusiness projections suggest that by 2028 farmers will be responsible for 10% of the added value in end-products, whereas food processing and distribution will be responsible for over 80%<sup>258</sup>. This contrasts with relative value added contributions of 32% and 50% in 1950 for farmers and food processing/distribution respectively. It is thought that an increasingly large percentage of varieties containing such specialised output traits will be produced under strict contractual guidelines<sup>259</sup>. It is further suggested that such contracts are likely to be managed by input suppliers who, in partnership with the farmer, will produce within contract parameters for specific niche markets<sup>260</sup>. A number of companies are using such types of legal contracts with farmers who act as contract growers<sup>261</sup>. In some cases farmers buying such proprietary seed have to sign contracts guaranteeing no reuse of seed in the following year<sup>262</sup>. Such contracts can also require that the growers use particular brands of inputs (e.g. herbicides) on the proprietary seed varieties.

Another development has been that of technology fees. To recapture private investments in plant biotechnology research some companies now make a legal distinction between the value of the original seed or variety *per se* and the value of the new technology embodied in the improved seed. Such companies now charge a 'technology premium' to farmers when they purchase improved seed. For example, the 1996 technology premium for Bt-based insect protection in cotton was reported to be approx. \$75 per hectare and \$25 per ha for maize. More recently, the technology premium list prices ranged from \$32 per acre for Bt cotton, to \$5 per unit for herbicide resistant soybeans. In some cases, such technology fees have been waived to facilitate market entry and it is expected that such fees would decline as more competitors bring substitute technologies to the market<sup>263</sup>.

In some instances, the developers of novel biotechnologically generated foods may opt to internalize the entire production and distribution process to the exclusion of other producers and suppliers. Calgene, owner of the FlavrSavr tomato, for example, was reported to be producing

exclusively under contract or using their own facilities. Where labour costs are lower in developing countries it is possible that contract growing of proprietary varieties containing output traits (e.g. especially for export crops) will begin to emerge.

#### **6.4 Technology protection systems.**

There has been some controversy generated over the development of 'technology protection systems' (TPS) which aim to ensure that saved seed containing proprietary technologies or genes is not re-planted without adequate payment for the novel embodied technologies. Such systems are likely to work for all self-pollinated and outcrossing seed propagated crops, and may have distinct biosafety benefits. At present no such systems have been developed for clonally propagated crops. Such systems may promote private investment in crop research for crops where the extent of re-planting of saved seed is a disincentive for recouping investments. One such technology dubbed the "Terminator" which was originally developed by the USDA and Delta & Pine, and is now owned by Monsanto, has been the focus of much attention<sup>264</sup>. However other companies are developing similar technology protection systems using a different suite of transgenes<sup>265</sup>. A number of countries (e.g. India) are reported to have banned the use of such TPS systems and the CGIAR has stated that such systems will not be used in its research programmes.

None of the technology protection systems under development have yet been commercialised (i.e. reached farmers fields) and are unlikely to be commercialised in the near future (e.g. 5-7 years). If developed further, the next generation of systems are likely to involve the failure of the proprietary genes to express their useful traits when the variety is re-planted, rather than the failure of the entire varietal genotype to replicate itself. The 'switching on' of such proprietary traits which rest upon the varietal platform may be contingent upon the application of proprietary chemicals which induce the proprietary transgenes to express the useful trait. Hence, farmers could choose whether on not to buy the proprietary chemicals which switch on the improved traits. The impact of such gene use restriction technologies (GURTs) is currently the subject of an independent international expert review process conducted by the CBD Secretariat as an agenda item for consideration at the next SBSTTA meeting<sup>266</sup>.

#### **6.5 Research exemptions under patent and PVP systems.**

A key consideration for researchers, and hence for the public concerned about the efficiency of agricultural research, is access to IPR protected materials and technologies for research or non-commercial purposes. An IPR research exemption refers to the permissible use of protected materials for certain research and product development/improvement purposes. e.g. non-commercial use. Research exemptions under IPR systems are critical to future scientific innovation and competitiveness. However there are signs that research exemptions under both patent and PVP systems are becoming less standard and more restrictive in the favour of the IPR holders.

Most patent legislation provides an exemption for scientific research or non-commercial uses of the patented technology. However the practical nature of such research exemptions can differ significantly between different patent systems. For instance, the nature of the research exemption under the US and Canadian patent systems is more restrictive than the research exemption provided under the European and Japanese patent systems. In some cases the research exemption is explicitly stated in national patent laws while in others it is not. Furthermore, there can be significant legal differences between experimenting on a patented invention—that is, using it to study its underlying technology and invent around the patent, which is what the exemption covers—and experimenting with a patented invention to study something else, which is not covered by the exemption. Many researchers in the USA and Canada work on the assumption that patent holders are unlikely to file a lawsuit against an academic researcher whose use of their invention is commercially insignificant<sup>267</sup>.



The research exemption under most PVP systems (e.g. UPOV) is typically called the breeders exemption. The breeders exemption refers to the right to use protected materials as the basis for developing a new distinct variety or other research use. Research or experimentation exemptions under patents are not as well defined. However, to prevent copying of research the breeders exemption under PVP laws such as promoted by UPOV 1991 is now contingent upon the questions of essential derivation and dependency. The 1991 Act of the UPOV Convention requires that varieties eligible for PVP shall not be essentially derived from other protected varieties or require the repeated use of the protected variety (e.g. inbred lines for F1 hybrid production). Essentially derived varieties may be obtained for example by selection of natural or induced mutants, by selection of somaclonal variants, by backcrossing or by genetic engineering.

The definition, either by molecular or phenotypic means, of thresholds which would define what extent of essential derivation and/or dependency would constitute an infringement is currently under discussion in UPOV, ASSINSEL<sup>268</sup> and FIS. It is likely that molecular profiling of varieties will be increasingly used to identify varieties which are essentially derived from commercially valuable elite germplasm. Some seed companies (e.g. Pioneer HiBred) are now hiring germplasm security officers trained in molecular diagnostics who will specialise in identification and prosecution of essential derivation situations where proprietary germplasm is being misappropriated. Unlike the case of state promoted DNA forensics for identification of humans in criminal situations, it is likely that the DNA forensics will be performed by the companies themselves rather than by independent agencies. It is also likely that criteria for judging what constitutes an “essentially derived” variety will have to be defined on a crop-by-crop basis<sup>269</sup>.

In the area of IPR protection for plants, utility patents are considered to be the IPR of choice in situations where the technology holder would like the strongest protection and the most minimal research exemption<sup>270</sup>. However, the legal interface between plant breeders rights and patents is currently unclear in many countries. Because plant molecular biotechnology is conducted in a modular fashion, a single variety (or transgene) can be subject to a multitude of different patents, each on different genetic components or processes, and each possibly owned by different owners in different countries. In addition, such varieties can also be subject to PVP and the legal provisions therein. ASSINSEL has stated that patented plant genetic components, traits or characteristics and commercialized varieties including their patented genetic components, traits or characteristics should be unrestrictedly accessible and/or usable for developing new plant varieties. However, to commercialize a variety incorporating a patented genetic component or expressing a patented trait or characteristic, ASSINSEL recognises that the authorization should be requested from the patent holder<sup>271</sup>.

Patent lawyers are typically paid to submit claims for IPR protection which are as strong and broad as possible<sup>272</sup>. There has been much international debate on the issue of agricultural biotechnology patents which are increasingly broad in scope<sup>273</sup>. In particular, when broad patents, or patents on basic research / enabling technologies occur there can be a tendency for the patent holders to engage in cross-licensing or patent pooling. Such practices can act as significant barriers to market entry for competitors and can act as disincentives for follow on innovation<sup>274</sup>.

Some of the larger companies with powerful patent portfolios on agricultural biotechnologies are now involved in cross-licensing or bartering of one patented technology for another. By comparison isolated public sector research institutions or smaller companies with relatively weak patent portfolios and legal expertise are not in a strong bargaining position to gain access to many useful proprietary technologies under standard research exemption clauses<sup>275</sup>. Threats of litigation or ‘sham litigation’ to slow down competitive entry into markets will also be disproportionately felt by weaker institutions or organizations<sup>276</sup>.

In the area of agricultural research, there is a greater need for more detailing of valid criteria for research exemptions under national patent law to ensure that researchers can gain access to

proprietary technologies for research and non-commercial purposes. In the context of food security in developing countries there may be some scope for obtaining research exemptions on use of proprietary technologies for non-commercial purposes e.g. orphan and neglected crops, non-export crops, subsistence farmers.

A more transparent elaboration of the research exemption criteria for non-IPR holders coupled to a greater specification of the utility and enablement doctrines for patent holders could increase incentives for follow-on and incremental research and help to deter anticompetitive cross-licensing schemes<sup>277</sup>. In particular, stronger research exemptions or compulsory licensing might be sought in situations whereby the patent owner “fails to practice” the patent in certain unprofitable “public good” type situations e.g. for improvement of non-commercial subsistence crops or for less lucrative markets. Generic material transfer agreements (MTAs) concerning genetic resources or technologies could also be developed which would broaden access to germplasm or technologies for certain purposes (e.g. non commercial use, non-export crops etc).

The relative lack of participation of public sector scientific NGOs as observers in international fora concerning food security, environment, agriculture and genetic resources may mean that important issues regarding research exemptions and access to technologies remain off policy agendas. There is a pressing need at the national or international level for greater involvement of membership based organizations representing public sector scientists in the elaboration of criteria and approaches for maintaining IPR research exemptions in a manner which best promotes research competition and equitable technology transfer.

#### **6.6 Farmers privilege to save and re-sow proprietary planting materials under patent and PVP systems.**

The farmers' privilege is the right to hold PVP protected germplasm as a seed source for subsequent seasons (farmer-saved seed). Where the privilege exists, farmers can use the harvested product of a protected variety for propagating purposes on their own holdings, where the harvested product was obtained by previous planting on their own holdings<sup>278</sup>. Under Article 15 of the UPOV 1991 Convention, the farmers' privilege is optional, within reasonable limits, for governments to include in their national PVP legislation.

The farmers' privilege to re-sow saved seed would generally be an infringement with most patented materials. Under most current patent systems, there is no farmers privilege to allow the saving and re-propagation of patent protected seed. This contrasts with the farmers privilege' under the UPOV plant breeders rights system where countries have the option to allow such a farmers privilege for PVP protected seed.

The International Seed Trade Federation (FIS) has stated that there is a need for a clear limitation or definition of those practices, which are carried out in some countries under the name of “farmers' privilege”. FIS considers that it should not happen that a situation of unfair competition should arise between the participants in the seed market because of the use of farm-saved seed with subsequent commercial use of the product obtained - whether it comes from the production of seed or from the production for consumption purposes<sup>279</sup>. FIS has also stated that despite the benefits of the UPOV system for protection of plant varieties, it will be useful for companies to take advantage of patent protection also for plant varieties, in case of maintenance of the abusive application of the possibility for the farmer to use his own seed without paying royalties, which is considered by FIS to not be justified. This would happen because the patent system, with its stronger degree of monopolization, legally excludes such a possibility<sup>280</sup>.

Nonetheless for both social equity and food security reasons there are justifications for providing a ‘farmers privilege’ for smallholder and resource poor farmers, especially in developing countries. This would essentially require a disaggregated ‘farmers privilege’ in both PVP and patent

legislation whereby poorer farmers who do not represent an immediate or lucrative market would enjoy the 'farmer privilege' to save seed, while their richer counterparts would be required to pay royalties on saved proprietary seed. Interestingly, both the EU's Directive on Protection of Biotechnological Inventions (Article 11) and the Andean Pact countries have opted to enshrine the farmers' privilege for a segment of their farmers, namely subsistence or smallholder farmers, whose livelihoods can be dependant on farm saved seed and planting materials.

### **6.7 IPRs and the agricultural biotechnology innovation system.**

Most innovations in biotechnology are developed using the knowledge or technologies generated from previous innovations<sup>281</sup>. Many plant biotechnology products or techniques are 'modular' in that they are assembled from a number of previously developed technologies/transgenes, each of which may be subject to a separate patent. The commercialisation of many proprietary biotechnology products is typically contingent on other proprietary biotechnology products or processes, and in particular on agreements between IPR holders regarding the relative contributions of different proprietary technologies to the product in question. Many biotechnology products (e.g. transgenic seeds or transgene cassettes) now have a complex IPR pedigree because a large number of proprietary products or processes are involved in developing the product.

The commercialisation of many plant biotechnology products will be dependent upon proprietary technologies owned by third parties. Therefore, both companies and public sector research institutions involved in plant biotechnology research will increasingly use their own patented technologies as bargaining or trading chips for access to other useful proprietary technologies. Most research institutions in OECD countries now have patent lawyers or specialised technology transfer units who negotiate terms of access to technologies or germplasm developed or acquired by the institutions. This applies to both institutions in the private (e.g. companies) and public sectors (e.g. universities).

Although knowledge is growing, the extent with which public sector agricultural biotechnology research institutes are now working with proprietary materials or technologies can sometimes be unknown from a legal standpoint. In some instances, public sector researchers may be unaware (until the point of commercialisation) that some of the products or processes they are working with are patented. For instance there is currently no efficient process for the genetic transformation of crop plants (i.e. to make transgenic crops) which is not patented. Some organizations may be unknowingly conducting research using patented technology which is not under license. Whether many public sector researchers are now working with 'unexploded' patents which will become apparent upon widespread commercialisation will largely depend on the propensity and financial ability of the patent holders to enforce their patents. Of particular concern to all plant biotechnologists is the 'freedom to operate' which can be loosely defined as legal access to all the technologies required to launch or commercialise a product.

### **6.8 Patents and access to key enabling technologies / research tools.**

Broad monopoly rights on key or early innovations which are unduly restrictive can stifle later innovation<sup>282</sup>. In particular it is thought that both over-broad patents and patents covering basic research tools (enabling technologies) may discourage incremental and follow up research<sup>283</sup>. In this respect, the technologies used to develop biotechnology derived products can be broadly divided into two major groups: genes and 'enabling' technologies or research tools. The genes or combinations of genes are typically responsible for the agronomic trait whereas the 'enabling technologies' are highly useful research tools which are routinely used for the actual research and development process, irrespective of what genes are being focussed upon.

Modern biotechnology research in both private and public sector institutions is increasingly reliant on a wide range of capital intensive research tools and processes. Among these technologies, there are key 'enabling technologies' which include plant transformation systems, selectable markers, gene expression technologies, gene silencing technologies, microarray/DNA chip technologies etc. Such basic research tools are highly valuable in themselves because they can increase the value and speed of research and development. Access to cutting edge research tools can confer competitive advantage for any research group. Hence access to improved research tools is continually sought after.

While a wide range of research tools, products and processes are still in the public domain, in the past decade many useful enabling technologies have become increasingly proprietary as a result of successful patent applications. Many 'enabling' technologies or techniques for conducting plant molecular biology research are currently subject to patents. For instance, all existing plant transformation technologies used to generate transgenic plants are proprietary and under the control of a small number of companies. Any commercialisation of transgenic plants by non patent holders without appropriate royalty payments may run the risk of patent infringement. In essence, one researcher's research tool may be another researcher's end product which has a commercial and marketable value. Hence, the distinction between basic and applied research regarding the development of enabling technologies can now be difficult to define.

It is precisely because of their value that many improved research tools and processes are patented. While the majority of such patents are held by private companies, some public (e.g. NARs) and semi-public (e.g. universities) sector institutions in OECD countries also patent any enabling technologies they develop. One risk is that the holders of patents on such research tools will choose to license them on an exclusive basis rather than on a nonexclusive basis which could have a stifling effect on the research activities of other institutions or companies. Another risk is that patent holders will use a device employed by some biotechnology firms of offering licenses that impose "reach-through" royalties on sales of products that are developed in part through use of licensed research tools, even if the patented inventions are not themselves incorporated into the final products. So far, such patent holders have had limited commercial success with such Reach-Through License Agreements (RTLUs).

There have been mounting complaints from both public and private sector researchers that the owners of rights to some research tools or 'enabling technologies' are increasingly reluctant to share them for research purposes i.e. restriction of the research exemption<sup>284</sup>. In June 1997 the US National Academy of Sciences communicated its concern about broad patents being issued for particular research tools such as DNA sequences (e.g. ESTs) to the US Patent and Trademark Office<sup>285</sup>. Expressed sequence tags (ESTs) are partial DNA sequences from genes which act as unique identifiers of each individual gene. In modern genomics research 1000s of different ESTs each corresponding to a different gene can be generated rapidly to give a snapshot of the majority of genes in a particular organism. The concern regarding EST patents was triggered in 1991 when the US NIH filed its first patent application on ESTs. Despite the later withdrawal of the patent applications, the concern over access to DNA sequence information continued to generate debate, both in the US and internationally. This debate has recently resurged since the US Patent and Trademark Office on 6 October 1998 issued the first patent for an EST<sup>286</sup>. In the European Union, it is unlikely that ESTs on their own will qualify for patentability under the EU's Directive on the Legal Protection of Biotechnological Inventions (Article 5). It is also now being questioned whether EST patents are likely to generate a profit over and above the high cost of filing patents on each individual EST<sup>287</sup>.

There are now other examples of scientific concern regarding patents over useful enabling technologies. For instance, while DuPont originally made available its powerful cre-loxP recombination technology without licensing, it then changed to requiring all researchers to buy or negotiate a license. However, DuPont is now providing this technology to some public research

institutions for medical but not for agricultural research purposes<sup>288</sup>. There has also been some concern among scientists regarding proposed changes to IPRs regarding databases. In October 1996, the US National Academy of Sciences also communicated to the US Department of Commerce its concern over the potential for proposed changes to intellectual property law over databases to have a negative impact on scientific research. In some instances, such as regarding the technologies necessary to make transgenic plants, it is not known whether the proprietary technologies which are in widespread use in plant biotechnology laboratories will be enforced by their owners upon commercialisation. All of the commonly used methods for generating transgenic plants (e.g. *Agrobacterium*, gene guns etc) are currently under patent and it is feasible that licenses may have to be paid to their owners upon commercialisation of transgenic plants<sup>289</sup>. Recently, the European Science Foundation (ESF) has stated its concern that a draft EU directive proposing changes to European copyright laws regarding electronic publishing could weaken the 'fair use' arrangements for researchers<sup>290</sup>.

In the USA concern over these issues among the scientific community has led to the National Institute of Health (NIH) establishing a Working Group on Research Tools which concluded that current negotiations over intellectual property rights are burdensome and that current IPR trends pose a serious threat to biomedical research and development. The NIH Panel urged a major review of the way patent law is applied in biotechnology in order to prevent overly broad patent claims. The Panel also made a series of practical recommendations for publically funded institutions that include; (1) the use of standard Material Transfer Agreements and (2) the development and promotion of Guidelines for recipients of public funds on what terms are reasonable in licenses and MTAs, both for importing and exporting research tools ([www.nih.gov/news/research-tools/index.htm](http://www.nih.gov/news/research-tools/index.htm)).

In the agricultural arena, separate reviews have also been conducted by the US Land Grant universities and the CGIAR of the extent of reliance of their agricultural biotechnology research efforts on proprietary technology. A preliminary poll of CGIAR centres determined that in almost 50% of the cases where IARC centres were using proprietary biotechnologies, there was some uncertainty regarding whether the results of their research could be applied freely without patent infringement<sup>291</sup>.

### **6.9 Preferential access to proprietary agricultural biotechnologies?**

The cost of licensing patented biotechnologies can vary widely and is a factor in determining whether plant biotechnologies will represent a cost-benefit, over and above conventional plant breeding approaches. In some instances key proprietary biotechnology tools have been nonexclusively licensed with very low fees. This has been the case for the Cohen-Boyer patent on recombinant DNA technology<sup>292</sup>. However, the cost of licensing can often vary according to the intended use of the patented technology and some companies or patent owners will license their technologies along a continuum from:

- licenses granted only in exchange for access to other useful proprietary technologies (i.e. joint-licensing)
- full royalty fee licenses (e.g. for any organization or competitor who can pay)
- limited royalty fee licenses (e.g. public sector / private sector partnerships)
- royalty free licenses (e.g. for non-commercial crops or non commercial markets)

Somewhat paradoxically, it would appear that research which is specifically targeted at the poorest sectors or markets in society, may have access to proprietary technologies in the most preferential manner, either freely or on concessional terms. There are reasons why owners might benefit from licensing their technologies, even at no cost (demonstration of the technology, creation of demand, provoking introduction of regulations, development of partnerships). Most patent-holders have an obvious interest in achieving wider demonstration of the applicability and advantages of the

patented technology, even in countries / sectors where significant license revenues might be unlikely, especially in the early years of establishing acceptability of a technology which has been controversial<sup>293</sup>

However commercially oriented owners are unlikely to license in situations where losing control of the technology damages them, either technically or financially. Licensing is highly unlikely if the licensed technology is used to compete with the licensor in profitable markets<sup>294</sup>. However, there are little economic obstacles to free licensing of technology for research and development, provided the resulting products did not undercut the licensor in markets where there was a profit to be made<sup>295</sup>.

#### **6.10 The importance of segmented markets for preferential access.**

The ability to segment non-commercial markets from commercial markets will be crucial to negotiating preferential access to patented technologies<sup>296</sup>. This can be equated with the disaggregation of clients to identify whom the intended primary beneficiaries of the research and development focus are. Where markets or clients can be defined which do not represent a commercial threat (e.g. resource poor farmers, orphan and under-utilised crops, non export production) to the market of the company holding the patented technology, then lower to no cost licensing of patented technologies may be possible. Such market segmentation approaches could feasibly increase access to proprietary technologies for poorer sectors of society. However it will be difficult to negotiate such access if there is any possibility of proprietary technology leakage into potentially commercially lucrative markets. Economic analysis of the international trade in crop commodities suggests that research exemptions might be easier to obtain for research to improve domestically consumed crops than for internationally traded export crops. In theory, it should be easier for public sector researchers to gain access to proprietary technologies for improvement of non exported orphan crops such as plantain, cassava, yams, cowpea etc. than internationally traded crops such as maize, wheat and rice etc.<sup>297</sup>

Segmentation of target crops into export and non export crops may therefore have a major bearing on access to proprietary tools and technologies, with access being easier for non-export crops which remain below a threshold value of competition with the technology holders<sup>298</sup>. The same probably applies to varieties which exhibit broad or specific adaptation, with the latter representing less of a threat to the patent holders of 'technology leakage'. Similarly research specifically targeted at farmers or rural groups which express little to no effective demand in financial terms is likely to have easier access to proprietary technologies than research for richer commercial farmers which may represent a lucrative target market for companies.

However if markets are not segmented, proprietary technology holders can only supply their technologies at only one price, which will be more than the poorest can afford<sup>299</sup>. In this respect regulations regarding parallel imports are of importance. Parallel imports refers to cross border trade in a product without the permission of the manufacturer or publisher. Such parallel imports can take place when there exists significant price differences for the same good in different markets. For instance, there are substantial price differences for the same pharmaceutical products in different countries. The advent of electronic commerce over the Internet is likely to increase the potential for parallel importation practices. In general, parallel imports are permitted under current international agreements on intellectual property under the so called "exhaustion" or "first sale" doctrine, whereby the owner of intellectual property cannot control the resale of a legally purchased good, and hence parallel imports are legal. Under Article 6 of the WTO TRIPs agreement countries are permitted to decide for themselves how to handle the issue of parallel imports. Regional trade agreements such as NAFTA or the European Union have their own rules regarding parallel imports. If proposals for 'universal exhaustion' of patent rights under the revised TRIPs Agreement are agreed, it will be more difficult to segment markets and allow differential terms of access to proprietary technologies<sup>300</sup>. A decision of the US Supreme Court (Loyalty King,

9 March 1998) upholding universal exhaustion of copyrights, is therefore of relevance to this issue<sup>301</sup>.

The International Service for the Acquisition of Agri-Biotech Applications (ISAAA) has been instrumental in facilitating technology transfer negotiations whereby proprietary biotechnologies have been made available to non-commercial or otherwise segmented markets<sup>302</sup>. ISAAA brokered examples include the provision of Monsanto's potato virus resistance technology for incorporation by CINVESTAV into some virus susceptible Mexican potato varieties. Most of the 10 varieties (e.g. Alpha) which could be transformed with the virus resistance transgene under the agreement were varieties which are not grown in moderate climates and export of transformed potatoes to the USA was reported to be explicitly excluded from the license agreement, as was any transformation of processing varieties other than Alpha<sup>303</sup>. In essence, the proprietary technology was made available for domestic production purposes only, including for some varieties (Rosita and Nortena) that were popular among small scale farmers in Mexico. ISAAA has also facilitated the transfer of Monsanto's transgenic sweet potato virus resistance technology to Kenya on a royalty free basis. Another example of such transfer of proprietary technologies to non commercial markets has been Merck's preferential licensing of the use of Ivermectin to treat river blindness in West Africa<sup>304</sup>.

### **6.11 Compulsory licensing.**

Patent systems use rules of law that attempt the difficult task of distinguishing between inventions that would occur even without patents and inventions that require the incentive of a patent. These legal rules call for a comparison between the invention and the "prior art," or pre-existing knowledge in the field. In some instances, the granting of a partial monopoly right to a patent holder can raise concerns about the supply of the market at reasonable prices. In response to those concerns, most national patent laws provide for some overriding conditions called 'compulsory licenses'. Compulsory licenses are granted by a government for the use of particular patents, copyrighted works or other types of intellectual property for particular purposes. Such compulsory licensing can be used as an instrument to promote competition in antitrust situations. However studies have shown that some companies that are subjected to compulsory legislation change their IPR strategy to one of relying on trade secrets to protect their inventions.

The Paris Convention for the Protection of Industrial Property states that each country shall have the right to take legislative measures providing for the grant of compulsory licenses to prevent the abuses which might result from the exercise of the exclusive rights conferred by the patent, for example, failure to work the patent. For instance, Canada presently allows for the granting of such licenses on several grounds, including the failure to work on a commercial scale in Canada (Patent Act P-4, Article 66). The WTO's TRIPS Agreement also provides for compulsory licensing of patents, but imposes some restrictions regarding the circumstances under which compulsory licensing may be applied (Article 31). These include circumstances whereby the patent is considered to be practiced in an anti-competitive manner or where the patent would be practiced only for the supply of the domestic market.

The EU's Directive on Protection of Biotechnological Inventions (Article 12) also provides for compulsory cross-licensing in situations where a breeder cannot acquire or exploit a plant variety right without infringing a prior patent. In such instances, the breeder may apply for a compulsory license for non-exclusive use of the patent. If, to exploit the variety the breeder needs a license from the patent holder but has been refused one, a compulsory license must be granted, "subject to payment of an appropriate royalty". In the EU Directive a symmetrical compulsory licensing provision also applies in situations where a patent holder cannot exploit their invention without infringing a plant variety right. In such instances, the patent holder can apply for a compulsory license for non-exclusive use of the protected plant variety. These provisions are dependant on the proviso that the applicants have applied unsuccessfully to the patent/PVP holder to obtain a

contractual license and that the new variety or invention constitutes significant technical progress of considerable economic interest.

If current IPR trends continue in the agricultural biotechnology sector, it is possible that compulsory licensing may be invoked by some governments to promote broader access to key proprietary 'enabling' biotechnologies which if restricted would have a negative effect on innovation, competition and/or the 'public good'. As compulsory licensing would be a national legislative issue it would probably require the national definition of 'public good' type criteria under which compulsory licensing would be necessary. Each country will have its own priorities for compulsory licensing. In the USA and Europe there is much interest in compulsory licensing for broad biotechnology patents, research tools and enabling technologies, dependent patents, and as a potential remedy for unreasonable prices. In some developing countries there is much interest in the use of compulsory licensing to obtain lower prices for pharmaceuticals for AIDS, tropical illnesses, vaccines and other essential medicines<sup>305</sup>. It is likely that ongoing disputes concerning compulsory licensing will eventually come before the WTO's dispute resolution framework. In the broader IPR context, there are also ongoing bilateral disputes between regions and countries regarding national differences in the interpretation and enforcement of intellectual property protection. For instance, the US government maintains a Special 301 Priority Watch List of countries where it is considered that there is a lack of adequate and effective intellectual property protection<sup>306</sup>.

#### **6.12 Public domain plant biotechnologies for poorer farmers?**

In the past, publically funded plant biotechnology research has often used prior publication in scientific journals to ensure that publically funded research and technologies is placed in the public domain. This approach has resulted in the availability of some useful and quite functional plant biotechnologies which are not patented and hence often freely accessible with minimum conditionalities. The details of many of these can be found in the extensive scientific literature, where if they are published prior to a patent application, can render the technologies unpatentable.

Many public sector plant biotechnology groups have adopted the prior publication approach to ensuring that technologies remain in the public domain. For instance, a key biotechnology laboratory at ETH in Zurich, Switzerland which is performing research of relevance to developing countries has adopted this approach. Similarly, the Cassava Biotechnology Network (CBN) IPR policy is based on a preference for publication and early disclosure rather than on IPR protection. Indeed, internet publishing of data from some public sector genomics research is increasingly used to ensure that data is placed in the public domain. As a result public sector biotechnology research is generating large amounts of publically available data and information. Hundreds of publically accessible biological databases now exist on the Internet although there are indications that some public databases are now on the verge of financial collapse due to lack of public sector funding<sup>307</sup>. However such prior publication approaches no longer ensure that the published research or technology in its original or a derived form will remain in the public domain. As a result a number of additional approaches have been used or proposed for those situations where scientists wish to legally ensure more open access to publically funded research and technologies.

Material transfer agreements (MTA) which are forms of contracts that typically delimit what can be done with exchanged genetic material or technologies. MTAs are a form of contract between two or more parties whose principal clauses are often (1) restricted sharing with third parties and (2) mandating an agreement be reached if the shared materials are subsequently to be commercialized or used for specific purposes. MTAs are legal contracts and may be used for non-patented or patented materials. Material transfer agreements (MTAs) or technology transfer agreements (TTAs) are now routinely used in transactions of research materials or data between biotechnology research institutions. Depending on the objectives of the research institution's technology transfer unit it may or may not be possible to develop derived proprietary products



from the transferred material or technologies. In many instances the limits of what can and cannot be done with the transferred research materials or technologies is legally specified in considerable detail.

To prevent exclusive appropriation of publically funded research, it may be possible to require the use of a standard MTA for the transfer of any research materials or technologies immediately resulting from such funding. Another alternative to ensure that the benefits of public sector funding are widely accessible may be to specify that any patented products or technologies directly resulting from the publically funded research will have certain types of specific exemptions. For instance, this approach is used in the IPR policy of the Rockefeller Foundation which states that IPR protected materials and technology resulting from Rockefeller Foundation supported research will be available at zero royalty rates for use in developing countries. Similarly ILTAB has a policy of free access by cassava growing developing countries to relevant proprietary technology it develops regarding cassava improvement. To ensure broader access to proprietary biotechnologies developed using public funding, publically funded institutions could for instance be limited from granting exclusive rights to any technologies which are of importance to national or global food security.

Another MTA type approach to promote access to technologies that is being used in the computer software industry is called 'copylefting' and is typically promoted by an organization called the Free Software Foundation (FSF). [See: <http://gnu.bilkent.edu.tr/home.htm>]. The simplest way to make a software program free is to put it in the public domain, uncopyrighted. This allows people to freely share the program and their improvements, if they wish to. But it is still possible for people to convert the program into proprietary software, through making changes, many or few, and distributing the result as a proprietary product. In essence, people who receive the program in that modified form do not have the freedom that the original author gave them by placing the software in the public domain. The FSF aim to give all users the freedom to redistribute and change GNU/Linux systems.software. However, instead of putting GNU software in the public domain, they "copyleft" it. Copylefting requires that anyone who redistributes the software, with or without changes, must pass along the freedom to further copy and change it. To copyleft a program, first it is copyrighted; then distribution terms are added, which are a legal instrument that gives everyone the rights to use, modify, and redistribute the program's code or any program derived from it but only if the distribution terms are unchanged. In this manner, the code and the freedoms become legally inseparable. There have been suggestions that copylefting might be used in some cases to promote greater research freedom in agricultural biotechnology, especially regarding enabling technologies<sup>308</sup>. Such MTA type approaches for publically funded research represent the other end of the technology 'accessibility' spectrum compared to trade secrets or exclusive licensing of patents.

Some public sector agricultural research institutions have become involved in 'defensive' patenting of technologies they develop which may have commercial value, or might have some value in the future. For instance, the Cassava Biotechnology Network recognizes that IPRs can offer protection against misappropriation of technologies developed within the Network. CIMMYT, in conjunction with ORSTOM, has patented its research on apomixis to help ensure that access of farmers in developing countries to such apomictic technologies could be ensured<sup>309</sup>. In the absence of standardised MTAs for what can be done with research materials and technologies developed from publically funded research it is likely that defensive patenting on an institution by institution basis will become a common feature for all of those agricultural research institutions (e.g. NARs) that can afford the legal costs of filing and defending patents. Such costs may not be trivial. The CGIAR is establishing a biotechnology transfer unit with expertise in IPR law in an effort to strengthen its negotiating position with other IPR holders of useful biotechnologies<sup>310</sup>. Defensive patents may also have value as bargaining chips to gain preferential access to other proprietary technologies from other institutions or companies. A similar type of approach is pursued by

CAMBIA which makes its proprietary biotechnologies freely available to public sector scientists in developing countries but charges private sector scientists a licensing fee.

While there are still many non-proprietary biotechnologies available, the cost of access to patented technologies is likely to be a growing issue for many public sector research institutions. It is illustrative that commercially oriented research in many biotechnology companies has to now follow the research route of least cost in terms of royalty payments to other companies for enabling technologies used to develop a commercial product<sup>311</sup>. Unfortunately no public sector body has yet compiled a directory of which useful plant biotechnologies are freely accessible in the public domain, especially for scientists in developing countries. Conversely, there is a corresponding lack of publically available studies on what the current patent situation is for key enabling biotechnologies. However, in 1998 the CGIAR Panel on Proprietary Science and Technology conducted a study of proprietary science and technology within the CGIAR system<sup>312</sup>. This CGIAR study included an initial review by ISNAR of the extent of use of proprietary plant biotechnology tools in each of the IARCs<sup>313</sup>. The US Land Grant universities are conducting a review of what proprietary plant biotechnology tools are used within the Land Grant universities and under what terms. The International Society for Plant Molecular Biologists (ISPMB) is currently undertaking a comprehensive study of different patent 'families' regarding key areas of plant biotechnology in order to publically provide better information regarding the current patent situation to its members

In the plant biotechnology arena, IPRs will have an increasing influence on any institutions access to the proprietary technologies of others. Institutions with large portfolios of relevant IP will be in a better negotiating position to access the IP of others. As IPRs are in greater use by the private sector than the public sector, it is likely that public sector research institutions such as the CGIAR, NARs and individual university researchers will not be in a strong negotiating position regarding access to useful proprietary plant biotechnologies.

## 7. Conclusions

Future food security is dependent on economic access to food, rather than solely on production levels of food. Food security is therefore largely a political and economic problem rather than solely a technical problem. Nonetheless technology will have an important role to play<sup>314</sup>. Even to maintain existing levels of access to food there is a need to increase food production significantly<sup>315</sup>. By 2020 cereal production will need to increase by 41%, meat by 63% and roots and tubers by 40%. Such production increases will be necessary without any significant expansion of agricultural area.

While there is little doubt that biotechnologies will contribute to food security through increasing the aggregate supply of food, whether such a contribution will be felt by the poorest sectors of society (e.g. rural poor) will depend to some extent on the objectives towards which the modern biotechnologies are applied. Current trends in private sector investment in plant biotechnologies suggest that only commercially lucrative markets, crops and clients are likely to be served by biotechnology research for the near future. At present there is a serious dearth of public sector funding which would have criteria to ensure that more demand driven biotechnologies are developed and applied to the crops and farming systems of resource poor rural communities, in a manner which improves both their food and livelihood security. In essence, there is a definite lack of a pro-poor bias in most agricultural biotechnology research.

At the governmental level, policy instruments are currently lacking which promote or incentivate biotechnological research which could contribute to food and livelihood security in resource poor situations, especially in developing countries. Agricultural biotechnology research which is targeted specifically to segmented non-commercial markets/clients groups such as orphan or under-

utilised crops, non-export crops, or resource poor farmers may have preferential access to proprietary biotechnologies than more commercially oriented research.

To promote national food security such research exemptions for orphan or under-utilised crops, non-export crops or resource poor clients could be incorporated in national policy instruments such as laws on patents, PVP and genetic resources. At present very few biotechnology research institutions world-wide have addressed how more innovative research exemptions on their proprietary technologies might be used to promote world food or livelihood security.

Similarly, the farmers privilege to save seed for subsequent re-planting could be more broadly applied to non-commercial markets and clients, which are unlikely to be served or targeted by the private seed sector in the near future. To promote national food security the farmers privilege for orphan or under-utilised crops, non-export crops or resource poor clients could also be incorporated in national policy instruments such as laws on patents, PVP and genetic resources.

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