Brazil: Biotechnology and Agriculture to Meet the Challenges of Increased Food Production

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Advances in science, and technological breakthroughs in the understanding of the molecular biology of plants, animals, humans, and organisms, combined with the power of new information technologies, have created a new technology platform, biotechnology. Combined with enhancing technologies such as genomics, bioinformatics, and proteomics it is helping to speed up the identification of useful genes that control valuable traits, shrinking the timelines to commercialize new products across a growing number of markets, particularly in agriculture (Shimoda 1998).

The needs and expectations are great. Plant biotechnology is required to generate the knowledge to produce new plants with a higher yield capacity and with better stress resistance. The world also expects the technology to produce plants that can be cultivated with lower inputs of environmentally toxic chemicals, plants that have additional value for specific niche markets, plants that can be turned into bio-factories, plants that can better harvest and transform sunlight, and plants that will be more resistant to UV radiation (an effect of the diminishing ozone layer). The R&D agenda is extensive.

Agriculture productivity will have to be boosted by the introduction of new plants, even wild species, to produce enough food for the world population expected to reach around 9 billion by 2050 (U.N. Population Division-Department of Economic and Social Affairs 1998). The time frame is short, but with biotechnological tools these traits will not sound so utopian in 10 years (van Montagu 1998).

However feasible it may sound, and knowing that humans have cross-pollinated plants and cross-bred animals for centuries to suit their needs, recent technological advances in molecular biology have provoked reactions from different parts of society, ranging from optimism to cautiousness to moral outrage (Background, *Sustainable Development*, 30(1), September 1999). Throughout the world biotechnology managers are involved in discussing the pros and cons with the press, politicians, policymakers, consumer representatives, and NGOs. The dialogue must improve in the scientific, social, cultural, and ethical areas to resolve uncertainties and eventually reach consensus.

Challenges

Brazil still depends heavily on agriculture, and a continuing supply of new technologies to increase its competitive advantage in the region and in export markets. Increased exports mean increased benefits to the general population. Poverty alleviation programs are always dependent on how well the country can manage its economy, including support for R&D.

Agricultural biotechnology promises to increase yields and market value for farmers. It promises to produce plants that will grow in harsh environments with less need for chemical input, therefore protecting the environment, to produce new cultivars with increased nutritional composition, and to reduce postharvest storage losses. The greatest research challenge, and maybe one that has not yet been seriously tackled by most of those holding the necessary knowledge, is the transfer of these new characteristics to social crops, to staple crops that will feed the hungry populations. We also need to simplify the use of traits, making them also available to the small-scale farmers in developing countries. The Rice Biotechnology Program financed by the Rockefeller Foundation is an excellent example of this approach (Conway 1999).

Intellectual Property Rights

The intellectual property rights (IPR) challenge is directly linked to the application of biotechnology tools outside the corporate world, where companies can afford to acquire rights, make alliances, or develop innovations on their own. Because the patent system has undergone a process of regulatory globalization and harmonization, and TRIPs has obliged most developing countries to move to some level of recognition of IPRs in agriculture, problems that were not common to research managers regarding IPR are now causing concern. The scope of patentable subject matter has also been given an inclusive interpretation, and restrictions on patentability have been narrowly interpreted enabling applicants for biotechnology patents to overcome existing bars (Drahos 1999).

Most of the basic tools used in many biotechnology projects in developing countries (promoters, markers, transformation processes (biolistics, *Agrobacterium*), broad scope enabling techniques) have been patented by their inventors in industrial countries, and are in the hands of a few large life sciences companies. Some of these R&D projects in developing countries are nearing completion. Initial material transfer agreements (MTAs) covered only research applications and laboratories, and some companies are now facing difficult negotiations to allow licensing the right of commercialization of their transgenic products (see Cohen, This volume)

Regulatory Matters

The regulatory/risk assessment challenge encompasses (a) food and environmental safety concerns that can exist anyway when dealing with a new technology; (b) financing of these extra phases of research; (c) ethical and religious concerns; (d) public awareness; (e) right of choice by consumers; (f) adequate labeling; and (g) the fact that genetic engineering has turned into a hot political issue for opposition groups to attack globalization, competition markets, technological substitution, monopolies/oligopolies of knowledge and of seeds by transnationals, and other concerns.

Despite efforts in Brazil since 1995 to develop biosafety legislation, and and to establish a regulatory infrastructure to deal with the arrival of transgenic crops in the market in an organized way, there is still a battle over soybean.

The commercial introduction of Monsanto's RR-soybean has coincided with strong EU refusal of transgenic foods since late 1998, and with the recent (1998-99) and aggressive acquisition of commodity seed companies, operated with national capital, by the same transnational companies that are being accused of building a potential global monopoly in agricultural biotechnology. The parallel approach of European supermarket chains, with promises of premium prices for GIO-free soybean of certified origin, has inflamed local politicians and farmers, who were looking for new export dollars. This has also given opposition groups a special tool to fight against the technology and against Monsanto and other biotechnology companies.

A critical point in the growing confusion was reached when Greenpeace and the Brazilian consumer's institute (IDEC) filed an injunction against Monsanto and against the National Biosafety Committee (CTNBio). They asked a judge to invalidate the approval for commercialization already given by CTNBio, because RR-soybean could be harmful to the environment, and because more tests were needed. Higher courts will review the appeal case in 2000, so no officially approved RR-seeds were planted in October-November 1999. News reports in late 1999 suggested that more than 2 million hectares of RR-soybean were being planted with illegal seeds brought from Argentina, possibly resulting in the appearance of new diseases not common in Brazilian fields. Five thousand identification test kits were acquired by the state government of Rio Grande do Sul, to guarantee, for commercial reasons, that the State is a GIO-free zone. According to the Law, identified GIO fields should be burned and farmers jailed. This may happen, unfortunately, to serve political ends and not because the RR-soybean is harmful to the environment. Public opinion is not well informed, with the media publishing inaccurate comments and creating growing confusion. Can this situation be corrected? The answer is yes, but players at all levels must help. Scientists must enter the the public dialogue instead of debating among themselves in scientific journals (Losey, Rayor, and Carter 1999; Horton 1999; Ewen and Pusztai 1999; Millstone, Brunner, and Mayer 1999; Kearns and Mayers 1999; Burke 1999). Dissemination of information based on trusted sources must be maximized for the benefit of society, showing clearly potential benefits, potential risks, and what is being done to increase knowledge in these areas.

Opportunities and Constraints

As highlighted in the online Nature Supplement "Science in Latin America." (*www.nature.com/server-java/Propub/nature/398A001A0.frameset?context=search*), the region enjoys a unique oppor-

Box 1 Genomics for Sugarcane Improvement

SUCESt - The Sugar Cane EST Project

Sugarcane is one of the world's most important crop plants and is cultivated in tropical and subtropical areas in more than 80 countries. In 1995, 1.2 x10^9 metric tons of sugarcane were produced on 18 million hectares and was used mainly for sugar consumption or as an energy source (ethanol and electricity). Brazil is responsible for 25 percent of the world's production, half of which comes from São Paulo State.

The cultivated sugarcane varieties are the result of interespecific hybridization involving *Saccharum officinarum*, *S. barberi*, *S. sinense* and the wild species *S. spontaneum* and *S. robustum*. It is thought that *S. officinarum* was originally selected by humans in Papua New Guinea, perhaps from *S. robustum* germplasm. Because of its multispecies origin, sugarcane is thought to have one of the most complex plant genomes carrying variable chromosome numbers (generally 2n = 70-120) with a commensurately large DNA content. This complexity complicates the application of conventional genetics and breeding techniques.

At present, sugarcane genome projects are being conducted in Australia, South Africa and the United States. In Australia and the United States, the projects are mainly focused on mapping and application of DNA markers for sugarcane genetics and breeding, whereas South Africa is conducting a small EST project. The molecular information developed to date for sugarcane is minimal, however, compared to the information necessary to identify and characterize loci encoding traits of physiological and agronomic importance. Genetic systems regulating differentiation and development or controlling important traits, such as pest resistance, amino acid and sugar metabolism, among many others, could be identified in a large scale EST sequencing project. The main goal of SUCEST is to undertake a large-scale EST program by sequencing random clones from cDNA libraries prepared from several sugarcane tissues (calli, root, stalk, etiolated leaves, flowers, and developing seed). The aim of the project is to identify around 50,000 sugarcane genes. The project will be considered finished when this goal is reached or when 300,000 reads are deposited. The information provided by SUCEST can be exploited by the research community in studies aimed to use the sugarcane genes as a source of markers for agriculturally significant characteristics. They could also provide a molecular basis for studies of plant growth and development that could be further used to solve questions in plant physiology, biochemistry, cell biology, pathology, and ultimately plant breeding. The cDNA clones, whose nucleotide sequence has been determined, will be used to complement the sugarcane molecular map and fabricate microarrays of immobilized DNAs that will be used to survey expression of each gene in different sugarcane tissues under different environmental conditions.

The project is part of the ONSA - Organization for Nucleotide Sequencing and Analysis Net, co-financed by the State Foundation FAPESP. It plans to provide contemporary training in basic molecular biology to graduate students needed to develop biotechnology and the "genome culture" in Brazil. It represents an opportunity for research groups not familiar with basic molecular biology to get hands-on training in these techniques for later incorporation into their own research programs. The sugarcane EST project has formed a network with 38 research groups located in many public and private Universities with the participation and support of Coopersucar, the major private Sugar Cane Institute in Brazil. The program is expected to be completed in 2004.

The same ONSA program is also coordinating the genome sequencing of *Xanthomonas campestris citri*, esponsible for citrus canker and of *Xylella fastidiosa*, responsible for the citrus variegated chlorosis (CVC). The group expects to start the citrus genome in two years.

tunity to win a more prominent place in the world of science. In Brazil, many lines of research and development are already benefiting from the application of biotechnology tools such as marker-assisted plant and animal breeding, genomic mapping of several species, embryo transfer applied to different animal species, genetic resources characterization and conservation, and transgenic products. Examples in genomics and transgenics are given in boxes 1 and 2.

The same Nature review article has identified, among others, three difficulties that relate to this forum: the lack of regional integration in science, scientists' reluctant acceptance of the free market, and a failure to acknowledge the importance of IPR in modern research. Biotechnology applications are teaching new lessons and adding new challenges in all three aspects.

Recognizing IPR is a behavioral change that will come as a consequence of understanding the system. Solutions, however, must accompany this acceptance. It is already far from easy to develop transgenic products. It is extremely difficult and expensive to negotiate license agreements (only possible in this case because the project is developed with Cornell University) with nine different companies to commercialize a papaya cultivar that carries resistance to a virus disease. Alliances and joint projects with CGIAR centers, U.S. universities, and other centers of excellence within the region could add strength to negotiations.

The integration of markets has made GM seeds and GM processed food hit Brazil faster than the internal research organization could deploy it. Consumers are in a confusing situation, because they receive no warning and are badly advised by conflicting information in the press and on the internet. Scientists are only beginning to learn how to deal with the constant questions about the safety of their work. The fact is that, with the exception of very well known traits already tested in the United States and consumed by millions during the last four years (for example, the RR-soybean), more research is needed to clarify basic questions in different environments. Tropical agriculture is very different from the temperate fields where most products have been tested. Protocols are required for field trials, risk assessment for environmental and food safety, registration of products, and public acceptance. The need is urgent, because these are constraints that will intensify as GIOs become an integral part of the research agenda in the region.

Role for the CGIAR Centers

Apart from well trained scientists two items are always part of the recipe for a successful research project: funds and tools, both tangible and intangible, such as IPR. We must now educate our politicians and the public, and involve lawyers in all future agreements involving research in biotechnology.

We must be careful not to infringe on the rights of others when developing new biotechnological projects in developing countries, where minimum TRIPs regulations are now in place. This also applies when a new transgenic plant or animal is

Box 2 Transgenic Plants – Some Examples from Brazil

Brazilian Corn to Produce Growth Hormone – Developed by the Molecular Biology and Genetic Engineering Center of the State University of Campinas (Unicamp) and the Chemistry Institute of the University of São Paulo (USP), these plants are ready to produce 250 grams of the hormone per ton of seeds – enough to treat hundreds of patients for months. The hormone is identical to the human form , and therefore better than the bacterial source that has one extra amino acid. It proved to be cheaper to produce and extract.

Papaya Resistant to Brazilian Strain of Ring Spot Virus – Developed in collaboration with Cornell University, these plants have been tested in greenhouses in Geneva, N.Y., and have now been transferred to Embrapa in Brasilia for field tests. In two years they should be ready for large-scale tests and should be as successful as their cousins being planted in Hawaii. The technology will bring the opportunity of papaya cultivation back to small farmers in areas where the crop has been decimated by virus disease. However, if the antibiotic marker is proven to be a real problem under Brazilian conditions, then another four to five years will be necessary to reconstruct the material.

Common Beans Resistant to Golden Mosaic Virus – Developed by Embrapa - Rice and Beans Center -these plants are undergoing greenhouse tests after a long research period, due to the difficulty of adapting existing technology to the specific virus strain. Researchers expect to complete the cross-breeding of the characteristic into commercial lines in two to three years.

going from the laboratory to the marketplace. Depending on the case, a complete inventory of the "freedom to operate" might be complicated and costly and has not been in the list of concerns of scientists until now. There are, of course, genes in the public domain but most of the well characterized traits and processes are patented in industrial countries and with TRIPs in place, there might be a chance that the patents would stand in developing countries. Access to this information is urgent.

CGIAR centers could develop, for the benefit of developing countries, more comprehensive partnerships with the private sector, with U.S. universities and other advanced research institutions (Serageldin 1999). This would give developing countries access to a minimum intellectual property platform that would guarantee that new products developed by their research institutes would reach farmers and consumers.

Another option would be to validate new discoveries, new methodologies (for example, those used to modify salinity resistance or control fruit maturation), and negotiate nonexclusive licenses for different applications, with regional market segmentation.

An interesting action that has been suggested many times would be for the CGIAR centers to act on the training of researchers, not only in biotechnology skills but also on IP management and policy development. Challenges were identified and options for solutions were proposed at a recent regional meeting in Costa Rica (September 1999) (see Cohen, This Volume). Some suggestions (Sampaio 1998) included:

- Development of a national competence in IPR, through human resource training
- Dissemination of IPR information and procedures through workshops, short courses, and seminars
- Dissemination of knowledge, and use of IPR systems as an important tool for technological development
- Training in negotiation skills, MTAs, and contract design (case studies)
- Provision by the CGIAR of legal support on the license and use of proprietary technologies and on contract management
- Financing of in-house development of biotechnological tools to enhance bargaining power when accessing IP in the private sector
- Provision by donors and CGIAR centers of licenses for enabling technologies, acquired from the owners in the private or academic sectors in industrial countries.

Helping developing countries resolve the biosafety and risk assessment issues is a major task for CGIAR centers and development agencies. Much more detailed research will be needed to change the present lack of public acceptance. This seems to be a fine example for regional collaboration. CGIAR centers could use their credibility, choose case studies, and issue a detailed manual to guide NAROs. This could also cover use of data to inform the public to ease their concerns about the use of new technologies for genetic improvement.

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