Agricultural Biotechnology and the Poor

An International Conference on Biotechnology

G.J. Persley and M. M. Lantin, *Editors*

Convened by
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Foreword

The eradication of poverty and hunger in developing countries represents a major challenge that is dependent on agricultural productivity and the discerning application of science and technology to ensure the health of people and environments globally. To explore these issues, an international conference focused on biotechnology and its potential impact on agriculture in developing countries was held at the World Bank in Washington, D.C., on October 21-22, 1999. The conference was convened by the Consultative Group on International Agricultural Research (CGIAR) and the U.S. National Academy of Sciences (NAS), and was cosponsored by: Biotechnology Industry Organization, Food and Agriculture Organization, Global Forum on Agricultural Research, International Council for Science, International Fund for Agricultural Development, Third World Academy of Sciences, UN Development Programme, UN Educational, Scientific and Cultural Organization, UN Environment Programme, UN Industrial Development Organization, and the Union of Concerned Scientists. We welcome the partnership with such a distinguished group of organizations in addressing these challenging issues of science and policy.

A steering committee comprised of Andrew Bennett, Department for International Development, U.K., Charlotte Kirk Baer, Board on Agriculture and Natural Resources, The National Academies, Joel E. Cohen, Rockefeller University, Nina Fedoroff, Pennsylvania State University, Timothy Reeves, Centro Internacional de Mejoramiento de Maiz y Trigo, and Donald Winkelmann, CGIAR Technical Advisory Committee, worked successfully to develop the conference program. The program was structured to draw from expert presentations as a basis for discussion, as well as sessions that were designed to encourage interaction and exchange of ideas on the challenges, opportunities, and constraints of biotechnology and its impact in developing countries.

The conference responded to the pressing need for an open, inclusive, and participatory debate on potential benefits and risks of biotechnology, grounded in scientific evidence, and concerned with the common good. Science-based discussions such as this one are critical in guiding the strategies of the international agricultural research centers of the CGIAR as they mobilize, in collaboration with their partners, cutting-edge science to combat poverty, hunger, and environmental degradation in the world's developing regions.

Over 400 people attended the conference, which was global in scope. Participants included representatives from the national research organizations of developing and industrial countries, nongovernmental and community-based organizations, the private sector, senior policymakers, academics, scientists, international agricultural researchers, development communicators, and media. Diverse technological, environmental, public health, economic, ethical, and social viewpoints were actively sought so that linkages could be explored. Our hope was that the elements of future activities could emerge that are directed specificallly toward the needs of small farmers and consumers in developing countries.

In his welcoming remarks, E. William Colglazier, Executive Officer of the U.S. National Academy of Sciences, outlined the key objectives of the conference: to broaden awareness of developing countries' views on issues related to biotechnology, and to contribute to a science-based understanding of the issues and public concerns and how these might be addressed. NAS member R. James Cook provided closing remarks including his perspectives and summary of the conference discussions. CGIAR co-convenor representative and World Bank Rural Development Department Director Alexander McCalla spoke on behalf of the CGIAR. Their insights provided a valuable synopsis of the event.

The coming together of our two organizations to convene this conference, in partnership with a distinguished and varied group of cosponsors, has shown the value of partnership when attempting to identify the challenges and opportunities that modern science presents through the tools of biotechnology. We hope that this volume will serve as a cornerstone for building on our current knowledge, as we head into the new century with a renewed determination to ensure food security, protect the environment, and reduce poverty in all developing countries.

Ismail Serageldin
Vice President, World Bank and
Chair, CGIAR

Bruce M. Alberts
President
U.S. National Academy of Sciences

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The Consultative Group on International Agricultural Research and the U.S. National Academy of Sciences wish to thank the staff members in both organizations, and those in the World Bank, for their contribution to the success of this conference, and to the publication of this book.

We are particularly indebted to Nina Fedoroff and Joel Cohen who worked with us in developing the conceptual framework of the conference. We are grateful to the distinguished speakers, session chairs, discussants, rapporteurs, resource persons, and all of the participants who came from around the world. Their input has ensured a high level of discourse and has helped to provide useful guidance on complex issues. The authors of individual papers have also assisted greatly by their additional contributions for this publication.

We thank also Manuel Lantin of the CGIAR Secretariat who served as Conference Coordinator and Gabrielle Persley of the World Bank, the Conference Rapporteur. Their joint efforts have resulted in this informative and timely publication.

We are especially grateful to the staff of the conference secretariat who handled the complex logistics for the conference, particularly Frona Hall, Danielle Lucca, Feroza F. Vatcha, and Waltraud Wightman. Shirley Geer, CGIAR Senior Information Officer, provided valuable assistance in finalizing this volume. Staci Daddona designed the cover and organized the printing, and Gaudencio Dizon provided skilled and cheerful assistance with the desktopping of this volume.

Agricultural Biotechnology and the Poor: Promethean Science

G. J. Persley

Prometheus, according to Greek mythology, was a Titan, responsible for introducing fire to humans, a remarkable innovation at the time, but having benefits and risks, depending on its use. *Promethean* has since come to mean *daringly original and creative.*

Science is an elegant way of getting at the truth, according to science writer Rick Weiss. It should follow then that molecular biology and other tools of modern biotechnology add elegance and precision to the pursuit of solutions to thwart poverty, malnutrition and food insecurity in too many countries around the world. In agriculture these enemies are manifest as pests, diseases, drought and other biotic and abiotic stresses that limit the productivity of plants and animals.

But not all appreciate the elegance of science in the pursuit of truth. The current debate about the potential utility of modern biotechnology for food and agriculture presents a challenge for modern science to contribute to the solution of human problems. This debate is currently focused on the initial applications of modern biotechnology in industrial country agriculture and its potential risks to human health and the environment. It is also intertwined with other often understated societal concerns such as food safety, animal welfare, industrialized agriculture, and the global role of large private-sector corporations.

A debate based on the best available empirical evidence on the relevance of modern science for poor people in developing countries is urgently needed. Its purpose would be to identify the most appropriate ways that molecular biology-based research might contribute to the solution of poor people's problems. These problems and the socioeconomic context in which they occur are so different from the problems and context of the countries where most of the biotechnology debate currently takes place that the positions and conclusions from the current debate are largely irrelevant for poor farmers and poor consumers in developing countries. Despite this, many of the arguments in the current debate are extrapolated to conclusions about the potential utility of biotechnology for poor countries and poor people. There is an urgent need for a more focused debate on the role of modern agricultural biotechnology in developing countries, a debate that should and is being led by people from developing countries themselves (Pinstrup-Andersen and Cohen 2000).

Because land and water for agriculture are diminishing resources, there is no option but to produce more food and other agricultural commodities from less arable land and irrigation water. The need for more food has to be met through higher yields per units of land, water, energy and time. As Swaminathan (2000) says, "*we need to examine how science can be mobilized to raise further the biological productivity ceiling without associated ecological harm. Scientific progress on the farms, as an ever-green revolution, must emphasize that the productivity advance is sustainable over time since it is rooted in the principles of ecology, eco-*

nomics, social and gender equity, and employment generation."

Current Status of Agricultural Biotechnology

The Gene Revolution

Mendel's laws of genetics were rediscovered in 1900. Mendel had published his work on inheritance patterns in pea in 1865, but it took 35 years for others to grasp their significance. Since 1900, we have witnessed steady progress in our understanding of the genetic makeup of all living organisms ranging from microbes to humans. A major step in human control over genetic traits was taken in the 1920s when Muller and Stadler discovered that radiation can induce mutations in animals and plants.

In the 1930s and 1940s, several new methods of chromosome and gene manipulation were discovered, such as the use of colchicine to achieve a doubling in chromosome number, commercial exploitation of hybrid vigor in maize and other crops, use of chemicals such as nitrogen mustard and ethyl methane sulphonate to induce mutations, and techniques such as tissue culture and embryo rescue to make viable hybrids from distantly related species. The double helix structure of DNA (deoxyribonucleic acid), the chemical substance of heredity, was discovered in 1953 by James Watson and Francis Crick. This triggered explosive progress in every field of genetics. As we head into the 21st century, we see a rapid transition from Mendelian to molecular genetic applications in agriculture, medicine, and industry.

This brief capsule of genetic progress from 1900 to 1999 (Swaminathan 2000) stresses that knowledge and discovery represent a continuum, with each generation taking our understanding of the complex web of life to a higher level. It would therefore be a mistake to worship or discard experimental tools or scientific innovations because they are either old or new. Just as it took 35 years for biologists to understand fully the significance of Mendel's work, it may take a couple of decades more to understand fully the benefits and risks associated with new genetically improved organisms.

The 1990s have seen dramatic advances in our understanding of how biological organisms function at the molecular level, as well as in our ability to analyze, understand, and manipulate DNA molecules, the biological material from which the genes in all higher organisms are made. The entire process has been accelerated by the Human Genome Project, which has invested substantial public and private resources into the development of new technologies to work with human genes. The same technologies are directly applicable to other organisms, including plants and animals. Thus, the new scientific discipline of *genomics* has arisen, which has contributed to powerful new approaches to identify the functions of genes and their application in agriculture and medicine. These new discoveries and their commercial application have helped to promote the biotechnology industry, mainly in North America and Europe.

Several large corporations in Europe and the United States have made major investments to adapt these technologies to produce improved plant varieties of agricultural importance for large-scale commercial agriculture. The same technologies have equally important potential applications to address food security and poverty of people in developing countries (see Box 1).

Agricultural Biotechnology in Developing Countries

The current use of modern biotechnology in Asia, Latin America and the Caribbean, sub- Saharan Africa, and West Asia/North Africa was reviewed at an international conference in October 1999 in Washington D.C. Senior policymakers from these regions led the discussion by addressing the following questions:

- What are the challenges?
- What are the opportunities for deploying biotechnological approaches?
- What are the constraints to using these approaches?
- How can the international agricultural research centers (IARCs) supported by the Consultative Group on International Agricultural Research (CGIAR) further assist?

Asia/Pacific

The current status of agricultural biotechnology in China, India, the Philippines, and Thailand was

Box 1 Definitions of Biotechnology and Its Component Technologies

Biotechnology is any technique that uses a living organism or substances from those organisms to make or modify a product, improve plants or animals or develop microorganisms for specific uses. The key components of modern biotechnology are:

- *Genomics*: the molecular characterization of all species.
- *Bioinformatics:* the assembly of data from genomic analysis into accessible forms.
- *Transformation*: the introduction of one or more genes conferring potentially useful traits into plants, livestock, fish and tree species.
- *Molecular breeding*: the identification and evaluation of desirable traits in breeding programs by the use of marker assisted selection, for plants, trees, animals and fish.
- *Diagnostics:* the use of molecular characterization to provide more accurate and rapid identification of pathogens and other organisms.
- *Vaccine technology:* the use of modern immunology to develop recombinant DNA vaccines for improving control against lethal diseases.

Source: Persley and Doyle 1999.

reviewed at the conference. All are committed to the use of modern biotechnology in agriculture, and are investing significant human and financial resources to this policy and have done so over the past decade.

China sees the greatest challenge as the use of biotechnology to increase food production and improve product quality in an environmentally sustainable manner. China has moved quickly to adopt new technologies. Over 103 genes have been evaluated for improving traits in 47 plant species. The crops include rice, wheat, corn, cotton, tomato, pepper, potato, cucumber, papaya, and tobacco. A variety of traits were targeted for improvement including disease resistance, insect resistance, herbicide resistance, and quality improvement. Approximately 50 genetically improved organisms (GIOs) have been approved for commercial production, environmental release or small-scale field testing in China. In a few cases, new genetically improved varieties have been approved for large-scale commercial production. These are being grown commercially on approximately 1 million hectares of land in China in 1999. It is expected that the area planted will increase rapidly in the next few years (Zhang 2000).

India has allocated large public resources toward infrastructure and human resources development in biotechnology. Current efforts are toward applications in improving agricultural productivity; bioremediation in the environment; medical biotechnology for the production of new vaccines, diagnostics and drugs; industrial biotechnology; and bioinformatics (Sharma 2000). Research and development (R&D) priorities in agriculture include new regeneration protocols for rapid multiplication of citrus, coffee, mangrove, vanilla and cardamom. Yield of cardamom has increased 40 percent using tissue-cultured plants.

Thailand is focusing on the applications of biotechnology to traditional foods, fruits and export commodities. R&D priorities are to raise production and cut costs by using new biotechnology on crops such as rice, sugarcane, rubber, durian, and orchids. An early success in Thailand has been in the application of biotechnology to develop new molecular diagnostics for the diagnosis and control of virus diseases in shrimps. These diseases cost the shrimp export industry over US$500 million in lost production in 1996 (Morakot 2000).

The Philippines began its biotechnology programs in 1980 with the creation of the National Institutes of Molecular Biology and Biotechnology, with a focus on agricultural biotechnology. In 1997, the Agriculture Fisheries Modernization Act recognized biotechnology as a major strategy to increase agricultural productivity. The Act will provide a budget for agricultural biotechnology of almost US$20 million annually for the next 7 years (4 percent of the total R&D budget), an increase from US$1 million per year. In 1998, five high level biotechnology research projects were funded by government: Development of new varieties of banana resistant to banana bunchy top virus and papaya resistant to ringspot virus; delayed ripening of papaya and mango; insect-resistant corn; marker-assisted breeding in coconut; and coconut with high lauric acid content. Public concerns have been vocal in the Philippines and this is constraining the commercial use of modern biotechnology in agriculture (de la Cruz 2000).

All four countries have regulatory systems in place at the national and institutional level to govern R&D programs and commercial developments where appropriate. Intellectual property management was considered to be a difficult issue for all four countries.

Latin America and the Caribbean

Agricultural biotechnology was reviewed in Brazil, Costa Rica, and Mexico, as examples of the diversity of uses and views of biotechnology across the region. The main challenges identified for the region were: management of intellectual property in relation to major and minor crops; assessment of several research options, not only a molecular approach, in assessing how best to tackle problems and challenges to improve agricultural productivity; identification of beneficiaries; prioritization of work on favored and/or marginal areas; use of GIOs as indicators of environmental damage; and need to monitor the behavior of GIOs in the environment after release. The ecological research effort for monitoring GIOs is needed to satisfy public concerns about the behavior of GIOs in the environment, and needs to focus on the key questions of : What are the specific concerns? How to do it? Who will do it? Who will pay for it?

In *Brazil*, many lines of research and development are benefiting from the application of biotechnology tools such as marker-assisted plant and animal breeding, genomic mapping of several species including sugarcane, embryo transfer applied to different animal species, genetic resources characterization and conservation, and use of genetic improvement to introduce new traits, such as papaya resistant to papaya ring spot virus and beans resistant to golden mosaic virus. The issues of field testing of genetically improved plants need to be addressed. Tropical agriculture is very different from the temperate fields where most of the new genetically improved products have been tested. Protocols are required for field trials, risk assessment (environmental and food safety), registration of products, and public acceptance. The need is urgent, because these are constraints that will intensify as new genetically improved organisms become an integral part of the research agenda in the region (Sampaio 2000).

Mexico was one of the first developing countries to begin the evaluation of genetically improved plants in the field, commencing in 1988, with trials of plants genetically improved for insect resistance (corn and cotton), virus resistance (potato), and delayed ripening (tomato) (Alvarez-Morales 2000). Some of these materials such as the virus-resistant potato are now being grown by Mexican farmers. There is a current debate in Mexico as to the desirability of testing genetically improved corn in Mexico, as it is the center of origin of the crop and wild relatives occur. Regulatory officials in Mexico are interested in continuing field trials with such new varieties if there is a clear benefit to Mexican agriculture, such as new varieties of corn with tolerance to aluminum. This phenotype has great potential to reclaim for agriculture tropical acid soils that were lost due to high levels of soluble aluminum ions (Herrera-Estrella 1999). Future field evaluations of corn are likely to be accompanied by a scientific monitoring program after release.

In *Costa Rica*, there is particular interest in using the tools of biotechnology to characterize and conserve biodiversity (Sittenfield and others 2000). Costa Rican institutions have developed some innovative partnerships for bioprospecting, which could serve as a model for other countries. In agriculture, pesticide use has increased three fold between 1993 and 1996, on crops such as banana, coffee, and rice. Much of this is used to control banana diseases where the excess pesticide use is leading to poisoning of field workers and contamination of land, water, and animals. Biotechnology-based solutions are urgently needed to replace chemical control of banana diseases. New virus resistance is being introduced into local rice varieties.

Sub-Saharan Africa

The current status of policy and programs using biotechnology in *Kenya, South Africa, and Zimbabwe* were reviewed and were complemented by interventions on the situation in other African countries. The major challenge identified was the persistent poor performance of agriculture in Africa, which is leading to a food and a poverty crisis. The issues concerning many countries are how to improve food security, increase productivity, conserve biodiversity, reduce pest management costs, deal with increasing urban migration,

Box 2 Molecular Breeding: Biotechnology at Work for Rice

Marker-aided selection (MAS) is the application of molecular landmarks-usually DNA markers near target genes-to assist the accumulation of desirable genes in plant varieties. There are many reasons why molecular markers are useful in plant breeding. The improvement of disease resistance in rice is a good example.

Bacterial blight is a widespread disease in irrigated rice-growing areas. In the pre- green revolution period, it caused widespread yield loss. The incorporation of host plant resistance through conventional breeding has been the most economical means of control, and has eliminated the need for pesticides. There are now over 20 genes available for use in rice improvement, but not all of these genes are equally effective in different production environments. The pest eventually overcomes the resistant gene. Using conventional approaches the plant breeder must be continually adding and changing genes just to maintain the same level of resistance. Breeding effort spent in “maintenance” is a potential loss of gains in other traits.

A more sustainable system can be developed by deploying more than one resistance gene at the same time. The challenge is to find the right combination of genes and put them into varieties most suitable for local production. When two or more genes are incorporated into the variety it is called “gene pyramiding.” Up to four genes for bacterial resistance have been pyramided in rice, and there is evidence that collectively they are more effective than would be ascribed to their additive effects. Because each gene may mask the presence of another gene, it is difficulty to pyramid more than two genes by conventional breeding and selection; but it can be done with molecular markers.

Over the past several years, scientists at the International Rice Research Institute (IRRI) and its national partners in the Asian Rice Biotechnology Network (ARBN) have applied DNA marker technology to address the bacterial blight problem. First, DNA markers are used to tag nearly all the bacterial blight resistance genes in available genetic stocks. Second, DNA markers are used to describe the composition of pathogen populations unique to each region. This parallel analysis of the host and the pathogen has enabled scientists to determine the right combination of genes to use in each locality.

In Asia, a number of resistance genes (Xa4, xa5, Xa7, xa13, Xa21), all with molecular tags, have been introduced in various combinations into locally adapted varieties. For example, in the Punjab of India, the popular variety PR106 carrying two-gene and three-gene combinations have been produced and are being evaluated by farmers. Similar gene pyramiding work is being conducted in eastern India but using different local varieties. In Indonesia and the Philippines, single- and two-gene pyramids for bacterial blight resistance have been produced in variety IR64. These lines are in the final stage of field evaluation before release to farmers.

ARBN is promoting sharing of these elite lines and gene pyramids from different countries amongst other countries in Asia so that the useful MAS products can be rapidly disseminated through collaborative field testing across the region.

Marker-aided selection has delivered some of the promises of biotechnology, and there are other examples of use in rice. The impact of MAS will continue to be significant particularly in an increasingly intellectual property(IP)-conscious environment. Marker technology is based on knowledge of endogenous DNA sequences; this has important practical implications as the rice genome will be completely sequenced by an international effort, led by the Rice Genome Research Program of Tsukuba, Japan. As long as there is a public commitment to maintain a rice genome sequence in the public domain, useful genes for MAS should be readily accessible to national and international rice breeding programs. Thus, because of their relative simplicity, easy integration into conventional breeding, and minimal background intellectual property, DNA marker technology and MAS are expected to be strong driving forces in crop improvement in the future.

Ken Fischer, Hei Leung and Gurdev Khush
(IRRI, Philippines)

and reduce poverty. Specific issues related to biotechnology are how to develop institutional capacity for risk assessment and management, to access information on developments in biotechnology elsewhere that may have application in Africa, and to develop the necessary human resources and infrastructure.

Several success stories are coming out of Africa, where biotechnological approaches have contributed to the solution of specific problems, reduced the cost of pest control, and created new employment opportunities in towns and villages. They include the wide adoption by farmers of rapid multiplication of disease-free banana plantlets in Kenya; use of new genetically improved pest-resistant cotton varieties by small farmers in South Africa; and use of new vaccines against animal diseases in Kenya and Zimbabwe

(Chetsanga 2000; Ndiritu 2000, Njobe-Mbuli 2000).

Some of the problems and constraints identified include: lack of awareness of the benefits and risks associated with modern biotechnology; lack of capacity in some countries to deal with assessing these benefits and risks and in regulating the use of modern biotechnology; high investment costs associated with biotechnological innovations; and increasing concerns being expressed in the media about the potential negative impacts of biotechnology and the need for public awareness of the issues.

In sub-Saharan Africa the need is both to improve awareness and institutional capacity to develop biotechnology-based products and, perhaps as importantly, for African scientists and policymakers to articulate an African scientific agenda and to participate in critical global debates on trade, economic growth, and the role of science (Njobe-Mbuli 2000).

West Asia and North Africa

Country status papers were presented for *Egypt, Iran,* and *Jordan* as examples from the region.

One of the major targets for biotechnology in Egypt is the production of transgenic plants conferring resistance to biotic and abiotic stresses, which are major agricultural problems leading to serious yield losses in many economically important crops in Egypt. AGERI (Agricultural Genetic Engineering Research Institute) was established in 1990 with the aim of mobilizing the most recent technologies available worldwide to address problems facing agricultural development (Madkour 2000).

The challenges identified were the need to increase agricultural productivity while preserving the fragile natural resource base in the region, and the need to conserve the rich indigenous plant and animal species. The opportunities include: using modern biotechnology to develop crop varieties tolerant to biotic and abiotic stresses, especially drought and salt tolerance; improving the nutritional quality of agricultural commodities; producing biofertilizers and biopesticides; and improving the availability of soil nutrients.

The main constraints in the region are inadequate financial resources, lack of qualified personnel, poor infrastructure, and insufficient regional and international collaboration. There is also a lack of clear strategies, policies, and regulatory frameworks to guide the use of modern biotechnology in most countries of the region.

Common Themes

The outcomes of all the regional reviews summarized above stressed the importance of making safe and effective use of the new developments in modern biotechnology to solve agricultural problems. The application of biotechnological advances could help countries deal with the major challenges of feeding expanding populations from the existing land and water resources, and also to alleviate poverty by stimulating the growth of bioscience-based industries, with an associated growth in employment. Developing countries that are pursuing the safe and effective use of modern biotechnology recognized the need to have in place effective regulatory systems at the national and institutional levels, compatible with international best practice. There was also a widely held view that intellectual property management is a major issue, in terms of enabling access to other people's technology and in stimulating rewarding local innovation. Countries need to have sufficient knowledgeable people to deal with these issues nationally, and in international negotiations and bilateral contractual arrangements.

Increasing Activity in Developing Countries

There is considerable work in progress in the use of modern biotechnology in developing countries, probably much more than is commonly recognized internationally. Much of the R&D in developing countries is being funded by national governments, and some by bilateral and multilateral development agencies. It is estimated that at least twice as much of the biotechnology-related R&D in the public sector in developing countries is being funded by national governments, as by the international development community at present. Only a small amount comes from the private sector. The total R&D effort is still substantially less than the high private sector investments in biotechnology in North

Box 3 Commercial Applications of Biotechnology in Crop Agriculture

Sustainable agriculture and sustainable intensification of agricultural systems are the challenges of the future. Sustainable agriculture is defined as the production of food to meet the needs of today without hindering the ability of future generations to meet their needs while maintaining a sustainable healthy environment.

World food supplies will have to more than double by 2025 to ensure sufficient quantity and quality, not only to meet increases in population, but also as a result of greater urbanization and spending power. In the past, world agriculture was in a position to produce enough healthy food for the growing population by gradually introducing yield-increasing technologies such as high-yield seeds, crop protection products, fertilizers, and improved irrigation systems and introducing more land to agriculture. Despite this, about 800 million people throughout the world are still undernourished. Full utilization of all technologies in crop production, including modern biotechnology, will play a decisive role in increasing yield to maintain sustainable global self-sufficiency in food.

In 1999 over 70 genetically modifed (transgenic) varieties of crops were registered for commercial cultivation worldwide. These include new varieties of cotton, chicory, potato, pumpkin, corn, soybean, rape, papaya, tobacco, tomato and clove). More than 15,000 field trials have been undertaken globally. New genetic modifications of more than 100 plant species are growing in laboratories, greenhouses, or in the field for experimental purposes.

The first wave of biotechnology crops is being grown commercially in the field, providing farmers with new agronomic traits, particularly herbicide tolerance and pest resistance that enable them to grow these crops more easily and more profitably. In 1999 the global area under genetically improved crops was 40 million hectares, mainly of corn (maize), soybean, cotton, canola (rapeseed) and potatoes. Eighty five per cent was grown in the USA, Canada, Australia, France and Spain and approximately 15 percent of the area was in developing countries, notably Argentina, China, Mexico and South Africa.

The private sector accounts for more than 80 percent of international biotechnology research. During 1997-99 transactions by the biosciences companies in the seeds industry have reached about US$18 billion. These investments were made to have access to the different crops and markets.

The second generation of genetically improved crops coming to commercialization over the next five years will include both other commodity and specialty crops, and also the introduction of new traits to improve the quality and nutritional value of the crops. There is also increasing interest in using crops to produce medicallly and/or industrially important compounds, such as vaccines in potatoes and biodegradeable plastics in corn.

Manfred Kern, Aventis Crop Sciences

America, Europe, and other Organization for Economic Cooperation and Development countries. Nevertheless, there is movement toward a critical mass of public sector investments in biotechnology in several developing countries (see also Box 3).

Agricultural Biotechnology in Industrial Countries

The greater specificity in the handling of genes has meant that inventors could protect their discoveries by means of patents and other forms of intellectual property rights. This has led to an explosion of private investment in the biosciences in the last 15 years, leading to a "biotechnology revolution." The greatest number of modern biotechnology applications are in health care, where they offer new hope to patients with AIDS, genetically inherited diseases, diabetes, influenza, and some forms of cancer. Biotechnology-based processes are now used routinely in the production of most new medicines, diagnostic tools, and medical therapies. The global market for these products in 1998 was approximately US$13 billion.

New developments in agricultural biotechnology (Box 3) are being used to increase the productivity of crops, primarily by reducing the costs of production by increasing the efficiency of use and decreasing the need for inputs of pesticides and herbicides, mostly in crops grown in temperate zones. The applications of agricultural biotechnology are developing new strains of plants that give higher yields with fewer inputs, can be grown in a wider range of environments, give better rotations to conserve natural resources, provide more nutritious harvested products that keep much longer in storage and transport, and continued low cost food supplies to consumers.

Private industry has dominated research, accounting for approximately 80 percent of all R&D.

Consolidation of the industry has proceeded rapidly since 1996, with more than 25 major acquisitions and alliances worth US$15 billion.

During the past decade, the commercial cultivation of transgenic plant varieties has commenced. In 1999, it is estimated that approximately 40 million hectares of land were planted with transgenic varieties of over 20 plant species, the most commercially important of which were cotton, corn, soybean, and rapeseed (James 1999). The value of the global market in transgenic crops grew from US$75 million in 1995 to US$1.64 billion in 1998.

The traits these new varieties contain include insect resistance (cotton, corn), herbicide resistance (corn, soybean), and delayed fruit ripening (tomato). The benefits of these new crops are better weed and insect control, higher productivity, and more flexible crop management. These benefits accrue primarily to farmers and agribusinesses, although there are also economic benefits accruing to consumers in terms of maintaining food production at low prices. Health benefits for consumers are also emerging from new varieties of corn and rapeseed with modified oil content and reduced levels of potentially carcinogenic mycotoxins.

The broader benefits to the environment and the community through reduced use of pesticides contribute to a more sustainable agriculture and better food security.

Other crop/input trait combinations presently being field-tested include virus-resistant melon, papaya, potato, squash, tomato, and sweet pepper; insect-resistant rice, soybean, and tomato; disease-resistant potato; and delayed-ripening chili pepper. There also is work in progress to use plants such as corn, potato, and banana as mini-factories for the production of vaccines and biodegradable plastics.

Scientific Advances

Further scientific advances will likely result in crops with a wider range of traits, some of which are likely to be of more direct interest to consumers, for example, by having traits that confer improved nutritional quality to food. Crops with improved output traits could confer nutritional benefits to millions of people who suffer from malnutrition and deficiency disorders. Genes have been identified that can modify and enhance the composition of oils, proteins, carbohydrates, and starch in food/feedgrains and root crops. For example, a gene encoding beta carotene/vitamin A formation has been incorporated experimentally in rice. This would enhance the diets of the 180 million children who suffer from the vitamin A deficiency that leads to 2 million deaths annually. Similarly, introducing genes that increase available iron levels in rice three-fold is a potential remedy for iron deficiency that affects more than 2 billion people and causes anemia in about half that number.

Applications of biotechnology in agriculture are in their infancy. Most current genetically improved plant varieties are modified only for a single trait, such as herbicide tolerance or pest resistance. The rapid progress being made in genomics may enhance plant breeding as more functional genes are identified. This may enable more successful breeding for complex traits such as drought and salt tolerance, which are controlled by many genes. This would be of great benefit to those farming in marginal lands worldwide, because breeding for such traits has had limited success with conventional breeding of the major staple food crops.

Functional Genomics for Trait Discovery

Although much of the discussion about molecular biology applications is focused on the opportunity of crop improvement by gene transfer through transformation, the same science brings new tools to assist plant breeders transfer genes through more conventional approaches. The complex traits for adaptation to abiotic stress are often difficult to identify. These are often difficult to identify and utilize in a breeding program without the additional help of modern science. Plant genomics is the engine to drive trait discovery and help solve intractable problems in crop production. To fully exploit the wealth of structural information obtained from the genome we must understand the specific biological functions encoded by a DNA sequence through detailed genetic and phenotypic analyses. Thus functional genomics requires diversity of scientific expertise as well as biological resources. In many important food crops the public sector has a large investment in biological resources, in plant breeding programs, and a long and skilled history of understanding biological function through national variety evaluation networks, as well as the global crop networks of the international agricultural research centers. These biological resources, scientific knowledge and expertise will become increasingly important in gaining knowledge about the function of genes and in developing markers for assisting the breeding process. (See also Box 2 on marker assisted selection in rice.)

Global Challenges

In order to better understand where science can contribute to achieving the goal of sustainable global food security in the 21st century, it may be useful to identify areas of consensus among the number of analyses and predictions that are currently available on world food supply, population, and poverty. These also relate the achievements/failures of the past to the prediction of important forces for change through the first quarter of the 21st century.

In global terms, increases in world food production have more than kept pace with the increases in the global population to date. The consensus of the various projections is that, although the world agricultural growth rate has decreased from 3 percent in the 1960s to 2 percent in the last decade, the aggregated projections show that, given reasonable initial assumptions, world food supply will continue to outpace world population growth, at least to 2020. Worldwide, per capita availability of food is projected to increase around 7 percent between 1993 and 2020 (IFPRI 1997). Therein lies a paradox.

The first aspect of the paradox is that despite the increasing availability of food, currently approximately 0.8 billion of the global population of 6 billion are food insecure. They dwell among the 4.5 billion inhabitants of the developing countries in Asia (48 percent), Africa (35 percent), and Latin America (17percent). Of these 0.8 billion a quarter are malnourished children (IFPRI 1997).

Children and women are most vulnerable to dietary deficiencies. Dietary micronutritional deficiencies accompany malnutrition. Vitamin A deficiency is prevalent in the developing countries and it is estimated that over 14 million children under five years of age suffer eye damage as a result. Up to 4 percent of severely affected children will die within months of going blind and even mild deficiencies can significantly increase mortality rates in children. Iron deficiency affects one billion people in the developing world, particularly women and children, and its effects are compounded by common tropical diseases. The anemia that results from the deficiency can diminish learning capacity and increase morbidity and mortality.

The second aspect of the paradox is that food insecurity is so prevalent at a time when global food prices are generally in decline. Over the 30 year period 1960-1990, world cereal production doubled, per capita food production increased 37 percent, calories supplied increased 35 percent and real food prices fell by almost 50 percent (McCalla 1998).

The basic cause of the paradox is the intrinsic linkage between poverty and food security. Simply put, people's access to food depends on income. Currently it is estimated that more than 1.3 billion people in the developing countries are absolutely poor, with incomes of a dollar a day or less per person, while another 2 billion people are only marginally better off (World Bank 1997). Rural poverty currently represents a very high percentage of the overall poverty. However with increasing urbanization, an increasing proportion of poor people will be living in the cities of the developing countries in the next century.

The most important global challenges are:

- Alleviating poverty, improving food security, and reducing malnutrition, especially amongst children;
- Providing sufficient income for the rapidly increasing numbers of urban poor;
- Using new technologies for environmentally sustainable development.

Global Problems Facing Agriculture and the Environment

The global problems facing agriculture are described by Swaminathan (2000) as:

- First, increasing population leads to increased demand for food and reduced per capita availability of arable land and irrigation water.
- Second, improved purchasing power and increased urbanization lead to higher per capita

food grain requirements due to an increased consumption of animal products.

- Third, marine fish production is becoming stagnant.
- Fourth, there is increasing damage to the ecological foundations of agriculture, such as land, water, forests, biodiversity, and the atmosphere, and there are distinct possibilities for adverse changes in climate and sea level.
- Finally, while dramatic new technological developments are taking place, particularly in biotechnology, their environmental and social implications are yet to be fully understood.

Knowledge is a continuum. There is much to learn from the past in terms of the ecological and social sustainability of technologies, including traditional technologies and those that underpinned the Green Revolution (Pinstrup-Andersen and Cohen 2000, Swaminathan 2000). New developments in science have opened up new opportunities to develop technologies that may lead to high productivity without adverse impact on the natural resources base. Blending traditional and frontier technologies leads to the birth of *ecotechnologies* with combined strength in economics, ecology, equity, employment, and energy.

Risks and Benefits

In considering the potential risks and benefits of modern biotechnology, it is useful to distinguish technology-inherent and technology-transcending risks (Leisinger 2000). Technology-inherent risks are those where the technology itself has potential risks to human health, ecology, and the environment. Technology-transcending risks include those that are not specific to the technology but where its use may have risks. For biotechnology these include the risk of increasing the poverty gap within and between societies, reducing biodiversity, and antitrust and international trade issues.

Risks to Human Health

Potential health risks of genetically improved organisms relate to assessing and minimizing the risk of food allergens in genetically improved food. New biotechnology based methods allow the identification, characterization, and minimization of risks of food allergens.

Genetically improved crops and food, and the risk of allergens associated with them, are now a concern throughout the world, especially in industrial countries. More than 90 percent of food allergens that occur in 2 percent of adults and 4-6 percent of children are associated with eight food groups. Allergenicity of genetically improved foods can be raised in crops and foods either by raising the level of endogenous allergen or by introducing a new allergen (Lehrer 2000).

Assessment of the risk of allergens is a challenge. The International Life Sciences Institute (ILSI) has developed a decision tree that provides a framework for risk assessment (Lehrer 2000). It uses the following criterion: that an introduced protein in a food is not a concern if there is (1) no history of common allergenicity, (2) no similar amino acid sequence to known allergens, (3) rapid digestion of the protein, and (4) the protein is expressed at low levels. Protocols enable assembly of the data to judge food against this criterion.

It is also important to inform consumers of any potential risk. A key concern of consumers is being able to identify where allergens are found. Consumers want to know where the potential for food allergens exists. Any protein added to food should be assessed for potential allergenicity, whether it is added by genetic engineering or by manufacturing.

There are several related areas of concern with regard to potential human health risks of genetically improved foods: toxicity, carcinogenicity, food intolerances; the risk of the use of gene markers for antibiotic resistance; other macromolecules aside from protein that could be potential allergens; and nutritional value. Methods of testing and evaluating risks of toxicity and carcinogenicity are well established for food (Lehrer 2000).

The question remains as to whether developing countries can implement and use currently available technologies and protocols to assess food allergens and other health risks. The techniques are well established, and should be readily implementable by trained professionals. Although no clear cases of harmful effects on human health have been documented from new genetically improved food, that does not mean that risks do not exist and they should be assessed on a case by case basis.

Ecological and Environmental Risks

The risks policymakers and regulators need to assess include the potential for spread of traits from genetically improved plants to the same or related species, plants (including weeds), the buildup of resistance in insect populations, and the potential threat to biodiversity posed by widespread monoculture of genetically improved crops.

- A transparent, science-based framework is required, which assesses risks on a case by case basis and takes account of all stakeholder views.
- Environment-related issues to be considered in each case include the possibilities for gene transfer, weediness, specific trait effects, genetic and phenotypic variability, and expression of pathogenic genes.
- Risk management needs to consider the prospects for managing any specific risks identified with a proposed release
- Experience is accumulating in the management of the Bt genes in transgenic cotton varieties in several countries and this needs to be closely monitored.
- An agricultural sustainability protocol that balances risks and benefits may have value for the approval and use of new crop varieties.

Cook (2000) describes the findings of recent field trials that conclude there appears to be no new issues in the testing of genetically improved plants. The same protocols to assess the effect in the environment of the introduction of genetically improved plants should apply to plants derived through conventional plant breeding. The "bar" should not be higher for genetically improved plants, and the protocols must cover all plants regardless of the process. This being the case, there seems minimal environmental risk in the plant itself. The risks lie in the management of the cropping system involving soil, water and other inputs. There is a need for the establishment of baseline information in the environment where such introductions are to be made. There is very little known on this, although some understanding has been gained over recent years, and further R&D is required (Cook 2000).

The information derived from such an assessment needs to be handled through risk management associated with "plants as plants." Risk management involves the consideration of traditional cultural practices that have evolved over time, and new knowledge gained from research in agronomy, plant pathology, entomology, weed science, plant biology, soils, microbiology, and other disciplines.

Biotechnology and Biodiversity

Risks to biodiversity and wildlife are important issues in particular environments.

Careful assessment is necessary of the risks associated with the possible creation of new selection pressures coming from the introduction of genetically improved organisms into the environment. Of special concern is the potential impact on biodiversity of genetically improved organisms as the selection pressures wield influence in the species composition of the ecosystem. These concerns merit further study, especially on the behavior of genetically improved organisms in the open environment. The framework for strategic planning in the deployment of genetically improved organisms should be formulated with sustain-ability as the primary concern (Johnson 2000).

Regulatory Systems

Both food safety and biosafety regulations should reflect international agreements and best practice and a given society's acceptable risk levels, including the risks associated with not using biotechnology to achieve desired goals.

The principles and practices for assessing the risks on a case-by-case basis are well established in most Organization for Economic Cooperation and Development (OECD) countries and several emerging economies. These principles and practices have been summarized in a series of OECD reports published over the past decade or more. National, regional, and international guidelines for risk assessment and risk management provide a basis for national regulatory systems. Biosafety guidelines are available from several international organizations including the OECD, United Nations Environment Program, United Nations Industrial Development Organization, and the World Bank.

Regulatory trends to govern the safe use of biotechnology to date, include undertaking scientifically based, case-by-case, hazard identification and risk assessments; regulating the end product rather than the production process itself; developing a regulatory framework that builds on existing institutions rather than establishing new ones; and building in flexibility to reduce regulation of products after they have been demonstrated to be of low risk.

Technology Transcending Risks

Biotechnology is not inherently different to other technologies with respect to economic and social impacts, as long as it focuses on the problems that affect poor people.

One important difference is that research on biotechnology has largely taken place in the private sector with proprietary technologies and an orientation to commercial agriculture. This implies the need for a strong role for the public sector, including increased resources, to address developing country priorities.

Socioeconomic Impact

- There is a risk that modern science may bypass the needs of poor people.
- Biotechnology is only one tool in addressing the challenges of food security and poverty.
- There is a need for biotechnology to be integrated with appropriate policies and other conventional R&D programs.
- The positive and negative impacts of biotechnology should be monitored over time in terms of who and what are affected and how they are affected. Monitoring impact will provide guidance for public policymakers in the future.

Pro-poor policies. Unless countries have policies in place to ensure that small farmers have access to delivery systems, extension services, productive resources, markets, and infrastructure, there is a risk that the introduction of agricultural biotechnology could lead to increased inequality of income and wealth. In such cases, larger farmers are likely to capture most of the benefits through early adoption of the technology, expanded production, and reduced unit costs.

Weighing Risks and Benefits of Biotechnology

Biotechnology has potential to reduce input use, reduce risk to biotic and abiotic stress, increase yields, and enhance quality—all traits which should enable the development of new crop varieties that are appropriate to poor producers and consumers.

Modern biotechnology is not a silver bullet for achieving food security, but, used in conjunction with other agricultural research, it may be a powerful tool in the fight against poverty. It has the potential to help enhance agricultural productivity in developing countries in a way that further reduces poverty, improves food security and nutrition, and promotes sustainable use of natural resources. Solutions to the problems facing small farmers in developing countries could benefit both farmers and consumers.

The benefits and risks need to be assessed on a case by case basis, weighing the risks and benefits for each particular situation.

The benefits of new genetically improved food to consumers are likely to vary according to how they earn their income and how much of their income they spend on food. Consumers outnumber farmers by a factor of more than 20 in the European Union, and Europeans spend only a tiny fraction of their incomes on food. Similarly, in the United States, farms account for less than 2 percent of all households, and the average consumer spends less than 12 percent of income on food. In the industrial countries, consumers can afford to pay more for food, increase subsidies to agriculture, and give up opportunities for better-tasting and better-looking food. In developing countries, poor consumers depend heavily on agriculture for their livelihoods and spend the bulk of their income on food (Pinstrup-Andersen and Cohen 2000).

Strong opposition to genetically improved foods in the European Union has resulted in restrictions on modern agricultural biotechnology in some countries. The opposition is driven in part by perceived lack of consumer benefits, uncertainty about possible negative health and environmental effects, widespread perception that a few large corporations will be the primary beneficiaries, and ethical concerns.

Ethical Issues

In regard to ethical issues:

- Environmental and food safety risks may sometimes be overstated as a means of gaining attention to technology-transcending risks and ethical concerns.
- It is important to pursue a dialogue on ethical issues to clarify the ethical and moral issues of concern and how they might be addressed in different societies.

The ethical challenges include the role of science, its risks, benefits, and impact on society. Moral and ethical standards are being used to develop laws governing some aspects of biotechnology (for example, in medicine laws governing human cloning). In 1998, the CGIAR system agreed to a statement of ethical principles underlying the work of the CGIAR centers in biotechnology (Box 4).

A major ethical concern is that "genetic engineering" and "life patents" accelerate the reduction of plants, animals, and microorganisms to "mere commercial commodities, bereft of any sacred character." However, all agricultural activities constitute human intervention into natural systems and processes, and all efforts to improve crops and livestock involve a degree of genetic manipulation.

Intellectual Property Management

Many R&D programs face the challenge and opportunities of managing intellectual property. Partnerships are critical to effective manage-

Box 4 Ethical Principles Underlying the Use of Biotechnology by the CGIAR Centers

Transparency

CGIAR scientists, whose research relies heavily on a wide range of partnerships, must do more than just honor their personal ethical codes. The system as a whole needs clear and uniformly applied ethical principles. These must be known and respected by all CGIAR staff and well understood outside the system. Such principles can exert a significant influence on the nature and extent of the partnerships that are formed with other organizations and individuals. The most effective partnerships are likely to occur when partners share common ethical principles. It is thus critical that the CGIAR system be transparent about its ethical principles, not least those underpinning its work in biotechnology, so that its partners will know what the system stands for—what it will and will not do, how it will and will not do it, and why.

Trust

There seems to be a growing mistrust of science and scientists in many parts of the world. The widespread publicity given by the media to biotechnology and especially to its negative aspects, requires that all involved in this work must be especially concerned that their behavior conforms to the highest ethical and moral standards. Relevant principles are those relating to honesty, intellectual rigor, openness and transparency, accountability, and precautionary approaches.

Statement of Ethical Principles

In 1998 the CGIAR adopted a Statement of Ethical Principles Relating to Genetic Resources, that asserts: *The CGIAR was founded on the ethical imperative of eliminating hunger and starvation and has…followed certain ethical principles. Increasing food security and alleviating poverty have long been central to the system's science-based humanitarian mission.* It further states that: *Greater transparency …is important in enabling strong and unambiguous relationships to be forged with a wide range of partners.…. The CGIAR works for the attainment of equity in the conservation, sustainable use and the sharing of benefits derived from genetic resources. This commitment to fairness requires that emphasis be given to the needs of resource poor communities and to disadvantaged members of society…. As trustees of genetic resources, the CGIAR Centers recognize their responsibility to be impartial, transparent and fair in their administration of the trust; to respect and observe national regulations and international conventions; to be accountable for their actions; and to exercise due care and diligence in conserving the material for the use of present and future generations and in making it readily available for use for the public good.* In relation to respect, responsibility and integrity in science, the statement says: *The CGIAR's work on genetic resources respects the general scientific principles of good faith and the search for truth. However, the CGIAR is guided by its particular humanitarian and equity-based concerns, and not the pursuit of knowledge for its own sake.*

Geoffrey Hawtin, IPGRI

ment and investment in intellectual property protection.

- Learning to manage intellectual property is a critical issue for many countries and institutions.
- Intellectual property management includes clarifying the role of institutions, developing an inventory of IP, developing ownership of intellectual property where appropriate, undertaking technology transfer, and marketing of the intellectual property.
- Human resource development is a major need in this area.
- Benefit sharing with holders of indigenous knowledge and genetic resources is an important issue that must be addressed.

It is most important to build up human resource capacity in intellectual property for scientists, managers, policymakers, and society as a whole. Societal changes are reflected in changing IPR requirements, and further changes are likely to result from further strengthening of IP protection and finding ways to reflect the contribution of indigenous knowledge.

Key Players

Public Investment is Critical to Food Security and Poverty Alleviation

Agriculture must figure prominently in poverty alleviation strategies of developing countries. Accelerated public investments are needed to facilitate agricultural and rural development through:

- Yield-increasing crop varieties, including those that are drought and salt tolerant and pest resistant, and improved livestock and fish
- Yield-increasing and environmentally sustainable production technologies
- Reliable, timely, and reasonably priced access to appropriate inputs as well as the credit often needed to purchase them
- Strong extension services and technical assistance to communicate timely information and developments in technology and sustainable resource management to farmers and to relay farmer concerns to researchers
- Improved rural infrastructure and effective markets
- Particular attention to the needs of women farmers, who grow much of the locally produced food in many countries
- Primary education and health care, clean water, safe sanitation, and good nutrition for all.

These investments need to be supported by good governance and an enabling policy environment, including trade, macroeconomic, and sectoral policies that do not discriminate against agriculture, and policies that provide appropriate incentives for the sustainable management of natural resources. Development efforts must engage poor farmers and other low-income people as active participants, not passive recipients; unless the affected people have a sense of ownership, development schemes have little likelihood of success (Pinstrup-Andersen and Cohen 2000).

Agricultural biotechnology can contribute to food security in developing countries, provided that it focuses on the needs of poor farmers and consumers in those countries, identified in consultation with poor people themselves. It is also critical that biotechnology be viewed as one part of a comprehensive sustainable poverty alleviation strategy, not a technological "quick-fix" for world hunger and poverty.

Biotechnology needs to go hand in hand with investment in broad-based agricultural growth. There is considerable potential for biotechnology to contribute to improved yields and reduced risks for poor farmers, as well as more plentiful, affordable, and nutritious food for poor consumers.

Public/Private Sector Roles

In order to maximize the use of modern molecular knowledge, both public and private sector research is required to bring innovation and choices to farmers and consumers. The private sector is likely to focus on those areas of opportunity which will repay their investmet in innovation. The public sector must maintain the freedom to operate in an era of increasing propriety technology. In developing countries the public sector will need to develop technologies that meet the needs of the non-commercial sector, including the needs of resource-poor farmers and poor consumers.

Public-private roles have been changing due to declining public sector investments in R&D, and increasing private sector investments especially in biotechnology. There are three dimensions to this change:

- change in leadership in biological research (from public to private)
- change in ownership of technology
- change in markets (the private sector is now more interested in developing country markets).

These changes have led to a major new issue: the private sector is interested in protecting its technology investments, and the public sector is interested in gaining access to private sector technologies. The challenge is: how to bridge the gap between the interests of the public and private sectors and redefine their roles.

The following lessons have been learned from public-private partnerships in biotechnology to date (Lewis 2000):

- Learning each others' ways is important for partnership success (differences in cultural perspectives need to be bridged).
- Both parties must have confidence in the technology being transferred.
- Trust is the glue that holds partnerships together. Scientist-to-scientist relations help establish trust.
- Having a capable catalytic/facilitating/intermediary institution is important (for example, USAID/Michigan State University, Rockefeller Foundation, CGIAR), as is generating seed funding.
- Developing awareness and understanding of IPR is important. This may require training and institution building with the partner in a developing country.
- IPR concerns should be addressed up front for the partnership to succeed.

How to Move Forward

There is a need for more investment in public research in NARS and the IARCs, to develop appropriate products. There is also agreement that this must be done in partnership with the private sector (especially local companies), and that farmers and consumers must be actively involved in driving the R&D agenda. Partnerships and dialogues with nongovernmental organizations and civil society are also needed to reach consensus. New institutional arrangements will be needed to facilitate new partnerships, including institutional experimentation.

Communicating About Biotechnology and Addressing Public Concerns

A special session on communications at the international conference on biotechnology in October 1999 concluded:

- Public opinion may sometimes not be based on scientific fact, but it cannot be ignored; fears based on perceptions are nonetheless very real.
- Improved dialogue is necessary to involve all stakeholders, including farmers and consumers and civil society, in the assessment of the risks and benefits of modern biotechnology.
- Trust is the key element to pursue in addressing public perceptions.
- Communicating about biotechnology is perception management, not just handing out information but engaging in dialogue.
- Dialogue needs to be specific about which applications of biotechnology are being pursued, for what purpose, and the potential risks and benefits (see also Box 5).

Issues Outstanding/Actions Required

There are uncommon opportunities now to harness the power and synergy of biotechnology and information technology to address contemporary development issues. Swaminathan (2000) notes that modern information technology provides opportunities to reach the unreached.

The future livelihood of small farm families will also depend on **precision agriculture**, which involves the use of the right inputs at the right time and in the right way. Biotechnology may play an important role in the major components of precision farming: integrated gene management, soil health care, efficient water management, integrated pest management, integrated nutrient supply, and efficient postharvest management. Ecotechnology-based precision farming can help to cut costs, enhance marketable surplus, and eliminate ecological risks. This is the pathway to an ever-green revolution in small-farm

Box 5 Communicating About Biotechnology: Case Studies

The German experience. The deep public opposition to genetic engineering in Europe is based on experience with previous food scandals (BSE, hormone beef) which were not handled well by governments and regulators, and which have led to a mistrust of people in their regulating agencies. In Germany, public opinion on biotechnology is grounded in an alliance of a subtle anti-Americanism and a not-so-subtle opposition to large multinational companies (which happen to be mostly American). Another public relations problem lies in the fact that the first-generation GIOs were perceived to be industry-driven, with very little benefit to the consumers. Although the public opinion battle on GIOs seems to have been lost in Germany, there might still be ways to turn it around. This would need a pro-active campaign, much like the Jubilee 2000 initiative on forgiving developing country debts. What is needed (and soon) are success stories that show how biotechnology can be used to alleviate poverty and reduce malnutrition in developing countries.

Carola Kaps

The Indian experience. There are many examples of biotechnologies that are not controversial, such as tissue culture and embryo transfer. It is the media's responsibility to provide a balanced viewpoint, and to provide an active platform for information exchange. The media also plays a role in awakening the public to potentially harmful technologies. Emerging issues in India relate to biopiracy and IPRs. Farmers' views are often not heard on these issues. The media in India also covers stories related to indigenous and local knowledge.

Govindan Venkataramani

The Corporate experience. How society accepts biotechnology will depend mainly on how well biotechnology-related issues are communicated. Communicating about biotechnology is perception management – not just handing out information, but engaging in a dialogue. It is extremely important to differentiate among the various fields of application (microorganisms, animals, plants, humans), and to be very precise in what is being debated - the fears of the public are different for different fields of application (e.g., ecological damage, public health).

Walter von Wartburg

The U.K. experience. The public is not as ignorant of the issues as many believe. People may not know every scientific detail, but they have a sharp sensitivity to the broad issues. The re-gulatory bodies, however, have not adequately addressed public concerns. The public wants answers to questions such as: Is GI food needed? Who stands to gain and lose? Are there are some ethical issues involved. How do we communicate biotechnology? Do we switch from scientific issues to legal, ethical and social issues? Do we move to a more participatory style of decision-making, involving the public more?

Jagdish Patel

agriculture. This is why increased public support to both the CGIAR and NARS is important for strengthening health and food security (Swaminathan 2000).

Role of the CGIAR System

Critical roles for the CGIAR system in the future are to enhance its role as:

- Protector of the interests of the poor and facilitator and bridge-builder in biotechnology partnerships.
- Facilitating public policy and innovative institutional arrangements.

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

Suggestions for the CGIAR System

Country needs are not all the same, so it is important to deal with the experience and needs of specific countries, and the specific problems in their agricultural sectors. There is a need to move the debate forward from the general to the specific. This would enable clarification of where the problems are and what can be done to solve them.

Specific suggestions emerged on areas of activity and issues where the various elements of the CGIAR system, especially the IARCs supported by the CGIAR could play a useful role in the future.

Facilitating information sharing. The CGIAR system could play a useful role, possibly in association with other cosponsors of the conference, in assembling and making accessible the factual information about what is happening in the use of modern biotechnology in developing countries. This could include analyses of the specific problems that need to be addressed in terms of the priorities, the science, the transfer of technology, the assessment and management of risks, and the associated public policy questions. These include regulation, public acceptance of new technologies, intellectual property management, trade and antitrust issues, capacity building, and investment.

Identifying problems and priority setting. The CGIAR system could assist in identifying the priority problems and opportunities to mobilize science to address the problems of the poor, and to identify specific technical, policy, and institutional problems and opportunities that need to be addressed, at the national, regional, or international level.

Supporting national capacity building. The CGIAR centers could provide further technical support for capacity building in NARS, in the centers' areas of expertise. They would be working with individual countries, UN and other international agencies, and other sources of expertise to assist countries to develop expertise in knowledge management, regulatory affairs for environmental and health risk assessment and management, legal and patent issues, science and technology, and financial and business management.

Ensuring compliance with agreed biosafety standards. The IARCs need to ensure that they comply with agreed national and international biosafety requirements and best practice in their host and partner countries. The IARCs may also be able to assist partner countries in the monitoring of environmental releases of GIOs and in identifying and using best practices in this rapidly evolving field.

Managing intellectual property. There is an urgent need for better management of intellectual property by the IARCs and NARS, in line with national policies and legislation, facilitating access to, and freedom to operate with, appropriate technologies, and finding means to stimulate and reward traditional innovation and local inventions. The current initiatives, such as the central advisory service for intellectual property at ISNAR and other initiatives, will go some way toward meeting this need.

Public/private partnerships. The CGIAR system should strengthen its efforts to develop and implement specific public/private sector partnerships, building on the experience of past efforts, and explore new modalities.

Communicating and addressing public concerns. Constant communication with stakeholders is required, to address public concerns and to engage in dialogue with proponents and opponents of new technologies, focusing on real issues that will have an impact on the poor in developing countries.

Actions Required

Beyond the work of the CGIAR, there is a need for:

- More public and private R&D investments on targets that affect the livelihoods of the poor, and that are perceived to benefit both farmers and urban consumers
- Local start-up companies to commercialize and distribute new technologies, including the continuing importance of local seed companies in the distribution of new plant varieties
- Innovative mechanisms to stimulate more R&D on the problems important to the rural and urban poor, including exploring the feasibility of tax concessions in OECD countries and a global competitive grants facility
- The need to explore new modalities for public/private sector partnerships, learning from past experience of those already in operation, especially in relation to intellectual property management.

Conclusion

Biotechnology is only one tool, but a potentially important one, in the struggle to reduce poverty, improve food security, reduce malnutrition, and improve the livelihoods of the rural and urban poor. The uncertainties and the risks are yet to be fully understood, and the possibilities are as yet not fully exploited. It seems important not to deny people access to new technology, so long as they are fully informed of the potential risks and benefits and able to make their own choices.

By assessing the current and potential usefulness of modern biotechnologies for the solution of specific problems in agriculture, new ground is being broken in analyzing how best to assess and mobilize:

- Rapid developments in science and technology
- New public policy requirements
- New institutional arrangements
- Dialogue amongst all interested parties.

The exchange of a wealth of knowledge, information and experience, and the discussion of a variety of sometimes differing perspectives, will be valuable in moving ahead with the responsible dialogue and debate on the use of the new developments in science and technology for the benefit of society.

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The Challenge of Poverty in the 21st Century: The Role of Science

Ismail Serageldin

Harnessing the best in agricultural science to fight poverty and hunger is the special contribution that the CGIAR has made to development in the past, and will continue to make in the future. In doing so, we want to be quite sure that we capture the benefits of advanced science and guard against its hazards and risks. We want to maintain an effective balance between the two viewpoints so clearly expressed by university witnesses testifying earlier this month at a hearing of the sub-committee on basic research of the US House of Representatives' Science Committee.

One witness opposed "a knee-jerk reaction and fears" that could deprive society of demonstrably beneficial, genetically improved crops. Another argued that to push ahead "without stepping back and taking reasonable precautions would be a mistake." These are crucial considerations for the CGIAR as it continues to develop and fine tune a set of practical guidelines that will direct its efforts in the next decade and beyond.

The CGIAR cannot do this alone. It has to do so in close consultation with its partners. The experience, concerns, and expectations of the developing countries must be heard, as well as the views of the scientific and environmental community, farmers, and consumers.

We can approach the issues dispassionately, and review them on the basis of scientific fact. Rigorous science-based discipline can be combined with a deep sense of caring and compassion. Such a combination will make this effort a celebration of all that science can do for the disadvantaged and disconnected in the human family.

Context

The relevance of biotechnology and, specifically, agricultural biotechnology to development, is now at the forefront of international interest. The perceived promise and perils of biotechnology are under intense public scrutiny. The debate is widespread, complex and, frequently, inconclusive. Discussions are sometimes scientific and impartial, at other times ideological, sensational, and visceral. Why this intensification of interest?

First, despite the great advances that have been made in the decade now ending and in the preceding years, development challenges have grown more complex. The global scale of demographic pressures in the new millennium will be unprecedented. The world's population is expected to exceed 8 billion by 2025, an increase of 2.0 billion in the next 25 years. Much of the increase will occur in developing country cities, where urban populations will more than triple. There will be many more mouths to feed in complex circumstances. Norman Borlaug calculates that "to meet projected food demands, by 2025 the average yield of all cereals must be 80 percent higher than the average yield in 1990." These increases must come primarily from increasing biological yields, not from area expansion and more irrigation, because land and water are becoming increasingly scarce.

Meanwhile, poverty and hunger remain pervasive in our world of plenty, despite the enormous burst of output and productivity, the dazzling changes wrought by science and technology, and the amazing achievements recorded on the social indicators for so many of the people on the planet. Let me remind you: in the 47 "least developed" countries of the world, 10 percent of the world's population subsists on less than 0.5 percent of the world's income. Some 40,000 people die from hunger related causes every day. A sixth or more of the human family has been marginalized.

Comprehending and preparing for unprecedented levels of global population is the first part of the challenge we confront. The second part is to ensure that this population has access to food in adequate quantities at adequate prices, everywhere, at all times. The third is to produce this food in a way that does not destroy the natural resources on which we all depend. This is the triple challenge we face, and the CGIAR is concerned with the last two facets that combine to form the challenge of sustainable food security.

The challenge is both technological (requiring the development of new, high-productivity, environmentally sustainable, production systems) and political (requiring policies that do not discriminate against rural areas in general, and agriculture in particular), and will have to be accomplished at a time when attention to agricultural development and rural well-being is diminishing. An essential aspect of the response to this challenge is to harness *all* instruments of sustainable agricultural growth. Agricultural biotechnology is one such instrument. It has moved to the center of the development debate fairly recently, and that marks it out for particular interest and, indeed, concern.

Second, the world of science has grown and changed beyond most expectations. Today, a revolution is taking place in the biological sciences. It is fueled by the groundbreaking work in modern molecular genetics, the enormous advances in informatics and computing, and the enormous sums being invested in biotechnology research. It is truly an exhilarating time for the biological sciences; similar to what physics experienced in the glorious 40 years between 1905 and 1945, when all the concepts were changed, from cosmology to quantum physics, from relativity to the structure of the atoms. We are decoding the very blueprints of life; we are learning to manage the deployment and expression of genes.

So, we live in a time unmatched for the opportunities that science provides. We can dream of new scientific breakthroughs and new products that can help humanity as never before: New higher yielding plants that are more environment friendly, new remedies for killer diseases, edible vaccines, single cell proteins to feed cattle and clean wastes, hyper-accumulating plants to take toxins out of the soil, expanding forests and habitats where more species thrive, and so much more. We can dream of a future of sustainable development where humans thrive in harmony with each other and with the environment.

These opportunities are a necessary focus of interest among all of us who believe that the full potential of science has yet to be realized in our continuing efforts to fight poverty, end hunger, and protect the environment.

A third reason for the current scrutiny of biotechnology is that in recent years, agrobiotechnology has exploded into a major private sector activity, mainly in the industrial countries, with possibilities of even greater expansion in the future. The global area planted with transgenic crops was 1.7 million hectares in 1996, 11.0 million hectares in 1997, 27.8 million hectares in 1998, and 39.9 million hectares in 1999. The US led the field in 1999, as before, with 28.7 million hectares of transgenic crops representing 72 percent of the global area, followed by Argentina—6.7 million hectares (17 percent), Canada—4.0 million hectares (10 percent), China—0.3 million hectares (0.1 percent), and Australia and South Africa—0.1 million hectares (1 percent). Mexico, Spain, France, Portugal, Romania, and Ukraine (in that order) completed the roster, each with <0.1 million hectares (less than 1 percent). Some 82 percent of the world's transgenic crops were grown in OECD countries, about the same as in 1998 (84 percent). The seven principal transgenic crops grown in 1998 were (in descending order) soybean, corn/maize, cotton, canola/rapeseed, potato, squash, and papaya (James 1999).

The global market for transgenic crop products has grown rapidly during the period 1995 to 1999. Global sales from transgenic crops were estimated at US$75 million in 1995; sales tripled in 1996 and again in 1997 to reach US$235 million and US$670 million respectively, more than doubled in 1998 to reach US$1.6 billion and increased by more than a third in 1999 to reach an estimated US$2.1 to US$2.3 billion. Thus, revenues for transgenic crops have increased by approximately thirty fold in the five-year period 1995 to 1999. The global market for transgenic crops is projected to reach approximately US$3 billion in 2000, US$8 billion in 2005, and US$25 billion in 2010**.** In the last three years alone, corporations commercializing transgenic crops and involved with seeds, agricultural chemicals, and the life sciences have been engaged in more than 25 major acquisitions and alliances valued at US$15 billion, and this consolidation is expected to continue.

So the biotechnology revolution is here. But it has so far been very much the preserve of the richer countries, a fact that has distorted the debate on what biotechnology can do for the poor. Moreover, like physics in the first half of this century, developments in biological science today compel us to confront profound ethical and safety issues, complicated by the new issues of proprietary science.

Key Issues

Opportunities

Many scientific studies have concluded that the promise of biotechnology as an instrument of development lies in its capacity to improve the quality and quantity of crops and livestock, swiftly and effectively. One of the most far-seeing and prestigious was a report prepared in 1997 by a distinguished panel led by our late friend and colleague, Henry Kendall. Their study reminded us that the time required to identify and eliminate unfavorable traits through traditional crop breeding is greatly reduced by the use of genetic engineering techniques. Increased precision in plant breeding translates into improved predictability of the resulting products in desirable areas, such as performance and survival (Kendall and others 1997).

The application of biotechnology can create plants that are more resistant to drought and soil acidity and salinization. These attributes are critical to the development of agriculture in the poorest areas where soils are poorly endowed. They are also vital at a time when water scarcity is expected to be a major deterrent to development and, perhaps, a threat to life on the planet as we know it. Additionally, plant characteristics can be genetically altered for earlier maturity, increased transportability, reduced postharvest losses, and improved nutritional quality. Vaccines against diseases afflicting livestock are already important products of biotechnological research (Morrison 1999).

Most of the early products of agricultural biotechnology focus on crop protection. In 1998, transgenic crops that are herbicide tolerant covered about 19.8 million hectares. Use of herbicide tolerant varieties greatly facilitates weed control using certain types of herbicide and greatly reduces the amount of herbicide applied to the crop for effective weed control. This also enables farmers to employ soil conservation practices such as minimum tillage. Decreased tillage reduces soil erosion.

Increased plant resistance to pests has also been a major focus of agricultural biotechnology research. In 1998, an estimated 7.7 million hectares were planted to transgenic crops with introduced genes that produce substances toxic to target insect pests. The use of pesticides has dropped in areas using these crops, a positive impact not only on farm income but also on the environment.

More recently, research conducted at the Swiss Federal Institute of Technology's Institute for Plant Science has shown that serious problems of malnourishment can be tackled by genetic engineering. Researchers have been able to modify rice grains genetically, to improve the supply of iron and vitamin A in the human diet. The genetically improved rices can help to reduce global rates of iron deficiency anemia (IDA) and vitamin A deficiency (VAD), especially in developing countries where the major staple food is rice. IDA and VAD are major contributors to childhood blindness and maternal mortality and morbidity primarily in developing countries.

That is a very brief summary of the promise of biotechnology as an instrument of agricultural research and development. It is a promise that attracts many developing countries. Agricultural biotechnology programs, some of them substantial and some, only exploratory, have been established in Brazil, Burundi, China, Colombia, Costa Rica, Cote d'Ivoire, Egypt, Honduras, India, Indonesia, Jordan, Kenya, Malaysia, Mexico, Philippines, Singapore, South Africa, Thailand and Vietnam, amongst others.

Threats

Simultaneously, however, biotechnology has become a lightning rod for an increasingly impassioned debate, with opposing factions making strong claims of promise and of peril. Opposition has been mounted to the spread of transgenic crops or genetically improved organisms (GIOs) and protest movements have developed across the globe.

Opposition to biotechnology and specifically to genetic engineering is derived from several viewpoints. They include fears of high-tech farming destroying the livelihood of smallholders, concerns about artificially created products competing with and destroying the marketability of "natural" products, and the presumption of environmental threat. Many critics fear that biotechnology is a scientists' obsession which is being exploited to bring quick profits to the few even though it can do great harm to the many. Those who hold such views are profoundly concerned that the increased application of biotechnology will harm not only ourselves but even generations of the future. These concerns are genuine and cannot be ignored.

To the extent that we would transform the genetic makeup of a particular variety of plant through genetic transfer from another variety of the same species, that should not pose much of an ethical problem. In fact, it would simply be an accelerated way of achieving by biotechnological means what could be achieved through conventional breeding programs. This process of acceleration should not pose ethical or safety problems for anyone who does not oppose conventional breeding programs.

We might arguably extend this acceptance to the bioengineered product of a genetic transfer involving related but different species of plants such as wheat and barley for instance. Here we are already tinkering with nature, but the boundary to the conventional "natural" breeding system is so close, that for many that would also be acceptable. The likely result of such a gene transfer is unlikely to significantly modify or denature the plant. *Triticale* is such an interesting cross.

Beyond that area, we get into the slippery slope leading to the design of new plant types, based on the assemblage of desirable traits collected from individual plant species or even from other organisms. Are we then "playing God" and tinkering with the natural order?

In all societies, there is a profound distrust of scientists, or anybody else, assuming the right to change the natural order of things. One can argue, rightly, that by our very presence on this planet we are changing the natural order of things, and that our increasing numbers, ever more powerful technology and insatiable appetites for consumption and pollution are indeed affecting nature, and mostly in negative, and potentially dangerous ways. Global warming and biodiversity loss are but two examples. Yet against that general proposition we must set the welfare of the human species.

For instance, dare we argue that hunter and gatherer societies living "in harmony with nature" should be encouraged to stay as they are, with people forced to live in squalor, want, disease, and premature death. A humane treatment of the people would deal with improved diet, education and health, although the resulting reduction in infant mortality and increases in consumption are likely to put pressure on the natural system. The question then becomes how to handle that pressure, how to ensure that the patterns of development adopted are sustainable, for surely, even arguing from a human-centric point of view, it does not make sense to undermine the ecosystems on which our long-term survival depends. Viewed thus, the matter becomes a calculus of the potential benefits and potential risks associated with change, including the adoption of new technology.

Ethical Issues

Safety Concerns

Ethical issues of safety acquire a different level of concern in the case of GIOs being released into nature. Is there a risk that we would harm the very ecosystems on which all life depends? What if the results of these scientific efforts produce "super weeds" or "super viruses" with an impact so broad that they are devastating? Anxieties about biosafety led to the adoption of restrictive laws in some countries in the 1970s totally banning research into the possibilities of genetic manipulation. These laws have been rescinded, but fears about biosafety continue to bedevil the debate. Here again the question is one of evaluating the scientific evidence and assessing, to the best of our ability, the likely risks and if these can be managed.

Clearly, it is not possible to exclude certain classes of risks entirely, any more than one would be able to exclude the risk of an asteroid hitting the earth or of being struck by lightning. Yet these risks are considered so remote that one in fact goes through life ignoring them. This is not to say that the potential risks of releasing GIOs into the environment are in the same class of probability as either of these two examples, but that the discussion should not start on the basis that ANY potential risk, no matter how remote, would automatically veto the potential application of a technology.

In a case much closer to everyday life, we could ask if people would be willing to accept a technology that is contributing to global warming, kills about 50,000 persons per year and maims another 500,000 in the US alone, and is adding nothing vital to our lifestyles except the added convenience of personalized fast travel. Yet, who would agree to ban the automobile?

Patent Rights

Another broad area of ethical issues involved in biotechnology is that of patenting. One of the ethical questions raised is whether the patenting of life forms is acceptable. There is no direct answer for that, but we must take note that the ownership of animals and plants is recognized, so is the right of owning a particular breed. We could argue that allowing ownership rights to other life forms is a matter of degree. After all the varieties of flowers or livestock are themselves owned and sold, breeding of horses and other show animals is recognized, so what is specifically more offensive in patenting, that is establishing an ownership claim, on a gene or gene sequence, in comparison with asserting ownership on a whole animal or plant or variety thereof?

The difference lies in the idea of owning a "building block of life" rather than the actual living creature itself. The assumption being that the building block in question can then be part of many other living things. This is an issue that I am personally still struggling with, and that I cannot easily define to my satisfaction.

Nevertheless, the issue is one that affects a lot of people and we should strive to understand their qualms and to accommodate them. No legislation can function if it does not have the broad based support of the majority of the population, and the views of the minority today could well be the majority tomorrow. But such a transformation is best achieved by education and scientific evidence, not by assertive preemptive action by a vocal minority.

Intellectual Property and Knowledge Management

There is another side to the patenting story that raises another set of ethical issues. These include the progressive monopolization of knowledge and the increasing marginalization of most of the world population with a concomitant selectivity in focus of research and applications of the new biotechnology and its benefits, skewing it to the potential markets of the rich and excluding the concerns of the poor.

The issues operate at two levels:

- the privatization of the scientific research enterprise, and the meaning of proprietary science in the coming century; and
- the proprietary aspects of the biotechnology in terms of both process and product.

On the first, I am concerned by a growing gap between the industrial and developing countries in the rapidly evolving knowledge frontier which is exacerbated by the privatization of the knowledge enterprise. Elsewhere I have called this an emerging *scientific apartheid* (Serageldin 1999).

Also very much at issue are patenting and intellectual property rights (IPR). Supporters of patenting point out that if the private sector is to mobilize and invest large sums of money in agricultural biotechnology R&D, it has a powerful claim to protecting and recouping what it has put into the exercise. On the other side of the argument is the fear that patenting and the exercise of IPR will lead to a monopolization of knowledge, restricted access to germplasm, controls over the research process, a selectivity in the focus of research and, thereby, the increasing marginalization of the majority of the world's population.

Regulatory Arrangements

These concerns are complicated by the fact that safeguards governing agricultural biotechnology are uneven and, in some countries, non-existent. Safeguards involve regulatory mechanisms and this calls for actions by governments to put them in place, and ensure that they function effectively. In the US, the Food and Drug Administration decided in 1992 that genetically improved products would be subjected to the same scrutiny, and be required to maintain the same standards, as all other foods. Extra scrutiny is undertaken only with the introduction of "something truly new." The FDA is presently undertaking a series of public hearings to see if its procedures should be modified.

The process in Europe is much more complex, involving a process of third party refereeing, a vote by the European Commission, and legislation by member states of the union. Regulatory traditions are advancing in developing countries, but not as extensively or as speedily as necessary, mainly because of a lack of capacity. However, ideas are being cross-fertilized, through the influence of international institutions, such as the Convention on Biological Diversity, and under the umbrella of the CGIAR. Special efforts have been made by CGIAR centers, the Rockefeller Foundation, OECD, UNIDO, and UNEP to build developing country expertise in this critical area.

A Balance Sheet

Let me try, now, to draw up a balance sheet that answers the question—where do we stand?

We know that substantial transformation of smallholder agriculture in developing countries is key to meeting the complex and demanding challenges of the new millennium.

The production side of agriculture is a necessary but not sufficient condition to meet the challenge of hunger. If the production side is inadequate, however, discussion of other policies and practices becomes largely academic. Productivity-increasing technologies have to be ecologically sustainable, economically viable, and socially equitable.

Agricultural biotechnology is not a magic wand that can replace poverty and hunger with a regime of plenty, but all the available evidence suggests that it can be an effective additional weapon on the development front.

Agricultural biotechnology holds promise of effectiveness in increasing crop yields, reducing the need for chemical pesticides that degrade the environment; supporting resource-poor farmers by nurturing the adaptability of plants to harsh growing conditions such as drought, salinity, and extreme temperatures; improving health by introducing desirable nutritional characteristics into new varieties.

The potential benefits of biotechnology should not divert our attention from the real concerns about the application of the new science. All that is scientifically possible is not ethically acceptable. But the issues of bioethics and biosafety, and of intellectual property rights will be ceaselessly and inconclusively debated unless all those concerned have a genuine desire to reach accommodation based on practical realities, not on emotion or ideology.

Safeguards and regulatory mechanisms have not been established in many developing countries because they are essentially a new branch of law that requires the accumulation of new expertise. A much stronger and more focused international effort is required to strengthen regulatory know-how and practice. In fact, capacity building across the whole spectrum of agricultural biotechnology activities is necessary.

Concerns have also been expressed by civil society representatives that a new wave of high-technology farming will destroy the interests of small farmers in developing countries. This could be particularly detrimental to women in Asia where 60 percent of the farmers are women, hence the need for national and regional policies that take account of the rights and interests of all concerned.

The private sector is at the forefront of every aspect of the agricultural biotechnology revolution—from R&D, through product creation, sales and sharing, to the development of regulatory mechanisms. So an important question for the future is: how can the strength of the private sector be harnessed for the development effort?

The many issues that touch on private/public sector partnerships come together in the work of the CGIAR System, which can serve as knowledge broker, bridge builder, and catalyst.

The Way Ahead

Biotechnology research efforts in the CGIAR were initiated in the mid 1970s by two centers, CIP and ILRAD (now ILRI). Today, twelve centers are engaged in various research activities involving the use of biotechnology techniques. The centers' laboratories vary in terms of the types of biotechnology techniques being employed, from the relatively simple cell or tissue culture to the more complex methods aimed at developing transgenic plants. The main areas of the centers' biotechnology work are in crop disease diagnosis/detection, crop improvement including molecular breeding, germplasm storage and exchange, crop propagation, improvement of microorganisms, livestock disease detection and treatment through new vaccines, embryo storage and exchange, and livestock improvement. Biotechnology research funding in the CGIAR centers represents a small fraction of the total funding for the CGIAR research agenda; some US$30 million. Compare this with a total CGIAR budget of some US$340 million, and total annual agricultural biotechnology research investment in the industrial countries of several billion dollars.

Can the CGIAR let the existing situation stand—in terms of its research program and the investment to support it— if, demonstrably, there is substantial potential for biotechnology to contribute to more rapid and sustainable agricultural growth in developing countries? Or should it take the lead in ensuring that:

- access to the potential benefits of technology is guaranteed for the poor and the environment
- the risks of biotechnology are minimized, and adequate institutional mechanisms are in place to ensure biosafety and bioethics
- biotechnology research is directed at solving the problems of poor farmers rather than toward solely scientific priorities, that is, technology should be needs driven rather than science driven, as the latter would run the risk of adding more technologies that are irrelevant to the majority of small-scale producers and to sustainable agriculture
- biotechnology is recognized as a tool to be used in conjunction with other tools, not as an end in itself.

We are listening closely to our partners from the national agricultural research systems, the international science community, the civil society, and the private sector as this conference seeks answers to these and related questions. We will pay the utmost attention to views expressed on the potential as well as the risks of biotechnology. And we will take the consensus that emerges from this meeting to the CGIAR where the thematic focus of attention will be: "Reducing Poverty through Cutting-edge Science."

We want your expertise and experience to be blended with ours in a science-based attack on poverty and hunger in the new millennium. For us in the CGIAR, the critical issue is that every instrument of agricultural transformation should be mobilized in our efforts to feed the hungry, help the poor, and protect the environment. We cannot, do not, and will not accept the notion that deprivation is imprinted on the genes of the poor and destitute, and that misery is their inevitable destiny.

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Feeding the Developing World in the Next Millennium: A Question of Science?

Alexander F. McCalla and Lynn R. Brown

Science played a major role in meeting the challenge of producing enough food to feed the additional billions of people added in the past 40 – 50 years. The Green Revolution in rice and wheat was responsible for securing major yield increases in those grains. In the period 1960 -90 global cereal production doubled, per capita food availability increased 37 percent, per capita calories available per day increased 35 percent, and real food prices declined 50 percent. This impressive global aggregate performance, however, masks considerable regional differences. In sub-Saharan Africa, in the same period, per capita food availability, and consequently per capita calorie availability, decreased due to sometimes negative growth rates in agricultural production and continuing high population growth rates. Increases in per capita calorie availability were also more muted in South Asia, home to about 140 million malnourished children under 5 years old.

Despite good global agricultural performance with respect to yield, the numbers of people undernourished fell by only 80 million, from 920 million to 840 million between the end of the 1960s and the early 1990s. As with the increases in per capita calorie availability, there were regional differences. While the share of the undernourished in East Asia declined markedly, the share in sub-Saharan Africa more than doubled. To make matters worse the numbers suffering from a deficiency in at least one micronutrient doubled between the 1960s and the early 1990s. Compared to the doubling in cereal production, the reductions in malnutrition were less impressive. This implies a lack of access to food on the part of the poor. This is of more concern today since the rate of yield increases, the source of most agricultural production growth outside of sub-Saharan Africa, has slowed considerably. If the rate of growth of food production relative to population and income growth falls, then price increases will likely follow, further compromising the ability of the poor to obtain food.

Production Challenges

In the first 25 - 30 years of the next millennium the world's population will increase by about 2 billion people. Most of this increase, about 95 percent, will take place in the developing world. This in itself is a challenge – feeding an extra 2 billion people while hopefully reducing the more than three-quarters of a billion people who do not have enough to eat today. We also must address the issue of more than 2 billion people who are deficient in one or more micronutrients such as iron.

The production challenge we face in the next millennium is not unprecedented. Between 1975 and now we have added close to 2 billion people to the world's population and production more than kept pace. Enough food was produced to feed everyone if it had been more equitably distributed. Poverty is the key reason why people do not have enough to eat. Over 1.2 billion people live on less than US$1 a day and a further 1.6 billion live on less than US$2.

The production challenge is more complicated, however, if we recognize two additional issues: the location of population growth and urbanization. At least 90 percent of the growth in population will occur in countries located between the tropics of Cancer and Capricorn. The question is Where will the food to feed them come from? In the last doubling of world grain supplies, the share of total grain production traded remained stable at around 10 percent. Stated another way, on average 90 percent of the world's food consumption takes place in the country where the food is produced. If the trend continues, then most of the food production must come from within the countries where the additional people will live. In other words, 90 percent of the increased food needed must be grown in farming systems prevalent in tropical countries. This area includes all of Latin America except for the southern cone of Argentina, Chile and Uruguay, all of Central America, and most of Mexico: all of Africa except the North Africa region and South Africa; the southern half of India and all of Southeast Asia including Indonesia. In these humid, sub-humid, and semi-arid tropical regions farming systems are highly complex, with heterogeneous mixes of annual plants, livestock, and trees. These are systems about which we are not knowledgeable. Most farmers are poor, with small landholdings. Productivity is low and agriculture is subject to water, wind, and temperature stresses. They are also the farming systems most likely to be adversely affected by global warming.

So in the next millennium we face a food, feed, and fiber production challenge in highly complex farming systems that will need to be addressed by science. The good news is that this has the potential to be a win-win challenge. Increasing smallholder agricultural productivity in these areas will not only increase food supplies, but also will increase smallholder incomes thereby reducing poverty, increasing food access, reducing malnutrition, and improving living standards of the poor.

Urbanization

There is a second issue - urbanization. During 1975-99 the urban population of developing countries increased by 1.2 billion. In the next 25 years it will increase by 2 billion, essentially doubling the urban population in just 25 years. Between 1750 and 1850 when industrialization was in full swing in Europe, it took 100 years to add 500 million to the world population. We will add about four times as many people in one- quarter of the time. The size of many of the developing country cities will far exceed most of the largest cities in the industrial countries. These cities will be in countries where agriculture is still the key economic sector. In 2015 Bombay will have over 26 million residents, Lagos 24.6 million, both of them more than double the 1950 population of New York City and far in excess of the predicted New York population in 2015.

Why does urbanization add to the food production challenge? Rural populations in developing countries obtain most of their food from subsistence production or local markets. Urban populations, on the other hand, obtain around 90 percent of their food from the marketplace. In India and China, two countries with the highest absolute numbers of people, indications are that less than 40 percent of rice and wheat production enters the market beyond the localized market at the point of production.

In the next millennium the fact that population growth takes place in urban areas, rather than rural, means that required growth in marketed food surplus in the developing world is increased more than proportionately. Every time a person transfers from a rural area to an urban one, their marketed food supply requirement doubles. Using conservative estimates we calculated that while population growth projected from now until 2025 is 42 percent, the required growth in marketed surplus of grains would be 60 percent.

The production challenge is therefore great because of three things: the absolute increase in population, where it will occur, and the doubling of urban populations. Given constraints on new land availability and increased competition for water, most of the food production increases must come from intensification of agricultural production on existing land. This is where molecular biology must play a role.

The Doubly-Green Revolution

The World Bank's interest in agricultural productivity improvement stems from its commitment to reduce poverty and food insecurity. Some have criticized the last Green Revolution, arguing that it disproportionately benefited the rich, in the early years, given the necessity for complementary increases in fertilizers, pesticides, and irrigation. It also contributed to environmental degradation in many areas. The next agricultural revolution must learn from the lessons of the past. It must benefit the poor and it must, at best, improve the existing state of the environment and, at worst, do no harm in terms of further environmental degradation. As Conway (1997) pointed out, the next technology- driven revolution must be doubly green – it must increase food production at a faster rate than in recent years and do it in a sustainable manner without significantly damaging the environment. It should also improve rural incomes and increase accessibility to food by the poor.

Biotechnology has the potential to contribute substantially to this objective, but it is controversial. The early days of the Green Revolution likely did not garner as much media interest despite producing genetically improved organisms. Genetic manipulation is not new. Traditional plant selection and breeding have occurred since the beginning of crop production, resulting in genetically improved organisms. Humans are also genetically improved organisms. Modern biotechnology has been used successfully in agricultural research institutes around the globe, including the centers of the Consultative Group on International Agricultural Research. Uncontroversial techniques include tissue culture, gene mapping, and molecular markers, which are used to improve the efficiency of plant breeding. A recent advance using biotechnology, by the West Africa Rice Development Association, has resulted in a successful cross of a traditional African rice with a high-yielding Asian variety. An exciting development from this work is the creation of a new plant type that can, during its early stages of growth, shade out weeds, similar to the African variety, but has the high yield capacity of Asian rice. In essence the best characteristics of both rice types have been combined, including drought tolerance, disease and pest resistance, and high yields.

The Role of Science

Although media controversy has talked of biotechnology in general, in essence the concern has largely focused on the transfer of genes between species as opposed to genetically improved organisms within the same genotype. The focus so far of much the commercial development of new crop varieties in industrial countries has been on introducing traits for herbicide tolerance and pest resistance in a few crops (rapeseed, corn, and soybean) by insertion of single genes. The *Bacillus thuringiensis* (Bt) gene from bacteria has been inserted in some crops to function as a pesticide. Little attention has been focused, for example, on micronutrient improvement.

Recent research in Switzerland, funded by the Rockefeller Foundation, shows the potential of modern biotechnology to address developing country micronutrient malnutrition problems. A gene that enhances vitamin A production was inserted into rice using a gene from a daffodil, and in a separate experiment, the bioavailability of iron for human consumption was also increased by introduction of a gene from a french bean. The potential of these advances is enormous. More than 2 billion people are anemic due to iron deficiency. In developing countries, 180 million children die annually from diseases linked to vitamin A deficiency, especially in Asia, where poor children are weaned on rice gruel.

The World Bank is committed to assisting developing countries develop the capacity to make fully informed decisions, including an assessment of the risks and benefits, of the new technological advances afforded by the biological revolution. It is important that developing countries not be left behind, nor their needs ignored in the process of technological innovation.

Public and Private Sector Roles

The Green Revolution took place mainly in public sector research establishments, in an era of open access to genetic resources. Today's biotechnology revolution is taking place largely in the private sector with associated intellectual property protection of emerging technologies. This intellectual property protection is important because it allows companies to recoup in the marketplace the often high R&D costs to develop these new products. The private sector likely will not undertake high-cost R&D without either a functioning marketplace and/or intellectual property protection. This explains why little private sector research is done on developing country food crops such as sorghum, millet, and cassava.

We need to explore ways to encourage such research by lowering the relative costs of R&D. We propose several options. The first is active public – private sector partnerships in research for developing country food crops. This benefits both parties through increasing the availability of crop germplasm to the private sector, and ensuring attention to the crops most important to poor farmers in developing countries. Intellectual property rights protection needs to be carefully explored in such partnerships. Two such activities deserve special mention. One is the work of Novartis Foundation on sorghum and millet in Africa. The other is the Donald Danforth Plant Science Center jointly funded by Monsanto, The State of Missouri, The Missouri Botanical Gardens, the University of Missouri, the University of Illinois, and Purdue University. Support from the State of Missouri is in the form of tax credits.

This leads to the question of whether tax concessions for such R&D activities should be further explored. Currently most of the multinational life science companies are located within the OECD. One incentive scheme could be tax concessions from host governments for R&D specific to developing country food crops, associated with some form of nonexclusive intellectual property protection. A second suggestion is the medical sector models whereby WHO, the World Bank, and other development agencies are collaborating with pharmaceutical companies in the development of new vaccines against major tropical diseases.

A third suggestion is the establishment of a global competitive grants research facility for R&D on developing country food crops, with nonexclusive intellectual property protection.

Why would companies want to undertake research for which their intellectual property protection was nonexclusive? First, the R&D could lead to new enabling technologies, which they could incorporate in R&D activities on crops other than developing country food crops, and which could have intellectual property protection on the final product. Second, increasing the productivity of developing country agriculture will reduce poverty and lead to agricultural commercialization, thus creating future competitive market opportunities for other commercial product lines.

Risks

Biotechnology has the potential to contribute to the solution of problems of food insecurity and malnutrition in developing countries. Use of biotechnology, however, could create potential export trade problems for developing countries, given the differing opinions regarding food safety and biosafety in industrial countries. This may lead to the development of non tariff barriers to trade, which developing countries have less ability and resources to address in the international arena. Therefore, it is important that the risks and benefits of any new technology be carefully evaluated. This should be done in both global and national open fora, ensuring that the risks and benefits to all potential beneficiaries are recognized and considered.

It is here that there may be an increasing role for CGIAR centers. Development of new transgenic varieties of developing country food crops is likely to fall outside present food and environment safety testing in industrial countries. Consumption patterns may render developed country biosafety systems less relevant. The lack of an export market for many of these food crops may also leave food safety testing outside of Codex. As well, many of these food crops are not consumed in industrial countries and so they would not have been tested for human consumption there.

For the poorest developing countries, biosafety regulatory systems are limited. If we succeed in getting increased public and private sector investment on the problems important in developing country food crops, then there will be a need to ensure independent testing with regard to human health and environmental safety. The CGIAR centers could potentially support countries in these evaluations. CGIAR centers already have partnerships with NARS to ensure improvement of new crop varieties for developing country agroecological needs. This role could be extended into capacity-building with regard to developing biosafety regulatory systems in conjunction with organizations such as Codex, OECD, UNIDO, and UNEP. Although new transgenic crop varieties are only grown at present in a few developing countries, media attention has ensured that safety concerns have been well publicized worldwide. Many consumers may know more about the perceived problems than they do about what biotechnology is and its possible benefits.

Conclusion

Biotechnology is one tool in our arsenal for feeding the world in the future. It is a solution not without problems, but it is one we cannot afford to ignore. We have fallen behind in educating consumers about the potential of biotechnology and in reassuring them about safety concerns. We could take some lessons from the pharmaceutical sector, where new drugs are introduced on a regular basis. We would submit that no new drug is absent of all risk, but careful evaluation through extensive clinical trials indicates that the benefits outweigh the risks when taken under prescribed conditions. Likewise there is no such thing as 100 percent safe food in today's world, and no one would claim such. There were 6.5 million cases of food poisoning in the United States of America in 1992, resulting in 9,000 fatalities. We need to fully assess the risks and benefits of all "new" foods, and when the benefits far outweigh the risk we need to move ahead. Incentives are needed for research attention to developing country food crops. Without them poor farmers and consumers in developing countries will not have access to, and benefit from, these new technologies that would allow them to increase their productivity.

If we turn our backs on modern biotechnology we may exacerbate malnutrition and micronutrient deficiency problems in developing countries. We need to move forward with both good science and effective public education.

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Genetic Engineering and Food Security: Ecological and Livelihood Issues

M. S. Swaminathan

As we say goodbye to the 20th century, we can look back with pride and satisfaction on the revolution that our farm men and women have brought about in our agricultural history. In 1969 I wrote in the Illustrated Weekly of India about the role our farm families played in initiating the Wheat Revolution in India: "Brimming with enthusiasm, hard-working, skilled and determined, the Punjab farmer has been the backbone of the revolution. Revolutions are usually associated with the young, but in this revolution, age has been no obstacle to participation. Farmers, young and old, educated and uneducated, have easily taken to the new agronomy. It has been heart-warming to see young college graduates, retired officials, ex-armymen, illiterate peasants and small farmers queuing up to get the new seeds. At least in the Punjab, the divorce between intellect and labour, which has been the bane of our agriculture, is vanishing."

While we can and should rejoice about the past achievements of our farmers, scientists, extension workers, and policymakers, there is no room for complacency. We continue to face several problems:

- First, increasing population leads to increased demand for food and reduced per capita availability of arable land and irrigation water.
- Second, improved purchasing power and increased urbanization lead to higher per capita food grain requirements due to an increased consumption of animal products.
- Third, marine fish production is becoming stagnant.
- Fourth, there is increasing damage to the ecological foundations of agriculture, such as land, water, forests, biodiversity, and the atmosphere, and there are distinct possibilities for adverse changes in climate and sea level.
- Finally, while dramatic new technological developments are taking place, particularly in biotechnology, environmental and social implications are yet to be fully understood.

Because land and water for agriculture are diminishing resources, there is no option but to produce more food and other agricultural commodities from less arable land and irrigation water. In other words, the need for more food has to be met through higher yields per units of land, water, energy and time. We need to examine how science can be mobilized to raise further the biological productivity ceiling without associated ecological harm. Scientific progress on the farms, as an "*ever-green revolution*," must emphasize that the productivity advance is sustainable over time since it is rooted in the principles of ecology, economics, social and gender equity, and employment generation.

The dimensions of the challenges faced by those involved in developing scientific strategies and public policies for sustainable food security are best defined in some statistics on India, which now has a population of one billion. In global terms, India today has 16 percent of human population, 15 percent of farm animal population, 2 percent of the geographical area, 1 percent of rainfall, 0.5 percent of forests, and 0.5 percent of grazing land.

The Green Revolution has so far helped to keep the rate of growth in food production above the population growth rate. The Green Revolution was, however, the result of public good research, supported by public funds. The emerging gene revolution, by contrast, is spearheaded by proprietary science and can come under monopolistic control. How can we take the fruits of the gene revolution to the unreached?

Meeting the Challenges Ahead

The Gene Revolution

Mendel's laws of genetics were rediscovered in 1900. Mendel had published his work on inheritance patterns in pea in 1865, but it took 35 years for others to grasp their significance. Since 1900, we have witnessed steady progress in our understanding of the genetic makeup of all living organisms ranging from microbes to man. A major step in human control over genetic traits was taken in the 1920s when Muller and Stadler discovered that radiation can induce mutations in animals and plants.

In the 1930s and 1940s, several new methods of chromosome and gene manipulation were discovered, such as the use of colchicine to achieve a doubling in chromosome number, commercial exploitation of hybrid vigor in maize and other crops, use of chemicals such as nitrogen mustard and ethyl methane sulphonate to induce mutations and techniques like tissue culture and embryo rescue to get viable hybrids from distantly related species. The double helix structure of DNA (deoxyribonucleic acid), the chemical substance of heredity, was discovered in 1953 by James Watson and Francis Crick. This triggered explosive progress in every field of genetics.

As we approach the end of the 20th century, we see a rapid transition from Mendelian to molecular genetic applications in agriculture, medicine, and industry. This brief capsule of genetic progress from 1900 to 1999 adequately stresses that knowledge and discovery represent a continuum, with each generation taking our understanding of the complex web of life to a higher level. It would therefore be wrong to worship or discard experimental tools or scientific innovations because they are either old or new.

Just as it took 35 years for biologists to understand the significance of Mendel's work, it may take a couple of decades more to understand fully the benefits and risks associated with genetically improved foods. It would be prudent to apply scientific and precautionary principles in areas of human health and environmental safety.

The 1990s have seen dramatic advances in our understanding of how biological organisms function at the molecular level, as well as in our ability to analyze, understand, and manipulate DNA molecules, the biological material from which the genes in all organisms are made. The entire process has been accelerated by the Human Genome Project, which has poured substantial resources into the development of new technologies to work with human genes. The same technologies are directly applicable to all other organisms, including plants. Thus, the new scientific discipline of *genomics* has arisen, which has contributed to powerful new approaches in agriculture and medicine, and has helped to promote the biotechnology industry.

Several large corporations in Europe and the United States have made major investments to adapt these technologies to produce new plant varieties of agricultural importance for large-scale commercial agriculture. The same technologies have equally important potential applications to address food security and poverty of people in developing countries.

Work in India has shown that genetic modification can do immense good in agriculture and food security. The 21st century may witness changes in temperature, precipitation, sea level, and ultraviolet b radiation, as a result of global warming. These changes in climate are expected to adversely affect India and sub-Saharan Africa. All human-induced calamities affect adversely the poor nations and the poorest among all nations the most. This led us to initiate an anticipatory research program to breed salt-tolerant varieties of rice and other crop plants in coastal areas, in order to prepare for seawater intrusion into farmland as a result of an eventual rise in sea level. The donor of salt tolerance was a mangrove species belonging to the family *Rhizophoraceae.* Transferring genes for tolerance to salinity from mangrove tree species to rice or tobacco is an impossible task without recourse to recombinant DNA experiments. This demonstrates the immense benefits that can accrue from genomics and molecular breeding.

Concerns

What then are the principal concerns? In industrial countries, the major concerns relate to the impact of genetically improved organisms (GIOs) on human health and the environment. These food and environmental safety concerns have been well documented and are widely known. The food and environmental scientists of developing countries are equally concerned about the food and environmental safety aspects of GIOs. The ethical and social issues relating to GM crops were dealt with in detail in a report published by the Nuffield Council on Bioethics in May 1999. What issues concern the public and professionals in developing countries?

The first issue of concern is biosafety. Why are large biotechnology companies averse to the labeling of GM foods? In spite of over three years of intensive discussion in meetings sponsored by the Secretariat of the Convention on Biological Diversity (CBD), the negotiations broke down at Cartagena, Colombia, in February 1999. Thus, there is as yet no internationally agreed biosafety protocol, as called for under Article 19 of CBD. The absence of such a protocol will hurt the private sector the most.

There are other issues of concern to the general public in India. First, India is a land of small farm holdings. There are now 106 million operational holdings in the country, and about 75 percent of them are one hectare or less. India has 25 percent of the global farming community, and farming provides a livelihood to nearly 66 percent of the population. There is concern that expansion of proprietary science and shrinking of "public good" research supported from public funds may lead to a situation where the technologies of the future remain in the hands of a few transnational corporations. Only resource-rich farmers may have access to them, thereby widening further the gap between the rich and poor. This could accelerate social disintegration.

Second, monopolistic control over crop varieties could lead to a situation where large areas are covered by very few genetic strains or hybrids. It is well known that genetic homogeneity enhances genetic vulnerability to biotic and abiotic stresses. Biotechnology companies are therefore recommending resistance management strategies, such as growing 30-40 percent non-Bt (*Bacillus thuringiensis*) corn with Bt-corn (see Gould and Cohen this volume). What will happen to the livelihood of farm men and women operating smallholdings with institutional credit and with no crop insurance, if GM corn, soybean, rice, potato or other crops are affected by serious diseases as a result of the breakdown of resistance? Will the companies agree to compensate them for the loss? This problem could become even more serious if companies incorporate genetic use restriction mechanisms, known popularly as "terminator" genes in the new varieties. Small farmers could then experience "genetic enslavement" since their agricultural destiny could be in the hands of a few companies if they have to purchase new seeds each year, similar to conventional hybrid seed.

A third issue relates to the potential impact of GM foods on biodiversity. This has two dimensions. The first deals with the replacement of numerous local cultivars with one or two new varieties, which could lead to genetic erosion. Modernization of agriculture has resulted in a narrowing of the base of food security, both in terms of the number of species constituting the food basket and the number of genetic strains cultivated (see NRC 1989, 1996). Local cultivars have often been the donors of many useful traits, including resistance to pests and diseases. Under small farm conditions, every farm is a genetic garden, comprising several annual and perennial crops, and several varieties of each crop. The need of the hour is to enlarge the food basket and not shrink it further.

The second dimension is equity in benefit sharing between biotechnologists and the primary conservers of genetic resources and the holders of traditional knowledge. The primary conservers have so far remained poor, while those who use their knowledge (for example, the medicinal properties of plants) and material become rich. This has resulted in accusations of *biopiracy*. It is time that genetic engineers and others promote and find ways to implement genuine *biopartnerships* with the holders of indigenous knowledge and traditional conservers of genetic variability, based on principles of ethics and equity in benefit sharing.

Unless R&D efforts on GM foods are based on principles of *bioethics, biosafety, biodiversity conservation, and biopartnerships,* there will be serious public concern in India, as well as many other developing countries, about the ultimate nutritional, social, ecological, and economic consequences of replacing numerous local varieties with a few new genetically improved crop varieties. To derive benefits from genetic engineering without undue risks, every nation should set up a multistakeholder Commission for Genetic Modification.

The Ecotechnology Revolution

Knowledge is a continuum. There is much to learn from the past in terms of the ecological and social sustainability of technologies. At the same time, new developments have opened up new opportunities to develop technologies that can lead to high productivity without adverse impact on the natural resources base. Blending traditional and frontier technologies leads to the birth of *ecotechnologies* with combined strength in economics, ecology, equity, employment, and energy.

In water harvesting and sustainable use, for example, there are many lessons to be learned from the past. In the desert area of Rajasthan, India, drinking water is available even in areas with 100 mm annual rainfall, largely because women are continuing to harvest water in simple structures called *kunds*. In contrast, drinking water is scarce during summer months in some parts of northeast India, with an annual rainfall of 15,000 mm. There is need therefore to conserve traditional wisdom and practices, which are tending to become extinct. The decision of the World Intellectual Property Organization (WIPO) to explore the intellectual property needs, rights, and expectations of holders of traditional knowledge, innovations, and culture is an important step in widening the concept of intellectual property rights (IPR). Principles of ethics and equity demand that this invaluable component of IPR be included when the TRIPs (Trade-related Intellectual Property Rights) agreement of the World Trade Organization (WTO) comes up for review. FAO has been a pioneer in the recognition of the contributions of farm families in genetic resources conservation and enhancement by promoting the concept of *Farmers' Rights*. Like WIPO, UPOV (Union for the Protection of New Varieties of Crops) should also undertake the task of preparing an integrated concept of breeders' and farmers' rights and assisting countries in developing equitable and effective *sui generis* systems for the protection of new plant varieties, as is required for all members of WTO (Barton, 1999; Leisinger, 1999).

Science and Basic Human Needs

The 20th century produced an impressive array of accomplishments in nearly every field of science and technology. The last part of the century was particularly rich in innovations in biotechnology, and information and space technologies. Such advances have had a beneficial impact on human food and health security. The global population was only 940 million in 1798 when Malthus expressed his apprehensions about human capacity to achieve a balance between food production and population. Human numbers reached 6 billion in 1999, and once in every12 years another billion will be added, if current growth rates continue in developing countries. Science-based technologies supported by appropriate public policies are responsible for food famines becoming rare. The famine of food at the level of an individual today is mostly due to inadequate purchasing power arising from a famine of jobs or employment opportunities.

In spite of an impressive stockpile of scientific discoveries and technological innovations, poverty and social and gender inequities are increasing. According to the World Bank, 1.3 billion people lived on less than US$1 per day and another 3 billion lived on less than US$2 per day in 1993. Nearly 1.5 billion of the world population of 6 billion will live in severe poverty at the dawn of the new millennium. Illiteracy, particularly among women, is still high in many developing countries. It is not only in opportunities for education that children of many developing countries remain handicapped, but even more alarming, in opportunities for the full expression of their innate genetic potential for physical and mental development. Between 25 and 50 percent of children born in South Asian countries are characterized by low birth weight (LBW), caused by maternal and fetal undernutrition and malnutrition. The UN Commission on Nutrition in a recent report has warned about the serious consequences of LBW for both brain development in the child, as well as the level of health in later life.

New technologies supported by appropriate services and public policies have helped to prove doomsday predictions wrong, and have led to the agricultural revolution (the Green Revolution) becoming one of the most significant of the scientific and socially meaningful events of the 20th century. Four thousand years of wheat cultivation led to Indian farmers producing 6 million metric tons of wheat in 1947. The Green Revolution in wheat helped to surpass in 4 years the production accomplishments of the preceding 4000 years, thus illustrating the power of synergy between science and public policy.

There are uncommon opportunities now to harness the power of such synergy to address contemporary development issues such as the growing rich-poor divide, feminization of poverty, famine of jobs, human numbers exceeding the population-supporting capacity of ecosystems, climate change, and loss of forests and biodiversity. Whether in economics or in ecology, experience has shown that a trickle-down approach does not work. Fortunately, modern information technology provides opportunities to reach the unreached. *Virtual colleges*, computer-aided and internet-connected, linking scientists and women and men living in poverty can be established at local, national, and global levels to launch a knowledge and skill revolution. This will help to create better awareness of the benefits and risks associated with genetically improved organisms, so that both farmers and consumers will get better insights into the processes leading to the creation of novel genetic combinations.

The future of small farm families will depend on *precision agriculture*, which involves the use of the right inputs at the right time and in the right way. Biotechnology will play an important role in the major components of precision farming: integrated gene management, soil health care, efficient water management, integrated pest management, integrated nutrient supply, and efficient postharvest management. Ecotechnology-based precision farming can help to cut costs, enhance marketable surplus, and eliminate ecological risks. This is the pathway to an ever-green revolution in small-farm agriculture. This is why increased public support to both the CGIAR and NARS is important for strengthening health and food security.

Conclusion

The industrial revolution in Europe marked the transition to a world where technology became a major causal factor in the prosperity gap between developing and industrial nations. How can we now enlist technology as an ally in the movement for social, gender and economic equity in an era of expanding proprietary science? Obviously, public good research supported from public funds must be stepped up. The following indicator of measuring the value of development efforts proposed by Mahatma Gandhi is the most meaningful yardstick for determining priorities in scientific research designed to help in meeting basic human needs: "*Recall the face of the poorest and the weakest man whom you have seen, and ask yourself, if the steps you contemplate are going to be of any use to him. Will he gain anything by it? Will it restore to him control over his own life and destiny?*"

If biotechnology research can be promoted keeping in mind the guideline Gandhi gave, it will become a powerful tool in ensuring sustainable food security in the world.

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China: Agricultural Biotechnology Opportunities to Meet the Challenges of Food Production

Qifa Zhang

Crop improvement using biotechnology has now become a reality. Globally, commercial production of transgenic crops has increased rapidly in the last few years (James 1998). There is considerable research and development (R&D) in agricultural biotechnology in China. The challenges, opportunities, and constraints to biotechnology R&D are reviewed here, especially those related to crop improvement and production in China.

Challenges

Increasing food production has always been the highest agricultural priority in China because of the huge population of the country. It is projected that the population of China will reach 1.6 billion by the year 2030. Demand for food production will increase by at least 60 percent to keep pace with population growth. This rapid population increase and vast urbanization will result in loss of valuable farmland and other natural resources. The only viable approach to increasing food production, therefore, is to increase the productivity of existing farmland. Statistics show, however, that the total production rates of the major grain crops has been decreasing in the last decade (Ministry of Agriculture 1996), because yield potentials of the newly released cultivars and hybrids have not been realized.

There is also a huge demand for quality improvement of food products, especially the grain quality of cereal crops. Quality improvement of rice, for example, was largely neglected in breeding programs in recent years. High yield cultivars and hybrids is frequently associated with poor quality; most of the widely used cultivars and hybrids have poor cooking and eating qualities, and thus are disfavored by producers and consumers.

Another major problem is degradation of the environment. We have seen increasingly frequent natural disasters such as floods, drought, insect pests, and diseases, and also expanding areas of soil desertification, salinity, and acidity. Extensive applications of chemicals have created a vicious circle in which the excessive use of the chemicals has resulted in a rapid deterioration of the environment, and this deterioration has made crop production even more dependent on chemicals.

The greatest challenge is to increase food production and improve product quality in an environmentally sustainable manner.

Developments in Biotechnology Research in China

Infrastructure

In the last 15 years there have been rapid developments in China in scientific infrastructure and also research programs in biotechnology and molecular biology of various crop plants. Infrastructure developments include the establishment of National Key Laboratories in the general areas of agricultural biotechnology and crop genetics and breeding, in north, central and south China. These laboratories are well equipped for biotechnology and molecular biology research. In addition, there are open laboratories supported by the Ministry of Agriculture, the Ministry of Education, and the Chinese Academy of Sciences. These laboratories have provided good opportunities for biotechnology research.

Financial Resources

During the same period, regular funding channels were formed at the central government level, which support basic and applied research. This includes the establishment of the National Natural Science Foundation of China and The Chinese Foundation of Agricultural Scientific Research and Education. Major research initiatives and programs were also established at the state level and by various ministries. The most important programs for biotechnology R&D are the National Program on High Technology Development (also known as the 863 Program) and the National Program on the Development of Basic Research (also known as 973), both of which included agricultural biotechnology as a major component. Programs were set up to promote young scientists by awarding special grants from the National Natural Science Foundation, the 863 Program, and also various ministries. Similar systems, although smaller, were also developed by local governments in many provinces.

International funding channels also opened to Chinese scientists during this period, including those of the Rockefeller Foundation, McKnight Foundation, the International Foundation for Science, and the European Union-China collaboration programs. The availability of financial support has enhanced research capacity and has promoted the development of young scientists. Some of the programs have a training component as well.

Scientific Advances

Rapid advances have been made in molecular biology and biotechnology research in China in the 1990s. These include genomic studies in rice and other cereals, development of molecular marker technologies, identification, and mapping and molecular cloning of a large number of agriculturally useful genes. These studies have resulted in powerful tools for crop improvement (for example, marker-assisted selection) that can be applied to develop new cultivars and hybrid parents.

Transformation technologies have also been firmly established in many laboratories for most of the crop species, including major cereal crops such as corn, rice, and wheat that are often considered difficult to transform. Transgenic plants can now be routinely produced for crops such as rice, corn, wheat, cotton, tomato, potato, soybean, rapeseed, and other crops, using *Agrobacterium*, particle bombardment or other methods.

The most up-to-date molecular technologies necessary for varietal development are now in place in China.

Opportunities

Genome mapping and biotechnology research in recent years offer powerful tools in crop improvement including genetic transformation and molecular marker-assisted selection. These techniques have opened enormous opportunities to meet the challenges of food production. These opportunities according to individual traits are described below:

Disease resistance: More than 20 genes for resistance to various plant diseases have been isolated in recent years (Baker and others 1997). Analyses of the DNA sequences indicate that the genes share many structural characteristics in common, despite the fact that diseases are caused by a variety of pathogens such as fungi, bacteria, viruses, and nematodes. The genes were isolated from a wide range of plant species including monocotyledonous and dicotyledonous species including tomato, rice, tobacco, and barley. These have provided a rich source of disease-resistance genes for improving resistance by genetic engineering.

Large numbers of genes have been tagged and mapped using molecular markers in many crop species (for examples see Zhang and Yu 1999). Closely linked markers flanking both sides of the genes were identified in many cases. These closely linked markers can be used as the starting points for isolating the genes using the map-based cloning approach. These markers can also be used as selection criteria in breeding programs to monitor the transfer of the genes, which is referred to as marker-assisted selection. New crop lines with improved resistance have been obtained using both approaches.

Insect resistance: Genes for resistance to various insects have been identified in many crop species and their wild relatives, including gall midge and brown planthopper resistance in rice, and pink borer resistance in cotton. A number of insect resistance genes has also been genetically tagged and mapped using molecular markers (Zhang and Yu 1999). These genes can be directly used in crop breeding programs using marker-assisted selection.

An important strategy in the development of insect resistant crop varieties is utilization of exogenous genes, including genes coding for endotoxin of *Bacillus thuringiensis* (*Bt*) and proteinase inhibitors from various sources (Krattiger 1997). Some of the genes have demonstrated strong insecticidal activities under both laboratory and field conditions. Several genes have now been widely used in transformation studies. Many insect-resistant transgenic cotton, corn, and rice plants have been produced from these transformation studies, which have now been advanced to the stage of commercial production (James 1998).

Large-scale utilization of the insect resistance genes in crop production will not only reduce labor and costs of production, it will also have long-term beneficial effects on the environment. These insect-resistant crops may have a major role to play in sustainable agricultural systems.

Tolerance to abiotic stresses: Drought, soil salinity, and acidity are among the most important threats to agricultural production that cause severe yield losses of all major food crops worldwide. In China, the northwest region is prone to drought, so water supply is a major limitation for crop production; in south and central China, soil acidity is a major limiting factor that reduces crop yield; salinity occurs in large areas in the east coastal region.

Drought resistance has been the subject of many studies in several major food crops including rice, corn and sorghum (Nguyen, Babu, and Blum 1998). Although many quantitative trait loci (QTLs), which explain certain genetic variations in drought tolerance in experimental populations, have been identified by molecular marker mapping, they are unlikely to have a major role to play for improving the drought tolerance of crops.

There have also been QTL studies on the tolerance of rice to acidic soil conditions, especially with respect to aluminum and ferrous iron toxicity (Wu and others 1999), showing that major gene loci may be involved in increasing the tolerance of rice plants. This may present an opportunity for using genes from rice itself to improve the tolerance of rice varieties to acidic soils.

A more promising line of research is the use of gene coding for citrate synthase, the enzyme for biosynthesis of citric acid (de la Fuente and others 1997). Transgenic sugar beet plants with elevated expression of this gene show an enhanced tolerance to aluminum, and also increased uptake of phosphate in the acidic soil as a result of excretion of citrate. This indicates that genetic engineering may be able to produce plants that can grow better in acidic soil even with reduced application of phosphate fertilizers. This work may have tremendous implications in crop improvement, especially for crops grown in tropical and subtropical regions.

Product quality: Biotechnology may have much to offer in the improvement of product quality. In rice, for example, the poor cooking and eating qualities of high- yielding cultivars and hybrids represent a major problem for rice production in China. Research has established that the cooking and eating qualities are to a large extent dependent on three traits: amylose content, gelatinization temperature, and gel consistency. It was recently shown that all three traits are controlled by the waxy locus located on chromosome 6 (Tan and others 1999).

The waxy gene was isolated from maize and rice (Shure, Wessler, and Federoff 1983; Wang and others 1990). Rice plants transformed with the waxy gene both in sense and antisense configurations showed reduced amylose content, thus demonstrating the usefulness of the transgenic approach in improving cooking and eating qualities. Moreover, the waxy locus has also been clearly defined in the molecular linkage map, and markers residing on the waxy locus and closely linked makers that flank the waxy locus on both sides were identified (Tan and others 1999). Thus, improvement of the cooking and eating qualities can therefore be achieved using marker-assisted selection.

Another example is the recent success in engineering the entire biochemical pathway for provitamin A biosynthesis (Al-Babili and others 1999), which significantly enriched vitamin A content in the endosperm of rice grains. This will be a great help to the poor peasant farmers to balance the micronutrients in their diets and hence alleviate malnutrition.

Increasing yield potential: Several of our major crop species have gone through two great leaps in yield increase in the last several decades: increasing harvest index by reducing the height by making use of the semidwarf genes, and utilization of heterosis by producing hybrids. Reduced rates of yield increase have been observed in a number of major food crops in the last 10-15 years (Ministry of Agriculture 1996). Increasing yield potential has therefore been a common concern in essentially all crop breeding programs.

Two approaches have been reported in the literature. The first approach is called "wild QTLs," in which efforts are devoted to bringing QTLs for yield increase from the wild relatives to enhance the yield of cultivars. The argument for such an approach is that only a portion of the genes that ever existed in the wild species was brought to cultivation in the processes of domestication, leaving most of the genes unused. With the help of molecular marker technology, it should therefore be possible to identify genes that can increase the yield of cultivated plants. Xiao and others (1996), for example, reported two QTLs from a wild rice that showed significant effects in increasing the performance of an elite rice hybrid. This has generated considerable interest in identifying genes for agronomic performance from wild relatives that are potentially useful for varietal improvement.

The second approach is to modify certain physiological processes by genetic engineering. Gan and Amasino (1995) reported a system conceived to delay leaf senescence by autoregulated production of cytokinin. The construct was designed by fusing a senescence-specific promoter isolated from *Arabidopsis* with a DNA fragment from *Agrobacterium* encoding isopentenyl transferase (*IPT*), an enzyme that catalyzes the rate-limiting step in cytokinin biosynthesis. The strategy for such a system is that the gene would be turned on at the onset of senescence leading to the synthesis of cytokinin, and the production of cytokinin would in turn inhibit the process of senescence, thus repressing the expression of this construct itself. Such a system would, therefore, be able to produce cytokinin for delaying senescence, and at the same time preventing overproduction of cytokinin, because overproduction of this hormone is detrimental to the plant. Transgenic tobacco plants carrying this construct showed a significant delay in leaf senescence, bringing about a large increase in the number of flowers, number of seeds, and biomass, indicating the possibility of increasing plant productivity by delaying leaf senescence. It is interesting, therefore, to determine if this system can provide a general strategy for yield increase in crop improvement.

There are many opportunities for biotechnology to contribute to sustainable food production, to achieve higher yields, better quality, and less dependence on chemicals, making crop production more environmentally friendly.

Field Testing of Transgenic Crops in China

According to statistics from the Ministry of Agriculture, transgenic research has been conducted in 47 plant species in China using 103 genes. A national committee for the regulation of biosafety of genetically improved agricultural organisms was established in 1996 to promote biotechnology in a healthy environment. This committee accepts applications twice a year for biosafety evaluation of genetically improved agricultural organisms such as crop plants, farm animals, and microorganisms.

By mid 1998, the committee had received 86 applications, of which 75 were for field testing of transgenic crops. Permission for 53 of the applications was granted for commercial production, environmental release, or small-scale field testing (Chinese Society of Agricultural Biotechnology 1998a, b). The crops used for transgenic research were rice, wheat, corn, cotton, tomato, pepper, potato, cucumber, papaya, and tobacco. A variety of traits were targeted for improvement including disease resistance, pest resistance, herbicide resistance, and quality improvement. In a few cases, transgenic crops have been grown for large-scale commercial production. We expect that the area planted in transgenic crops will increase rapidly in the next few years.

Constraints

Intellectual Property Rights

One of the major constraints relates to intellectual property rights (IPR). China does not yet have effective IPR in place for large-scale biotechnology research to develop new genetically improved crops. Most of the genetically improved crop plants that have been developed so far involve complex IPR issues. There is a major shortage of experts in China with knowledge of IPR, and experience in dealing with these issues. China urgently needs help in training people in IPR. Scientists and breeders do not fully understand IPR, which are not always recognized and honored. Education is therefore urgently needed on these issues.

Delivery Systems

Another major constraint is the lack of delivery and extension mechanisms that take the products of biotechnology research to the farmers. China had a network system to dispense agricultural technologies, seeds, and other related materials. With the development of a market economy, the old distribution systems are gradually losing their effectiveness, and are now evolving into profit-driven seed companies undergoing the processes of privatization. Although this may be a good movement in itself, it may take several years for the system to become effective, because the funding situation does not appear to be promising at the moment. Governmental support mainly goes to the research component, and there is not enough funding to support initiatives and startups of seed companies.

Scientific and Technical Constraints

There are also a number of scientific and technical constraints to the application of technology in crop improvement. One of the constraints is the lack of understanding of the mechanisms governing the traits that are very important in crop improvement. Drought causes severe yield loss worldwide, and it will continue to be among the most damaging stresses in crop production. Tolerance of the crop to drought as a trait, however, has not been well defined, and it is still not clear what aspects of plant morphology or physiology are the most important for drought tolerance. Research is still needed to define a clear target for improving drought tolerance.

There is also a huge need for germplasm. Germplasm has not been found for a number of important traits such as resistance to fungal diseases and resistance to a number of pests in crop species, for example, sheath blight of rice, scab disease of wheat, and yellow wilt of cotton. These have become the most devastating diseases worldwide, as have borer insects of a number of crops that cause heavy damage. International collaboration, coordinated by CGIAR centers, may have a crucial role to play in germplasm identification, exchange, and utilization.

Perspectives

Recent developments in genome mapping and genetic engineering have provided a knowledge base, identified germplasm resources, provided useful genes, and offered effective tools for crop improvement. Integration of the knowledge, the tools, and the genetic resources into breeding programs will greatly increase the efficiency of new varietal development.

Molecular Marker-Assisted Selection

It is expected that molecular marker-assisted selection will have a major role to play in future genetic improvement of many crops. This is not only because the technique itself has provided a highly efficient tool for speedy and precise selection, but also because it possesses several distinct advantages. First, it does not require the isolation of the targeted gene, which often takes years and considerable resources to accomplish. Second, most of the gene constructs such as those commonly used in many transformation studies are now covered by IPR, hence are not freely available for varietal development. Third, the progeny developed by marker-assisted selection in general does not suffer from adverse effects such as over- or underexpression and transgene silencing, which are now frequently reported with transgenic plants. The performance of the progeny resulting from marker-assisted selection is therefore much more predictable than those from transformation. The large number of genes that have been precisely tagged and mapped will provide a rich source for marker-assisted breeding.

Gene Isolation

The most common practice for obtaining new genes is map-based cloning. Molecular markers that are closely linked to genes of interest can serve as the starting point for cloning the genes following the map-based cloning approach. It can be expected that the process of gene isolation using this approach will be greatly accelerated with advances of the international effort in DNA sequencing. It is highly likely that all the genes that are accurately mapped with closely linked markers can be quickly isolated with the availability of the sequence information.

The recent development in DNA-chip technologies may also provide a powerful tool for large-scale isolation of new genes in the near future (Lemieux, Aharoni, and Schena 1998). It can be expected that large numbers of genes will become available for crop improvement in the next decade.

Biotechnology will soon play a major role in crop improvement in China. The area planted to cultivars, developed using modern biotechnology, will increase steadily in the years to come. Biotechnology will contribute significantly to food production and food security in China in the coming century.

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India: Biotechnology Research and Development

Manju Sharma

Biotechnology has transformed many parts of the chemical industry, agriculture, and medicine. This area of science has little demarcation between basic and applied research, and new discoveries and innovations, in most cases, can find direct application. Innovations, techniques, and tools that have emerged and revolutionized modern biotechnology include genetic engineering, cell fusion technology, bioprocess technologies, and structure-based molecular designs including drug development, drug targeting, and drug delivery systems.

In the 1980s the Government of India considered the need for creating a separate institutional framework to strengthen biology and biotechnology research in the country. Scientific agencies supporting research in modern biology included: Council of Scientific and Industrial Research (CSIR), Indian Council of Agricultural Research (ICAR), Indian Council of Medical Research (ICMR), Department of Science and Technology, and University Grants Commission. Biotechnology was given an important boost in 1982 with the establishment of the National Biotechnology Board. Its priorities were human resource development, creation of infrastructure facilities, and supporting research and development (R&D) in specific areas. The success and impact of the National Biotechnology Board prompted the Government to establish a separate Department of Biotechnology (DBT) in February 1986. There have been major accomplishments in areas of basic research in agriculture, health, environment, human resource development, industry, safety, and ethical issues.

Basic Research

Basic research is essential on all aspects of modern biology including development of the tools to identify, isolate, and manipulate the individual genes that govern the specific characters in plants, animals, and microorganisms. Recombinant DNA (rDNA) technology is the basis for these new developments. The creativity of the scientists and the basic curiosity-driven research will be the keys to future success. India led through the work of G.N. Ramachandran, in which he elucidated the triple helical structure of collagen. The Ramachandran plot has proven to be fundamental in solving the protein structure. Areas of biosystematics using molecular approaches, mathematical modeling, and genetics including genome sequencing for human beings, animals, and plants, will continue to have priority as we move into the next century. The tremendous impact of genome sequencing is increasingly evident in many fields. As an increasing number of new genes are discovered, short, unique, expressed sequenced tags segments are used as signatures for gene identification. The power of high throughput sequencing, together with rapidly accumulating sequenced data, are opening new avenues in biosciences.

In the plant genome area, the sequencing of *Arabidopsis* and rice genome will soon be completed and cataloging and mapping of all the genes will be done.

There have been major achievements in basic bioscience in the last decade or so in India, where we have expertise in practically all areas of modern biology. The institutions under the CSIR, ICMR, ICAR, DST, and DBT have established a large number of facilities where most advanced research work in biosciences is being done. In the identification of new genes, development of new drug delivery systems, diagnostics, recombinant vaccines, computational biology, and many other related areas, considerable success has been achieved. Breakthroughs include studies on the three-dimensional structure of a novel amino acid, a long protein of mosquito (University of Poona), and demonstration of the potential of the reconstituted Sendai viral envelops containing only the F protein of the virus, as an efficient and site-specific vehicle for the delivery of reporter genes into hepatocytes (Delhi University).

Agriculture and Allied Areas

The post Green Revolution era is almost merging with the gene revolution for improving crop productivity and quality. The exploitation of heterosis vigor and development of new hybrids including apomixis, genes for abiotic and biotic resistance, and developing planting material with desirable traits and genetic enhancement of all important crops will dominate the research agenda in the next century. Integrated nutrient management and development of new biofertilizers and biopesticides would be important from the view- point of sustainable agriculture, soil fertility, and a clean environment. Stress biology, marker-assisted breeding programs, and studying the important genes will continue as priorities. We will have to switch to organic farming practices, with greater use of biological software on a large scale.

In India we have achieved the cloning and sequencing of at least six genes, developed regeneration protocols for citrus, coffee, mangrove species, and new types of biofertilizer and biopesticide formulations, including mycorrhizal fertilizers. Research to develop new genetically improved (transgenic) plants for brassicas, mung bean, cotton, and potato is well advanced. Industries have also shown a keen interest in the options of biotechnology and are participating in field trials and pilot level productions. The successful tissue culture pilot plants in the country, one at TERI in New Delhi and the other at NCL in Pune are now functioning as Micropropagation Technology Parks. This has given a new direction to the plant tissue culture industry. The micropropagation parks serve as a platform for effective transfer of technology to entrepreneurs, including training and the demonstration of technology for mass multiplication of horticulture and trees. Considerable progress has been made with cardamom and vanilla, both important crops. Yield of cardamom has increased 40 percent using tissue-cultured plants.

Between 1996 and 1998, in just eight countries, the area covered by new genetically improved transgenic plants (from 16.8 to 27.8 million hectares) (James 1998). Some of the main crops grown are soybean, corn, canola, cotton, and potato. The United States, Argentina, Brazil, and China have moved ahead quickly. The new plants exhibited herbicide, insect, and viral resistance, and overall improvement in product quality.

While the Green Revolution gave us self-reliance in food, the livestock population has provided a "White Revolution," with 80 percent of the milk in India coming from small and marginal farms. This has had a major social impact. A diverse infrastructure has been established to help farmers in the application of embryo transfer technology. The world's first IVF buffalo calf (PRATHAM) was born through embryo transfer technology at the National Dairy Research Institute, Karnal. Multiple ovulation and embryo transfer, in vitro embryo production, embryo sexing, vaccines and diagnostic kits for animal health have also been developed. Waste recycling technologies that are cost effective and environmentally safe, are being generated. The animal science area is also opening up many avenues for employment generation.

With a coastline of more than 8,000 kilometers, and two island territories of Andaman and Nicobar and Lakshadweep, there is great potential for marine resource development and aquaculture. To achieve an annual target production of 10 million metric tons of fish, scientific aquaculture offers great possibilities. In fact, aquaculture products are among the fastest moving commodities in the world. We have to continuously improve seed production, feed, health products, cryopreservation, genetic studies, and related environmental factors. This is an area which will help substantially in the diversification of the breadbasket, and in combating nutritional deficiency.

Food Security

Food security is another area in which biotechnology offers major inputs for healthier and more nutritious food. Millions of people are malnourished, and Vitamin A deficiency affects 40 million children. There are also serious deficiencies of iodine, iron, and other nutrients. A recent UNICEF report on food and nutrition deficiencies in children describes this as a "silent, invisible emergency with no outward sign of a problem." Every year over 6 million children under the age of 5 die worldwide. About 2.7 million of these children die in India. More than half of these deaths result from inadequate nutrition.

With the advent of gene transfer technology and its use in crops, we hope to achieve higher productivity and better quality, including improved nutrition and storage properties. We also hope to ensure adaptation of plants to specific environmental conditions, to increase plant tolerance to stress conditions, to increase pest and disease resistance, and to achieve higher prices in the marketplace. Genetically improved foods will have to be developed under adequate regulatory processes, with full public understanding. We should ensure the safety and proper labeling of the genetically improved foods, so consumers will have a choice.

It is scientifically well established that an environmentally benign way of ensuring food security is through bioengineering of crops. For the 4.6 billion people in developing countries, one billion do not get enough to eat and live in poverty. Is there any other strategy or alternative? Biotechnology will provide the new tools to breeders to enhance plant capacity. Since we know that 12 percent of the world land is under agricultural crops, it is projected that the per capita availability may be reduced from 2.06 hectares to 0.15 hectare by 2050.

Plant Biotechnology

With more than 47,000 species of plants and two hot-spots of biodiversity, 8 percent of the total biodiversity of the earth is available in the Indian subcontinent. The bioresource and biodiversity constitute the mainstay of the economy of the poor people, and special emphasis is required for plant biotechnology research. Isolation of genes for abundant proteins, combining molecular genetics and chromosome maps, and a much better understanding of the evolutionary relationship of the members of the plant kingdom, have led to the potential of plant species being the major source of food, feed, fiber, medicine, and industrial raw material. Molecular fingerprinting and areas of genomics and proteonics will penetrate the barriers of fertilization to allow transfer of important characters from one plant to another. By identifying appropriate determinants of male sterility, we can extend the benefit of hybrid seeds to more crops. We must help the farmer by ensuring hybrid vigor generation after generation. Additional research on apomixis would open up such possibilities.

We have set up a National Plant Genome Research Centre at Jawaharlal Nehru University. A number of centers for plant molecular biology in different parts of the country were initially responsible for training significant numbers in crop biotechnology. There are innumerable possibilities of producing more proteins, vitamins, pharmaceuticals, coloring material, bioreactors, production of edible vaccines, therapeutic antibodies and drugs. Promising leads are available in these areas, and a number of genetically improved crops are ready for field trials of transgenic plants. Work on developing transgenic cotton, brassica, mung bean, and potato has significantly advanced.

Environment

A special area of global concern amongst the scientific community is environmental protection and conservation, and the need for a policy of sustainable development in harmony with the environment. The Stockholm Conference in 1972, and the UNCED Conference in Rio de Janeiro in 1992, both focused world attention on areas of pollution, biodiversity conservation, and sustainable development. Plants and microbes are becoming important factors in pollution control. World Bank estimates show that pollution in India is costing almost US$80 billion, as well as the human cost in terms of sickness and death. New developments such as bioindicators, phytoremediation methods, bioleaching, development of biosensors, and identification and isolation of microbial consortia are priority research areas. Significant work has been done in India, but developing a more biologically oriented approach towards pollution control would be extremely important. Cleaning up the large river systems and ensuring the destruction of pesticide residue in large slums in the city are priorities in which a biotechnological approach would be environmentally safe.

Phytoremediation to remove the high levels of explosives found in the soil has become a reality. Although it was known that some microbes can denitrify the nitrate explosives in the laboratory, they could not thrive on site. French and others (1999) have transferred this degradative ability from the microbe to tobacco plants, and these have produced a microbial enzyme capable of removing the nitrates.

Biodiversity

The global biosphere can survive only if resource utilization is about 1 percent and not 10 percent. The global environment is regulated by climate changes and biosphere dynamics. Knowledge about biodiversity accumulated in the last 250 years is being used by scientists throughout the world. There are many gene banks, botanical gardens, and herbaria for conservation purposes. There are also molecular approaches including DNA fingerprinting for plant conservation. The totality of gene species and ecosystems has become exceedingly important, not only to understand the global environment but also from the viewpoint of the enormous commercial significance of the biodiversity.

Biotechnology is becoming a major tool in conservation biology. Twelve percent of the vascular plants are threatened with extinction. Over 5,000 animal species are threatened worldwide, including 563 Indian species. India also has about 2000 species of vascular plants that are threatened.

Biodiversity is under threat, and understanding the scale of this destruction and extinction is essential. Questions such as who owns the biodiversity, who should benefit from it, and what is the role of society and the individual are pertinent. There is a Kashmiri proverb that says: *We have not inherited the world from our forefathers, we have borrowed it from our children.*

More research is needed on forests, marine resources, bioremediation methods, restoration ecology, and large-scale tree plantations. The last has reached 180 million hectares and may increase substantially in the next decade. Marine resources provide many goods and benefits including bioactive materials, drugs, and food items and must be characterized and conserved.

Medical Biotechnology

A major responsibility of biotechnologists in the 21st century will be to develop low-cost, affordable, efficient, and easily accessed health care systems. Advances in molecular biology, immunology, reproductive medicine, genetics, and genetic engineering have revolutionized our understanding of health and diseases and may lead to an era of predictive medicine. Genetic engineering promises to treat a number of monogenetic disorders, and unravel the mystery of polygenetic disorders, with the help of research on genetically improved animals. Globally, there are about 35–40 biotechnology-derived therapeutics and vaccines in use and more than 500 drugs and vaccines in different stages of clinical trials.

Every year about 12 million people die of infectious diseases. The main killers according to WHO are acute respiratory infection, diarrheal diseases, tuberculosis, malaria, hepatitis, and HIV-AIDS. There are vaccines being developed for many diseases, and diagnostic kits for HIV, pregnancy detection, and hepatitis are being developed. The technologies have been transferred to industry.

The Department of Biotechnology has developed guidelines for clinical trials for recombinant products, which have now been accepted by the Health Ministry and circulated widely to industry. Promising leads now exist to develop vaccines for rabies, *Mycobacterium* tuberculosis, cholera, JEV, and other diseases. Recombinant hepatitis B vaccine and LEPROVAC are already on the market. There is a Jai Vigyan technology mission on the development of vaccines and diagnostics. A

National Brain Research Centre is being established to improve knowledge of the human brain and the brain diseases.

The discovery of new drugs and the development of the drug delivery system are increasingly important. Bioprospecting for important molecules and genes for new drugs has begun as a multi-institutional effort. A recombinant vaccine for BCG and hepatitis is being developed. The age-old system of Ayurveda practiced in India needs to be popularized and made an integral part of health care. The global market for herbal products may be around US$5 trillion by 2050.

Industrial Biotechnology

Advances in biotechnology can be converted into products, processes, and technologies by creating an interdisciplinary team. The pharmaceutical sector has had a major impact in this field, as rare therapeutic molecules in the pure form become available. Diagnostics have expanded, with over 600 biotechnology-based diagnostics (valued at about US$20 billion worldwide) now available in clinical practice. The polymerase chain reaction (PCR)-based diagnostics are the most common. Indian efforts in the diagnostic area have been commendable, and it is expected that sales will rise from about US$235 million to US$470 million in the next century.

The consumption of biotechnology products is expected to increase from US$6.4 billion to about US$13 billion by 2000. Industrial enzymes have emerged as a major vehicle for improving product quality. In India a number of groups are gearing up to produce industrial enzymes such as alpha-amylose, proteases, and lipases, increasing three-fold by the end of the century, which will match or surpass the computer industry in size, importance, and growth. India is now producing 13 antibiotics by fermentation. Capacity exists to produce important vaccines such as DPT, BCG, JEV, cholera, and typhoid. Cell culture vaccines such as MMR and rabies, and hepatitis-B, have also been introduced

Bioinformatics

The coming together of biotechnology and informatics is paying rich dividends. Genome projects, drug design, and molecular taxonomy are all becoming increasingly dependent on information technology. Information on nucleotides and protein sequences is accumulating rapidly. The number of genes characterized from a variety of organisms and the number of evolved protein structures are doubling every two years. DBT has established a national Bioinformatics Network with ten Distributed Information Centres (DICs) and 35 sub-DICs. A Jai Vigyan Mission on establishment of genomic databases has been started, with a number of graphic facilities created throughout the country. This system has helped scientists involved in biotechnology research.

Ethical and Biosafety Issues

The bioethics committee of UNESCO established in 1993 has evolved guidelines for ethical issues associated with the use of modern biotechnology.

Biosafety guidelines for genetically improved organisms (GIOs) need to be strictly followed to prevent harm to human health or the environment. A three-tier mechanism of Institutional Biosafety Committees has been instituted in India: the Review Committee on Genetic Manipulation, the Genetic Engineering Approval Committee, and the state level coordination committees. It is important to give a clear explanation of the new biotechnologies to the public to allay their fears. New models of cooperation and partnership have to be established to ensure close linkages among research scientists, extension workers, industry, the farming community, and consumers.

Gene transformation is done worldwide with four broad objectives: (a) to develop products with new characteristics; (b) to develop pest and disease resistance; (c) to improve nutritional value; and (d) to modify fruit ripening to obtain longer shelf life. Thus the aims and objectives are laudable and the tools are available. The new technology does, however, call for a cautious approach following appropriate biosafety guidelines.

About 25,000 field trials of genetically modifed crops have been conducted worldwide. The anticipated benefits are better planting material, savings on inputs, and genes of different varieties can be introduced in the gene pool of crop species for their improvement. The potential risks include weediness, transgene flow to nontarget plants, and the possibility of new viruses developing with wider host range and their effects on unprotected species. For crops such as corn and cotton with single gene introductions, there is very little problem expected. When multiple genes are involved scientists have to be more cautious.

The time has arrived for a serious look at ethical and biosafety aspects of biotechnology. Researchers, policymakers, NGOs, progressive farmers, industrialists, government representatives, and all concerned players need to come together and share a platform to address the following issues.

- Environmental safety
- Food and nutrition security
- Social and economic benefits
- Ethical and moral issues
- Regulatory issues.

Human Resource Development

There are about 50 approved MS, postdoctoral, and MD training programs in biotechnology in progress or just about to start, in different institutions and universities covering most Indian States. Short-term training programs, technician training courses, fellowships for students to go abroad, training courses in Indian institutions, popular lecture series, awards, and incentives form an integral part of the human resource development activities in India. A special feature of the program has been that since 1996 many students after completion of their training course join industries or work in biotechnology-based programs in institutions and laboratories. National Bioscience Career Development Awards have been instituted. Special awards for women scientists and scholarships to the best students in biology help promote biotechnology in India and give recognition and reward to the scientists.

Some Special Programs

Biotechnology-based activities to benefit the poor and weaker sections and programs for women have been launched. A unique feature is the establishment of a Biotechnology Golden Jubilee Park for Women which will encourage a number of women entrepreneurs to take up biotechnology enterprises that benefit women in particular. This will also encourage women biotechnologists to develop relevant technologies.

States are taking a keen interest in developing biotechnology-based activities. The States of Uttar Pradesh, Arunachal Pradesh, Madhya Pradesh, Kerala, West Bengal, Jammu and Kashmir, Haryana, Mizoram, Punjab, Gujarat, Meghalaya, Sikkim and Bihar have already started large-scale demonstration activities and training programs.

Investment Required

The Indian Government has made substantial investments in biotechnology research. Bringing Indian biotechnology products to market will require the involvement of large and small entrepreneurs and business houses. This will require substantial investments from Indian and overseas investors. The worldwide trend is that large companies are becoming major players in development of biotechnology products, and also in supporting product-related biotechnology research.

Expectations

In the years ahead, biotechnology R&D should produce a large number of new genetically improved plant varieties in India, including cotton, rice, brassicas, pigeonpea, mung bean, and wheat. Tissue culture regeneration protocols for important species such as mango, saffron, citrus, and neem will lead to major commercial activities. Micropropagation technology will provide high-quality planting materials to farmers. Environment-friendly biocontrol agents and biofertilizer packages will hopefully be made available to farmers in such a way that they can produce these in their own fields. The country should be in a position to fully utilize, on a sustainable basis, medicinal and aromatic plants. The development through molecular biology of new diagnostic kits and vaccines for major diseases would make the health care system more efficient and cheaper. Genetic counselling clinics, molecular probes, and fingerprinting techniques should all be used to solve the genetic disorders in the population. The establishment of ex situ gene banks to conserve valuable germplasm and diversity, and a large number of repositories, referral centers for animals, plants, and microorganisms should be possible. Detailed genetic readouts of individuals could be available. Information technology and biotechnology together should become a major economic force. It is expected that plants as bioreactors would be able to produce large numbers of proteins of therapeutic value, and many other important items. The recent discovery of the gene for recalcitrant species was a landmark event. In vitro mass propagation can be carried out on any desired species with nonrandom programming. Certainly the 21st century could witness a major increase in new bioproducts generated through modern biology.

To achieve the goal of self-reliance in this field, India will require a strong educational and scientific base, clear public understanding of the value of new biotechnologies, and involvement of society in many of these biological ventures. India has a large research and educational infrastructure comprising 29 agriculture universities, 204 central and state universities, and more than 500 national laboratories and research institutions. It should therefore be possible to develop capabilities and programs so that these institutions act as regional hubs for the farming community, where they can get direct feedback about new technological interventions. It will be equally important to establish strong partnerships and linkages with industry, from the time a research lead has emerged until the packaging of the technology and commercialization are achieved. Arther Kornberg, Nobel Laureate, stated: *"Much has been said about the future impact of biotechnology on industrial development, but this does not yet apply to the less developed countries that lack this infrastructure and industrial strength. In view of the current power of biotechnology and its even brighter future, there is no question that the less developed countries must now position and strengthen their status in biotechnology."*

Kornberg further stressed that :"*What a tragedy it would be if these enlarged concepts of genetics, biology and chemistry were available only to a small fraction of the world population located in a few major centres of highly developed countries."*

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Philippines: Challenges, Opportunities, and Constraints in Agricultural Biotechnology

Reynaldo E. de la Cruz

The Philippines has a land area of 30 million hectares and a population of over 70 million (1998). In 1997, the combined area devoted to agriculture was 10.3 million hectares, with coconut being the most widely planted crop, followed by rice, corn, banana, pineapple, and others. The area and production of some important agricultural crops are presented in Table 1. Rice and corn lead in area and production. The country is a major producer of coconut, sugarcane, banana, and pineapple. The export value of sugarcane has gone down considerably in recent years.

More than 70 percent of the population is directly or indirectly dependent on agriculture. Most of the land is owned by small farmers. Significant increases in population have placed tremendous pressure on agricultural lands. Prime lands are now being converted into resettlement areas and for industrial uses. Agricultural land area has therefore been decreasing through time.

Table 1 Area and production of some important agricultural crops

Agricultural crops	*Area in million hectares*	*Production in million metric tons*
Rice and corn	4.75	26.9
Coconut	4.00	12.0
Sugarcane	0.70	3.4
Banana	0.21	21.6
Pineapple	0.04	1.6
Coffee	—	0.1
Others	0.60	2.4
Total	**10.30**	**68.0**

Source: Bureau of Agricultural Statistics Report, 1997.

Biotechnology in the Philippines

The Philippines started its biotechnology programs in 1980 with the formal creation of the National Institute of Molecular Biology and Biotechnology (BIOTECH) at the University of the Philippines at Los Baños (UPLB). In 1995, three other biotechnology institutes were established within the University of the Philippines System. They are located in the UP Diliman campus to focus on industrial biotechnology, UP Manila to focus on human health biotechnology, and UP Visayas to focus on marine biotechnology.

The biotechnology institute in UP Los Baños continues to provide leadership in agricultural, forestry, industrial, and environmental biotechnology. Other research institutes at UPLB are also doing biotechnology research. Among these are the Institute of Plant Breeding, Institute of Biological Sciences, Institute of Animal Sciences, Institute of Food Science and Technology, and the College of Forestry and Natural Resources. Outside UPLB, other research institutes and centers such as the Philippine Rice Research Institute, Philippine Coconut Authority, Cotton Research and Development Institute, Bureau of Plant Industry, the Bureau of Animal Industry, and the

Industrial Technology and Development Institute are also involved in biotechnology R&D.

The type of research undertaken in the Philippines from 1980 to 1999 is mainly conventional biotechnology, with the exception of a small amount of work on molecular markers and the development of genetically improved organisms (GIOs) with useful traits. The results of a survey on the budget spent for biotechnology R&D in the country from 1980 to 1999 are given in Table 2.

In 1998, five high level biotechnology research projects were funded by government:

- Transgenic banana and papaya resistant to banana bunchy top virus and papaya ringspot virus, respectively
- Delayed ripening of papaya and mango
- Bt corn
- Marker-assisted breeding in coconut
- Coconut with high lauric acid content.

Almost 80 percent of the total annual budget for biotechnology R&D comes from the government. Fifteen percent comes from international development agencies, while the private sector contributes approximately 5 percent. The private sector is expected to provide more funding in future as they see the potential of biotechnology in agriculture.

In 1997, the Agriculture Fisheries Modernization Act (AFMA) became law. The main objective of AFMA is to modernize agriculture, including infrastructure, facilities, and R&D.

Table 2 Type of biotechnology R&D, number of projects, and percentage of total projects funded from 1980 to 1999

Type of biotechnology R&D	*Number of projects*	*Percent of total*
Biocontrol	55	20.5
Soil amendments	44	16.5
Food/beverage	43	16.3
Tissue culture	52	19.5
Feed component	20	7.5
Enzymes	16	6.0
Diagnostics	7	2.6
Farm waste utilization	4	1.5
Vaccines	3	1.1
Animal reproduction	3	1.1
Molecular markers	12	4.6
GMOs	7	2.7
Total	**266**	**100.0**

Source: Survey conducted by UPLB BIOTECH, 1999.55

AFMA recognized biotechnology as a major strategy to increase agricultural productivity. The law states that AFMA will provide a budget of 4 percent of the total R&D budget per year for biotechnology during the next 7 years. This allocation provides an annual budget for biotechnology of almost US$20 million. Before AFMA, the annual budget for biotechnology averaged less than US$1 million.

AFMA operates through National Research, Development and Extension (RDE) network systems of 13 commodities and five disciplines. The 13 commodity networks are rice, corn, root crops, coconut, plantation crops, fiber crops, vegetables/spices, ornamentals, fruit/nuts, capture fisheries, aquaculture, livestock and poultry, and legumes. All of these commodities include biotechnology in their RDE agenda. The five discipline-oriented RDE networks are fishery postharvest and marketing, soil and water resources, agricultural and fisheries engineering, postharvest, food and nutrition, social science and policy, and biotechnology. As a discipline, biotechnology focuses on upstream basic research, which includes work in molecular biology. The commodity networks focus on downstream (application) research.

The main goal of biotechnology R&D under AFMA is to harness the potential of this cutting edge technology to increase productivity of all the commodities in the agriculture and fishery sectors. Biotechnology will therefore play a major role in the selection and breeding of new varieties of plants and animals. It will also provide the inputs required such as biofertilizers and biocontrol of harmful pest and diseases. Biotechnology will also be tapped to produce genetically improved crops with resistance to harmful pests and diseases, for accurate diagnosis and control of diseases in plants and animals, for bioremediation of the environment, and for bioprospecting. AFMA envisions that the benefits derived from biotechnology will reach the small farmers and fishermen.

The Philippines does not have the critical human resources required for biotechnology R&D. As of 1999, there were about 250 scientists qualified to do high-level biotechnology R&D. Most of the researchers are affiliated with universities, particularly UPLB.

Adequate laboratory facilities and equipment for upstream biotechnological research exist at a number of institutions in the Philippines, including BIOTECH based at UPLB and UP Diliman, the Institute of Biological Sciences, Institute of Plant Breeding, and Philippine Rice Research Institute. There is a need, however, to upgrade most of the laboratories in the country.

Challenges

Although the country recognizes the tremendous potential that can be achieved from biotechnology, several challenges need to be met before the goals set can be achieved.

Increase Productivity

Yields of crops and livestock have been declining, while demands are increasing, because of the rapid increase in population. Conversion of prime agricultural lands into other uses has placed tremendous pressure on the agricultural sector to increase productivity per unit area. Productivity has been affected by poor soil fertility, the incidence of pests and diseases, abiotic stresses such as drought caused by El Niño and climatic factors especially typhoons. The challenge is to use biotechnology to increase productivity and yield on the farms using minimal inputs.

Global Competitiveness

With impending trade liberalization, the country expects to receive cheap agricultural products from other countries, thus widening its balance of trade. In 1997, the value of Philippine exports was US$25.2 million while imports were valued at US$35.9 million giving a negative trade balance of US$10.7 million. The challenge is to use biotechnology to produce local products that are highly competitive with those from foreign sources, thereby promoting exports of quality products while reducing imports.

Biosafety and Risk Assessment

The Philippines is sensitive to the issue of biosafety. We have one of the strictest biosafety guidelines in the world to undertake R&D and for field testing. The challenge is to improve and better implement the current biosafety guidelines, taking advantage of knowledge generated worldwide. Protocols are needed to assess risk of GIOs and to manage any identified risk factors. The challenge is for the Philippines to develop its capability to undertake risk assessments and management, based on scientific evidence.

Regulation of Biotechnology Products

The commercial release of new products must be regulated. At present, all regulatory bodies such as the Bureau of Plant Industry (BPI), Bureau of Animal Industry (BAI), Fertilizer and Pesticide Administration (FPA), Bureau of Food and Drugs Administration (BFAD), and the Environment and Management Bureau (EMB) do not have a policy and guidelines to regulate the commercial release of new genetically improved products. In addition, the institutional support system, such as laboratories and infrastructure is not in place. The challenge is to create guidelines to regulate commercialization of GIOs, the establishment of support laboratories and infrastructure, and the training of people for these regulatory bodies.

Transfer of Technology/Commercialization

Products of research will not create any measurable impact unless they are transferred to end-users and/or commercialized. The challenge is to transfer products to users, particularly to small farmers and fishermen. This requires the proper packaging of the product to attract private investors for eventual commercialization.

Trade-Related Issues

Transgenic crops and other GIO products may become trade-related issues in the future because of trade liberalization. It is expected that new genetically improved crops will be imported into the Philippines. The challenge is to create public awareness of the benefits and risks of any new product and assist acceptance of new technologies by consumers, where these are beneficial.

Intellectual Property Protection

Because the process, products, and genetic materials used in biotechnology R&D have proprietary considerations, issues of intellectual property protection by patents and plant variety protection (PVP) will arise. The present Intellectual Property Code of the Philippines allows the patenting of microorganisms, but not plants and animals. Plant varieties will be protected by *sui generis* mechanism if the PVP bill is passed by both houses of Congress. The challenge is for the country to strengthen its IPR laws to provide protection to researchers, discoverers, and investors.

Opportunities for Biotechnology

Although the Philippines is lagging behind the industrial countries and its ASEAN neighbors in terms of R&D in biotechnology, many windows of opportunities are open.

Increased Yield of Plants

Biotechnology provides the opportunity for researchers to improve plant growth, development, and yield by providing for the basic needs of the plant such as biofertilizers and biocontrol agents.

Genetically Improved Plants

The country recognizes the tremendous potential of improved crop plants containing genes that provide pesticidal properties, resistance to herbicides, tolerance to pests, disease, and stress (salt, heavy metals, and drought), or combinations of these properties. Such improved plants are expected to reduce considerably production costs such as inputs of fertilizers and pesticides. Once the issues of biosafety regulations and intellectual property have been settled, the country will be open to use such new plant technologies that are now limited to only a few countries.

Marker Technologies

These technologies may help speed up the selection and production of more effective hybrids. Most breeding work in the country is now using this technology, specifically in rice, corn, banana, and coconut.

Livestock

Tremendous opportunities are available for livestock biotechnology, including the production of vaccines for foot and mouth disease and hemorrhagic septicemia, for diagnostics, and *in vitro* fertilization.

Microbial Products

Opportunities are available for the use of microorganisms for biofertilizers, biopesticides, and bioremediation of the environment.

Bioprospecting

The Philippines is blessed with rich genetic resources waiting to be tapped for food, fiber, enzymes, and drugs. New beneficial genes are expected to be discovered in the highly diverse species of plants, animals, microorganisms, and marine organisms. The challenge is to save and use judiciously the rich biodiversity of the country which make it one of the *hotspots* of biological diversity in the world.

The rich biodiversity of the country offers many opportunities in the search for novel genes and gene products. The Philippines has in place a law governing access of genetic resources by foreign and local bioprospectors. This law is designed to protect both the bioresource and the bioprospectors.

Introduction of Foreign Technologies

Because of the importance given to R&D in biotechnology under AFMA, introduction of foreign technologies, including genes that offer unique advantages, may have great potential for the country. For example, the sugar industry had been declining because of competition with high fructose syrup and other sugar substitutes. There are opportunities to use sugarcane, a highly efficient plant to produce high-value products such as oral vaccines, biodegradable plastics, and other products.

Joint R&D Collaboration

Collaboration between Philippine and overseas researchers is one opportunity that is now well in place. Many researchers actively collaborate with researchers from Australia, Canada, USA, Japan, South Korea, and countries of the European Union.

Constraints

Although the R&D opportunities are evident, there are some additional constraints that need to be addressed.

Difficulty in Accessing New Technologies

Development of the local biotechnology industry has been hampered because of the inability of researchers to access state-of-the-art technologies. Researchers are therefore repeating work done elsewhere rather than being able to adopt current technologies.

Antibiotechnology Groups

Some NGOs and individuals in academe and government services do not support biotechnology. These groups are well organized and well funded, and are highly successful in promoting anti-biotechnology sentiments in the country. They are also instrumental in convincing legislators to enact resolutions imposing moratoria on research and commercialization of GIOs. While they focus on GIO products produced and brought into the country by multinational companies, they also affect the R&D of local researchers.

Biosafety Guidelines

The present set of biosafety guidelines is one of the strictest in the world. The guidelines were originally patterned after those first used in the United States, Australia, and Japan during the early 1980s. Since then, all these countries have relaxed most of their guidelines as a result of new technical data and familiarity in dealing with new products. However, the Philippines did not relax its guidelines.

Commercial Release

New genetically improved products cannot be commercialized in the country because the regulatory bodies cannot issue the required permits or licenses. The regulations allow only limited field trials of genetically improved organisms. The regulatory bodies lack the proper guidelines and institutional support to regulate the new products. This is a major constraint because any potentially useful new product cannot be commercialized after the field trials.

How CGIAR Centers Can Help

The CGIAR centers can play a larger role in assisting national centers develop their R&D capabilities in biotechnology. Some activities that CGIAR centers can undertake include:

Germplasm Exchange

Most CGIAR centers hold extensive collections of germplasm, the starting point for selection, breeding, and genetic manipulation. The centers are in a position to share or exchange this germplasm with local researchers or institutes.

Joint Collaborative R&D

Centers should encourage more joint collaborative research with local institutes and share their financial and human resources and infrastructure with less well-endowed local research institutes. Centers are also in a position to assist through training, workshops, and scholarships, human resources development.

Regulatory Arrangements

Centers should help countries develop their biosafety protocols and competence in risk assessment and management of biotechnology products. Centers may also be able to assist countries in developing regulatory mechanisms and institutional capabilities for the commercialization of biotechnology products.

Advocacy

CGIAR Centers should be more proactive in promoting popular awareness and acceptance of the products of modern biotechnology.

Conclusion

Researchers, policymakers, industry people, and the CGIAR system must address the challenges, opportunities, and constraints that face R&D in biotechnology at this critical time of increasing population, globalization, trade liberalization, concerns with biosafety, regulation, and intellectual property. All countries share these same challenges, opportunities, and constraints although at different levels.

The above challenges, opportunities, and constraints can be addressed by CGIAR centers at the international level and by national R&D centers at a country level, with harmonized activities at internatiobnal, regional and country levels.

For developing countries, the small farmers and fisherfolks should be the main beneficiaries of biotechnology R&D. Biotechnology will only prosper if the private sector actively participates in the R&D aspect as well as in the commercialization stage.

Thailand: Biotechnology for Farm Products and Agro-Industries

Morakot Tanticharoen

Before the economic crisis in 1997, Thailand was named one of the Asian Newly Industrialized Countries (NICs) with an average economic growth rate of 8-9percent during 1993-95. The crisis resulted in a negative growth rate of –7.8 percent in 1998. Moreover, the impact of the economic recession in the world market has affected the country's total exports, which amounted to US$57 billion (US$1=31.5 bahts) and US$53 billion (US$1=41.6 bahts) in 1997 and 1998, respectively. The economic growth forecast for 1999 is expected to be around 3-4 percent.

Efforts to revive the economy are currently being implemented in both the government and the private sector. The linkage between the status of science and technology and the economic status of a country has long been noted. At this stage, it is crucial for Thailand to increase the technological capability of the country, to make efficient use of its resources, and to reduce the cost of production, thereby increasing economic growth and competitiveness.

Despite the country's industrialization, agriculture has remained a significant part of the economy. Thailand has been moving towards industrial-based agriculture and has focused on the development of postharvest and processing technologies that are the major problems for industry. Biotechnology has become the country's priority for research and development (R&D) and for the benefit of the private sector as well as rural development.

Farm Products and Agro-Industries

Though most of the economic sector registered negative growth rates, the agriculture sector has expanded by about 2.8 percent in 1998. Thailand's Ministry of Agriculture estimated that farmers would earn 650 billion bahts (US$16.2 billion) for 1998, of which 74 percent would come from the major products listed in Table 1.

Estimated earnings might only be 404 billion baht (US$ 9.85 billion), a 16 percent decline in 1999. The situation could result from a weaker demand abroad, coupled with the stronger baht. (Values in this paper are based on a baht/US$ exchange rate of 41). Water shortage will have a major impact on agriculture, particularly with paddy from the second crop.

The government promotion to develop agribusinesses since 1976 has greatly contributed to the expansion of agroprocessing. Thailand's top 10 export products in 1997 and 1998 are rice, canned foods, rubber, frozen shrimp and prawn. Export earnings for the first nine months of 1998 were US$6 and US$3.9 billion for agricultural products and agro-industry products, respectively. Combined export earnings from agriculture accounted for 23 percent of total earnings

Table 1 Production of key agricultural products and earnings in 1997-98 and 1998-99

	Earning [a] (US$ billions)		*Production [c] (million metric tons)*	
	1997-98	*1998-99 [b]*	*1997-98*	*1998-99 [b]*
Rice	4.43	3.27	23.38	21.5
Black tiger prawn	1.56	1.42	0.21	0.20
Rubber	1.33	1.18	2.20	2.31
Swine	1.25	1.23	no data	no data
Sugarcane	0.77	0.60	42.20	42.60
Cassava	0.69	0.45	15.44	16.37
Chicken	0.68	0.70	0.83	0.84
Maize	0.42	0.50	3.84	4.99
Chicken eggs	0.38	0.38	no data	no data
Oil palm	0.023	0.02	2.63	2.67
Soybean	0.009	0.009	0.36	0.37

a. Commerce Ministry.
b. Estimates.
c. Ministries of Commerce and Agriculture.

(Department of Business Economics). Thailand's top ten food exports in 1998 are:

	Export Value (US$ millions)
Rice	2.17
Canned fish	1.69
Fresh chilled/frozen shrimps, prawns and lobsters	1.45
Sugar	0.66
Tapioca (cassava) products	0.57
Chilled/frozen poultry cuts	0.41
Prepared/preserved fruits in air-tight containers	0.38
Fresh chilled/frozen cuttle fish, squids and octopus	0.29
Prepared/processed foods for animal feeds	0.25
Processed poultry	0.22

The value of agricultural exports rose dramatically because of the weakened local currency. However, exports of agricultural products declined in dollar terms 13.1 percent, followed by a 12.1 percent decline in agro-industry products. Recent exports have been hit by tough price competition from lower-wage Asian countries. The result showed that Thailand could not depend solely on its weaker currency to boost exports. To remain competitive, Thailand will have to focus more on the country's development, and be more innovative and creative in R&D.

R&D Priorities

Improving crop yield and protecting agricultural crops from diseases and pests, improving postharvest handling, and diversifying products are all priorities for Thailand.

There is a need to improve productivity of Thai crops, while retaining their unique qualities (for example, the fragrant Thai rice Khao Dawk Mali). Rice productivity in Thailand averages only 2.42 metric tons/hectare compared to 6.3, 6.0, 4.3, and 3.6 metric tons/hectare in the United States, China, Indonesia, and Vietnam, respectively. Thai sugarcane yields are only 48.8 metric tons/hectare compared with 93.8 in Brazil. The country's 46 sugar mills, meanwhile, have the capacity to process more than double the amount of cane they now receive. Another problem with Thai cane is the sweetness. The international grading system has given a rating of 11 ccs (commercial cane sugar) for Thai sugar compared with 13 to 14 for other countries. The Office of the Cane and Sugar Board's main activity at the moment is to develop better sugarcane varieties with the goal of increasing the sweetness grade of Thai cane to 15 within five years. The new varieties should also be resistant to drought, salty soil, and diseases.

Agricultural Development Priorities

A master plan for Thailand's agricultural development was approved by the government in early 1998 to make exports more competitive. The objectives are supported by a master plan for industrial restructuring approved in April 1998. Thirteen industries will be promoted to make Thailand a key export center in Asia within two years. Three industries using agricultural products (food and animal feed, rubber and rubber products, and wooden products including furniture) are included in 13 industries. Key agricultural projects planned by a committee chaired by the Deputy Agriculture Minister are:

- The establishment of integrated agricultural zones for exports.
- R&D to raise production and cut costs by using new technology with emphasis on biotechnology. Rice, livestock, rubber, durian, longan, and orchids have priority.
- Bringing product quality and processing up to international requirements. A center to control quality from the raw material stage to the finished product will be established.
- Restructuring the Agriculture Ministry to modernize its management and services.
- Encouraging farmers to use less chemical fertilizer while promoting natural alternatives and organic production.
- Improving management of land use and ownership, natural resources, irrigation, and coastal areas.
- The establishment of weather warning systems in high-risk areas.
- Improving farm methods and technology.

The Agriculture Ministry outlined five strategic plans for 1999 with a budget of about US$1 billion:

- Increase competitiveness of farm products for export and import substitution (US$305 million), and to promote self-sufficient farm projects (US$24 million)
- Management of natural resources and the environment (US$372 million)
- Development of agricultural institute (US$225 million) to encourage community-based production
- Plans initiated by His Majesty the King (US$78 million)
- Preparation for the 21st century (US$4 million).

Apart from the government's annual budget, the ministry has obtained US$600 million, mainly from the Asian Development Bank (ADB) to improve the agricultural economy through a series of short and long-term programs.

National Center for Genetic Engineering and Biotechnology (BIOTEC)

The Center, known as BIOTEC, was first set up under the Ministry for Science, Technology and Energy on September 20, 1983. In 1991, Thailand established the National Science and Technology Development Agency (NSTDA), and BIOTEC became one of the NSTDA centers, operating autonomously outside the normal framework of civil service and state enterprises. This enabled the Center to operate more effectively to support and transfer technology for the development of industry, agriculture, natural resources, environment, and the socioeconomy.

BIOTEC policy provides the resources for the country to develop the critical mass of researchers necessary to achieve Thailand's national R&D requirements in biotechnology. This is achieved through R&D projects, the facilitation of transfer of advanced technologies from overseas, human resource development at all levels, institution building, information services, and the development of public understanding of the benefits of biotechnology.

BIOTEC is both a granting and implementing agency. BIOTEC allocated approximately 70 percent of its R&D budget to several universities and research institutes around the country and 30 percent to carry out in-house research projects. The infrastructure of national and specialized laboratories is made available for in-house research programs as well as visiting researchers. It is expected that the construction of a Science and Technology Park will be finished in early 2001 and will house BIOTEC's main laboratories including pilot plant, greenhouse, and incubator unit.

Several research programs have been undertaken by a BIOTEC-appointed committee of recognized experts in the field. Some major programs and activities are described below.

Shrimp Biotechnology Program

Until recently, basic knowledge about the major cultivated shrimp species has lagged far behind technical innovations that have led to successful intensification of culture, and to ever-increasing world production. Basic knowledge must be addressed to maintain high levels of production. Moreover, sustaining high production levels will also require further innovation to minimize adverse environmental impacts. Biotechnology will play a central role in helping us to understand the shrimp and to improve rearing practices. BIOTEC's support will focus on issues dealing with shrimp diseases and with improvement of the seed supply. The disease work has so far emphasized the characterization, diagnosis, and control of serious shrimp pathogens, particularly yellow-head disease (YHD) and white-spot syndrome (WSS) disease. Luminescent bacterial infections have contributed to the declining production to a lesser degree. These diseases become progressively more serious threats to the industry as it has grown and intensified. Indeed, the work on YHD virus and WSS virus supported by BIOTEC has been instrumental in substantially reducing the losses caused by these viruses in Thailand during 1995-97. The losses to YDH (probably exceeding US$40 million in 1995) and those to WSS (probably exceeding US$500 million in 1996) could have been much worse without the basic knowledge and the DNA diagnostic probes made available to the industry by Thai researchers. Checking for subclinical WSS virus (WSSV) infections by PCR has been a common practice in Thailand, to help farmers in screening out WSSV +ve PL (post larvae) before stocking (Flegel 1997).

The Shrimp Biotechnology Service Laboratory was established in July 1999 at BIOTEC to summarize the reference PCR methods for shrimp viral disease detection for Thai shrimp farming. SBSL objectives are to serve as the reference laboratory for major shrimp pathogen diagnosis based on molecular techniques, to conduct research, and to provide assistance for molecular detection of various shrimp viruses.

It has been reported that WSSV can be vertically transmitted and widespread among wild broodstock. In addition to the disease problem, a decline in the growth rate of shrimp produced from currently available wild broodstock has also been observed. Production of specific pathogenic free (SPF) animals and the development of specific pathogen resistant (SPR) strains are now being used in the USA, Venezuela, and French Polynesia with *Penaeus stylirostris* and *P. vannamei.* This could be considered a breakthrough since production of *P. vannamei* more than doubled during 1992-94. Currently the most important program involves the domestication and genetic improvement of *P. monodon* stocks (Withyachumnarnkul and others 1998). The project will lead to the development of SPR stocks and improved growth performance through selective breeding. The first domesticated stocks from this program were to be ready for pond production tests in 1999. BIOTEC is also supporting advanced studies on DNA characterization and DNA tagging of the shrimp stocks. These studies are providing the tools that will be important for rapid genetic improvement strategies.

BIOTEC is dedicated to the principle that the players in the shrimp industry should take an active role in the R&D effort for their industry, in both planning and finance. BIOTEC took an active part in promoting the formation in 1996 of an industry consortium (the Shrimp Culture Research and Development Company) dedicated to solving problems common to the shrimp aquaculture industry as a whole. This consortium serves the industry directly and also serves as a bridge to other public and private institutions involved in relevant research, not only in Thailand, but throughout the world.

Cassava and Starch Technology

About 70 percent of the 16 million metric tons of cassava roots produced in 1998 is used in the production of pellets and chips, and the remaining 30 percent is mainly used to produce flour and starch. A production shortage in 1997-

98 prompted the Thai Tapioca Development Institute (TTDI) and Kasetsart University to recommend a new variety with a higher yield. Kasetsart 50 is the new variety with an average yield of 26.4 metric tons of roots per hectare, and a starch content of 26.7 percent compared with 13.75 metric tons per hectare and 18 percent starch content of the best strain available.

The tapioca starch industry is one of the largest in Thailand. In 1998, tapioca starch was worth about US$120 million. About 40 percent of starch was used domestically for the production of modified starch, sweetener, and monosodium glutamate. Most of the remaining 60 percent was exported. Efficient production, low production costs, and the development of value-added products are vital to the starch industry and the farming sector (total of 1.3 million hectares planted in cassava).

The program on starch and cassava products was established to provide support and funding for R&D. The program is funded jointly by BIOTEC and TTDI to carry out R&D in three core activities. The short-term project aims to improve the processing efficiency of starch production, in particular to minimize water and energy consumption. This will reduce water use and costs, and also reduce wastewater treatment. Wastewater discharge varies from 13 to 50 cubic meters/ton of starch produced, with an average of 20 cubic meters. A benchmark on water use is a priority for the Thai starch industry.

Biotechnology can play an important role in waste utilization. Solid waste (after starch extraction) still contains 50 percent of starch (dry weight) and has been utilized as animal feed. Tapioca, however, is not suitable for the production of feed requiring high protein content. Attempts have been made for protein enrichment using various microorganisms such as *Aspergillus* and *Rhizopus*. Nevertheless, the economic feasibility is still in doubt and further technological development is needed. In contrast, turning wastewater into energy through high-rate anaerobic digestion is promising. Though the technology is proven, an adaptation to such high-strength wastewater and low buffering capacity is required to ensure stability of the system. In comparison with the UASB technology, the fixed bed is easier to control and operate. R&D, however, is focused on increasing loading efficiency. Based on calculations, methane generated from anaerobic treatment of starch wastewater from 60 factories would be approximately 630 million cubic meters annually. This could be substituted for fuel oil used in drying, saving energy costs of about US$4 million annually. There is also the environmental cost of large land areas required for conventional pond systems. In addition to native starch, production of modified starch is increasing, leaving an excessive amount of sulfate in wastewater. This may interfere with the anaerobic digestion intended for energy production. A number of papers have been published recently on the interactions between the sulfate reducing bacteria (SRB) and the methanogenic bacteria (MGB). Molecular diagnosis has been developed and applied for the mixed cultured system. A better understanding of these anaerobic microbes could lead to the biological removal of sulfate, which is the main problem of various industries.

EU has set a quota for tapioca pellets imported from Thailand. Product diversification is part of the second core research activity. As a result, production of biodegradable plastic from cassava starch is being investigated. Increasing use of cassava as a raw material for fermentation industries such as amino acids and organic acids must proceed at furthering the development of value-added products. To reduce costs of production, however, research is oriented toward the production of good quality cassava chips as a starting material to replace the starch.

Finally, basic research on cassava starch structure and properties will add to our knowledge and help increase the use of cassava starch. The Cassava and Starch Technology Unit, a specialized BIOTEC laboratory established in 1995 at Kasetsart University, has been engaged in studying the physicochemical properties of cassava. The unit is well equipped, and provides regular service and training on instrument analysis of starch properties to the private sector and government agencies.

Rice Biotechnology Program

Rice yields in Thailand are low. One of the major constraints in cultivation is blast disease, especially in high-quality rice cultivars such as the aromatic "Khao-Hom Dawk-Mali." In northern Thailand, about 200,000 hectares of rice were affected by blast in 1993, causing serious economic loss and resulting in government intervention of about US$10 million to assist disease-struck farmers. Another US$1.2 million was spent on fungicides (Disthaporn 1994). Attempts have been made to breed higher resistance levels to blast in Thai rice. Limiting factors, however, are lack of insight and information on resistance genes, and the complex structure of the pathogen populations. Genetic analysis provides an efficient tool to identify useful resistance genes in the host while analyzing the race composition of the pathogen population. Recent research activities applying molecular genetic methods (DNA fingerprinting of a blast isolate collection at Ubon Ratchathani Rice Research Station, mapping of host resistance genes by the DNA Fingerprinting Unit at Kamphaengsaen campus of Kasetsart University) are providing baseline data on the interaction between rice and blast. The project is working on three closely related areas as follows:

- Establishment of a suitable differential cultivar series; identification of resistance genes conferring complete and partial resistance to blast disease in rice. This activity follows up on the project "Identification, mapping and utilization of rice blast resistance QTLs in improved aromatic rice varieties for Thailand."
- Pathotype and molecular genetic characterization of the blast pathogen population in Thailand. So far, more than 500 monospore isolates have been deposited with the BIOTEC specialized culture collection.
- The special case of fertile isolates; the potential of using Thai isolates of *Magnaporthe grisea* for the development of a molecular, diagnostic tool for pathogen race analysis. The degree of fertility can be assessed from the timing and number of perithesia that develop. BIOTEC has the capacity to test the mating type of about 80 isolates per month.

This project is a nationwide, network-type collaboration combining molecular genetics and classical approaches to help scientists breed rice cultivars with improved blast resistance.

BIOTEC provided US$1.5 million in 1999 to fund the "Rice Genome Project Thailand." BIOTEC on behalf of Thailand has joined an International Collaboration for Sequencing the Rice Genome [ICSRG] by sequencing 1 Mb annually of chromosome 9 for the next five years. BIOTEC is expected to provide about US$3.7 million to cover this work. Chromosome 9 was selected based on the previous extensive work on the fine genetic and physical maps surrounding the submergence tolerance QTL, the prospect of gene richness, and the small chromosome size. Joining ICSRG will allow Thai scientists to access directly the rest of the genome sequence made available by the other collaborating members. Gene discovery from wild rice germplasm will be undertaken in parallel to use efficiently the genome sequence data. The project will bring Thailand into the international scientific arena, incorporate state of the art technology, and improve Thailand's competitive edge in the international rice market.

Dairy Cow Program

In 1997, Thai milk consumption was 12 liters/person/year. Milk production is still insufficient to meet local demand, and Thailand has to import more than 50 percent (worth US$305 million) of the dairy products consumed in the country. To meet the national demand, it is estimated we need an additional 130,000 dairy cows, assuming present productivity averaged from total cows.

Reproductive efficiency is a primary determinant of dairy herd production profitability. Milk yield is still far below the average of most developing countries at approximately 10 kilograms/day, as compared to 30 kilograms/day. It is, therefore, important to promote an increase in dairy production through science and technology. The major programs are breeding and feeding. The lack of proper management is another major contributing factor to an underproductive dairy industry.

Traditional breeding practices in Thailand have been too slow to meet national requirements, and importing pregnant heifers and/or young quality-bred calves from abroad is too costly. Cutting-edge technologies such as embryo transfer, in vitro fertilization, embryo sexing, and semen sexing have been studied by Thai scientists for more than ten years. Nevertheless, the technologies have not yet been adopted, for several reasons. Technology transfer and training of Thai researchers at the leading laboratories/companies are now under discussion. The goal is to increase production of high-quality heifer calves at the most economical cost.

Agriculture and Gene Engineering

By the mid 1970s, with modern biotechnology developing through the use of recombinant DNA technology and molecular biology, Thailand was ready to adopt the new tools and apply them to various practical problems, in the biomedical field first and later in agriculture and other areas. A few specific examples will be given here to highlight the application of molecular biology and genetic engineering to agricultural development. Efforts in agricultural biotechnology and genetic engineering have been focused on three main areas: crop improvement through plant transformation, DNA fingerprinting, and molecular diagnosis of plant and animal diseases.

Crop Improvement

Crop improvement should lead to the production of genetically improved (transgenic) plants with superior properties including resistance to diseases, insect pests, and abiotic stresses. The Plant Genetic Engineering Unit (PGEU), the specialized laboratory of BIOTEC at Kasetsart University, Kamphaengsaen Campus was established in 1985 to carry out work on plant biotechnology and genetic engineering. A transgenic tomato plant carrying the coat protein gene of tomato yellow leaf curl virus was first developed to control this serious virus disease of tomato (Attathom and others 1990). The same approach was taken to develop transgenic papaya and pepper for resistance to papaya ringspot virus and chili vein-banding mottle virus, respectively (Chaopongpang and others 1996; Phaosang and others 1996). Sri Somrong 60, a Thai cotton variety, was successfully transformed with cryIA[b] gene expressing a toxin from *Bacillus thuringiensis.* Development of transgenic rice varieties has been supported by the Rice Biotechnology Program launched by BIOTEC and Rockefeller Foundation. An example is the transformation of Khaw Dawk Mali 105, an aromatic Thai rice with D^1 pyrroline-5-carboxylate synthetase (P5CS) for salt and drought tolerance. Most transgenic plants are now being tested under greenhouse conditions in accordance with the Biosafety Guidelines (Attathom and Sriwatanapongse 1994; Attathom and others 1996). Field testing of transgenic plants developed in Thailand is expected to get under way in 2000.

DNA Fingerprinting

Each living creature has a unique DNA sequence. Using DNA fingerprinting and polymerase chain reaction (PCR) scientists can identify organisms and genes. Important genes can be located (genetic maps). Moreover, the availability of DNA probes and specific sequence has made it possible to develop appropriate molecular methods for diagnosis of plant and animal diseases. Molecular mapping of genes in rice involving flooding tolerance, rice blast, aroma, cooking quality, and fertility restoration were accomplished using three mapping populations. A backcross breeding program for the improvement of Jasmin rice was initiated. In the first stage, resistance to bacterial leaf blight, flooding tolerance, resistance to brown planthopper/gall midge, and photoperiod insensitivity were main areas of focus. RFLP-based markers were an important limiting factor for high throughput and cost effectiveness. The PCR-based marker for Xa21 is the most reliable marker for marker-assisted backcrossing in rice.

Tomato production in the tropics and subtropics faces serious constraints due to bacterial wilt (BW), a disease caused by the bacterial pathogen recently reclassified as *Ralstonia solanacearum* (formerly *Pseudomonas solanacearum*). In Thailand, an endemic outbreak of BW in tomato, potato, pepper, ginger, and peanut occurs each year, causing a yield loss of approximately 50-90 percent depending on growing conditions. BW-resistant varieties cannot easily be developed due to the nature of the (quantitatively inherited) resistance that involves several genes. Marker-assisted selection (MAS), a breeding method of selecting individuals based on markers linked to target genes in addition to phenotypic measurement, is essential and useful only for enhanced resistance to diseases. At this time, three putative QTLs (quantitative trait loci) corresponding to BW resistance have been found using AFLP ('A' fragment length polymorphism) markers. Once markers closely linked to BW-related QTLs are well established, they can be used for marker-assisted breeding for enhanced resistance to bacterial wilt in tomato. A tomato consortium has been set up to extend public-private collaboration.

BIOTEC has set up the DNA Fingerprinting Service Unit at Kasetsart University. The unit has provided services to public and private concerns for more than two years. The main services are DNA fingerprinting and DNA diagnosis (Table 2).

Biocontrol Program

In 1996, Thailand imported 38,000 metric tons of chemicals, mainly insecticides and herbicides. The global trend of going organic is an opportunity for Thai farmers to supply fresh organic produce, especially fruit and vegetables, to the world. Over the past decade, the developmental work on biocontrol in Thailand has continued to receive active support from BIOTEC and the Thailand Research Fund (TRF).

Two companies are now producing commercially *Trichoderma* to control *Sclerotium rolfsii* Sacc., and *Chaetomium* to control soil fungi such as *Phytophthora* (Yuthavong 1999). BIOTEC and the Department of Agriculture have set up a pilot-scale production facility to produce NPV (nuclear polyhedrosis virus), *Bacillus thuringiensis* and *B. sphericus*. NPV is widely used to control *Spodoptera* moth in grapes. *Bacillus thuringiensis* (Bt) produced locally has gained popularity over the last few years. The capacities of pilot plants at Mahidol University and King Mongkut's University of Technology (Thonburi) are taken up with Bt production. Commercial production may begin soon. A project at Mahidol University to transfer the chitinase gene into *B. thuringiensis* subsp. *israelensis* has received support from BIOTEC.

Table 2 Services provided by the DNA Fingerprinting Unit

Service	*Organism*	*Marker technology*
DNA fingerprint	Maize, rice	SSLP
	other plants	AFLP
DNA diagnosis		
animal (paternity test)	Dairy cow	SSLP
plant (hybridity, purity	Maize, rice	SSLP
test)	others	AFLP
agricultural product		
adulteration	rice	
GMOs	soybean	
species diversity	tuna	

SSLP= Simple sequence length polymorphism
AFLP=Amplified fragment length polymorphism

Trade in Agricultural Products

Although Thailand is a leading exporter of food products, it also imports food commodities that are not available or that cannot be adequately supplied through local production. Among Thailand's top ten food imports in 1998 are fresh and frozen tuna used for canning and vegetable materials for animal feed preparation. Exports of frozen and processed chicken are expected to remain at 1998 levels of 140,000 metric tons for the next two years. Maize, soybean meal, and fishmeal are key ingredients for feed industries. Maize production for the 1998-99 crop year will be approximately 4.9 million metric tons, whereas local demand, mainly from animal feed factories, is expected to be 3.8 million metric tons. With adequate supplies, no maize imports were permitted in 1999 beyond the 53,250 metric tons that Thailand had committed to allow under the World Trade Organization agreement. In contrast, soybean output was about 375,000 metric tons in 1999, with consumption expected to increase marginally to 1.17 million metric tons. This means that soybean imports will rise to 800,000 metric tons. In addition, about 680,000 metric tons of soybean meal were produced in 1999 —100,000 from local soybeans and the rest imported.

Over 50 percent of world soybean production comes from new genetically improved varieties, mainly from North America. Regulations governing the movement of new genetically improved crops are becoming more restrictive. In mid 1999, for example, the European Agriculture Commissioners made a political agreement with regard to the ban on the use of GIOs in feed. As a net food producer, Thailand should be able to deal with potential problems. DNA diagnosis has been used to confirm the origin of raw materials used in food processing to comply with trade agreements. For example, the DNA Fingerprinting Unit will check the species identification of tuna already canned. This addresses the conflict between global free trade and environmental protection. The US Department of Commerce proposes to inhibit the importation of Atlantic-caught bluefin tuna harvested from countries using methods that are inconsistent with the International Convention for the Conservation of Atlantic Tunas.

Biosafety Issues

Biosafety issues are increasingly being debated in Thailand. The National Biosafety Committee (NBC) was established in January 1993 under BIOTEC. The NBC has introduced two biosafety guidelines: one for laboratory work, and the other for field work and the release of genetically improved organisms (GIOs) into the environment. The establishment of institutional biosafety committees (IBCs) at various public institutes and private companies was also strongly recommended by the NBC, and in many cases these recommendations have been implemented.

The importation of prohibited materials under Plant Quarantine Law B.E. 2507 implemented by the Department of Agriculture also controls to a certain degree the use of GIOs. Article 6 empowers the Ministry of Agriculture to impose rules regarding prohibited organisms. Ministry regulation II (B.E. 2537) identifies certain prohibited transgenic plants. Permission from the Ministry of Agriculture is required to perform field testing of genetically improved plants brought into Thailand. The following have received permission to be evaluated in Thailand: the Flavr Savr tomato produced by Calgene for the production of seeds (1994); a field trial of Monsanto Bt cotton was carried out under restricted containment in a netted house in 1996; in 1997, a Bt corn field trial was approved to be carried out by Novartis at their experiment station under netted screenhouse.

The public seems to pay more attention to the introduction of GIOs into the country by the multinational companies than to considerations of technological information. An issue not presently discussed or debated, in particular at the political level, is whether or not Thailand should be more aggressive on the development of genetically improved organisms, making best use of Thailand's genetic resources. Thailand is rich in biodiversity, and several genes resistant to biotic and abiotic stresses embedded in wild plants and other bioresources need to be discovered and utilized. This illustrates the potential benefits of biotechnology and genetic engineering. In the 1980s, when genetic engineering and biotechnology first made their impact felt, genetic engineering capability was present in only two or three institutions in Thailand (Yuthavong 1987). Ten institutions now have genetic engineering capability. Nevertheless, the most important challenge for the future of GIOs is not technical in nature, but the attitude of the public towards the technology. These issues need to be studied and debated among the scientists, the public, and the policymakers, and an optimal policy needs to be developed. BIOTEC realizes that genetic engineering depends critically on public support, so the Center has emphasized public education, with information programs on biotechnology and GIOs being introduced to the public and to industry.

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

Maria José Amstalden Sampaio

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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Costa Rica: Challenges and Opportunities in Biotechnology and Biodiversity

Ana Sittenfeld, Ana Mercedes Espinoza, Miguel Muñoz, and Alejandro Zamora

Modern biotechnology in agriculture came into prominence in the 1990s. From 1986 to 1997, approximately 25,000 transgenic crop field trials were conducted in 45 countries on more than 60 crops with 10 different agronomic traits. Seventy-two percent of all transgenic field trials were conducted in the United States (James 1997). Approximately 40 percent of field trials being conducted in developing countries are for virus resistance, the balance being for herbicide-resistance crops (25 percent), and for insect resistance (25 percent) (Sasson 1999). By late 1997, 48 transgenic crops involving 12 cultivars and six traits were approved for commercialization in at least one country. More than 90 percent of the owners of this technology were private-sector operators (James 1997). The crops included soybean, cotton, oilseed rape, potato, corn, tomato, papaya, and squash. Agronomic traits included insect, virus, and herbicide tolerance, delayed ripening, male sterility, and changes in oil composition (Nutfield Council on Bioethics 1999; Sasson 1999). Research on the genetic modification of rice, cassava, banana, oil palm, yam, and sorghum is being undertaken in public and private sector institutions (Krattiger 1998; Simon Moffat 1999).

Agricultural biotechnology is being adopted at very high rates. In 1998, approximately 28 million hectares were planted with transgenic crops, around 60 percent of this acreage being in the United States, followed by China and Latin America. This figure was up from 11 million hectares in 1997 and 1.7 million hectares in 1996 (Sasson 1999). Argentina grew 4.3 million hectares of transgenic crops in 1998, a three-fold increase from 1997. Europe planted a small acreage of genetically improved (GI) crops: about 8,100 hectares of transgenic corn in 1997 mainly in France and Spain (Nutfield Council on Bioethics 1999; Sasson 1999). In addition more than three-quarters of the cheese produced in the US is made from a gene-spliced version of an enzyme called chymosin (Miller 1999).

The principal benefits of transgenic crops include more flexibility in crop management, decreased dependence on conventional insecticides and herbicides, and higher yields. In 1997, the economic benefit to U.S. farmers was estimated at US$133 million for *Bacillus thuringiensis* (Bt) cotton, US$119 for Bt corn, and US$109 million for herbicide-tolerant soybean, with an overall total of US$381 million, up from US$159 million in 1996. In a 1997 survey of the US Corn Belt, Bt corn produced an average of 32.8 bushels more per hectare than did non-Bt corn. Corn productivity is around 388 bushels per hectare, showing yield improvements of 10 percent and reductions of herbicide use of up to 40 percent (Holzman 1999). A study produced by the U.S. National Center for Food and Agricultural Policy (Washington, D.C.), estimates that new genetically improved corn raised yields in the United States by 47 million bushels on 1.6 million hectares in 1997 (a year of high corn borer infestation) and by 60 million bushels on 5.8 million hectares in 1998. Around 0.8 million fewer hectares of corn were sprayed with insecticides as a result of the technology. For cotton, yields were up to 38 million kilograms and 2.05 million fewer hectares were treated with insecticide (Business and Regulatory News 1999).

Challenges

The initial commercial goals of agricultural biotechnology were directed at the markets of the industrial world. There is a growing realization, however, that agricultural biotechnology could make a valuable contribution toward solving the urgent problem of food supply, protecting the environment, and reducing poverty in developing countries. There is no doubt that agricultural biotechnology has opened up new possibilities, particularly in crop and livestock development. The question remains as to just how agricultural biotechnology will improve livelihoods and increase the standard of living in developing countries.

A sustainable strategy to provide food security for a growing population must promote biodiversity conservation, and avoid further habitat loss of natural ecosystems. The strategy must also seek to: reduce unsustainable technologies such as the overuse of chemical fertilizers and pesticides, unsustainable irrigation procedures, and soil preparation methods that promote soil erosion; increase nutritional composition; reduce postharvest storage losses; and increase production from the present 2 billion metric tons per year to 4 billion. The strategy must also deal with issues of ethics, biosafety, and intellectual property rights (IPR) in the use of new biotechnologies.

Food security today must be defined in terms of grains, meat, and milk production and supply. Over the next 20 years there will be an increase in demand for meat, with most of the increased demand coming from developing countries, thus making investment in livestock research a necessity. The relative importance of different livestock species varies: cattle are generally more important for Latin America and the Caribbean, small ruminants in sub-Saharan Africa, small ruminants and buffalo in South Asia, and pigs and poultry in East Asia and Latin America (Delgado and others 1999).

Good science and technology development is fundamental to the successful use of biotechnology in agriculture. Developing countries are not homogeneous, however, in terms of scientific capabilities, social structures, and economic goals, so there is not a single solution for all countries. There are countries with very little capacity in agricultural biotechnology. They require different strategies than countries with an up-to-date biotechnology program. The latter countries may also have a national policy and strong connections within the country between the public and private sectors, and between both those sectors and their equivalent sectors in more advanced countries (Brink, Prior, and DaSilva 1999). It is not surprising, therefore, to find first-class biotechnology laboratories in China, India, Thailand, Brazil, Argentina, Mexico, Egypt, and South Africa, which are perfectly capable of competing in the world of agricultural biotechnology.

In a recent study, Solleiro and Castañón (1999) indicate that Latin America has arrived late on markets for biotechnology products and services, a situation related to an industrial structure that is traditionally reluctant to introduce changes, and has little capacity for R&D. The authors give several explanations: Most R&D in Latin America is conducted at universities and public sector institutions, with minor participation of the industrial sector; human resources are not sufficient to cover all demands, and biotechnology in the region is not structured in a multidisciplinary way with capacity in molecular biology as well as management and marketing. A few successful efforts have incorporated competitive strategies on the intelligent management, combining inhouse skills with excellent capabilities to locate, acquire, and assimilate external technologies.

A significant portion of the improvements in agricultural biotechnology are being developed by and/or controlled by a few major multinational companies, making it more difficult for developing countries to access know-how in this area. For many of the food production companies the objective is to become more integrated by promoting vertical coordination of food systems, from the field to the supermarket. Different forms of acquisitions, mergers, and alliances continue to be a dominant characteristic of the biotechnology industry (Thayer 1998). By 1998, companies that were primarily chemical in origin had taken over most of the seed business.

Through joint ventures and acquisitions, Monsanto and DuPont now market over half of the seeds for the two largest U.S. crops, soybean and corn (Thayer 1999).

Intellectual Property Issues

Patenting and IPR are promoting privatization of scientific research in agricultural biotechnology, and might increase the gap of biotechnology know-how and its applications between developing and industrial countries (Serageldin 1999). Alternatives for developing countries include increasing research capacities at national institutions and at the CGIAR centers. This will allow the development of their own tools and know-how, which could be protected by IPR, and to acquire the necessary negotiation power to exchange licenses and implement strategic alliances with the private sector. The provision by donors of free licenses, acquired from the private sector and academic institutions, for basic enabling biotechnologies should also be considered when supporting projects in developing countries and CGIAR centers. Obtaining free licenses from the private sector, to be applied in providing solutions to tropical crops that are not on the agenda of industries, offers another alternative for developing countries. In general, learning how to use IPR as a tool to advance biotechnology in developing countries, together with public and private investment, as well as new and imaginative public-private collaboration, is needed to promote technology transfer and better use of resources.

Some arrangements involving transfer of proprietary technologies by the private and public sectors in industrial nations, without royalties, to developing countries are already taking place (Krattiger 1998). The benefit for developing countries is obvious; by increasing crop yields, new genetically improved crops reduce the constant need to clear more land for producing food; seeds designed to resist drought and pests would be especially useful in tropical countries, where crop losses are often severe. Scientists in industrial countries are already working with colleagues and individuals in developing countries to increase yields of staple foods, to improve quality for better market acceptance, and to diversify economies by creating new exports (Simon Moffat 1999).

Opportunities and Constraints

Biodiversity-rich countries can take advantage of their biological/genetic resources from wildland diversity, locally adapted varieties and races, and wild relatives of crops to increase yields. This can be performed by applying agricultural biotechnology tools, implementing bioprospecting activities, and by establishing partnerships with public and private sector institutions in industrial and developing countries, including the CGIAR centers. Required investments in infrastructure are much lower than for any other high technology field, with the exception of software development.

Linking Biodiversity and Biotechnology

Several countries and institutions are implementing bioprospecting agreements with the private and public sector, based on the opportunities and obligations offered by the Convention on Biological Diversity, and on the new developments in biotechnology and molecular biology, which are rapidly generating new tools and bioproducts. Bioprospecting collaborations are occurring in both developing and industrial countries (Sittenfeld 1996; Varley and Scott 1998). In this process, the definition of policies on access to genetic resources by governments and nations, as part of well-planned bioprospecting frameworks, are of particular importance for the success of national programs. These activities integrate the search for compounds, genes, and other nature-derived products with the sustainable use of biological resources and their conservation, along with scientific and socioeconomic development of source countries and local communities.

Agricultural biotechnology, specifically the search for new genes for plant improvement, offers advantages to biodiversity-rich countries compared to pharmaceutical research. Infrastructure and capital equipment costs are higher for the pharmaceutical area than for agriculture research (Tamayo, Nader, and Sittenfeld 1997). The need for alternatives to production and protection of crops and livestock and the increasing capacity in biotechnology (for example, differential gene expression techniques and genetic engineering), offer new opportunities for bioprospecting. Biotechnology can facilitate the transfer of several traits from wild biodiversity into cultivated crops. However, as with traditional plant breeding, there is a need to select the precise traits that consumers would reward in the market (Carter 1996). Advances in biotechnology also provide choices of diversity beyond traditional use of *ex situ* collections in germplasm banks. It is important to incorporate *in situ* collections (in the form of wild biodiversity) into agricultural research. Together with this concept, the need to develop innovative systems to connect to agricultural practices, biodiversity conservation and intelligent use of biological resources becomes apparent (Sittenfeld and Lovejoy 1996; Sittenfeld 1998).

Many of the advances in agricultural biotechnology are developed in industrial countries, in close proximity to growing biotechnology companies, and therefore favor the agricultural practices of the industrial countries. This may pose a problem for the primarily agricultural economies of several countries in Latin America, and other developing countries, because these developments may displace or transfer the production of these countries to the farm fields of the industrial countries, or even possibly to industrial bioreactors (Tamayo, Nader and Sittenfeld 1997). The concept of modern biodiversity prospecting, already proved in drug research (Sittenfeld and Villers 1993, 1994), offers an alternative to this threat by transferring biotechnology to developing countries in exchange for access to their biological resources. This will enable developing countries to use their own biological resources while retaining a competitive edge with industrialized countries. We can find examples of this practice in Mexico, Surinam, Peru, Argentina, Chile, and Costa Rica. The Instituto Nacional de Biodiversidad (INBio) in Costa Rica is negotiating agreements with scientific research centers, universities, and private enterprise that are mutually beneficial to all parties (Sittenfeld 1998). These pioneering agreements provide significant returns to Costa Rica while simultaneously assigning an economic value to natural resources, and providing a new source of income to support bioechnology and the maintenance and development of the country's Conservation Areas.

Linking biotechnology and biodiversity through modern bioprospecting, requires the creation and implementation of adequate frameworks integrating favorable macropolicies, biodiversity inventories and information systems, technology access, and business development. The principle of bioprospecting may be simple, but the link between biotechnology, biodiversity conservation, and its sustainable use requires several considerations, including: a realization that a wider range of skills are required for research, product development, and approval; the creation, use, and management of multidisciplinary teams dealing with the complexities of legal and regulatory frameworks for biotechnology and biodiversity conservation and use; and the use of advanced applications of biotechnology to broader arrays of bioresources. Finally, understanding the opportunities and problems derived from international collaborative research and the linkages with commercial organizations represents a key point for favorable bioprospecting activities (Sittenfeld , Lovejoy, and Cohen 1999).

The Costa Rica Experience

Importance of Agriculture

Agriculture has been one of the most important sectors for the economy of Costa Rica, promoting democracy, national values, and political stability. Agricultural expansion, however, has resulted in poor natural resource management, with low value-added prices for most of the crops (Mateo 1996). The agricultural sector, although still contributing about 18 percent of the GNP and representing 70 percent of the total exports from 1970 to 1997 (Proyecto Estado de la Nación 1998), is currently undergoing changes caused by shifts and pressures of globalization, and fluctuating export prices in coffee and banana. A few successful exceptions are niche export markets for nontraditional products such as high value-added vegetables, fruits, and ornamentals (Mateo 1996). In 1997, agriculture exports accounted for US$1.7 billion, although the size of the crop area diminished 32 percent from 179,034 hectares in 1970 to 120,118 in 1997. The active population in the agricultural sector dropped from 25.3 percent in 1990 to 20.2 percent in 1997.

Research in agriculture has generated a number of useful technologies, contributed to national food security, and developed successful research systems on a few selected export crops such as coffee and banana. However, agricultural research has attempted to maximize production using models based on high inputs that caused pollution and contamination of land, water, and animal life (Mateo 1996). Importation of pesticides and herbicides increased six-fold in three years from 13,770 kilograms in 1993 to 60,886 kilograms in 1996. The use of pesticides on crops such as banana in Costa Rica has lead to increasing numbers of poisoned field workers, higher than the numbers reported for other Latin American countries, the United States or Europe (Proyecto Estado de la Nación 1998).

Conservation Strategies

Costa Rica is a small country of 51,000 square kilometers that has enjoyed a long history of conservation. The accelerated growth of protected lands, coupled with deforestation and lack of institutional coordination, led to the formulation of a National System of Conservation Areas (SINAC) in 1986. Today SINAC comprises a system of clearly defined protected areas encompassing about 25 percent of the national territory (1,266,395 hectares in 1997), including National Parks, Forestry Reserves, Wildlife Refuges, and other means of protection under the administration of the Ministry of the Environment and Energy (MINAE). Biodiversity in protected areas represents a major renewable resource and a potentially powerful engine for Costa Rica's intellectual and economic development (Mateo 1996; Sittenfeld 1996). Conservation areas are the main attraction for tourism, an industry that generated US$719 million in 1997. Total exports in 1997 were US$3.3 billion, indicating that protected areas are contributing to the economy in a substantial manner.

Having a quarter of its territory separated for wildland protection, and realizing that only 15 percent of the soils are adequate for agriculture (Proyecto Estado de la Nación 1998), Costa Rica needs to find ways to take advantage of its biodiversity. It is a major challenge for sustainable development to find innovative ways to link conservation and biotechnology to increase agricultural production on less land, with lower pesticide use, and to maximize the benefits of bioprospecting.

Biotechnology in Costa Rica

Rice Biotechnology Program at CIBCM. Rice is the most important staple crop in Costa Rica, providing almost one-third of the daily caloric intake, with a per capita consumption of 55 kilograms/year. Production is based on rainfed and irrigated rice varieties developed several decades ago at the CGIAR-supported Centro Internacional de la Agricultura Tropical (Cali, Colombia). However due to a narrow genetic background, all the varieties are susceptible to similar pests and diseases such as planthoppers, rice hoja blanca virus, and rice blast fungus *Magnaporthe grisea*, as well as physiological disorders such as iron toxicity and zinc deficiency.

Because of a lack of resistance or tolerance to the factors mentioned above, the use of pesticides and fungicides has increased costs, which reduces profit margins and competitiveness of rice production in Costa Rica. Moreover, yield has remained fixed at 4.5 metric tons/hectare, leading to a strong dependency on international markets. A strategy based on pesticide spraying is also leading to pollution of water and wildlife refuges. Weed control, especially of red rice, a complex of *Oryza* species, represents nearly one-third of production costs.

The Rice Biotechnology Program has been supported by several institutions, including the Rockefeller Foundation and the Costa Rican-United States Foundation for Cooperation (CRUSA). It is centered on the use of biotechnology to make biodiversity available for crop improvement and to diminish or eliminate some constraints to rice production in Costa Rica. The strategy includes the molecular characterization of wild rice germplasm found in the country, which may harbor useful agronomic traits for future use in crop improvement. A second approach is bioprospecting for bacterial genes with insecticide activity isolated from different genera, such as *Bacillus thuringiensis*, *Photorhabdus* spp.

and *Xenorhabdus* spp., in different ecosystems. Isolated genes might be incorporated into the rice genome through genetic engineering. The strategy also includes genetic characterization of *M. grisea* lineages, in both cultivated and wild rice species to define sources of disease resistance.

Facilities were developed for plant genetic engineering at the CIBCM to offer a new tool to rice breeding programs. The first attempt at genetic transformation of rice was focused on the development of commercial rice cultivars resistant to hoja blanca, using viral genes and modified versions of those genes, which upon expression in plants may induce tolerance or resistance to the disease. This project started in 1989, with the molecular characterization and sequencing of the rice hoja blanca virus (RHBV), the development of plant tissue culture protocols for regeneration of Costa Rican "indica" rice varieties, and epidemiological studies on transmission and dispersion of RHBV by its insect vector, the planthopper *Tagosodes orizicolus*, which is also a pest of rice. Transgenic plants were produced using the RHBV coat protein gene as well as modified versions of the gene. The bacterial minichromosome used as a transformation vector included a bacterial gene to detoxify the herbicide glufosinate. This gene renders the plant resistant to the herbicide and is currently used for selection of transformed calli as well as in regenerated plants and their progeny. Herbicide-resistant plants may offer an alternative to control weeds, since a broad spectrum of them may be affected by the herbicide without harming rice plants.

Biological tests are conducted to demonstrate that the expression of RHBV capsid protein in transgenic plants is leading to resistance against the disease. Preliminary experiments are showing the lack of viral symptoms in transgenic plants; in order to determine whether the expression of the new trait is stable and inherited to the offspring, these lines will be tested in field trials during 2000-01.

Since a delphacid transmits the RHBV, it would be desirable to have genes that may affect *T. orizicolus*. We have conducted transformation experiments for expression of a lectin (GNA) that has anti-planthopper activity. The lectin gene was modified to achieve high levels of expression in the phloem tissues where the insect feeds, and transgenic plants will be tested shortly under greenhouse conditions. This strategy plans to lead to cultivars containing two levels of resistance to hoja blanca disease, one against the virus and the other against its insect vector.

In addition to that work, a set of different genes is currently being transferred to rice cultivars. These genes include resistance to bacterial blast (*Xanthomonas oryzae*), the viral replicase gene against RHBV, and protein inhibitors for insect control. Several other genes activated during stress (drought and salinity) are going to be used in rice transformation. The ultimate goal is to pyramid genes on several commercial cultivars, which may be used in rice breeding programs.

The population of Costa Rica is increasing and cultivated land area is diminishing, so our ultimate goal is to increase yield per area through the use of biotechnology. In the long term we expect to have a pool of useful genes from wild rice relatives, bacteria, or even nonrelated plants, and to transfer them to commercial rice cultivars. Wild rice species have proved to be useful resources for enriching the genetic pool of cultivated rice. Interespecific crosses with *O. rufipogon* have increased yield up to 20 percent. Also, the Xa21 gene from *O. longistaminata* has been cloned and introduced into the rice genome, thus conferring the plants with resistance to *Xanthomonas oryzae*. Some of the characteristics that could potentially be used for the improvement of rice are: pests and pathogen resistance, higher protein content, plant vigor, tolerance to high metal concentrations, salinity, and soil acidity.

The Rice Biotechnology Program includes research to identify, map, and characterize the native relatives of rice that occur in Costa Rica. This research is conducted at CIBCM in collaboration with the International Rice Research Institute (IRRI), Manila, Philippines. The location of the plants was recorded with a geographic positioning system (GPS), and the distribution of wild rices was correlated to a series of ecological and geographical variables. The identification and characterization of the wild species were done by morphological methods, and the genetic variability of these species is being studied using rice microsatellites and isozymes.

Populations of three of the four *Oryza* species reported for tropical America have been found in natural ecosystems throughout the country, accounting for three of the six described genome types of *Oryza*. Of these, *O.latifolia* is the most variable, abundant, and widely distributed. *Oryza grandiglumis* and *Oryza glumaepatula* are reported for the first time for Costa Rica. These two species have restricted distributions and need to be preserved, since they are not appropriately protected at the moment. Furthermore, two native populations of putative sterile hybrids that reproduce asexually have been found. Multivariate discriminant analysis revealed significant morphological differentiation of the species found. It also made clear the differentiated and intermediate position of the putative hybrids, one believed to have originated from the interspecific cross of *O. glumaepatula* and *O. grandiglumis. Oryza rufipogon*, native of Asia, and *O. glaberrima*, from Africa, have also been found in different rice plantations around the country, but not in natural habitats. These plants, now considered weeds, may also constitute valuable genetic resources for future use.

Oryza latifolia is a tetraploid species with a CCDD genome type. It occurs in a wide range of zones, soil types, and weather regimes, from 0 to 650 meters. A principal component analysis showed that there is significant differentiation of some of the populations of this species, mainly those from the Atlantic and Pacific slopes of Costa Rica. Isozymes have revealed genetic differentiation in the populations of this species, and a correlation between morphological and genetic variability has been observed. Some populations have agronomically important traits, such as drought and salinity tolerance, resistance to planthoppers, and shorter heading time. *Oryza grandiglumis* (CCDD genome) is a robust plant that occurs only in Caño Negro Wildlife Refuge. It has the biggest seed of the native *Oryza* species and it may have tolerance to *M. grisea*. There are two populations of *O. glumaepatula* located in unprotected marshlands in northern Costa Rica. This species belongs to the *O. sativa* group (AA genome), thus being the closest native relative of cultivated rice. Microsatellites are being used to assess the genetic diversity and structure of this species. The population at the Medio Queso River has two alleles per locus, whereas the one at Guanacaste is fixed at both markers studied. There is, as well, a cline at the Medio Queso population, which could be the result of a limited gene flow between subpopulations. This information will be useful to design *in situ* conservation strategies for these species, as well as in the breeding plans and in risk assessment for the introduction of genetically improved rice. Pathogens and other organisms related to these wild species are now being identified. Tolerance to biotic and abiotic stress factors will be an important characteristic in selection of germplasm to be used in interespecific crosses, and in selection of offspring.

Intellectual Property Issues

Two main concerns have arisen out of this experience. First, IPR on the vectors and genes used in the transformation process may be under patent protection in the hands of private companies and academic institutions. This principle also applies to patents on technologies and tools used, such as plant transformation systems, selectable markers, and gene expression technologies. When broad patents, or patents on basic research, are obtained by the private sector, the consequences for public research products are important. This is the case for biolistics (DuPont), *Agrobacterium*-mediated transformation (Japan Tobacco), and coat protein-mediated resistance (Monsanto). If those technologies are used only for research purposes, there is a general agreement that no infringement occurs. However, this is not the case when research is translated into products in the marketplace. This situation is affecting the commercail development of new genetically improved plants in Costa Rica. In addition, the Patent Law of 1983 excludes the protection of biotechnology products and procedures. By 2000 the law is expected to be changed to meet TRIPs requirements.

In Costa Rica, as in other countries, the distribution channels and agricultural extension in the public sector to reach farmers fields are in a process of change toward privatization. Broad IPR protection of enabling technologies in the hands of the private sector might have serious impact, as seed distribution channels are undergoing privatization around the world (Spillane 1999).

Regulatory Issues

The second concern is related to biosafety regulations and the risk of using genetically improved rice cultivars in tropical environments. No documented experience on this topic has yet been published, to the best of our knowledge. It is one of the most contentious arguments against the use of genetically improved plants in the tropics, since it is assumed that wild relatives might under specific conditions hybridize and give rise to a new hybrid that may pose a threat to agriculture if it behaves as a weed. No scientific evidence has been presented to support this argument, though a large body of speculation is shaping the opinion about plant biotechnology among consumers and even regulatory offices. The mapping of native relatives of rice species in Costa Rica is providing important information to select field trial locations and crop areas. Conducting this type of study, in connection with the production of different genetically improved rice plants, offers an interesting model to manage risks associated with agricultural biotechnology developments. It is important to note that in 1997Costa Rica included biosafety regulations in its Phytosanitary Protection Law No. 7664.

Will Costa Rica benefit from agricultural biotechnology? The answer may lie more heavily on the solution of the two concerns of intellectual property and biosafety above mentioned than on the ingenuity of the plant breeders and molecular biologists.

Bioprospecting

The Bioprospecting Program of Costa Rica's National Biodiversity Institute (INBio), established in 1989, is a private nonprofit research institute. Its mission is to promote greater awareness of the value of biodiversity, and thereby promote its conservation and improve the quality of life of Costa Rican society. The institute generates knowledge about biodiversity and disseminates and promotes the sustainable use of biological and genetic resources. Several of INBio's programs, including its National Biodiversity Inventory, Bioprospecting, Information Management, and Information Dissemination and Conservation Program, document what biodiversity exists in Costa Rica, where it can be found, and how the country can find sustainable, nondamaging ways to use it and to conserve it (Tamayo, Nader, and Sittenfeld 1997). The collaborative agreement established between INBio and the Ministry of the Environment and Energy (MINAE), provides the framework for inventory and bioprospecting activities in collaboration with the SINAC. INBio, through specific access permits, collects samples for its Inventory and Biodiversity Prospecting Divisions and shares intellectual and monetary benefits with MINAE.

Bioprospecting involves the screening of biological and genetic resources for their potential use, and the development of innovative strategies for capacity building, and adding value, and the generation of resources to invest in conservation activities. Within this framework bioprospecting is carried out in collaboration with local and international research centers, universities, and the private sector. The set of criteria used by INBio, to define its research agreements, include access, equity, and transfer of technology and training. Agreements stipulate that 10 percent of research budgets and 50 percent of any future royalties be awarded to MINAE for investment in conservation, according to the Biodiversity Law of 1998. The remainder of the research budget supports in-country capacity in biotechnology and value added activities, also oriented to conservation and the sustainable use of biodiversity.

Management requirements for a successful bioprospecting enterprise, based on the INBio experience, include the following:

- Defining and implementing a bioprospecting framework, meaning favorable macropolicies, biodiversity inventories, information management systems, technology access, and business development
- Creating interdisciplinary and multidisciplinary teams of scientists, lawyers, conservation managers and business developers
- Distributing the benefits obtained from bioproducts into building biotechnology capacity and improving biological resource management.

Benefiting from Biodiversity

INBio builds on sound biodiversity knowledge, which helps to define market needs, major actors, and national scientific and technological capacities (Sittenfeld 1996; Tamayo, Nader, and Sittenfeld 1997). The principal markets for bioprospecting are the pharmaceutical, agricultural, and biotechnological sectors, with an estimated market size of over US$600 billion worldwide (Sittenfeld, Lovejoy, and Cohen 1999). Important requirements for bioprospecting include knowledge of national and institutional strengths and weaknesses, market surveys, and evaluation of conservation needs. Most of INBio's bioprospecting activities are concentrated on the development of new pharmaceutical products; however, the basic issues and strategies can be applied to the agricultural sector as well (Sittenfeld and others 1998).

Because "raw" biological samples have low market value (Reid and others 1993), bioprospecting should seek to increase value by moving beyond simple resource collection and distribution services. Research contracts should concentrate on augmenting the value of biological resources by carrying out research in the source country. Additionally, involving in-country academics and researchers ensures that technologies transferred or accessed remain in the developing country. Increasing value is particularly important when negotiating royalty fees. In general, royalties for raw samples and collecting information are usually low, but adding information on activity, structure, and use of compounds and genes will allow increasing sharing of profits, up to 15 percent or more, depending on the area of activity and market size of the product (Reid and others 1993; Ten Kate 1995).

Guidelines provided by the Convention on Biological Diversity, and research experiences with different commercial and academic entities, allows INBio to follow basic rules such as the fair and equitable sharing of benefits, the implementation of collection methods with reduced impact on biodiversity, technology transfer, biotechnology capacity building, and up-front contribution to conservation activities. Examples of INBio agreements with academic and commercial entities are described elsewhere (Sittenfeld and Villers 1993, 1994; Sittenfeld 1996; Nader and Rojas 1996; Mateo 1996).

Recent experience in biodiversity prospecting negotiations have succeeded in establishing favorable terms for technology transfer, royalties, and direct payments among others, for INBio, and Costa Rica's Conservation Areas. Agreements have been developed between INBio and public and academic research institutions in Costa Rica and abroad, INBio and Merck & Co. Inc., INBio and the British Technology Group/INBio and Hacienda La Pacífica, INBio and the Bristol Myers Squibb Corporation, and others. The issue of benefits accrued from bioprospecting is difficult, given the inherent complexities of assigning value to the accumulated knowledge of biodiversity, the transfer of know-how and technology, and enhanced capacity building. Up to this time products obtained from samples processed by INBio have not reached the marketplace. From 1992 to February 1998 INBio conducted bioprospecting agreements worth over US$6 million. The use of this money can be broken down as follows: US$3.5 million for investments and research expenses at INBio (taxonomy, information management, and biotechnology), US$1.2 million which have been distributed to MINAE and the Conservation Areas; and US$0.8 million to support biotechnology development at public universities. It is important to take into consideration that the figure of over US$2.5 million for conservation and biotechnology development is significant for a country the size of Costa Rica, with a GNP of only US$ 9 billion for 1997 (Proyecto Estado de la Nación 1998). MINAE has used its share to support the management and upkeep of Costa Rica's National Park at Coco Island, a unique site. This is a good example of direct bioprospecting benefits flowing to conservation (Mateo 1996).

The economic value of bioprospecting should not be overestimated. Bioprospecting can only complement other activities to advance human development and biodiversity conservation. Recent national policies, for example, established in Costa Rica to promote ecotourism, to protect wildlands, and to stimulate private reforestation and secondary forests, together with the promotion of reforestation programs on carbon offset for carbon fixation, produced a forest coverage of 40 percent, with an increase of 2.6 percent of secondary forest in the last year. The deforestation rate went from 22,000 hectares in 1990 to 8,000 hectares in 1994 and continues to decline (Proyecto de la Nación 1998).

Role of the CGIAR Centers and the World Bank

Biotechnology is a necessary, but not sufficient, condition to advance social good in food and medicine. However, the CGIAR centers together with the World Bank have a pivotal role in ensuring that agricultural biotechnology impacts, in a positive way, the standard of living, food security, and poverty reduction in developing countries, by assisting these countries to take competitive effective advantage of their natural resources. Some considerations for both institutions are:

1. Establishment of system of soft loans for biotechnology development and capacity building consistent with the Kendall report (Kendall and others 1996).
2. Provide NARS with information, in particular with regular reviews of worldwide developments in the area of agricultural biotechnology and with studies of the likely impacts and appropriate developments in agricultural biotechnology for the country or the region.
3. Identification of realistic objectives and strategies for the sustainable use of biodiversity and guidance in the implementation of adequate bioprospecting frameworks.
4. Identification of opportunities to avoid or reduce negative impacts of agricultural biotechnology.
5. Promote activities to increase north/south, south/south and south/north interactions and understanding of biosafety, biodiversity conservation and national capacity development in both science and markets.
6. Development of in-house and in-country development of good quality agbiotechnology and negotiating skills, to enhance bargaining power when accessing IPR from the private sector, together with the provision by donors and CGIAR centers of licenses for enabling technologies, acquired from the private and academic sectors to NARS.
7. Promote national cooperation between national and international public and private sectors, to increase food production and well-organized distribution systems in the country. In particular, more emphasis should be devoted to applications of biotechnology in livestock research.
8. Increase public sector biotechnology R&D on traits where the technology is not economically attractive to the private sector in the short term.
9. Promote education in key areas for agricultural biotechnology development and public awareness on biotechnology.

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Mexico: Ensuring Environmental Safety While Benefiting from Biotechnology

Ariel Alvarez-Morales

World population, now 6 billion, is expected to reach 8 billion people by the year 2025 and maybe 9-10 billion by the year 2050 with around 97% of this population growth occurring in the developing countries (Fedoroff and Cohen 1999 and references therein). To face the challenge posed by the need to feed this huge increase in population, food production will have to double or triple by the middle of the next century. These challenges cannot be faced with the so-called traditional technologies in agriculture, and the new technologies, known collectively as biotechnology, will be essential to reach these goals.

However, although in principle most people with a certain knowledge of the potential of biotechnology agree with these statements, most of the people living in either the industrial or developing countries have not yet seen any product derived from this new technology benefiting them directly as consumers, either through lower prices for products or improved nutritional quality.

This has led many consumer associations and environmental groups to find unjustified any possible risk to the environment posed by the introduction of genetically improved organisms (GIOs), given the apparent lack of benefit to society. In most societies there are groups that will not trust either industry or the regulatory agencies that they perceive as allied to the chemical industry, often now bioscience companies.

This has led to a serious deterioration of confidence by the public to the safety claims regarding new genetically improved (transgenic) crops, as expressed by scientists, industry, and government. In some cases this has led to open confrontation and destruction of tests sites by the public, national governments proposing a moratorium on transgenic crops, or retailers of food products refusing to sell or removing food products that are either transgenic, derived from transgenic crops, or have a component from a transgenic crop in them. All this has happened, unfortunately, without an open and serious discussion of the facts between the opposing groups.

With respect to the possible risks to the environment posed by the release of transgenic crops, most scientists involved in the development of such products would consider them safe. In fact, some would be considered safer and in most cases, at least as safe as a comparable product obtained through traditional breeding methods. However, the appearance of conflicting information concerning the safety of GIOs in scientific journals, such as the report on the effect of pollen from Bt-corn on the larvae of the monarch butterfly (Losey, Rayor, and Carter 1999), has contributed to increased pressure being exerted by environmentalists and the public on the regulatory authorities in different countries.

The pressure may be felt more in countries where some or all of the following situations prevail:

- Incomplete or missing legislation regarding the experimental release or commercialization of GIOs
- Limited experience with GIOs
- Limited scientific and technological capabilities to assess the risk of GIOs
- Substantial areas rich in biodiversity

- The presence of wild relatives of one or more cultivated species for which a transgenic derivative exists
- Limited public education.

Unfortunately, all or at least some of the situations mentioned, occur to various degrees in most developing countries.

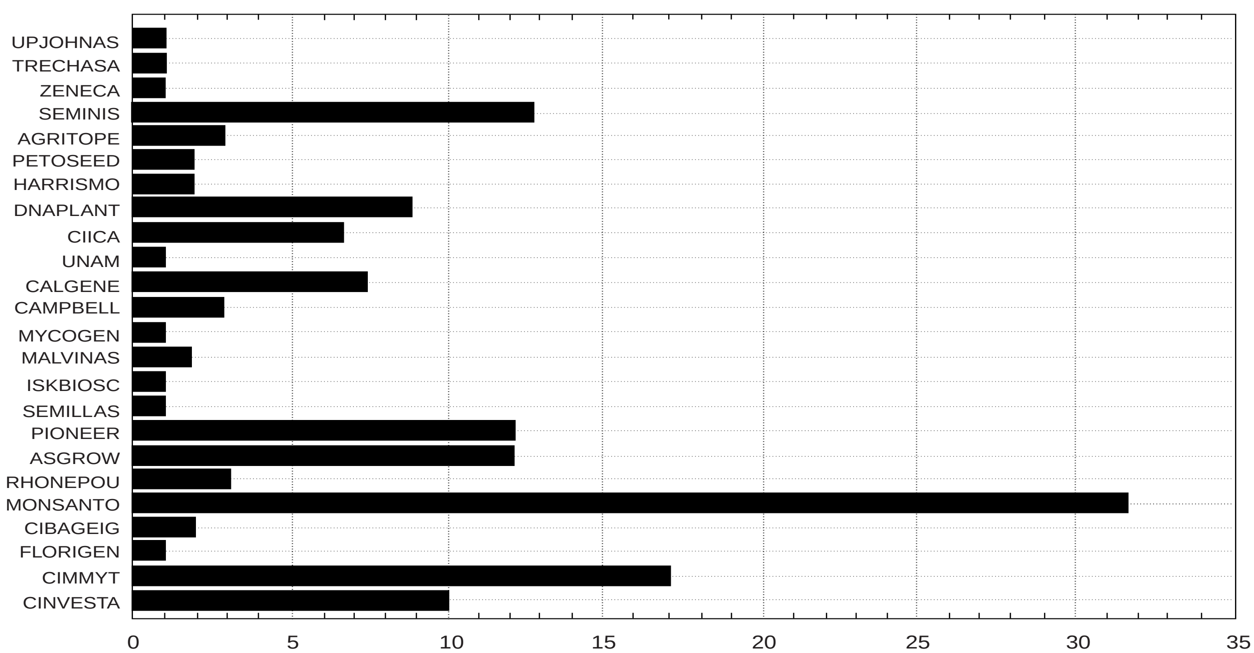
The Case of Mexico

In Mexico, field testing of transgenic crops started in 1988, and by July 1999, 141 permits to release transgenic material had been granted by the General Directorate of Plant Health (DGSV) of the Secretary of Agriculture, Livestock and Rural Development (SAGAR). The permits were first reviewed by the National Biosafety Committee on Agriculture (CNBA), which is a consulting body to the DGSV.

Most of the field evaluations have come from commercial organizations wishing to introduce their material into the Mexican market (Figure 1). The Center for Research and Advanced Studies at Irapuato (Cinvestav-I), the International Center for Wheat and Maize Improvement (CIMMYT), and the National Autonomous University (UNAM) have also conducted field trials for research purposes or as part of the development of socially oriented products. The latter include a PVX/PVY-resistant potato variety developed by Cinvestav-I in collaboration with Monsanto, with funding from the Rockefeller Foundation (Qaim 1998).

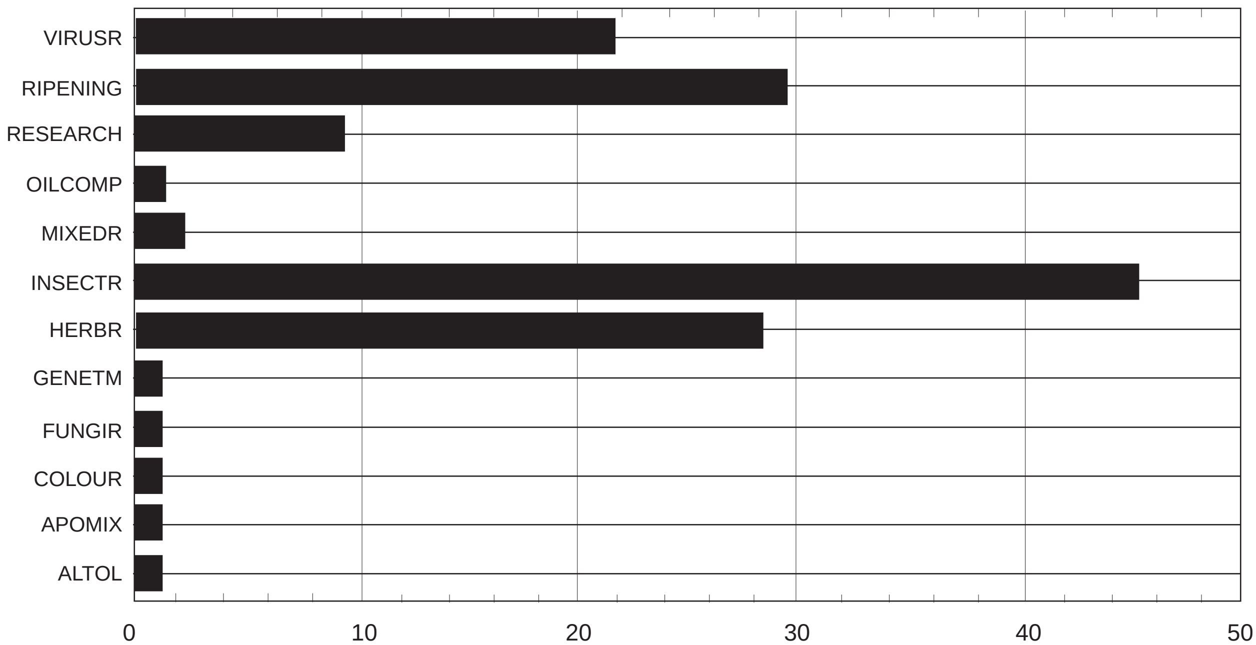
The traits that have been most widely tested by the companies, such as insect resistance, herbicide tolerance, or virus resistance (Figure 2), do not offer any direct benefit to consumers, nor do they help to address any serious local or national problem in Mexico. Delayed-ripening products developed and deregulated in Mexico are the FLAVRSAVR tomato, intended to be sold as a fresh product, and the corresponding tomato from Zeneca for industrial purposes. FLAVRSAVR tomato, however, was intended for the U.S. market and has not been promoted in Mexico, where there is no real need for it because fresh tomatoes are available throughout the year.

Figure 1 Releases of transgenic material by applicant (1988-July 1999)



Note: Applicants are (from top to bottom): Upjohn-Asgrow, Trechas, Zeneca, Seminis, Agritope, Petoseed, Harris-Moran, DNA Plant Technology, CIICA, UNAM (National Autonomous University of Mexico), Calgene, Campbell-Sinalopasta, Mycogen, Malvinas, ISK-Bioscience, Semillas Hibridas, Pionner, Asgrow, Rhone-Poulec, Monsanto, CIBA-GEIGY, Florigen Europe, CIMMYT, Cinvestav-Irapuato.

Figure 2 Releases of transgenic material by trait (1988–July 1999)



Note: The traits tested are, from top to bottom: virus resistance; delayed ripening; marker genes or any other construct used for research purposes; modified oil composition; mixed resistance — insect and herbicide resistance; insect resistance; herbicide resistance; genetic modification (for a *B. thuringiensis* release); fungi resistance; flower colour; apomixis, aluminum tolerance.

Maize has been the most tested crop, followed by tomato and cotton (Figure 3). Mexico is the center of origin and/or diversity for all three crop species, and wild relatives of them can be found in different areas of the country. A fierce campaign against GIOs started in Mexico around 1997-98, however, mainly as a result of transgenic maize being tested in Mexico, and most criticisms have been targeted at this crop.

It is not difficult to understand why this has happened, because maize has played a major role in the development of prehispanic cultures, and is deeply immersed in the traditions and culture of the Mexican people. As could be expected, transgenic maize has been portrayed by all of those opposing it as a threat to maize biodiversity and culture.

Regulatory Issues

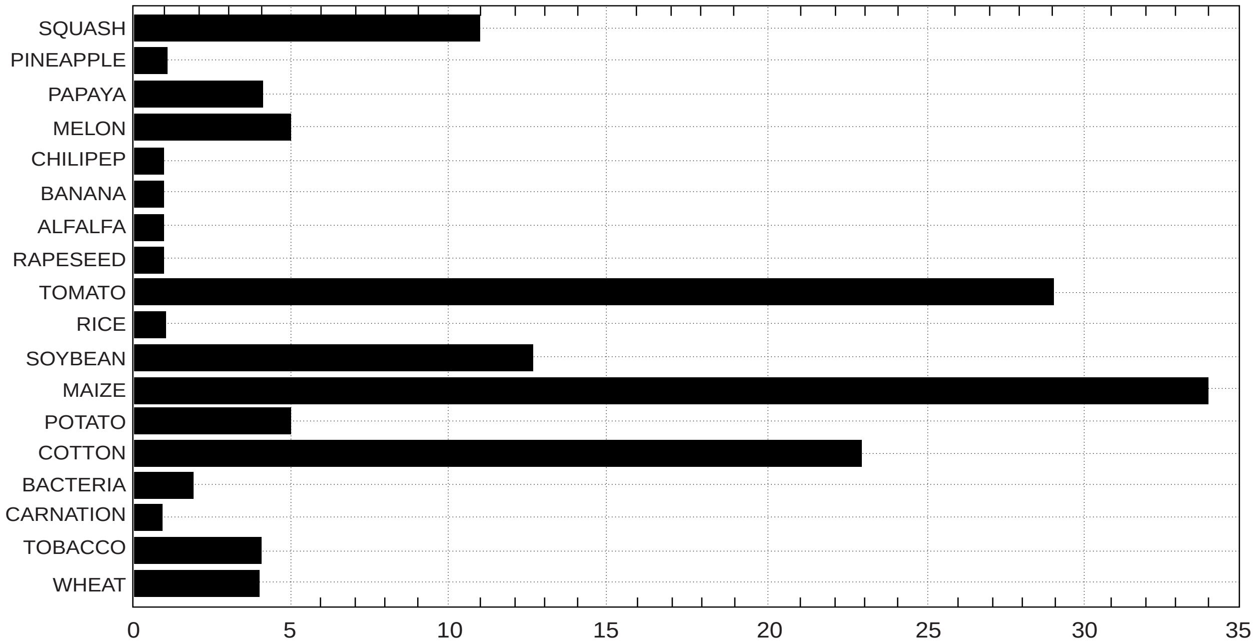
Regulatory bodies cannot dismiss the importance of public opinion and the concerns of interested parties such as NGOs with an interest in preserving the environment. However, extreme positions are difficult to deal with because usually there is no room for compromise.

So far the environmental safety of the genetically improved materials released has been assessed with data concerning past experience with nontransgenic crops. These data provide a sound base to allow the release of these materials based on a "negligible risk" hypothesis, which often means that whatever risk may be involved in the release of the transgenic material, it is similar or less than what would be expected with comparable nontransgenic material, based on the principle of familiarity.

Some want to ban transgenic materials arguing potential risk to the environment, and scientists or regulators stress the safety of these same materials based on nonGIO data. Both groups lack substantial evidence to back their claims, leading into a vicious circle of having to obtain risk-related data, and continuing to test because there is insufficient data to ensure their safety.

The consequences of this situation are worrying. In Mexico, the DGSV bowed to pressure from groups opposed to the release of transgenic

Figure 3 Releases of transgenic material by type of GIO (1988–July 1999)



maize, and stopped, in July 1998, the approval of field trials with commercial varieties of GM maize. They have since allowed two limited field trials with research material from CIMMYT. In Brazil, the State government of Rio Grande do Sul is considering a ban on all transgenic crops, despite the opposition of the Brazilian scientific community (Bonalume Neto 1999).

Finding a Possible Solution

Regulatory officials in Mexico are interested in continuing field trials with transgenic maize if there is a clear advantage or benefit to Mexican agriculture. An example of this could be the generation of transgenic varieties of maize with tolerance to aluminum, which has been obtained at Cinvestav-I, through the over-expression of a gene coding for a citrate synthase (De la Fuente and others 1997). This phenotype has great potential to reclaim for agriculture tropical acid soils that were lost due to high levels of soluble aluminum ions (Herrera-Estrella 1999).

However, even situations where there seems to be a clear or potential benefit to the country are vulnerable to criticism. A solution to avoid this situation must be proposed that will satisfy all parties involved. This possible solution is the medium-and long-term monitoring of GIO releases, which has already been proposed and which is being implemented or planned by the governments of the United States and Japan (Reichhardt 1999; Saegusa 1999).

Monitoring should, in principle, be acceptable to the scientific community if it is acknowledged that releases are being approved on a "negligible-risk" hypothesis, which may still be subject to confirmation or modification through the collection and analysis of field data. The nonextremist public and NGOs should see monitoring as a serious exercise that could produce different outcomes, such as: (l) early detection of environmental damage; (2) identification of new potential or real effects on the environment; (3) no damage or negative influence on the environment by introduced GIOs. Each outcome would be met with an appropriate response by the regulating authorities.

Implementation of an Environmental Monitoring System

Medium- or long-term environmental monitoring of the release of transgenic plants into the environment would probably not be a simple matter. Difficult questions need to be answered before setting up such a system: When, where and what to monitor? What transgene(s) to include? How long should the monitoring be carried out? How would the meaningfulness of the results be assessed? Other relevant nontechnical questions are: Who will carry out the monitoring? Who will pay for it?

Mexico, and many other developing countries in a similar situation, view answers to the last two questions as critical, because having the answers to the technical questions becomes secondary if the human or economic resources to implement the process are missing. I will, therefore, try to propose an answer to the last two questions, and assume that the specific technical issues would have to be answered by an interdisciplinary technical group (see Johnson, this volume).

There is already a well structured Biosafety Committee in Mexico, with a good level of expertise, that could very well serve to coordinate the monitoring efforts. A company that wishes to test transgenic material in Mexico would then be required to choose any of the following possible schemes:

1. Include, along with the normal request for a field trial permit, a monitoring program that would be revised and approved by the CNBA. The monitoring program should include, in addition to company researchers, local universities, research institutions, agronomy colleges, and others.
2. Submit a request for a field trial permit and request from the CNBA guidelines or a monitoring program that should be followed by the company during the course of the field trials. In this case the CNBA would also invite different local institutions to collaborate on this program.
3. Submit a request for a field trial permit and provide the funding for the CNBA to contract the monitoring to local research institutes, colleges, or universities.

In all cases, partial and final reports of the results obtained through the environmental monitoring program should be revised and approved by the CNBA, and would be made publicly available.

In the first two instances above, funding should be covered by the company or by the company and the institutions involved. It is not unreasonable to think that academic institutions would be willing to collaborate on such programs. There should be funding available through national or international agencies, or through programs to promote collaborations between industry and academe.

The inclusion of academic institutions would provide a higher level of confidence to a society that in many cases distrusts large international companies, and also would be a way to involve local expertise in the complex interaction between agriculture and the environment. This is an area for which there should be an ever-increasing interest and need, if agriculture, whether or not it uses GIOs, and conservation of the environment and biodiversity are expected to coexist in the future.

A Special Case for Mexico: Maize

The proposal for environmental monitoring can certainly be applied to any crop, and would be most relevant in those situations where there are sexually compatible wild species of the transgenic crops under test. Therefore, in principle, this may be especially applicable to transgenic maize in Mexico. However, the large diversity of land races and the very wide distribution of these, and the wild species such as *Tripsacum* and teocinte, may call for a special program to closely monitor the behavior of transgenic maize that may be released into the environment.

CNBA, CIMMYT, and the National Institute for Research on Forestry, Agriculture and Livestock (INIFAP), concerned with the possible risks involved in the release of transgenic maize, organized in September 1995 a forum to discuss these issues (Serratos, Willcox, and Castillo 1996). At the time, no mention was made of the possibility of monitoring because the speed at which these materials would be available and ready to be tested or even commercially used in Mexico was not foreseen. The outcome of that forum was a set of guidelines to safely test transgenic maize, and the identification of different "risk zones" along the Mexican territory according to the abundance of teocinte and *Tripsacum* growing in them.

During 1996 and 1997, however, commercial interests were requiring more than just field trials of reduced size and confined to specific locations. These tests were also intended to assay agronomic traits rather than assess the safety of the materials. These trials were therefore not giving any answers to the questions posed by those sectors interested in the effect of these GIOs upon the environment.

This led to a second forum in October 1997, organized by the North American Plant Protection Organization (NAPPO), the CNBA, and grower organizations. It was intended to revise the situation, at a time when the United States, the main maize/corn supplier to Mexico, was already producing a considerable amount of grain from transgenic materials, and people were already fearing that this unstoppable influx of transgenic maize would be a risk to the environment in Mexico.

The conclusions drawn from this forum were, in my opinion, more academic than practical. More research was considered necessary into the ecology of the wild species and their interactions with the land races and hybrids already being used. There were also proposals on how to obtain funds to implement the research needed. At the same time, however, requests to conduct field trials were being submitted to the DGSV, and Mexico was importing maize from the United States. All of this could not wait for the implementation of research programs to obtain the data required to evaluate the risks.

The final outcome has been severe restrictions being imposed on field trials of transgenic maize by the DGSV. The criterion being used is that there is no benefit to Mexico with the use of these materials, so no risks should be taken. But are there any real risks? We do not know for sure, and by assuming risks *a priori* we close the door to any possibility of finding the correct answer. We may also be losing any potential benefits that may come from the use of these materials, such as the use of reduced amounts of herbicides and/or pesticides on our land.

Role of the CGIAR

The solution to the impasse of maize in Mexico may be to call upon an independent institution to set up programs that would answer some of the questions regarding the biosafety of these materials. It could plan and conduct short, medium, and long-term monitoring of the behavior of GM maize in different settings in Mexico.

An institution with the capability, the resources, and the expertise to meet this challenge, and that could use this information, would be CIMMYT. The 16 centers that collectively form the Consultative Group on International Agricultural Research (CGIAR) represent the largest global effort toward collecting, preserving, and utilizing agricultural resources. This action could assist Mexico's response to the recognition of the potential of wild species such as teocinte and *Tripsacum*, as a source of valuable genetic traits like apomixis and resistance to *Striga* infestations (Hoisington and others 1999).

CIMMYT is actively pursuing the application of biotechnology to improve the productivity and sustainability of maize and wheat production, and has received at least 17 permits to conduct field trials with GM maize or wheat. It would therefore seem to be in CIMMYT and Mexico's best interest to warrant the safety of maize biodiversity—one of the best genetic resources—and to assure the people living in those places where these materials are planned to be released that they will indeed benefit from their use, without sacrificing their natural resources.

It would seem natural for CIMMYT to lead this effort to measure the effects of genetically improved materials on the environment. One would expect, however, that this would be a concerted effort that would include interested people from research centers, universities, agricultural colleges, and other interested groups. As well, this should not be an isolated exercise, because the biggest threat to biodiversity is ignorance and poverty, not GIOs. Appropriate efforts and models should be used to conserve biodiversity. Fortunately, there exist interesting propositions that acknowledge the need to consider socioeconomic context of the environmental situation that exists in Mexico, and probably in many other developing countries (Gómez-Pompa 1999).

Regulators should be proactive and respond with specific and prompt actions to the anxieties of society, because inaction makes society more vulnerable to misinformation and fear. This leads to unrest and distrust of the people and institutions that were created to protect them.

We cannot explain to and convince all the people of the potential benefits of GIOs in agriculture. We should also not tell them that we have stopped testing because of some perceived risks. What we should be able to tell them is that we are making our best effort to find the facts so that we can prevent any damage to our environment, if that were the case, or to decide if the use of a technology will enhance their living standards and that of their children.

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Egypt: Biotechnology from Laboratory to the Marketplace: Challenges and Opportunities

Magdy A. Madkour

The Government of Egypt places great importance on the significant role the agricultural sector plays in the national economy. Agriculture accounts for 20 percent of both GDP and total exports, and 34 percent of the total labor force. The agricultural sector contributes to the overall food needs of the country, and provides the domestic industry with agricultural raw materials.

The agricultural sector has undertaken major steps to reform its economic policy program such as:

1. Gradual removal of governmental controls on farm output prices
2. Increasing farmgate prices to cope with international prices
3. Removal of farm input subsidies
4. Removing governmental constraints on the private sector in importing and exporting agricultural crops
5. Imposing limitations on state ownership of land and sale of new land to the private sector
6. Adjusting the land tenancy system
7. Confining the role of the Ministry of Agriculture (MOA) to agricultural research, extension and economic policies.

As the government moves toward privatization, transfer of technology to the private sector has occurred (for example, in vitro micropropagation of virus-free potato). This shows the capacity and interest of the private sector to adopt new technology. Technology transfer is expected to grow dramatically in the short term as the research programs become more product oriented.

One of the major targets for biotechnology in Egypt is the production of transgenic plants conferring resistance to biotic stresses resulting from pathogenic viruses, bacteria, fungi, and insect pests, and abiotic stresses such as salinity, drought, and high temperature. These biotic and abiotic constraints are major agricultural problems leading to serious yield losses in many economically important crops in Egypt.

AGERI (Agricultural Genetic Engineering Research Institute) was established in 1990 at the Agricultural Research Center (ARC) to promote the transfer and application of this technology. AGERI aims to adopt the most recent technologies available worldwide to address problems facing agricultural development (Table 1).

Strategic Goals of the Agricultural Sector

1. Optimizing crop returns per unit of land and water consumed
2. Enhancing sustainability of resource use patterns and protection of the environment
3. Bridging the food gap and achieving self-reliance
4. Expanding foreign exchange earning from agricultural exports.

Opportunities for Deploying Modern Biotechnological Approaches

1. Producing transgenic plants resistant to indigenous biotic and abiotic stress
2. Reducing the use of agrochemicals and pesticides and their environmental risks

Table 1 Examples of current plant genetic engineering research at AGERI/EGYPT

Discipline	*Potato*	*Tomato*	*Cotton*	*Maize*	*Faba bean*	*Cucurbits*	*Wheat*	*Banana*	*Date palm*
Virus resistance		☐			☐	☐		☐	
Insect resistance	☐	☐	☐	☐					
Stress tolerance		☐	☐		☐		☐		
Genome mapping and fingerprinting		☐		☐					☐
Fungal resistance		☐		☐	☐				

3. Improving the nutritional quality of food crops
4. Reducing the dependency on imported agricultural products (Seeds-Crops).

The private sector has access to biotechnology, and has invested heavily in research and development (R&D) of technology and the necessary ancillary expertise to bring a product to market. The competitive edge of a private company depends on the proprietary nature of its R&D and the protection offered by intellectual property laws.

A private company might engage in development of a product in conjunction with a developing country because (a) it addresses a technical problem critical to its own product development, (b) it presents an opportunity to enhance its public relations, and/or (c) it provides a window to an important market, technology, or germplasm of interest.

Developing country institutions may be interested in working with private companies to gain access to important technology, develop managerial and business expertise, build intellectual capacity, or form a partnership with an entity that has an existing capability of bringing a product to market.

Pioneer Hi Bred/AGERI; a Private/Public Partnership

The relationship between AGERI, an Egyptian public sector institution, and Pioneer Hi-Bred, a U.S. private company, was forged through a relationship that involved common business interests. The importance of codevelopment of technology as opposed to technology transfer is especially pertinent in the case of Pioneer Hi-Bred's relationship with AGERI. In this partnership, a public sector institution was able to bring a significant contribution to the table. AGERI has isolated a number of strains of *Bacillus thuringiensis* (Bt) that had pesticidal activity of interest to a private sector company. AGERI filed a patent in Egypt on January 11, 1996 (No. 019797) on Bt derived bioinsecticide against a wide range of insects, and in the United States on January 10, 1997 (No. 5178-3) on Bt isolates with broad spectrum activity.

AGERI also has a state of the art biocontainment facility, and a team of trained scientists. AGERI can provide access to the local Egyptian market and the broader Middle East market, both of which are sufficiently developed to be attractive. In turn, Pioneer Hi-Bred came to the discussion table with technology as well as with marketing, regulatory, and legal expertise of value to AGERI.

AGERI has therefore initiated a partnership with Pioneer Hi-Bred through a USAID R&D grant to achieve the following:

1. Research and training for AGERI scientists to be trained at Pioneer/Iowa in methodologies relating to agricultural biotechnology
2. Potential for product development; Pioneer was granted access to evaluate certain novel Bt proteins and genes patented by AGERI.

Four parties have signed this agreement: Pioneer-USA, AGERI-Egypt, ABSP/MSU-USA, and USAID-Cairo/Washington D.C. Both collaborators, Pioneer and AGERI, have provided inputs to this research and training effort.

Joint discoveries resulting from the work will be shared and patent rights will be sought according to terms of the USAID agreement. Pioneer Hi-Bred will retain sole ownership of its proprietary Bt gene(s) and proprietary germplasm, and AGERI will retain sole ownership of its proprietary Bt gene(s).

Under a separate agreement, AGERI granted material transfer agreements (MTAs) for Pioneer Hi-Bred to evaluate the Bt toxin protein. Options for possible commercial development of maize have been also considered. This is one of the examples of USAID-sponsored collaboration as also described by Lewis (this volume).

BIOGRO/AGERI; a Business Partnership

A second model of moving research into commercial application is elaborated through the successful interaction between scientists at AGERI and the University of Wyoming, who have been involved in collaborative research studies for the past six years on Bt. The research efforts led to the development of a biological pesticide based on a highly potent strain of Bt isolated from the Nile Delta. This strain is extremely effective against a broad range of insects: Lepidoptera (moths), Coleoptera (beetles), and Diptera (mosquitoes). An additional significant feature of this strain is its capacity to kill nematodes.

AGERI has successfully managed to manufacture its first biopesticide *Agerin* based on the insecticidal bacterium *Bacillus thuringiensis*. Agerin is capable of protecting a broad range of important agricultural commodities, of controlling a number of biomedically significant pests, and has the potential for sales on a worldwide scale.

To fulfill its commitments to bring research results into application and large-scale commercial distribution to the farmers, AGERI, in collaboration with a private investor, succeeded in establishing a commercial business entity under the name "BIOGRO International." This company is responsible for the commercialization of research results conducted in AGERI and will be in a position to sell AGERI products. This is essential to guarantee that sales revenue generated from product sales will be invested back into the Institute to support the continuation of its activities.

It is envisaged that BIOGRO will link with the Genetic Engineering Services Unit (GESU), which was established at AGERI to work out any commercial agreements to benefit both the institute and BIOGRO. It will also allow for the free flow of information and products related to genetic engineering being produced by the institute for commercialization purposes.

AGERI attaches a high priority to collaborating with the private sector, which will be fully informed of R&D in the field of genetic engineering and biotechnology in Egypt through (a) the circulation of newsletters and reports, (b) having representatives of the private sector participate in the design of product R&D, and (c) representation of the private sector on the governing board of AGERI.

As one of the leading institutions in agricultural genetic engineering in West Asia, North Africa, and the Middle East, AGERI is planning to share its know-how and experience with other countries within the framework of Technical Cooperation among Developing Countries (TCDC). This will be achieved through specialized workshops, seminars, and internships. The institute can also provide professional consultation in the field of molecular biology and agricultural genetic engineering.

Role of the CGIAR centers

The CGIAR centers could usefully expand their activities in the following areas, to further assist national institutes in the applications of modern biotechnology:

Biosafety

1. Setting up regional linkages to share biosafety data and to pool information
2. Providing training and guidance on risk assessment and risk management issues
3. Providing technical training in biosafety reviews, prior to releases
4. Building consensus among nations on biosafety protocols and guidelines
5. Assisting in the development of media and information materials to increase public awareness

R&D collaboration

6. Increasing CGIAR/NARS collaboration in biotechnology R&D
7. Setting up programs for the use and management of technology

Intellectual property management

8. Increasing awareness on intellectual property and its fundamentals (copyrights, trademarks, patents, licensing, plant variety protection, plant breeders' rights)
9. Establishing intellectual property policy and institutional policies
10. Building capacity and human resources development in the field of technology transfer and intellectual property rights.

Iran: Hopes, Achievements, and Constraints in Agricultural Biotechnology

Behzad Ghareyazie

To take advantage of biotechnology, countries such as Iran need sufficient funds, biosafety regulations, intellectual property rights (IPRs), and policies on ethical and trade-related issues.

Considerable investments in human and financial resources are required for biotechnology research and development (R&D). Developing countries rely mainly on public funds for their research. As a percent of GDP devoted to science and technology, the investment ranges from 2-4 percent for industrial countries to up to 1 percent for developing countries. In Iran, the figure is less than 0.3 percent. Most of the investments in the industrial countries are made by the private sector, whereas in developing countries the private sector investment is negligible.

Investment is not only required for biotechnology R&D products, but also to prepare, ratify, and implement a sound regulatory framework to prevent risks to humans and the environment that may be associated with recombinant DNA technology. Biosafety regulations are needed to improve and introduce new genes from different sources into different species. There are concerns about the safety of the genetically improved organisms (GIOs). The public has some concerns about the broad application and release of GIOs in the environment. The magnitude of the deliberate field release of such organisms has intensified the need for biosafety.

There are only a few developing countries that have their own biosafety guidelines. Iran is one of those countries that have not yet put in place any guidelines. These countries will have to follow international agreements and treaties. Many developing countries do not have the financial and human resources to participate in the international debates that result in internationally approved agreements, so there is little or no input for some developing countries.

There is a need for strong protection in intellectual property rights (IPRs), including patents, plant breeders' rights, and trade secrets. For emerging countries to take advantage of biotechnology, they should have a sound policy on IPR that includes comprehensive patent and plant variety protection laws. Without strong IPRs, cooperation and partnership between the public and private sector is difficult. Many of the methods and products of modern biotechnology are owned by transnational companies in industrialized countries. Strong IPRs are needed to access these technologies and to build a research capacity inside the country. Upgrading and strengthening IPR laws is usually opposed in developing countries.

Agricultural Biotechnology in Iran

Human Resources

Iran has 339 scientists recognized as biotechnologists, and 141 are involved in agricultural research. Recently educated scientists (both in Iran and abroad) have a good knowledge of genetics and molecular biology, and have good laboratory skills in the application of molecular tools and DNA/protein technology.

The Iranian government has made a considerable investment in developing human resources and in training (both classical and non-degree training) scientists in biotechnology. There are now several hundred Iranian graduate students studying biotechnology abroad.

Iranian universities also have started to offer courses in biotechnology in different faculties. There are three major universities in Iran that offer MSc and Ph.D. degrees in agricultural and medicinal biotechnology. The capacity of these courses is, however, limited and cannot meet the demand for experts in this field.

Institutions

There are 46 institutes/centers in Iran involved in biotechnology (in whole or in part). They include a range of well developed and well equipped modern institutes. There are 19 institutes/centers in Agriculture and Natural Resources, 12 in Medicine, 8 in Basic Sciences, and 7 in Industry and Environment. These institutes rely mainly on public funds. Some are well funded and equipped with modern and advanced facilities, while others are fragile with limited resources. In addition to the public institutions there are several private companies active in biotechnology. These companies also rely on loans and support from government. In some cases joint ventures with foreign investors have been put in place. The companies are successful and their businesses are profitable.

Razi Institute. One of the most important applied R&D organizations in Iran, this Institute is under the Ministry of "Jihad e Sazandegi," with a current annual budget of about US$10 million. The institute has about 130 scientists, and a record of scientific achievement and innovation. It has been internationally recognized and designated as a Reference Organization/Laboratory in diagnostics. Razi was one of the first institutes in the world able to mass produce poliomyelitis vaccines.

National Research Center for Genetic Engineering and Biotechnology (NRCGEB). This center was established in 1988 under the Ministry of Culture and Higher Education, and is involved in basic and applied research in biosciences, medicine, agriculture, and pharmacology, using the tools of molecular biology, genetic engineering, and biotechnology. NRCGEB holds practical and theoretical specialized workshops in biotechnology and molecular biology for specialists, researchers and graduate students. The center is currently located in a temporary site with a huge expansion project under construction. The new home for the NRCGEB is being constructed in a 15 hectare site 16 kilometers west of Tehran with 60,000 square meters of laboratory, library, pilot plant, and administrative buildings.

The center has a good record of achievements in medicinal biotechnology such as production of recombinant growth hormone for humans, and DNA vaccine production project for hepatitis B. It is relatively new in agricultural biotechnology research. Transformation of sugar beet and rape seed, promoter analysis of Psr3, production of salt tolerance in plants by T-DNA activation insertion mutagenesis, and gene isolation and characterization are some of the ongoing activities.

Biotechnology Center of Iran Research Organization for Science and Technology (IROST). IROST is a major research institute established in 1979. The Biotechnology Center of this organization was established in 1982. The Biotechnology Center is active in environment, medicine, agriculture, food biotechnology, and bioprocessing engineering. The center is well equipped with large and modern laboratories. The production of biological fertilizers and single cell proteins (SCPs) from agricultural by-products, production of lysine and giberrelic acid, on a large scale; alpha amylase, gluco amylase, gluco isomerase, pectinase, and many other enzymes on a laboratory scale, and application of bacterial and fungal agents in agricultural pest control, are some of the activities of the agriculture branch of the center.

The center has the Persian Type Culture Collection (PTCC), which is a large collection of microbes of interest to industry and agriculture.

One of the other outstanding achievements of this center is the industrial scale production and marketing of a *Bacillus thuringiensis* (Bt. M-H-14)-based insecticide for combating malaria in southern and eastern provinces of Iran.

Private sector. The private sector has started investing and has some activities in Iran in biotechnology in recent years. Rana Agro-Industry Corp. is one the pioneering private companies in this field. Rana was established in 1992. In a joint venture with a British company, Rana produces tissue culture-derived date palm and banana, with an expansion program for lage-scale production of other fruit trees and ornamental plants. During the Persian Gulf war, hundreds of thousands of palm trees were destroyed. These trees need to be replaced. Added to the plantlets required for plantation expansion projects and the replacement of older trees with the younger and more productive ones, there is an annual market for over 200,000 palm plantlets in the country. There is a huge demand and market in neighboring countries as well. Rana is currently producing about 100,000 plantlets per year. The company will have the capacity to produce 400,000 date palms or 6 million other plant varieties per year.

Cina Gene is the leading company in Iran producing and offering restriction enzymes and other enzymes used in molecular biology, PCR kits, DNA markers, plasmids and many other research items. Considering the lengthy and bureaucratic procedure of placing orders for these items from abroad, and considering the cost of shipment, the company has been welcomed by Iranian research institutes and universities.

Agricultural Biotechnology Research Institute of Iran (ABRII). The Agricultural Research Education and Extension Organization (AREEO) is an umbrella policymaking and funding organization under the Ministry of Agriculture, under which all the national agricultural research institutes are organized. AREEO supervises, among others, several crop-specific research institutes in Iran such as Rice Research Institute of Iran (RRII), Sugar Beet Seed Institute (SBSI), and Pistachio Research Institute of Iran (PRII). In addition there are several discipline specific research institute such as Seed and Plantlet Improvement Institute (SPII), Soil Water Research Institute of Iran (SWRII), and ABRII under AREEO. On behalf of these research institutes, AREEO has several international collaborating institutes and laboratories worldwide. It is one of the donors to the CGIAR, and has separate collaborative projects with its centers such as ICARDA, IRRI, CIMMYT, CIP, and ISNAR.

ABRII was established in 1980 as the Plant Biotechnology Department of SPII. It has recently been upgraded to the level of an independent institute. All biotechnology research activities of the research institutes under AREEO are supervised and monitored by ABRII. ABRII is government funded, with a current annual budget of about US$2 million, and has modern and advanced research facilities such as 10 large phytotrons, several greenhouses and controlled rooms, tissue culture facilities, radioisotope application facilities, and an optical room.

Mass production of uniform and disease free plants. Efficient protocols have been established for mass production of date palm, cherry, apple, banana, potato mini tuber, and sugarcane through tissue culture at ABRII. Hundreds of hectares of these tissue culture-derived plants are being grown in Iran, and demand is increasing dramatically due to their good performance and farmer satisfaction. ABRII's facilities were not designed for large-scale production of tissue culture-derived plants, so new greenhouses and tissue culture rooms with higher capacity are under construction. In addition, we are transferring our experience and the protocols to large-scale private-sector contractors and government-owned private companies. One successful example is the technology transfer of the tissue culture of Karoon Sugarcane Agro-Industry Company.

Haploid Breeding

We are currently incorporating different methods of haploid breeding in our plant improvement programs at ABRII, particularly anther culture and maize X wheat crosses. Seventy-nine double haploid (DH) lines of wheat were produced using wheat X maize technique from four crosses at F1 and F3 stages. Eight promising lines with high yield (up to 10 metric tons/hectare) and enhanced resistance to yellow rust and leaf rust were selected.

Enhancing resistance to biotic and abiotic stresses. Agricultural products constitute Iran's main export items after oil. Iran, however, is also one of the major food importing countries. The import of rice, for example, has increased dramatically in the last 20 years, partly because of population growth (from 19 million in 1956 to 60 million in 1996).

In 1998 Iran imported 1.3 million metric tons of rice, making it one of the largest rice importing countries in the world. More food will be required by the year 2010, considering the limited available land for agriculture, and limited supply of water in Iran. With an average annual rainfall of 240 mm (compared to the 860 mm average annual rainfall in the world), Iran is categorized as one of the dry regions of the world. Major expansion of the area under rice cultivation is not possible. Rice is susceptible to several insect pests including striped stem borer, the major insect pest of rice in Iran, causing estimated crop losses of up to 20 percent. There is no known resistance source in the world collection of rice germplasm maintained at IRRI. In collaboration with IRRI, a synthetic cryIA(b) gene was introduced to Iranian aromatic variety Tarom Molaii using a biolistic approach. The molecular analysis showed the stable integration of the gene into a single locus expressing at a high level (Ghareyazie and others 1997). Bioassays indicated enhanced resistance against four different pests of rice up to the 6th generation (unpbulished data).

Combating salinity problem. About 15 percent of Iran's land area is covered by salt-affected soils. Salinity and drought are the main causes of reduced agricultural productivity. There are increasing lands where none of the known crop plants can be economically cultivated. Breeding for salinity tolerance was not effective in producing crop varieties that can tolerate extreme salinity. Plant physiologists in ABRII are hoping to improve the agronomic characteristics of wild species for cultivation in salt-affected soils. Iran is considered as the center of origin for many crop plants, ornamentals, and fruit species. It is estimated that more than 10,000 plant species with high intraspecifc genetic variation exists in Iran. A large collection of seeds of crop varieties of different species including wheat, barley, rye, rice, pea, melon, grape, and many other important plants and their wild relatives is being maintained in Genetic Resources and National Germplam Center under SPII. We have collected several wild species of both Graminaecea and Poaceae families from extremely salt affected lands covered with salt crystals. In addition to improving their agronomic characters for animal fodder, we are interested in determining their salt tolerance, potassium transport and their osmotic adjustment mechanisms. We are attempting to isolate and characterize the candidate gene conferring additional tolerance in these varieties. In an attempt to increase the tolerance of rice cultivars to salinity a manitol-1-phosphate dehydrogenase gene was transferred to an Iranian rice variety. The stable integration and Mendelian inheritance of the gene was assured by molecular analysis. The increased level of manitol in transgenic rice is under investigation. Greenhouse experiments, however, did not show significant increased salinity tolerance when compared with control plants. Protein analysis will tell us whether the gene has been silenced, or if the approach was (increasing the manitol level) inappropriate. The same gene is also being introduced to Iranian elite wheat cultivars.

Isolation and characterization of high affinity potassium transporter genes from rice. We are interested in potassium transport mechanism for its putative involvement in salinity tolerance. It has been documented that the capacity to maintain a high [K+] /[Na+] in shoots is correlated with salt tolerance in several crop plants including rice. In collaboration with IRRI in a German/BMZ-funded project, we isolated and characterized a high affinity potassium transporter gene from a salt tolerant variety; Pokkali, and a slat sensitive variety IR 29 (Ghareyazie and others 1999). An additional high affinity potassium transporter gene from a different family was also isolated and is being characterized at ABRII. There is no report of the availability of any complete gene of this kind (including its promoter). The promoter analysis is being carried out at ABRII to determine the factors affecting the expression of these proteins. Attempts are being made for isolation and characterization of other genes of agronomic importance including candidate genes involved in pathogen resistance.

Application of Molecular Markers

Application of molecular markers such as isozyme and random amplified polymorphic DNA (RAPD) to study genetic diversity and germplasm management is a routine practice in ABRII and other institutes. About 1000 accessions from Iranian rice germplasm have been characterized in collaboration with RRII and IRRI. Using restriction fragment length polymorphism (RFLP), and PCR-based DNA markers including amplified fragment length polymorphism (AFLP), RAPD, sequence tagged sites (STS), and PCR-based RFLP. Three groups were distinguished among Iranian rices. These are indica and japonica and varieties that are genetically distinct from both indica and japonica types, indicating the varieties probably evolved independently within the country (Ghareyazie and others 1995). Classification of wheat germplasm and fingerprinting walnut and olive trees are some of the ongoing projects at ABRII. Molecular markers have been used to tag quality related genes such as aroma (in collaboration with IRRI) and gelatinization temperature (gt) at RRII (Nematzade 1995; Alavi and others 1999). Mapping QTLs for salinity tolerance genes is one of the ongoing projects at ABRII.

Constraints

Human resources. Most developing countries are suffering from similar constraints. There has always been a move of senior scientists from developing to industrial countries. The public sector (even the private sector) in most of the developing countries cannot offer salaries comparable to industrial country companies. Developing nations spend considerable amounts on education and training, but they often do not benefit from it. In Iran, the trend has been more promising in the past few years. More scientists are returning home and the number of specialized and qualified scientists in universities and research institutions is increasing significantly. In spite of this positive trend, agricultural biotechnology R&D is still suffering from the shortage of senior scientists.

Insufficient funding. Lack of money for science has been another common problem for most developing countries. Iranian agricultural research institutes do not receive sufficient support and contributions from foreign sources. There have been some positive moves by government, however, to increase funding for agricultural research, and agricultural biotechnology in particular. Nevertheless, currently funding is not considered as the top problem in agricultural biotechnology research and development in Iran.

There is a lack of a biosafety regulatory framework in Iran. In addition to the risks associated with the irresponsible deployment of GIOs, it creates problems in legally acquiring and safely releasing products of biotechnology.

There is also a serious lack of protection of IPRs in Iran, and little or no capacity in protecting national IPR at the international level.

Hopes

The establishment of the National Council for Scientific Research under the presidential office has raised hopes among the scientists in Iran. This council is a planning and priority-setting and granting council that receives scientific advice from 11 commissions. Biotechnology, agriculture, and soil and water commissions are the three related to agriculture. Some of the promising developments are: inclusion of both agriculture and biotechnology among the top priorities at the national level for funding and support; identifying the research priorities for funding in both agriculture and biotechnology commissions; submission to Majlis of the draft to ratify the "breeders' rights law"; preparation of a biosafety draft for ratification; full support of the President's administration to biotechnology; and the scientific achievements by both private sector and the public institutions.

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Jordan: Status and Future Prospects of Biotechnology

Moh'd M. Ajlouni and H. Malkawi

Biotechnology is considered to be a frontier area offering a new technological base for the provision of solutions to some of mankind's problems. This technological base involves interactions amongst people, microorganisms, biomass, and industry, underscoring the utilization of renewable resources with a low environmental impact and high regenerative capacity.

Biotechnology has produced new products and processes in a number of economic sectors including agriculture, food processing, chemical and pharmaceutical industries, pesticides, detergents, feed stocks, recycling, and waste treatment.

Biotechnology has advanced rapidly in industrial countries. Jordan still lags behind because of the lack of:

- Major funding to establish laboratories and to have the needed infrastructure and facilities
- A national strategy for biotechnology and its applications
- Know-how at the technical level
- Experienced scientists, many of whom go to the industrial countries
- Insufficient collaboration with international institutions and agencies that are involved in biotechnology development.

Despite these major shortcomings, Jordan has made some progress in biotechnology projects for research and development. Projects have been undertaken by university laboratories, research institutions, and private companies in the following fields: plant tissue culture and basic biotechnology research (in medicine, biological nitrogen fixation (BNF), and in vitro selection for salt tolerance.

Current Status

Jordanian universities have covered research and development (R&D) fields in biotechnology, in the following activities:

- Embryo transfer in animals
- Early diagnosis using monoclonal antibodies
- Applied microbiology
- Biogas
- Single cell protein
- Enzymes and antibiotics
- Plant growth inhibitors
- Natural products
- Cloning
- Protein solvent concentration
- Bioreaction
- Gene isolation
- Biological nitrogen fixation.

Most of the activities are in the field of natural products, early diagnosis using monoclonal antibodies, applied microbiology in food, and biogas production. Antibiotics, growth regulators, embryo transfer in animals, bioreaction, and biological nitrogen fixation are all considered important.

In one of the surveys conducted among the researchers working in biotechnology, the respondents identified areas of importance for Jordan (Table 1). The absence of some fields such as insulin and interferon production, separation technology, process development, developing equipment and biosensors, which are all consid-

Table 1 Research areas specified by biotechnology researchers working in Jordanian universities

Field	*No. of researchers*
Amino acid sequence determination	2
Applied microbiology	8
Biochemical engineering	4
Biological response modifiers	1
Bioreactor modeling	2
Environmental engineering	3
Eukaryotic molecular genetics	1
Gene mapping , transfer, and synthesis	3
Hormone synthesis	2
Hybridoma technology	4
Molecular genetics	4
Molecular immunology	4
Molecular modeling	1
Monoclonal antibodies	8
Plasmid vector fusion	3
Process engineering	1
Protein engineering	4
Recombinant DNA technology	4
Single cell protein	6
Enzymes	6
Tissue culture	14
Vaccine production	10
Viral molecular genetics	1

ered to be important, clearly reflects the absence of scientific specialization and implies shortages in these fields. Researchers have also shown a willingness to work as a group with common concerns to develop their research programs.

Private industry is pursuing R&D in the following areas: tissue culture, biofertilizers, monoclonal antibodies, production of pesticides, developing some equipment used in biotechnology, and yeast production. Future projects planned include enzyme production, veterinary drugs, and laboratory equipment.

Current and future areas, in addition to those considered of a great interest to researchers and technologists in the industrial sector, are given in Table 2.

There are many common interests between the industrial sector and Jordanian universities in important activities such as tissue culture, vaccine production, monoclonal antibodies and applied microbiology, single cell protein, and enzyme production.

The industrial sector, however, highlights its interest in environmental engineering, process engineering in industries and its improvements, and other areas. This results from their sense of the importance of industrial production over the academic research which may not result in any direct products or goods.

Constraints

A recent survey on constraints to the applications of biotechnology in Jordan identified the following issues:

- Lack of financing is the most important restriction in universities and institutions in the pri-

Table 2 Current, future, and essential biotechnology research in the industrial private sector

Current activities	*Future activities*	*Essential activities*
Tissue culture	Enzyme production	Amino acid sequence determination
Natural fertilizer	Veterinary drugs	Applied microbiology
Monoclonal antibodies	Scientific laboratory equipment	Biochemical engineering
Pesticides		Bioreactor modeling
Scientific equipment evolution		Environmental engineering
Yeast production		Gene mapping, transfer, and synthesis
		Hormone synthesis
		Molecular genetics
		Molecular immunology
		Monoclonal antibodies
		Process engineering
		Protein engineering
		Single cell protein
		Enzymes
		Tissue culture
		Vaccine production

vate sector (over 40 percent in the survey).

- Although financial support is a serious problem, researchers (15 percent) cited other problems such as the shortage of professional technicians trained on advanced and specialized scientific equipment. Also of concern is the approvals procedures for biotechnological research, especially the long time between presenting the proposal and its implementation. The result is decreased interest of the researcher, who will often pursue other areas of research.
- Another problem facing researchers in this area is the lack of consumable materials and routine ordering procedures.
- It is important to mention that the right scientific atmosphere is often absent for this type of research activity; the importance of this type of research is not made clear; it is expensive; it does not directly produce goods for people; and there is a lack of scientific literature and other materials. This lack of public awareness of the importance of biotechnology research and the absence of scientific groups who will provide the necessary cooperation and technical assistance to the researcher were cited by 30 percent in the survey.
- University professors claim they do not have enough time to do their research, and the system itself does not allow the appointment of research staff. Professors in the universities should teach and do research at the same time, but because of the heavy teaching load, they cannot find enough time for research. The research would be of an academic nature and not applied research.
- The industrial sector in this field is unable to compete with other international brand products, especially at the beginning of the production and development processes. This results in reduced financial support. As a result, the industry prefers not to be involved in this activity, which requires that most of the products be manufactured locally. The private sector, therefore, concentrates on accumulating imported products and promoting them locally, or dealing in international products only.
- There is an additional problem regarding lack of cooperation among institutions in the same field to reach common objectives and solve problems. There are many drug companies, for example, but there is no common interest in biotechnological R&D.
- There is a prevalent lack of knowledge in both private and governmental sectors about the importance of biotechnology adoption, and what is necessary to facilitate and expedite work in this field.

Conclusions

- Most biotechnology research activities are restricted to universities, with a limited activity adopted by the private sector, which is represented by some industrial institutions.
- Universities pursue basic rather than applied science.
- The role of the private sector is limited in biotechnology R&D, mostly concentrating on improving and promoting current products or producing new ones.
- There is some fragmented biotechnology research in Jordan, mainly of conventional biotechnology.
- There is limited cooperation between Jordan's universities and the private sector.

Constraints and problems encountered by biotechnology researchers at universities and in the private sector include:

Universities: Technical and financial problems; lack of time for research by teaching professors; environment not conducive for research and innovations; lack of public support for research; lack of specialized equipment and information; shortage of laboratory materials and spare parts, and maintenance of scientific equipment.

Private Sector: Marketing problems; technical production and its improvement, which limits the concentration on R&D as a necessity for economic growth in these institutions; lack of appreciation by decisionmakers and the private companies on the role of biotechnology.

The following suggestions may help solve some of the problems and obstacles, and improve and develop biotechnology activities in Jordan in universities, the private sector, and the public sector.

1. Establish a biotechnology center to:
    - Encourage biotechnology research activities and development

- Create a suitable environment for researchers
- Establish specialized and well equipped laboratories
- Direct research into fields of interest in Jordan, which could be applied in industrial institutions
- Encourage private sector research where possible.

2. Supervise and link the various institutions doing biotechnology research by:
   - Providing the requested technical support and finance for the researchers in universities and the private sector
   - Creating a connecting link among different sectors to integrate information and research between the private sector and universities.

Kenya: Biotechnology in Africa: Why the Controversy?

Cyrus G. Ndiritu

This is a time of intensive discussions of Africa's agricultural and economic performance, and the potential impact of biotechnology on the economy and the welfare of the continent. The two issues that dominate the debate are the persistent poor performance of agriculture with associated widespread poverty, and the ability of biotechnology to resolve Africa's food crises taking into account its potential and perceived effects on the continent's enormous biological diversity.

Socioeconomic Situation

At a 3.1 percent growth rate, Africa's population was about 200 million 30 years ago; it is 520 million today and is projected to increase to 1.3 billion in the next 25 years. The continent has the highest population growth rate in the world.

Africa's present and growing population makes it difficult to maintain adequate food consumption levels. Although global food production has reached a stage where sufficient food is produced to meet the needs of every person on earth, the per capita food production and availability has, and still remains, lowest in Africa. Western Europe's per capita food availability stands at some 3500 kilocalories/day, those of North America at 3600 kilocalories/day. In sub-Saharan Africa, only 2100 kilocalories are available per person per day making this the lowest level of per capita food availability in the world.

Although Europe and America have large food surpluses, food availability in Africa is far from being adequate for all people to have access to food at all times. The notion that, at the global level, the problem is not one of inadequate food production but of distribution is correct in a statistical sense, but it is trivial and highly misleading. It suggests, for example, that redistribution of static food supplies is the solution to food deficiency, and further, it relegates the need to increase production in regions like Africa to a subsidiary role.

African people find themselves in a condition of inadequate food consumption levels because they do not earn sufficient income to obtain enough food to satisfy their needs. The situation may not necessarily be one of food scarcity but rather the scarcity of income or purchasing power. This in essence is poverty which prescribes undernutrition. Between 55 and 60 percent of the rural people in sub-Saharan Africa are absolutely poor, subsisting on less than US$1 per day. More than 200 million people (over one-third of the African population) suffer chronic undernutrition. Infant mortality in Africa is about 103 in every 1000 compared to 8 per 1000 in high-income countries. Most urban residents spend more than 80 percent of their earnings on food. This leaves very little for spending on human welfare including nutrition, education, and public health. About 32 out of the 48 low-income countries in the world are in sub-Saharan Africa.

Given that the notion of redistribution of the globally abundant food supplies to meet the needs of the poor countries is of more theoretical than practical significance, the proposition is to increase production in the African countries themselves. A more productive agriculture in these countries should without exception be made an integral part of the process to increase food production. It is with this background that most governments in sub-Saharan Africa have the attainment of food-self sufficiency as their long-term national policy on food production and economic growth. Agricultural improvement to raise food production to "acceptable" levels is an urgent priority for these countries.

Agricultural Performance in Sub-Saharan Africa

Most of the African people earn their living by producing food, and employment and income earning opportunities are closely linked to productive agriculture. In sub-Saharan Africa 50-75 percent of the population and labor force are engaged in agriculture. In 1990, agriculture provided, on average, 32 percent of Africa's GDP, 66 percent employment (for 1987), and about 20 percent of its exports (World Bank 1989, 1992). In this context, agricultural development is critical to present and future economic growth and improvements in the welfare of Africa. Increases in incomes from a productive agriculture are needed to raise food purchasing power and to reduce poverty.

African agricultural growth has been slowing considerably during the last two decades. The annual growth rate fell from 2.3 percent in the 1970s to 2.0 percent in 1980-92. Of the major developing regions of the world, only in sub-Saharan Africa has the per capita food cereals output been declining over the last 30 years.

The stagnation of agriculture in sub-Saharan Africa is due to both internal and external factors. After independence, many African governments were committed to industrialization and to the political support of their urban residents (Lofchie 1987). Exports from agriculture have been heavily taxed to generate the capital for industrialization, thereby reducing incentives for agricultural production. Producer prices for agricultural exports in many countries in the 1980s were generally lower than 50 percent of world prices (World Bank 1986). In addition, a major indirect tax on agriculture has been imposed by overvalued exchange rates. This implicit tax on agricultural exports has been a disincentive to increased agricultural production and exports. With these low agricultural prices and other distortions unfavorable to agriculture such as importation of cheap competing foods, domestic food production has stagnated with farmers retreating from commercial activities to subsistence. There has been little incentive for farmers to invest in new technologies or in other agricultural enterprises. The low profitability has encouraged low productivity, risk avoidance measures including multiple cropping, minimum input use, and extensive agricultural activities based on human labor. The welfare of farmers has been reduced not only by these direct and indirect taxes on their exports, and distortion-reducing prices of competing imports, but also by poor rural marketing systems for industrial and food crops. Policy measures that remove such disincentives and promote productivity are needed.

The external considerations constraining African agricultural performance include a number of biotic and abiotic factors such as shortage of arable land, poor moisture availability, declining soil fertility, limited access to costly farm inputs, limited technological base, and pests and diseases.

Shortage of Arable Land

Past increases in agricultural productivity resulted from an expansion of land under cultivation. Because new arable land is no longer available, intensive techniques provide the best hope for increased production of the principal food crops in Africa.

Inadequate Rainfall

Comprehensive studies of African rainfall have shown a progressive drying trend, with drought a common occurrence over large parts of the continent. The frequent droughts in Africa have often been blamed on human agricultural activity, particularly overgrazing and deforestation. The fact remains that agricultural growth is severely constrained by extensive and severe rainfall shortages. We therefore need to develop crops and livestock breeds that are early maturing and adaptable to the harsh climatic conditions of Africa.

Soil Fertility

The problem of rainfall shortages in many parts of Africa is enormous, and is often compounded by low soil fertility such as in the semi-arid zones where soils tend to be sandy and prone to soil erosion and degradation. These soils lack important nutrients such as sulfur and phosphorus and have low organic matter content. Agricultural production in most parts of Africa therefore requires capital-intensive chemical fertilizer inputs. Fertilizers in Africa are expensive, so farmers use considerably less per hectare than in Europe and America. In 1993 a farmer could purchase 41 kilograms of DAP fertilizer for the price of 90 kilograms of maize. By late 1999 he/she can purchase only 25 kilograms of fertilizer for 90 kilograms of maize. Farmers in Africa therefore use suboptimal levels of fertilizer, averaging 11 kilograms/hectare compared to 90 kilograms/hectare in Asia.

The suboptimal application of fertilizer creates eutrophication of water sources, modified soil structure, and pH changes leaving the soil even more prone to erosion. Organic manure has low nutrient content, so frequent applications are needed. This leads to negative environmental consequences, and associated labor problems. We need to develop new and cheaper agricultural inputs to alleviate the current burden to farmers, and to enhance production.

Pests and Diseases

The devastating effects of plant pests and diseases in Africa is reflected in the amount of resources spent by farmers on their control. In Kenya in 1995, for example, farmers purchased the following agricultural chemicals: 1.36 million kilograms of insecticides, 3.4 million kilograms of fungicides, 113,000 kilograms of plant hormones, and 1.7 million kilograms of herbicides (Kenya 1996), plus large expenses incurred on livestock pest and disease control. Huge crop and livestock losses are incurred in Africa as a result of pre- and postharvest pest and disease damage. The issue of pest and disease resistance in crops and livestock is, therefore, of crucial significance to Africa.

Technological Base

Although area expansion and the use of conventional methods of breeding and agricultural R&D have served African agriculture well in increasing output in the past (for example, in Kenya the production of Katumani Mpya maize, Kenya Mtama sorghum, and rinderpest vaccines), these options can no longer sustain productivity. New intensive production techniques are now needed to augment yields and reduce losses, while conserving the natural resource base. Innovative technologies are urgently needed to transform agricultural growth and development in Africa. Biotechnology offers scope to resolve many of the problems affecting crops and livestock production in Africa.

Role of Biotechnology in Africa

The debate on biotechnology for Africa must be considered in the context of the continent's need for more food and the survival of its people. Biotechnology-derived solutions for biotic and abiotic stresses, if built into African genotypes of plants and animals, could reduce the need for, and the high costs of, agrochemicals and water. New solutions could also reduce the deleterious effects of diseases and weeds, thus promoting sustainable agricultural production in Africa. Several countries, especially South Africa, Kenya, Zimbabwe, and Egypt, are putting in place structures and capacities for R&D in biotechnology. Improvements in productivity are beginning to emerge from the applications of conventional and modern biotechnology.

For example, to address the problems of soil fertility and fertilizer application, for example, a number of countries have embarked on the use of *Rhizobium* inoculant in the production of grain legumes. The application of tissue culture to address constraints of availability to farmers of adequate disease-free planting materials and rapid improvement in crop production, is now commonplace in several countries. In Kenya, for example, the application of tissue culture technology has been initiated in different crops and has resulted in increased production of banana, pyrethrum, potato, cassava, sugarcane, and flowers, most of which have become commercial enterprises. The demand for such materials is demonstrably high, and the changes at the household income levels of growers are becoming increasingly noticeable.

The use of DNA-based molecular markers is now applied in various forms to construct linkage maps of different species. This helps locate particular genes of relevance to the rapid improvement of crop and livestock breeding in Africa. Mapped markers are useful in speeding up selection of traits for use in conventional cross-breeding procedures. These techniques are applicable to many African crop improvement programs such as those seeking to enhance resistance to diseases (for example, maize streak virus) or to generate tolerance to insect pests and drought conditions. Specific programs and capacities in this field are rapidly emerging in Kenya and Zimbabwe, to address resistance to maize stem borer and drought tolerance.

The relevance of genetic modification to produce transgenic crop varieties with resistance to pesticides, insects, and diseases cannot be ignored, given the prohibitive costs to farmers of agricultural chemical inputs and yield losses. Improved food security, poverty alleviation, and environmental conservation in Africa will be enhanced using crops that have a high yield, and resistance to pesticides, insects, and diseases. Great strides are being made in the use of genetic engineering in Africa. Tangible examples include Kenya's virus-resistant transgenic sweet potato project, which is under development with Monsanto Company of the United States, Egypt's transgenic potato, maize, faba bean and tomato developments, and South Africa's new tobacco and cotton varieties with resistance to herbicides.

Recombinant animal vaccines have considerable application in Africa to combat rampant and devastating livestock diseases such as rinderpest and Rift Valley fever. Not only can such vaccines be produced inexpensively, but they also offer the advantages of multiple protection, low costs, as well as allowing the easy distinction between vaccinated and naturally infected animals. This feature is highly desirable in Africa with respect to livestock export to industrial countries, and in continental disease eradication efforts.

Although not exclusively DNA-based, plant and animal disease diagnostic kits, based on the products of biotechnology such as monoclonal antibodies and recombinant antigens, are important modern agricultural applications relevant to Africa. There are important economic implications for pathogen monitoring and disease control programs. Many laboratories in Africa are at present involved in the generation and application of these technologies in the study and control of human, animal, and plant diseases, including HIV/AIDS, theileriosis, trypanosomosis, rinderpest, and streak and mosaic viruses of different crops. Biotechnology therefore has tremendous potential in the improvement of agriculture and food production in Africa. There are numerous challenges, however, that need to be addressed if the people and the continent are to benefit in a sustainable way.

Challenges to Biotechnology Use in Africa

Although many initiatives have been taken to put in place structures and mechanisms for development of biotechnology in Africa, major differences exist between countries in relation to the level of application. Countries face a challenge in making decisions about their level of biotechnology. These include: (1) the development of a knowledge base appropriate to decisionmaking in the use of biotechnological approaches; (2) priority setting for biotechnology aimed at solving specific problems of national importance; (3) establishment of policy and regulatory structures for biosafety and intellectual property protection; (4) capacity development for enhancement of the above issues; and (5) establishment of linkage and cooperative mechanisms for biotechnology development, its transfer, and sustainable applications in Africa.

Why the Controversy?

There is overwhelming evidence and knowledge that the needs and drive for biotechnology in Africa are quite different from those of industrial countries. Africa's agenda is based on the urgent needs for technological change to enhance food production and to alter the course of widespread poverty, hunger, and starvation. Industrial countries are driven by market and profit. These distinctions must be understood and appreciated at the national, regional, and global levels.

The ongoing debate creates fear, mistrust, and general confusion to the public, and has failed to seek the views of African policymakers and stakeholders. The debate about biotechnology for Africa should not be whether or not the continent needs biotechnology, but how biotechnology can be promoted, supported, and applied in safe and sustainable ways that contribute to improved agriculture and to the social and economic welfare of the people of Africa. The need for biotechnology in Africa is very clear, and should not be confused with the marketing/food surplus-driven forces of the industrial countries.

Areas for Collective Consideration

Many countries in Africa face severe reductions in agricultural research funding. Because most biotechnology R&D is more expensive than conventional research, it should be focused on solving priority national or regional problems where it has a comparative advantage. This means that African countries must develop appropriate policies for biotechnology, and mount efforts to identify key national priorities for biotechnology, bearing in mind the needs of the resource-poor who depend on agriculture for their livelihood. This approach should take into account national development policies, private sector interests, market possibilities, technology diffusion mechanisms, and linkages. Diverse stakeholders should be involved in the formulation of national biotechnology policies, strategies, and plans.

The development and application of biotechnology in a safe and environmentally sustainable manner is the subject of considerable debate. Potential environmental hazards from new products of biotechnology, especially genetically improved organisms (GIOs), have raised concerns that, in the absence of adequate legislation and biosafety instruments, some companies may use African countries as test sites for their products, without prior informed agreement by the countries concerned. Appropriate regulatory arrangements need to be in place to help ensure that this does not occur (Doyle and Persley 1996).

The question today should not be whether or not Africa requires biotechnology, but rather how African countries can be assisted to harness and safely apply biotechnology to support development. Egypt, Kenya, South Africa, Zimbabwe, Botswana, Malawi, Mauritius, Cameroon, and Zambia either have or are in the process of adopting explicit biosafety regulations and guidelines, and some are involved in negotiations for an international biosafety protocol. Biosafety frameworks should be accommodative and promotional, rather than prohibitive, advocating the establishment of adequate and sound biosafety regulations, risk assessment and management regimes, and instruments for monitoring use and compliance. What Africa needs most at this time of intense European - American debate on developments and use of GIOs, is the creation of widespread public and policymaker awareness and education on all facets of biotechnology and biosafety. This will enable the countries to make judicious decisions on the path to biotechnology use.

Biotechnology R&D in Africa is presently focused on improving agriculture, with only very few initiatives targeting the ecological impact of GIO development. The greatest effort is still focused on tissue culture application. Over 85-90 percent of the biotechnology R&D in the region is within the public sector, with universities and agricultural research institutions taking on most of the responsibilities. Except for South Africa, local private sector engagement in biotechnology is limited. The private sector is dominant in biotechnology development in industrial countries.

African countries face a compelling need to develop long-term policies on biotechnology that (a) promote national biotechnology needs assessment and targeted research; (b) provide incentives for creation and financing of local private biotechnology enterprises; (c) promote local public R&D of foreign industry partnerships; (d) improve and enhance scientific capacities and technological infrastructure; and (e) integrate biotechnology risk management into existing environmental, health, and agricultural regimes.

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South Africa: Biotechnology for Innovation and Development

Bongiwe Njobe-Mbuli

This paper briefly reviews the South African experience in biotechnology, identifies the challenges, and thereby may stimulate positive debate and lend strength to the African voice in global debate.

What is often pointed out in reference to biotechnology in developing country agriculture is the food security problem, a poverty eradication challenge, and a rapidly growing population. All of these challenges are magnified in sub-Saharan Africa, and biotechnology may be a viable option to meet the needs of the people.

Can a new type of Green Revolution happen in Africa as it did in Asia? Could it work in a different sociopolitical context, and even economic context? Would African farmers adopt new technologies and hope for the same dramatic outputs?

Biotechnology is a reflection of a quantum leap in agricultural scientific endeavor, and we should not lose sight of that fact. We are in an era of declining funds for public sector agricultural research, so there is pressure to develop private-public partnerships.

Ethical issues surrounding biotechnology, including consumer or environmental issues, are largely a concern of industrial countries. Often overlooked is the fact that the African continent sees itself in the process of renewal. There is a strong sense of renewal, and of hope. There is a new energy emerging and a new frankness in dialogue. People are starting to look at political and economic constraints that have often limited opportunities for agricultural development, particularly public investments in research. This is an opportunity that must not be overlooked.

The African continent, particularly sub- Saharan Africa, has been moving rapidly on trade liberalization. There is also a heightened awareness of the cultural and biological diversity that exists in sub-Saharan Africa, which is being seen as an asset for the continent.

There is increased consumer awareness, but this varies from country to country. This level of awareness has a major impact on the way we discuss biotechnology. A negative consumer reaction to genetically improved (GI) products puts us on the defensive, rather than allowing us to deal with the contextual issues and needs.

Crop Improvement in South Africa

South Africa's crop improvement experience may parallel that of many other African countries, which have long experience in plant breeding and particularly genetic modification of plants.

Plant breeding research in South Africa was established about 1950, and the first gene bank was established in 1960. Legislation on plant breeders' rights was passed in 1964 and put into place in 1966. It was largely to support the established commercial sector, and was therefore part of a government instrument supporting large-scale commercial grain and related industries. Most plant research was therefore aimed at those enterprises.

In 1977, South Africa ratified UPOV as part of the overall support for plant breeders' rights, and field trials on GIOs started in 1992. In the intervening years, there was an increasing awareness of the fact that the agricultural challenge in South

Africa was not just about large commercial entities, but that it included a broad group of stakeholders.

With the growing emphasis on strong plant breeders' rights, and the appearance of GIOs in the 1990s, particularly in terms of our markets because the push came from the private sector, there was increased awareness that we needed to reassess the government approach to plant breeding.

The first conditional commercial releases of GM varieties came in 1997. Considerable work has been done on GIOs in South Africa, mainly with cotton, strawberries, and pest management issues. We also did some experimental work in animal breeding.

Over the last ten years South Africa has put in place institutional structures to support appropriate controls in agricultural plant breeding. Opportunity exists for a quantum leap in terms of using new technologies. We are looking at the combination of biotechnology and information technology, without going through the whole process of learning how to deal with resource-limited farmers through improving extension and other activities. We are trying to find something more dynamic that will propel farmers into a new era where they will be able to increase their incomes per unit of land.

The private sector in South Africa is quite active in biotechnology, and has been doing this without government involvement. A private sector NGO watchdog was a strong lobby group on the pro-biotechnology side, leading to the actual drafting and the promulgation of the GIO Act.

The public sector attitude is understood at the political level as being in support of good science, responsible behavior, and access to quality information. That is a framework within which one could garner support from consumers and other interest groups.

On a more cautionary note, we have learned that in this debate we need to recognize that there is a need to balance the interests of the breeders, the farmers, and the consumers, and those interests are not always in harmony.

There is a high cost in both technology development and in technology transfer. It is not a simple issue of developing a technology and simply giving it to the poor farmers. There is a high cost in technology development and meaningful transfer, which can then result in an increase in incomes at the resource-poor farmer level.

When private sector dominance is debated, it usually refers to the U.S. private sector. Very little mention is made of the small businesses that are starting up in South Africa and other African countries. The dynamics of the different levels of private sector involvement in this debate mean that as we structure public-private partnerships, we realize it is not a simple issue of getting into a partnership with the CGIAR centers and two or three large conglomerates. Instead we need to take into account the fact that, in areas where poverty is dominant, there are other types of entities within the private sector.

The Challenges

We need short, medium, and long term strategies. In the short term, we should identify the issues, and deal with any conflicts of interest. In the longer term, we should look at sustainability of whatever kind of partnerships may emerge.We must ensure information for and communications with all stakeholders.

Risk assessment and the management techniques and capabilities must be in place to support the introduction of GIOs, and to deal with the conflicts of interest that may emerge, particularly from environmental and consumer groups. The biosafety protocol that the scope of definition of GIOs and the applications of ALA procedures is critical in determining whether or not one starts to facilitate the free flow of GIO products. The reality is that very few countries actually have the institutional capacity to manage risks and inspire consumer confidence that these products carry no risk, and that we have done the necessary work to support our position. We also need to declare persuasively that there is no problem with the use and propagation of these materials.

Sub-Saharan Africa will probably need to be the starting point for risk assessments, changing management techniques in the scientific and regulatory areas, and also at the field level to be able to accommodate the number of applications that will be made to test GIOs.

Another challenge is to answer: Innovation for whom? Who innovates? What is the nature of the innovation? If it is a scientist who innovates, does it necessarily translate into development when it goes into the field? That question needs to be dealt with because there is no equity in the technology transfer options that are currently on the table.

No matter how successful social development programs of Monsanto are on the continent, the reality is that when commercial production is achieved, you do get into a conflict of interest.

Certain of our cotton producers in Guazu, Natal, are using improved GI seed, but this has happened in an ad hoc manner, with seed not readily available on the market. The farmers did have yield increases, and one of them won a Female Farmer of the Year Award because her yields went up so high. We have not, however, been able to play this out for the large numbers of resource-poor farmers who would need to benefit from the application of such technologies.

What about the future? In sub-Saharan Africa we need to improve our awareness and our institutional capacity to develop biotechnology-linked products. Inherent in our ability to plan for technologies and advanced technologies is our ability to articulate an African scientific agenda, because if that is not articulated, then we will always be on the receiving end rather than being part of the creative process.

We must have greater involvement in critical debates on trade and economic growth, because the subtleties of understanding biotechnology and its application are tending to confuse what are essentially trade and other economic interest debates at the global level. The African voice must be stronger in future.

The CGIAR Can Help

Much of what the CGIAR centers are doing is good, and it should continue to promote informed opinions for all. The proceedings of this conference should be made widely available to research institutions, to government officials, and to decisionmakers worldwide.

The CGIAR needs to disengage from what I think is a simplistic equation of food security as a factor of poverty eradication and declining research funding, plus biotechnology equals development. I think it goes beyond that equation. The CGIAR is a system whose research, fraternity, and leadership must go deeper into the issues, and actually come to grips with the conflicts and help find strategies to deal with those conflicts. Only then will we have meaningful development in sub-Saharan Africa.

The CGIAR centers have a challenge to move beyond the current emphasis on the U.S.-based private sector issues and to look for other alternatives, identify other options. It is not necessarily true that the kind of public-private partnership that would emerge out of a CGIAR-linked process would be of benefit to poor people across the world. This presents a major challenge, as we strive for equity, sustainability, and development through biotechnology innovation.

Zimbabwe: Exploitation of Biotechnology in Agricultural Research

Christopher J. Chetsanga

Zimbabwe is a small country (390,000 square kilometers) with a population of 12 million. Agriculture and mining are the pillars of the Zimbabwe economy, with limited industrialization to add value to products. The main sources of revenue for Zimbabwe are agricultural products and mineral export. The leading contributors to GDP are tourism, tobacco, gold, ferroalloys, sugar, and nickel.

Zimbabwe's main agricultural products are tobacco, maize, cotton, and soybean. Maize is the staple food crop, and tobacco, cotton, and soybean are cash crops. Tobacco farmers have established a sustainable support system that ensures their success. The farmers have instituted a levy system whereby they raise money to support tobacco research, which is under the oversight of the Tobacco Research Board. Earlier funding from Government has essentially been replaced by levy funds from stakeholders.

The tobacco industry Kutsaga Research Station has laboratories where scientists work on improving tobacco breeding, pathology, and other areas using biotechnology. The farmers get good yields of tobacco leaf, and market it at the Harare Tobacco Auction Floors from April to October. Harare boasts the largest tobacco auction floors in the world.

Agriculture is reasonably developed in Zimbabwe. The two major farming groups are the commercial farmers, and the smallholder farmers largely in villages. The main divisions of farming are crop and animal breeding. The main constraints to Zimbabwe agriculture are the unpredictable rainfall patterns and the high cost of fertilizer.

About 90 percent of crops are grown under rainfed conditions. There are limited provisions for irrigation, largely on commercial farms. There is increasing donor interest in supporting dam construction in village areas to improve the agricultural performance of resource-poor farmers.

Maize Cultivation

There is a strong desire to improve the agricultural performance of Zimbabwe. Considerable research has been done by the Department of Agricultural Research and Specialist Services over many years in developing hybrid maize using traditional crop breeding techniques. Zimbabwe hybrid maize seed is grown in most of the Southern African Development Coordination Conference (SADCC) countries. The different hybrid varieties are now bulked and marketed by Seed Co., a local seed company. In recent years the sales of Zimbabwe hybrid maize seed encountered increasing competition from imported maize seed marketed by Cargill and Pioneer Hi-Bred.

The patchy rainfall patterns in recent years have heightened awareness of the need to develop drought-tolerant crop varieties. Conventional plant breeding through pollen transfer is time consuming. It generally takes about 10 years to fully develop an improved hybrid maize variety. The slowness associated with conventional maize breeding is due to the number of generations required to cross, select, and evaluate new progenies.

Efficiencies in conventional breeding are only acquired from long experience working with a particular crop. The experience enhances a breeder's efficiency in developing a maize variety that gives higher yields in a targeted farming area.

Using conventional maize breeding, the records show that U.S. maize yields were increasing at an annual rate of 1 percent. Half of this gain was from improved plant breeding, and the other half from improved management practices.

In the 1997-98 growing seasons U.S. farmers planted 32.6 million hectares of maize, and got an average yield of 8.1 metric tons/hectare. The total production was 263 million metric tons. During the same period, the whole of sub-Saharan Africa planted about 22 million hectares of maize with an average yield of 1.2 metric tons/hectare. Total annual maize production in sub-Saharan Africa is 26 million metric tons. These low yields frequently result in food deficits.

African farmers need to improve these low maize yields, by improving management practices and having access to the best available maize breeding technology. Biotechnology offers the best opportunity to increase maize yields. It also offers opportunities to develop new crop varieties with desired characteristics more rapidly than conventional crop breeding.

Biosafety Considerations

The United States has led in field trials of genetically improved (GI) crops (14,153 trials from 1986 to 1997). Canada had 3,747 trials during the same period. South Africa has done significant field testing of some genetically improved crops.

Dominant traits introduced to transgenic crops include: maize and soybean tolerant to glycophosphate herbicide; insect-tolerant Bt maize and Bt cotton; virus-resistant tobacco; late-ripening tomato; and herbicide-tolerant canola. These transgenic plants have been transformed by the introduction of new genes. The general safety concern about transgenic crops is: Will the gene and its protein product transform the crop into a new variant with harmful properties to the environment? This concern relates to other crops and live forms in the ecosystem.

There is no evidence to date of demonstrated risk in the presently available genetically improved crops that should cause concern. The approvals for commercial use have only been granted after field evaluation to satisfy biosafety requirements.

There might, in a few cases, be reason for concern that the field evaluations have not always been exhaustive. There is some evidence, for example, that the monarch butterfly may be damaged by Bt maize, in laboratory experiments.

There needs to be careful assessments of benefits and risks, and monitoring of the behavior of genetically improved crops in the environment, so as to identify any unintended impact on the ecology.

Biotechnology in Zimbabwe

In the early 1980s biotechnology education was expanded through a masters degree at the University of Zimbabwe. A number of graduate biotechnology specialists are now working in agricultural and pharmaceutical biotechnology laboratories, food processing companies, and medical research institutions in Zimbabwe. The Zimbabwe Biotechnology Program, especially its capacity-building component, has benefited considerably from funding by the Dutch Government, SAREC (Sweden), and the Rockefeller Foundation.

Maize Biotechnology

The government has established a Biotechnology Research Institute (BRI), which is one of seven under the Scientific and Industrial Research and Development Centre (SIRDC). The major project in BRI is maize research carried out in collaboration with CIMMYT. The main priority is to develop a drought-tolerant maize strain. This project is at an advanced stage.

Large biotechnology research laboratories have been built for a long-term maize research program. We are seeking international research funding and hope to attract international maize research specialists to spend periods of time in the laboratories. So far we have a team of four molecular biologists and two breeders. We are also pursuing research on sweet potato, mushroom, and cassava, to exploit their potential as both food and cash crops.

Zimbabwe's Biosafety Regulations are to be gazetted as Statutory Instrument 1999 by the Zimbabwe Government. A Biosafety Board has been established to oversee the conduct of biotechnology in Zimbabwe. Intellectual property rights in biotechnology provide an environment that meets the prevailing international statutes.

Biotechnology in its broad sense does not always have to involve genetic engineering. In Zimbabwe micropropagation technology has been used to generate seedlings of root tuber crops (sweet potato and now cassava and banana) and make them available to resource-poor farmers.

Biotechnology in Agriculture and Medicine

Biotechnology has so far had its greatest impact in medicine. Its application in making recombinant vaccines and recombinant insulin for treating diabetes has been a great success. The applications of biotechnology to agriculture could be equally as powerful.

It is appreciated that genetic engineering can be used to make a number of unique products. Those of us in the field have a responsibility to apply it in ways that benefit human existence and the environment.

Science-Based Risk Assessment for the Approval and Use of Plants in Agricultural and Other Environments

R. James Cook

The use of plants as crops to produce food, fiber, and other products has an amazing record of environmental safety. The greatest risk with any plant deliberately introduced into a new environment is its potential for invasiveness beyond the planted area—to become a weed—but even here crop plants have an outstanding record of safety. Crop plants typically must be managed as "weedy" volunteers after harvest, and some varieties of crop plants are more prone than others to carry over in the field after harvest. I am not aware, however, of a crop plant having become an invasive weed because of plant breeding. This remarkable record of safety for crop plants would indicate that either (1) the risks to the environment presented by crop plants are low; (2) the extensive field testing prior to commercial use and the institutional assessments and decisions on which plants or varieties to grow as crops have been sound; and/or (3) the management practices in place have been adequate to mitigate any risks inherent with plants.

Of the "risks" that have been associated with plant-based agriculture, virtually all are the consequence of the *management* practices needed to grow crop plants and keep them healthy. The environmental risks include soil erosion because of tillage used to form a seedbed and control weeds, nitrates left unused in the soil because of overfertilization (or underutilization because of disease), nontarget effects of pesticides on beneficial insects, and smoke from burning crop residue. These are just some of the more important environmental impacts associated with the growing of crops. Genetic modification of crop plants is unquestionably the best route to mitigation of these risks, but must be accomplished without introducing new risks.

In spite of the safety record, there is public concern worldwide that plants with genes introduced from outside their normal range of sexual compatibility—the so-called "genetically improved" plants (GIs)—might present new risks to the environment. Some of the more frequent claims expressed in the popular press or on the many websites established for the express purpose of raising concerns, include: virus-derived genes used as a source of virus resistance in crop plants will lead to new viruses with potential to kill native plants; the use of genes from *Bacillus thuringiensis* (Bt) as a source of resistance to insect pests will lead to super pests; the antibiotic-resistance genes used as selectable markers will transfer from plants to human pathogens, further exacerbating the medical dilemma of antibiotic resistance in these pathogens; or the use of crops with resistance to glyphosate (Round-up) will lead to greater use of herbicide in amounts that would "annihilate many life forms." Claims such as these are not supported by science. Nevertheless, governments, research organizations and companies must respond to these claims, and must have in place the means to scientifically assess and report on real risks presented by crop plants. This paper outlines an approach to a science-based risk assessment for plants intended for use in agricultural and other managed environments.

Focus on the Product Rather than Process

Numerous studies have been conducted over the past 20-25 years by governments and scientific societies on the safety of rDNA-modified organisms. One of the earliest studies was released by the National Academy of Sciences (NAS 1987). The four conclusions given in that landmark study still apply and are repeated here, with my notes of clarification or emphasis provided in parentheses.

- There is no evidence that unique hazards exist either in the use of rDNA techniques or in the transfer of genes between unrelated organisms.
- The risks associated with the introduction of rDNA-engineered organisms are the same in kind as those associated with the introduction into the environment of unmodified organisms and organisms modified by other genetic techniques.
- Assessment of the risks of introducing rDNA-engineered organisms into the environment should be based on the nature of the organism and the environment into which it will be introduced (product), not on the method (process) by which it was modified.
- There is an urgent (and ongoing) need for the scientific community to provide guidance to both investigators and regulators in evaluating planned introductions of modified organisms from an ecological perspective.

A follow-up study of the National Academy of Sciences on field testing of genetically improved organisms was released two years later (NRC 1989). A key conclusion in this report was that: "Crops modified by molecular and cellular methods should pose risks no different from those modified by classical genetic methods for similar traits."

Thousands of field trials have been conducted with transgenic crop plants during the past 10-12 years, with no evidence that the conclusions stated in the NAS and NRC reports were wrong. On the contrary, the evidence only continues to accumulate in support of the conclusions in these reports. Nevertheless, the rigor of tests for environmental and human health risks conducted with transgenic plants and food made from these plants has been taken far in excess of that done with plants genetically improved by more conventional methods or by induced mutations. Should the bar on safety standards be kept high only for transgenic crops, or should the bar be equally high for all new varieties of crops regardless of the method used to genetically modify them?

Accepting the principle that "the risks associated with the introduction of rDNA-engineered organisms are the same in kind as those associated with the introduction into the environment of unmodified organisms and organisms modified by other genetic techniques," and that "crops modified by molecular and cellular methods should pose risks no different from those modified by classical genetic methods for similar traits," then any risk assessment for the approval and use of plants in an agricultural or other managed environment should be the same regardless of whether that genotype or collection of related genotypes are unmodified genetically, genetically improved by a "traditional" method, or genetically improved by rDNA techniques.

Accepting further that the focus should be on the product and not the process, then the steps used to conduct a risk assessment should be the same for all crops plants, regardless of the source of genes or method(s) used to transfer these genes. How else can the risk assessment be "science based"? Furthermore, whether the risk assessment is done by a government regulatory agency, an institutional variety release committee, or private organization, the assessment process as well as the conclusions on safety should be public information.

Risk Assessment for Plants

What possible hazards are inherent with plants *as plants* (not the management used to grow them) that should be considered when deciding whether to use a particular plant to produce food, fiber, fuel, or grow it for some other purpose? This question pertaining specifically to environmental safety has been addressed in a study released in 1993 by the Organization for Economic Cooperation and Development (OECD 1993). This study represents possibly the first attempt at identification of the environmental safety issues, including worker safety issues, presented by plants and how any risks identified can be managed. Six safety issues with brief explanations or comments follow:

- *Gene transfer*, meaning the movement of genes through outcrossing. This issue could also include gene transfer from plants to microorganisms. Although transfer from plants to microorganisms is possible based on laboratory studies (Gebhard and Smalla 1998), and obviously has happened in evolutionary time (Doolittle 1999), the probability of a functional and medically important antibiotic gene moving from a plant to a human pathogen is negligible.
- *Weediness*, meaning the tendency of the plant to spread beyond the field where first planted. This issue would seem particularly relevant to new crops or old crops introduced into new areas. The classic example is kudzu, introduced into the southeastern United States to control soil erosion, but which now has become a major invasive weed in this region. The tendency with plant breeding is to reduce rather than increase the weediness characteristics of crop plants.
- *Trait effects*, meaning effects of traits harmful to nontarget organisms. Plants with spines or thorns can present a hazard both to workers and wildlife, and many plants produce secondary metabolites that are toxic to animals, or possibly to beneficial insects. As with weediness, plant breeding has tended to reduce rather than increase trait effects on nontarget organisms, sometimes making the domesticated plant more susceptible to pest attack than its unmodified wild relatives.
- *Genetic and phenotypic variability*, meaning the tendency of the plant to exhibit unexpected (pleotropic) characteristics in addition to the expected characteristics. This trait is well known from conventional breeding, but becomes an identifiable hazard only if the variability leads to one of the other safety issues, such as greater weediness or greater tendency for outcrossing.
- *Expression of genetic material from pathogens*. An avirulence gene from a pathogen expressed as a transgene in a plant, for example, has been shown to trigger an uncontrolled hypersensitive response that is potentially lethal to those plants (de Wit and others 1998). Such "genetic disease" would be eliminated early in R&D. Another potential hazard would be the probability of recombination of a virus gene expressed by the plant with genes from another virus infecting that plant. This risk would be similar to the risk of genetic recombinations following mixed virus infections.
- *Worker (human) safety*, such as the effects of nicotine uptake through the skin of workers who handle tobacco. This effect is actually a variation on trial effects discussed above.

Two points regarding these safety issues should be made clear. First, the term "safety issue" is used in the OECD report as the first step to hazard identification; it does not mean that a hazard actually exists. A crop plant known for outcrossing, for example, would raise the issue of gene transfer, but unless there are sexually compatible plants within the range of movement of pollen, there is no hazard. The transfer of resistance to glyphosate from a Round-up Ready® soybean variety in not a hazard in North America because there are no sexually compatible relatives of soybean growing wild in North America. Second, these six safety issues apply regardless of whether the plant has been introduced into cultivation directly from the wild (without genetic modification) or modified genetically. Weediness would have been a safety issue when soybeans were first introduced into North America during the earlier part of this century, but is no longer an issue because (1) observations in small plots during the early years of work with these plants showed that weediness was not a likely problem, and (2) practices are in place to manage any propensity for weediness of this crop plant.

Since risk = hazard x exposure, a low hazard could be considered high risk if the exposure was high and, conversely, a low exposure could be considered high risk if the hazard was high.

Gene Transfer

Returning to the example of gene transfer, a trait that requires a chemical treatment to be expressed (genetic-use restriction technology or GURT) might, because of the phenotype, be identified as a potential hazard if the trait transferred to a wild relative from the crop plant. Without the necessary spray treatment of the fertile hybrid, however, there would be no exposure and therefore no known risk. Conversely, the trait itself may provide no competitive or reproductive advantage (or disadvantage) to a fertile offspring even if transferred by outcrossing, therefore representing a potentially high exposure but low or no risk because there is no identifiable hazard. Gene transfer with no consequence does not, of itself, present an environmental risk. Many traits intended to improve harvestability or other production characteristics, and most if not all traits intended to improve the nutritional quality of the harvested products of crop plants, could fall into this category.

Weediness

A weediness hazard might be identified for a trait for resistance to a pest if the plant population to which the trait might transfer is under selection pressure (biological control) from that pest. If, however, that pest plays no significant role in the ecology of the wild or weedy plant population, then transfer of resistance by outcrossing to an individual within this plant population would constitute no identifiable hazard regardless of exposure. In cases where a relative of the crop plant is both a weed intermingled with its domesticated counterpart, and a source of pests or pathogens of that crop plant, a fortuitous buildup of resistance to that pest within the weedy relative could constitute a component of IPM for that pest. In other words, gene transfer could be beneficial in some cases.

Trait Effects

One of the most significant breakthroughs, with practical implications for control of plant viruses through genetics, was the discovery that expression of a virus coat-protein gene as a transgene in the plant then makes that plant resistant to that virus in direct proportion to the amount of coat protein produced by the transformed plant (Beachy, Loesch-Fries, and Turner 1990). This discovery opened an entirely new genetic approach to control of diseases caused by plant viruses—diseases that heretofore have defied all attempts at their control by traditional plant breeding. One of the latest success stories is the control of papaya ringspot in Hawaii by coat-protein mediated resistance (Gonsalves 1998). This approach is an example of "pathogen-derived resistance," whereby a gene for production of a pathogen protein, when produced in the host plant, results in the expression of resistance if not immunity by that host plant to that pathogen.

The question has been raised as to whether virus coat protein produced in a transgenic plant could encapsidate the naked nucleic acid of another virus also present in that plant (mixed infections are common in plants), and thereby create a "new" pathogen (OECD 1993). Coat protein plays a role in the transmissibility of some plant viruses by insects; were this the case for a coat protein produced in a transgenic plant, then the nucleic acid of a virus not transmissible by a leaf-feeding insect might become insect-transmissible if encapsidated by that plant-produced coat protein. This would be an identifiable hazard. The exposure, on the other hand, would be limited to plants with ability to make that coat protein, since the new virus, being dependent on its host plant rather than its own genome for its coat protein, when moved to a plant lacking that coat-protein transgene, would essentially come to a dead end. Such viruses would then be limited to plant genotypes with the coat-protein transgene. This would be an example of a plant made resistant to one pathogen only to find that it is now susceptible to another pathogen.

The issue of "trait effects" led the U.S. Environmental Protection Agency to propose in November 1994 that traits intended for pest control would be subject to regulation under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) as "plant-pesticides." The regulation, which is still not final, would apply specifically to any substance(s) produced by the plant for its defense against pests and the gene(s) needed to produce the substance(s). A consortium of eleven scientific societies, led by the Institute of Food Technologists and the American Society of Agronomy, challenged the EPA concept that the traits used by plants for their defense against pests and diseases could be equated scientifically with pesticides applied to plants (Cook and Qualset 1996). Most plant defense responses involve the coordinated expression of many genes and a cascade of biochemicals no one of which could be singled out and subjected to meaningful toxicological tests used for pesticides. The consortium of scientific societies then produced a decision guide that categorized plant defense mechanisms into six groups, five of which included defense traits not of a character to be considered as pesticides. The sixth group included traits such as Bt, pyrethrum, nicotine, and other defense mechanisms where the substances involved could be subjected to toxicological tests and were of a character to be considered as pesticides.

Impact of Agriculture on the Environment

Agriculture, by its very nature, is disruptive to nontarget organisms in the environment. Tillage is highly destructive to populations of earthworms that return in numbers only after a few years of no-till management. Rotating maize with soybean—or changing any field from one crop to another—must be disruptive to populations of insects, soil microorganisms, even to macrofauna such as birds and other wildlife. Insecticidal sprays, used to protect crops, kill insect pests and beneficial insects alike. *Science-based* should mean that we know the baseline for non target environmental effects, and can then assess any additional nontarget effects of the new trait that would elevate the risk measurably above this standard.

Assembling a complete picture of this baseline as a defined standard would be costly in human and financial resources that could well be spent on higher priorities, such as developing better varieties. The unfortunate situation is that, having only a fragmentary or incomplete picture, the baseline is treated as virtually nonexistent. Every effort must be made to bring about a greater public and scientific understanding of (1) the environmental disruptions and perturbations that result from simply growing crops to feed and clothe people, and (2) the remarkable trends through genetics that are making agriculture not only more productive but also environmentally more benign.

The baseline also includes the tens of thousands of new varieties of crop plants with new traits added for improved performance or end-use quality during the past century or more using the range of technologies now grouped under "traditional breeding." For example, some 200 crops are grown in the United States, the great majority of which were, at one time, alien introductions to North America. Over the years they have been subjected to extensive genetic modifications to make them more adapted to local conditions, resistant to local or introduced pests, and acceptable to the preferences of U.S. consumers and export customers. Each of the crop plants introduced presented new exposures when first grown in American soil and encountered by American wildlife. Because of the detailed understanding of transgenes, and the fact that only the gene(s) of interest are introduced into the recipient plant, crop plants genetically improved to express transgenes are arguably safer to the environment than their traditionally bred counterparts.

Risk Management for Plants

Risk assessment cannot be discussed without also considering *risk management*. Many highly effective methods in place are in place for management of risks specifically associated with plants as plants, whether as new crops or old crops with new traits. Risk management for crop plants includes that combination of (1) cultural practices evolved over centuries of agriculture, and (2) the knowledge gained during the past century or more from research in agronomy, plant pathology, entomology, weed science, plant biology, soils, microbiology, and the many other disciplines that make up the agricultural sciences. These disciplines, along with engineering, provide the science and technology in place to mitigate any risks that might be associated with a new crop or new trait expressed in a familiar crop.

The risk, for example, of gene transfer by outcrossing from an herbicide-resistant crop plant to some relative that grows as a weed comingled with that crop plant (for example, from canola to weedy mustard), can be managed by the use of a different herbicide (many herbicides are available to manage weedy mustard) or through use of a crop rotation that allows the "rotation" of different weed-management practices. The risk of introducing seed of a fertile hybrid between the crop plant and its weedy relative into a cropped area can be managed by use of seed grown under stringent certification procedures designed to identify crop-weed hybrids when they appear in the seed-production field. The risk of gene transfer from a transgenic crop to a nontransgenic crop can be and is managed by maintaining a certain minimum distance between the crops, such as has long been done in areas that produce both oilseed rape for industrial oil and canola for edible oil. Where there is an identifiable hazard of gene transfer between a crop plant and wild relatives of that crop plant (for example, in an area considered to be the geographic center of origin of the crop plant), serious consideration should be given to whether that crop plant should even be grown in such an area.

There is a great deal of experience and technology available for management of any risk of weediness that might be inherent with a crop plant. Crops such as canola are well known for their tendency to carry over after harvest and to become weeds in the next crop, unless managed by tillage or herbicide treatment. Small grains such as wheat and barley are notorious as volunteer in the field for several weeks or months after harvest and must be controlled. In Washington State, the spring barley variety 'Steptoe' eventually fell from favor among growers because of its unusual ability to survive as volunteer over the winter and become a grass weed in a following pulse crop or, worse, contaminate a subsequent wheat crop. This variety has since been replaced by varieties no less prone to volunteer but significantly less likely to survive an eastern Washington winter.

Replacing the variety with one that reduces or eliminates any identified hazard is another effective and well-established approach to risk management. When it was discovered that the 1970 southern leaf blight epidemic on maize was due to a race of the pathogen, *Bipolaris maydis* [=*Cochliobolus heterstrophus*], uniquely virulent on maize hybrids having the Texas male-sterile cytoplasm (used as a genetic alternative to detasseling in the production of hybrid seed), this method for producing the male-sterile inbred lines was replaced within the next one or two crop years.

Balancing Risks Against Benefits

The overall measure of any cropping system should be its sustainability. It might be useful, therefore, to establish a series of tests for each new crop variety—transgenic or conventional—aimed at helping to determine the contribution the new variety may make to the sustainability of the cropping system in which it will be used. Tests for contributions to sustainability may help identify the benefits of the new variety or new trait, which can then be weighed against any risk(s).

Sustainability includes consideration of economics, impact on environment/natural resource base, and social costs and acceptance. Of these three factors, agriculture needs to pay particular attention to the match between the cropping system and the environment/natural resource base as the test for long-term sustainability, because of the fundamental importance of the environment and natural resource base to both economic vulnerability and social acceptance. Examples of tests for potential to contribute to sustainability based on the need to protect the environment and natural resource base are posed below as questions. These questions can be answered with existing technology and knowledge of cropping systems and required inputs. Whether or not the variety is approved for commercial use could then depend on the answers to these questions.

- Will the variety help reduce the dependency of this crop or cropping system on pesticides?
- Is the pest resistance expressed by this variety of the "durable" type, that is, not likely to be defeated by the pest during the first 10 years and preferably 15-20 years of its use?
- Will the variety help to save soil by making it possible to grow this crop with less or no tillage?
- Will the variety help to improve soil quality, prevent runoff of water from the planted field, or provide wildlife habitat by producing at least as much if not more crop residue than other varieties of this crop likely to be grown?
- Will this variety produce to its full potential without the aid of field burning?
- Will this variety capture as much if not more of the nitrogen added as fertilizer for its production than other varieties of this crop likely to be grown?
- Will this variety assure that no more water and possibly less water will be required to grow the crop than other varieties of this crop likely to be grown?

As an example, Washington State University is working to develop a variety of barley with resistance to Rhizoctonia root rot caused by *Rhizoctonia solani* AG8. Resistance to this disease is needed to reduce the risk and achieve the full yield potential of barley seeded directly (no-till) into standing stubble of cereals. Research in Australia and the U.S. Pacific Northwest has shown that this disease is of only minor importance on barley and wheat seeded into conventionally prepared seedbeds, but is potentially devastating, especially on barley seeded directly into stubble as needed to save soil, fuel, and water (Rovira and Venn 1985; Weller and others 1986). The pathogen has a wide host range and can survive through at least two years of breaks to broadleaf crops. Varieties of wheat and barley differ slightly in tolerance, but these differences are inadequate to reduce the risk of this disease.

Rhizoctonia species are naturally parasitized in soil and on plant roots by *Trichoderma* species, of which the best studied is *T. harzianum* (Kubicek and Harmon 1998). One of the several mechanisms by which this natural enemy of *Rhizoctonia* can inhibit or kill its prey includes a gene with potential, when transferred to plants, to provide a natural defense within the plant. The gene is for production of endochitinase, an enzyme produced by *Trichoderma* to soften and penetrate the chitin-containing walls of *Rhizoctonia* hyphae. Chitinase genes from plants also provide some level of resistance to *Rhizoctonia* species, but the endochitinase genes from *Trichoderma* have proved highly effective in potato and tobacco (Lorito and others 1998).

What are the possible risks of barley varieties transformed to express a *Trichoderma* endochitinase gene for defense against *Rhizoctonia*? Gene transfer is not an issue since there are no wild relatives with ability to hybridize with domestic barley in the area where the varieties will be grown. There would also be no plant pest risk because of the transformation and no risk to workers that would handle the straw or grain. The production of the *Trichoderma* endochitinase enzyme could affect nontarget fungi present within the root or other plant tissues, most or all of which will be endophytic fungi, but some of which may be other fungal pathogens of barley with chitinous cell walls. Such effects would not likely affect soil ecology any more than rotating crops. One identifiable hazard might be ability of transgenic plants to volunteer and survive the winter since the volunteer plants, like the crop produced from these varieties, would be healthier and therefore more robust and more likely to withstand freezing.

Although the risks are small and manageable, the benefits following the proposed agricultural sustainability protocol above would be enormous. There are no fungicides used at present on barley for control of Rhizoctonia root rot, other than traditional seed treatments, but plants with resistance to Rhizoctonia root rot, being more robust, would be more competitive with weeds and therefore would require less use of herbicides in some fields some years. There is no evidence of the emergence of *Rhizoctonia* strains insensitive to endochitinase, and therefore the resistance expressed by barley transformed with this gene should be of the "durable" type. Furthermore, these varieties, by making it possible to grow barley with less or no tillage, would allow for practices that save soil and improve soil quality, prevent runoff of water, provide wildlife habitat as standing stubble, and encourage the return of earthworm populations. Since stubble burning is largely to reduce pressure from root diseases (Cook and Haglund 1991), varieties of barley with resistance to Rhizoctonia root rot would reduce if not eliminate the need for some field burning. Because of healthy roots, these varieties would also then be more efficient in outreach and absorption of nutrients such as nitrogen that otherwise could move below the rooting zone. Crops produced from these varieties of barley would probably need more water, because of their ability to produce more grain, but it would be water that would otherwise be left unused in the soil. Clearly the benefits of these transgenic barley varieties would be enormous, especially when balanced against the risks which would be negligible to the environment and nonexistent to consumers.

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Genetically Modified Crops and Other Organisms: Implications for Agricultural Sustainability and Biodiversity

Brian Johnson

We are at the dawn of a revolution in how we grow food and many other products on this planet, a revolution that is pushing society into rethinking what we want out of agriculture. Biotechnology and other advances in plant and animal breeding and crop technology are already offering an unprecedented range of choices for how we use agricultural land, and how we produce fish and forests. Visions of the future for agricultural land vary between weedless and pestless "green concrete" and visions of a new organic agriculture producing high-quality, high-yield crops yet protecting and nurturing biodiversity. Given the rapid pace of new developments in agricultural biotechnology and the culture of the research world, consumers, farmers, policymakers and regulators throughout the world are struggling to come to terms with these choices. Some consumers, especially those in Europe, are perplexed, anxious, and desperate for information about the potential effects of biotechnology on their food and their environment. The media have sensed that this issue is not going to go away from public consciousness in the foreseeable future, and are actively promoting widespread debate on how we should best use the profound discoveries emanating from the new genetics. This is perhaps the most important debate of the new millennium, because its outcomes will have global implications for food and raw material production for the rest of our history.

I will explore some of the implications of using the present outputs from the agricultural biotechnology industry, draw attention to the science which seems to be missing from the debate, and to look toward the future, when we may well turn to biotechnology to build a more sustainable agriculture. The views are mostly those of the UK statutory conservation bodies and inevitably Eurocentric, but I will try to pose some fundamental questions about the implications of agricultural biotechnology for developing countries.

Statutory conservation advisors in the UK are *not* opposed to genetic modification as a technique for changing the characteristics of plants and animals. It is simply another, but very powerful, tool for plant and animal breeding. On the contrary, we see real promise in genetic modification for eventually producing more sustainable and environmentally friendly crops and farming. Biotechnology *could* give us a future where perennial crops have in-built resistance to pests and diseases, fix their own nitrogen, and give higher yields. We may eventually be able to produce entirely new plants, designed specifically to produce food, medicines, industrial chemicals and fuel. But let us not be blinded by such dreams; like all new technology, genetic modification is risky. European society is deeply concerned about the direction that research and development (R&D) in this technology appears to be going, and the statutory conservation agencies are trying hard to stimulate a debate, not on *whether* genetic modification should be used, but on *how* and *where* it might best be used.

In Europe, where our landscape and wildlife are inextricably mixed with, and dependent upon, farming, we already have serious environmental problems with "conventional" chemical-dependent agriculture. We have surface and groundwater pollution, soil degradation and erosion, and alarming declines in biodiversity. These are the costs of increasing yields, aimed at driving down costs of food to consumers and attempts to compete on world markets. We are still overproducing some commodities and the damage to our environment continues. These agricultural processes were enabled by the introduction of new plant varieties and more effective chemical regimes, including new generations of pesticides. In whatever way we measure the impacts of intensive agriculture, we must conclude that in its present form it is probably not sustainable. By this I mean that, although *levels of production* may be sustainable for perhaps decades, the *social, environmental, and economic consequences* of these processes may not be sustainable for that period of time.

Biotechnology may offer a way out of this dependence on unsustainable agriculture by eventually producing crop plants that enable agriculture to sustain yields but minimize environmental impacts. But the perception in Europe is that some of the present generation of genetically modified (GM) crops, especially those developed for the US agricultural situation, which are herbicide-tolerant and insect-resistant, may present yet further risks to biodiversity in our present intensive agricultural system. I will explore some of the reasons why these GM systems are being proposed and I will argue that the advent of genetic modification has thrown into sharp focus the need for reappraisal of agricultural strategy in Europe. We need clear thinking, scientific information, and realistic views to minimize the risks and maximize the benefits, which I see not just in terms of yet more production and profit.

Before exploring the potential benefits of genetic modification in agriculture, I would like to look more closely at some of the perceived risks associated with growing the present generation of GM crops in Europe. I believe that some of these have been understated by both the industry and by some regulatory authorities both in Europe and overseas. I believe there has been a *laissez faire* attitude toward the potential environmental effects of GI crops. This attitude toward such a powerful technology is potentially damaging not only to the industry but also to politicians, policymakers, and regulators. It is they who are faced with the task of convincing the public that GM crops will bring real benefits to the public and the environment, at minimal risk. It would not be unfair to suggest that up to now the European public are far from impressed by the arguments in favor of GM crops put forward by the biotechnology companies.

Risks to Natural Biodiversity

There are many genetic transformations in crops, such as altered starch, oil, and fat content, which will probably have little or no adverse impact on biodiversity. Most of the present generation of GM crops carry transformations for the insertion of genes for herbicide tolerance and insect resistance into existing crop varieties. My comments will therefore focus on the genetically modifed herbicide tolerant (GMHT) and genetically modifed insect resistant (GMIR) crops which are closest to commercial use in Europe, but are being used commercially now over some 40 million hectares worldwide.

Gene Flow and Transfer of Traits to Other Species

Recent research confirms that genes introduced into some genetically improved crops will spread into related native species (Chevre and others 1997). Gene transfer is almost inevitable from crops that have interfertile relatives in adjacent natural ecosystems, but not from crops such as the maize and cereals grown in Europe, whose closest relatives are on the other side of the oceans. Should we worry about this? After all, genes have been moving for many years from "conventionally" bred crops to wild relatives; for example, in the UK hybrids occasionally occur between oilseed rape (*Brassica napus)* and native species like wild turnip (*B. rapa)* (Raybould and Gray 1993; Department of Environment, Transport and the Regions 1999). The difference of course is that genes inserted into GM crops are often derived from other phyla, giving traits that have not been present in wild plant populations, and if introduced accidentally, may change the fitness and population dynamics of hybrids between native plants and crops, eventually backcrossing into the native species and becoming established. So the issue is not so much the *rate* of gene flow (on which there has been copious research), rather the *impact* that this might have on agriculture and biodiversity (on which there has been almost no research). Conventional plant breeding, using mutagenesis and embryo rescue techniques, also produces lots of completely new genes in crops, about which we know very little. Interestingly, these are often the very crops being used by organic farmers and being sold as "natural foods"!

Most geneticists would argue that most "foreign" genes introduced into crop/native hybrids would in fact *decrease* their fitness in the wild, leading to rapid selection of these genes out of the population. This is particularly true of genes designed to prevent germination of saved seed, like the so-called terminator gene - if this were to "escape" it would commit instant suicide and certainly not spread into the natural world as has been suggested by some anti-GM campaigners.

There is no difference to the farmer between buying seed with terminator technology and buying hybrid seed, because neither can be saved and grown next year. There is a serious issue about whether farmers in the developing countries should become locked into a cycle of dependence on patented seed, but the genetics of this technology is not a direct environmental threat(see Pinstrup-Andersen and Cohen, This volume).

Transfer of certain genes, such as resistance to insects, fungi and viruses could *increase* fitness (ability to reproduce) of any resulting hybrids, possibly forming aggressive weeds or plants that swamp wild populations. Weeds having tolerance to a range of herbicides could also emerge; these would be difficult to control in agriculture, or in natural ecosystems like grasslands. Farmers may eventually need mixtures of herbicides to control them, causing yet more damage to biodiversity. There is already evidence from North America that this "multiple tolerance" and resistance to herbicides is beginning to emerge(see Cook, This volume).

If nontarget plants acquired insect resistance from GM crops, they could damage food chains dependent on insects feeding on previously nontoxic wild plants. Not only would there be a direct effect, for many insects are entirely dependent on single plant species, but acquisition of resistance in wild plants may change their population dynamics, increasing the risks of them invading agricultural land and natural ecosystems. These ecological genetics principles also apply to virus and fungus resistances. This is an even more serious issue for developing countries where control of invasive plants is a major problem for subsistence farmers and may have implications for biotopes of global importance.

The science we urgently need to be able to assess these risks is simply not being done. At the moment we do not know what effect escaped genes might have on natural and farmland ecosystems. This lack of science is disturbing, given the commercial pressure and rapid timetable for the introduction of GM crops into our landscapes. Science will never tell us *everything* about what might happen, but no science will tell us *nothing*.

Genetic transfer to native ecosystems not only carries ecological risk, but also undermines fundamental reasons for conserving plants and their dependent ecosystems *in situ*. Our understanding of ecological genetics depends on research on gene pools of species making up native ecosystems, and the genetic code of each wild species holds information which may eventually benefit us. So-called "genetic pollution" of native gene pools raises some legitimate questions about the loss of basic scientific resources. As scientists, we are keenly interested in the genetics of native populations, so to add genes from other phyla unwittingly and randomly to gene pools is not necessarily a good idea.

There is clearly a need to set up effective monitoring systems to detect gene transfer and research to assess ecological impacts. Research in this area would be in the interests of both the industry and the environment. It would be far better for biotechnology companies to produce the next generation of GM crop plants with in-built mechanisms, such as pollen incompatibility, to prevent gene flow. Perhaps the ecologically simplest way to ensure genetic isolation is to make sure that wherever possible plants used for genetic modification are unrelated to native species and edible crops whose center of origin is within the intended market territory. Biotechnology companies should start thinking now about which plants are chosen as platforms for biomedical and industrial product transformations. If biotechnology is ever to become a standard technique for plant breeding, I predict that genetic isolation of crops from the rest of the living environment will become normal practice, as will the removal of certain genes such as antibiotic resistance.

Genetic Modification of Native Species

At least two research programs in Europe and the United States have recently inserted novel genes into *native* species. One is concerned with inserting herbicide tolerance and genes for increased yield into native grasses, aimed at establishing monocultural high-output forage crops. The other is aimed at inserting genes for insecticide immunity into predatory mites, so when a field is treated with insecticide the mites survive and set about mopping up any surviving pests.

These developments greatly increase the risks of gene transfer and may run unacceptably high risks, because such genetically improved native organisms are completely cross-fertile with native species. From a farmland management perspective, the long-term prospect of having most pasture planted with herbicide-resistant grasses, and then sprayed to eliminate all other plants, could have devastating effects on remnant populations of wild plants, invertebrates, and birds that live in these agricultural grasslands. There is also a real danger that such new varieties of native plants would be fitter than natives and colonize natural ecosystems with unpredictable results.

This scenario is especially important in Europe, where we farm a much greater proportion of land than in the United States, and have less wilderness. The UK and other European governments are committed to several international agreements to conserve wildlife, and we know we cannot do so solely by trying to protect isolated sites. This means that we need to farm in a way that allows biodiversity to thrive within farmland, alongside or within crops, unlike in the United States where intensively farmed areas are often quite separate from large protected wildernesses. Why then are commercial companies and research institutions introducing agricultural biotechnology without assessing properly and holistically the potential risks and benefits to biodiversity? Perhaps regulatory systems throughout the globe need to give some clear signals to the industry about where the boundaries between the possible and the unacceptable might lie. In other words, like in medical R&D, we may need an ethical framework to help science and industry to develop R & D strategies for different agro-ecosystems.

Genetically Improved Crops and Agricultural Intensification

The prospect of gene transfer causes concern for crops that have wild relatives in the same ecosystem, and occupies reams of headline comment in the press. Perhaps of greater importance is the fact that management of some genetically improved crops would be very different from conventional intensive agriculture or organic farming.

In the United States, genetically modifed herbicide tolerant (GMHT) crops are grown under a regime of broad-spectrum herbicides applied during the growing season. Farmers report almost total weed elimination from GMHT crops, which include cotton, soybean, maize, beet, and oilseed rape.They also report substantial reduction in herbicide use (see Pinstrup-Andersen and Cohen, This volume). Recent research in the United Kingdom confirms that weed control in GM beets and other GMHT crops is likely to become much more efficient (Read and Bush 1998). These results are hardly surprising since this is the main purpose behind the technology.

This GMHT system will soon be available, at least experimentally, for virtually all mainstream agricultural crops, including vegetables. Broad-spectrum herbicides used on commercial scale GMHT crops during the growing season may be far more damaging to farmland ecosystems than the selective herbicides they might replace. Using these herbicides in the growing season may also increase the impact of spray drift onto marginal habitats such as ancient hedgerows (field margins common in Europe) and watercourses. It is not only the *volume* of herbicides that is the issue but their *efficiency* and *impact* on wildlife.

When insect resistance and herbicide tolerance are combined in the same crop variety, there may be few insects capable of feeding on the crops and few invertebrates and birds would be able to exploit the weed-free fields. In Europe we already have massive declines in farmland birds, with several previously common species now close to extinction.

The problem with assessing the environmental impact of these changes in management is that the regulatory system and the public has very little scientific data on which to assess the real risks, and potential benefits, from adopting GMHT crop systems. Formal risk assessments submitted by the biotechnology companies as part of the regulatory process deal with this issue inadequately. In the United Kingdom, the Department of Environment, Transport and the Regions and the Ministry of Agriculture, Food and Fisheries have realized this, changed the regulatory system, and commendably have started some field-scale experiments to try to answer some of these important questions.

The development of new crops with improved tolerance to abiotic factors (such as drought, salinity, frost) and the potential advent of 'pharmed' crops producing vaccines and GM biomass systems, may also change crop management, perhaps increasing demand for arable land in the long term, and putting further pressure on natural biodiversity on marginal land.

Agricultural Intensification and Declining Wildlife

If we want to make predictions about how intensification enabled by GM crops could affect biodiversity, we can turn to evidence of declines in farmland plants, insects, and birds resulting from agricultural intensification in Europe over the past 30 years. Factors responsible include abandoning traditional crop rotations, increased pesticide efficiency and drift, use of artificial fertilizer, drainage, and intensification of soil cultivation(McLaughlin and Mineau 1995). There is overwhelming evidence demonstrating that the use of more effective pesticides (including herbicides) over the past 20 years has been a major factor causing serious declines in farmland birds, arable wild plants, and insects. Pesticides not only have direct toxic effects on wildlife but they also *enable* modern crop management changes to take place. Winter-sown crops, for example, rely heavily on effective fungicides. Thirty years ago winter sowing was unknown in the United Kingdom and winter stubbles were widespread, providing an essential food source for wintering flocks of birds. There are many examples of declines in farmland wildlife in the UK and these are typical of intensively managed farmland throughout Europe.

It is important to remember that although these declines in biodiversity have been severe in many intensively managed areas, there are still viable populations of many farmland-dependent species throughout Europe. Some of these, however, are only just surviving the impact of intensive agriculture.

Twenty-five of the 200 species of British "arable plants" are now "Nationally Scarce" and a further 24 are "of conservation concern" and included in the 1983 IUCN Red Data Book (RDB) (McLaughlin and Mineau 1995; Wilson 1994). Not only have many arable plants become threatened but there has also been a marked shift towards a less diverse, grass-dominated flora (Kleijn and Snoeijing 1997). More effective herbicides are responsible; similar trends have been observed elsewhere in Europe (Eggers 1984; Andreasen, Stryhn, and Streibig 1996; Wilson 1992, 1994). Changes in herbicide practice have also been a major factor in reducing the distribution of insects such as the common blue butterfly (Aspinall 1988), the larvae of which feed on broad-leaved weeds.

Over half of British farmland birds are now in serious decline and 13 are red-listed (Siriwardena and others 1998). The 78 percent drop in grey partridge (*Perdix perdix*) numbers observed in the United Kingdom between 1972 and 1996, has been directly attributed to increased herbicide and pesticide efficiency. Skylark (*Alauda arvensis*) populations have declined by 75 percent over this period mainly due to increased pesticide efficiency (Campbell et al. 1997). Recent research implicates agricultural intensification in the decline of other songbirds(Ewald and Aebischer 1999).

Besides the aesthetic and scientific reasons for conserving biodiversity within and around agricultural crops, there is another important utilitarian reason for wanting to do so. This is the need to maintain the food chain links between native species and crop systems. This link is vital if we are to preserve the function of biodiversity to deliver early warning of dangers in crops or the chemicals used to manage them. Without these links, we are unlikely to be able to detect any dangers arising from the new agriculture by monitoring wildlife; the first organism in the food chain will increasingly be *Homo sapiens.* This "natural early warning system" has served agriculture and the public very well over the past 50 years. It detected the toxicity of DDT and aldrin-based organochlorine pesticides (Sheail 1985) and showed up the potentially lethal effects of PCBs before toxic levels built up in humans. This is not just an issue for the industrial countries. It is a natural alarm system which is probably the most cost-effective way of monitoring environmental safety in developing countries. We abandon this biological system at our peril.

Regulatory Arrangements in the U.K.

Until research makes the ecological consequences of using new genetically modified crops clearer, the UK government, acting on advice from regulatory committees and statutory conservation agencies (English Nature 1997), have negotiated a delay in commercial releases of GIHT and GIIR crops for at least the next 3 years, to enable sufficient time for ecological research such as the present field scale trials to take place. In the UK alone, at least 27 studies have started. Information from such research can then be used by regulators to make more informed and publicly defensible decisions about whether GM crops should be commercialized, and under what conditions and in what environments. The delay also allows time to develop better regulations controlling where and how these crops may be grown. In the United Kingdom there is currently no mechanism for on-farm regulation of GM crops, but we believe that for some GM crops this should be put in place. Delaying commercial release could also allow development of better genetically improved crops with, for example, in-built safeguards against gene transfer. The crops coming to commercialization today are the first generation of new biotechnology products. We are therefore engaged in science aimed at determining whether these products are appropriate for release into the English landscape.

Biotechnology and Biodiversity

In Britain, over 70 percent of our land is farmed, and much of our wildlife depends on this farmland. Farmland is important to biodiversity throughout Europe and if we cannot stop degradation of biodiversity on this land, we risk failing to deliver the requirements of international treaties such as the Convention on Biological Diversity (CBD) and EU Directives such as the Birds Directive and the Habitats and Species Directive. Conventional intensive agriculture is already threatening our farmland wildlife and several EU Governments are now trying to introduce agri-environment measures to reverse these declines.

The irony is that biotechnology may hold the key to *less* damaging forms of agriculture, yet it appears that it is currently being used by some parts of the industry in some countries to produce the opposite effect. We are challenging the industry to change direction in R&D, toward producing crops that contribute to more sustainable forms of agriculture, demonstrating real and tangible benefits for the environment. I believe this needs to be done wherever the products of biotechnology are intended to be used, whether in industrial or developing countries.

Environmental damage resulting from the unwise use of biotechnology in agriculture would be a serious issue in developing countries where biodiversity and environmental factors such as unpolluted ground and surface water are fundamental resources used by large numbers of people. Intact and rich ecosystems are important not only for their intrinsic values but also as sources of revenue, whether from sustainable harvesting or from tourism.

Future Strategy

Europe needs to decide the right path for its future agricultural strategy. We need a much clearer and more confident view of what we require from our agriculture, particularly in terms of food production levels, biodiversity, and sustainability. In the United Kingdom we have recently adopted farmland bird populations as a key measure of agricultural sustainability. In other words, we will test the effects of our agricultural policies and practices in terms of whether they increase or decrease farmland bird numbers. It is quite possible that farming systems involving GM herbicide-tolerant and perhaps some insect-resistant crops will fail that test, but we need more research before we can be certain. Other countries may well have different indicators.

We also urgently need to send clear signals to the biotechnology industry about what *we* as the customers want them to produce. Some challenges for the immediate future might include:

- Securing fungal resistance in adult plants by "switching on" resistance genes that are active in the seed, but not currently in adult plants. This seems to be an elegant and safe use of biotechnology which could lead to significant reductions in fungicide use.
- Achieving insect resistance by altering physical characteristics of plants, perhaps by increasing hairiness or thickening the plant cuticle. This could reduce insecticide use, without using in-plant toxins.
- Altering the growing characteristics of crops (for example, shortening the growing season or changing the timing of harvests), offers the prospect of allowing more fallow land and less autumn planting. The recent discovery of dwarfing genes by the John Innes Institute in the U.K. could be a significant step towards the production of higher yielding and more reliable spring-sown cereals.
- Developing crops (including trees) that can tolerate high levels of natural herbivory yet remain viable.
- Preventing outcrossing by engineering pollen incompatibility and other mechanisms into crops. This could significantly reduce the risk of spread of GM traits into native species.

Many of these new traits could be simply transferred from one crop variety into another or be accomplished by switching on or off genes already present in the plant. Such transformations are likely to be more acceptable to the public than moving genes between phyla. The consequences of short-circuiting genetic distance between species, which has been maintained over long periods of time and geographic isolation, are simply not well enough understood to be able to assess the risks.

The real challenge is developing traits like these, which could eventually form part of organic farming systems of value for society as a whole.

Conclusion

Biotechnology and the new science of genomics, which is giving us new insights into how genes function, offer a whole new range of options for how we could use land, because for the first time in our history we really can design crops to suit the land and the purpose rather than having to adapt land and purpose to suit the crop. New sustainable agricultural systems will need support from packages of possible incentives, subsidies, and regulatory measures to make them profitable and attractive to growers.

Perhaps we also need new institutions, and more multidisciplinary teams dedicated to the search for more sustainable farming systems, to think through and explore how we might design new agricultural systems such as mixing different crops in the same fields or having nitrogen-fixing perennial crops in sustainable permacultures. We need to break free from the paradigms of the past, where advances in agricultural yield have always meant retreats in sustainability. This is also important for developing countries where biotechnology may be able to offer new solutions to old problems of crop pests and disease in otherwise ideal crops, rather than trying to export conventional, chemically-based agriculture with its damaging effects on biodiversity and the wider environment and on human health. These are serious scientific and strategic challenges for agricultural biotechnology, for regulators, policymakers and for politicians; they are urgent issues for all of us, for the pace of discovery will not slacken.

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Sustainable Use of Genetically Modified Crops in Developing Countries

Fred Gould and Michael B. Cohen

When potential risks to the environment from new genetically modified (GM) crops are discussed, the focus is generally on risks of genes escaping to wild relatives that become "superweeds," risks of crops themselves becoming weeds, and the potential that toxins produced by the GM crops (or toxins used to kill pests of engineered crops) will harm nontarget organisms (for example, Johnson, This volume; Rissler and Mellon 1996; Snow and Moran Palma 1997) . These are all tangible risks, that can be diminished if taken seriously. Their worst-case negative impacts on the overall environment in developing countries are relatively small compared to the impact on the environment of rural populations without food security and living in poverty.

Because poverty can lead to environmental degradation, we will examine a potential chain of interactions between genetic modification, increased yield, variation in yield, food security, and environmental degradation. We believe that new genetic modification has great potential for increasing yield and decreasing yield variation, but that such accomplishments will require vigilance by scientists and society.

Giving farmers the right kind of seeds can never ensure food security, but giving them the wrong kind of seeds always can make things worse. Social scientists know that you cannot alleviate poverty just by growing more food, but agricultural scientists are always being pushed by philanthropic and development organizations to produce more food because food production is a necessary but not sufficient condition for food security (Serageldin 1999). This has led to increased yield becoming a focus of international attention.

About 50 years ago agricultural scientists were told that the growing world population would demand that we substantially increase crop yields. Amazingly, agricultural scientists, with the financial aid of many government and private organizations, did a reasonable job of meeting this demand (Conway 1998). Today agricultural scientists are being told to do this again because world population growth by the year 2025 or so will demand that we increase production by 30-50 percent (see Pinstrup-Andersen and Cohen, This volume). A special report in Science (Mann 1999) reviewed recent debates about whether, with or without biotechnology, plants could be pushed to become that much more productive. Even if agricultural science can push plants and soils to meet this demand, what happens in 2025 if the optimistic forecasts of no population growth after that date are incorrect? Do we once again ask agriculturalists to raise yields?

Importance of Yield Stability

One thing that crop and animal breeders have learned over the years is that when you select strongly for improvement in one trait of an organism, be it speed in a race horse, appearance in a dog, or yield in a crop, there are tradeoffs (Falconer and Mackay 1996; Mann 1999). The race horse may be frail, the dog less intelligent, and the crop less capable of dealing with stress. In our efforts to keep increasing maximal or average yield, we must be vigilant not to produce crops that have high variation in yield because they are less capable of withstanding stresses associated with unusual weather or pest outbreaks. There has always been support given to programs that breed for stress resistance, but these programs are often funded with the goal of increasing yield rather than decreasing variation in yield. A number of recent reviews have attempted to determine if the variation in crop yields (statistically adjusted for change in the mean) have changed during the 20th century. The conclusions of these assessments indicate that on a global and continental level overall adjusted variation in yield has not generally increased (Naylor, Falcon, and Zavaleta 1997; Calderini and Slafer 1998), but that the component associated with genetic crop improvement has increased (Calderini and Slafer 1999). This means that the variation in yield is being pushed upward by the varieties of crops grown, but that other factors such as improved irrigation may be balancing out this increase caused by breeding.

Unpredicted spatial and temporal variation in yield has a different relative importance depending on your perspective. Local variation in yield gets partially averaged out at the world market scale, and it can be dealt with reasonably well by individual farmers if they have the resources to farm on a three or four year time horizon. But for the subsistence farmer, variation in yield can be critical. If you were a subsistence farmer who could not save harvested corn for more than 12 months, would you rather have a corn cultivar that in five successive years produced 48, 72, 12, 24, and 84 bushels per hectare or a second cultivar that produced 46, 36, 41, 43, and 38 bushels per hectare? Your choice would probably depend greatly on the details of your social and economic situation (for example, whether you had alternative crops or alternative sources of income, and whether you had cash crops; Walker 1989), but in many cases your concern over the 15percent lower average yield of the second cultivar would not outweigh concern over the year when the first cultivar yields 12 bushels per hectare, especially if you could not predict when that year would come. Having the right seed cannot ensure that you will not have variation in yield, but having the wrong seed can guarantee that you will have high variation. The "race horse" seeds we produce for resource-rich farmers may not always be the best seeds for subsistence farmers. Our contention is that there is a need to pay substantially more attention to yield stability as we strive for higher average yields. A more radical stance is that increasing yield stability rather than increasing average yield should be the primary goal.

Because at the local level, drought, flooding, and pests vary significantly from year to year, cultivars bred with resistance or tolerance to any of these disruptive factors would decrease yield variation and could also result in increased average yield. Genetic engineering has improved and should continue to improve, these traits, but care must be taken in how this is done if a major goal is decreased variability in yield.

Pest Resistance Management and Yield Variation

Crop breeders have long known that some conventionally bred cultivars with resistance to insect and microbial pests may perform wonderfully for the first few years after they are deployed commercially, but then fail miserably in controlling the targeted pests in later years because the pest has evolved a way to cope with the resistance mechanism in the cultivar. Sometimes there is a slow decline in effectiveness of the cultivar, but in other cases the onset of control failure is rapid and unpredictable. If you are a subsistence farmer, the failed performance of such cultivars can mean hardship, especially if the cultivar had previously performed well and long enough for you to gain confidence in it. Indeed some of the criticisms of the Green Revolution of the 1960s and 1970s centered on rice cultivars that were rapidly adapted to by insect and microbial pests. For example, brown planthopper populations adapted to the single-gene resistance in the first Green Revolution rices within 2-3 years of their widespread cultivation (Gallagher, Kenmore, and Sogawa 1994), and single-gene resistance to the rice blast fungus has been notoriously unstable (Ou 1985). The longevity of cultivars with single blast resistance genes in Japan has been less than 3 years (Kiyosawa 1982).

In industrial countries, breeders and seed producers sometimes try to deal with pest adaptation to widely used crops that have one resistance mechanism by maintaining, in reserve, replacement cultivars with different resistance mechanisms, for example wheat rust (McIntosh and Brown 1997). These systems are sometimes able to replace cultivars in a single season as was the case with the southern corn blight epidemic in the USA. In developing countries, instituting such a system for subsistence crops is difficult or impossible because of limited infrastructure and resources.

Not all pest-resistant cultivars are rapidly adapted to by their target pests. Entomologists and plant pathologists have worked hard to predict whether a specific resistant cultivar is likely to work well for a long time under field conditions. This characteristic called "durable resistance" has proven to be partially predictable, but many plant pathologists are only willing to judge the durability of a specific type of pest resistance in retrospect.

The general problem of pests adapting to any approach used to control them has been the bane of agriculturalists for centuries. Weeds, pathogens, and insects have all overcome various cultural, chemical, and biological approaches used for their control (Gould 1991). Over 500 insect species are known to have adapted to at least one insecticide (Georghiou and Lagunes 1988), and it often takes less than three years for this adaptation to evolve (Forgash 1984). In many developing countries this can severely disrupt food production because replacement insecticides are often not available, and the beneficial insect populations have been decimated by insecticide use.

In 1997 and 1998, there was a tragic series of over 400 suicides among cotton farmers in Andra Pradesh, India in response to crop failures that were in part the result of pest adaptation to insecticides (Verma 1998; McGirk 1998). The farmers were heavily in debt because of several seasons of crop failures, caused by irregular rainfall and heavy infestations of the insect pests *Spodoptera litura* and *Helicoverpa armigera*. Application of large doses of highly toxic insecticides such as monocrotophos and methomyl were not effective because of pest resistance to these compounds, and their toxicity to predatory and parasitic arthropods which otherwise could have provided some level of natural biological control.

In the 1970s entomologists, plant pathologists, and weed scientists began a concerted effort to use knowledge of evolutionary biology and population genetics to develop strategies for slowing the rate at which pest populations evolved adaptations to control tactics such as pesticides and pest-resistant crops. This approach called "pest resistance management" now seems highly appropriate for crops developed using genetic engineering, because there is good reason to predict that some approaches to the development and deployment of engineered pest-resistant crops will last much longer than others.

Bt Crops as a Case History

When new genetically improved crops that expressed insecticidal proteins from *Bacillus thuringiensis* (Bt) were first developed, there was much concern in the United States about insects adapting to these toxins. Unlike conventionally bred resistant crops, where a resistance mechanism can only be moved within a single crop species, the Bt toxins were being moved into multiple crops, so insects that fed on more than one crop would get multiple exposures. Unlike insecticides that are sprayed only during some time periods in the season when pest pressure is high, the newly developed crops produce the toxin all season long, so all insects in a population can be exposed to the toxin. Everything known about pest adaptation indicated that overuse of such crops could give great control for a limited number of years followed by failure (Tabashnik 1994).

In the United States there was one other pertinent fact about Bt crops. *B. thuringiensis*, the bacterium that was the source of the toxin genes in the crops, has long been sprayed on crops by organic farmers and others as an alternative to chemical insecticides. Organic farmer groups and their supporters protested that the overuse of Bt toxins in genetically engineered crops, and the subsequent development of adapted pests, would leave them without an effective pest control tool. This highlighted two issues: one was the plight of the organic farmer and the other was the unique, environmentally benign nature of Bt toxins compared to conventional pesticides. A set of

Bt toxins, sometimes referred to as Bt endotoxins, were known from previous uses to be effective at killing either some caterpillars or some beetle species, but they had no effect on almost all other species. From an environmental perspective these are wonderful toxins, and unless other toxins with this high target specificity can be quickly found, the overuse and loss of Bt toxin efficacy in transgenic crops could send cotton and potato farmers back to spraying environmentally disruptive chemicals.

All of the above issues led the United States Environmental Protection Agency (US-EPA) to finally require that Bt crops be developed and deployed in a manner that would decrease the risk of rapid pest adaptation. EPA staff have worked hard in pushing companies to develop workable resistance management plans (Matten 1998), but to date this has only been partially successful. It is worth examining some of the processes that led to the current situation in the United States to understand better some of the issues that will face developing countries if they attempt a similar approach. We are not privy to all of the workings of the US-EPA so we can only provide an observer's perspective.

Bt-Resistance Management

Prior to the commercialization of any genetically improved crops, the US-EPA held meetings of Scientific Advisory Panels to get advice from experts outside EPA regarding risks of genetically improved crops. One of the recommendations of these panels was to institute resistance management programs. When EPA granted conditional registrations for the first Bt corn cultivars in 1996, one of the conditions was the development of resistance management plans by the year 2000. The EPA felt that such plans were not immediately needed because they expected adoption of these Bt cultivars to proceed more slowly than it actually did. The conditional registration for Bt cotton included a resistance management plan, but this plan is now being reexamined because it lacks rigor. More recent conditional registrations of newer corn cultivars have included more stringent resistance management plans. The imposition of resistance management plans is something new for the US-EPA and the agency has been gaining sophistication in this area over time.

In 1998 the EPA convened a Scientific Advisory Panel to reassess the issue of Bt resistance management. The report of this panel (EPA 1998) laid out some clear recommendations to the EPA. After considering a number of potential resistance management strategies, the panel recommended that "a refuge/high dose strategy must be employed for target pests within the current understanding of the technology." They added that "regulatory strategies should serve to provide growers with a sustainable approach that encourages compliance." These were important recommendations worthy of careful examination.

We would like to discuss the refuge/high dose strategy in some detail because it is often misunderstood. The high dose portion of this strategy is most easily understood by analogy to the use of antibiotics. When doctors prescribe antibiotics they often give their patients the admonition that even if they feel completely cured after three days, they should continue to take the antibiotic for the full time prescribed. The reason for this is to produce a high dose of antibiotic for an extended time period that will kill even those rare bacterial cells that have a mutant gene conferring partial tolerance of the antibiotic. After three days you may have killed 99 percent of the targeted bacteria, but if the 1 percent that survive have a gene that confers partial tolerance and are transmitted to another individual, his or her infection will be more difficult to treat. More importantly, when that next individual takes the antibiotic, the partially tolerant bacteria may evolve even higher tolerance if among the millions of bacteria involved in the infection there are a few bacteria with other mutations that add to the tolerance conferred by the initial mutation. When a patient takes an antibiotic for the full period prescribed, the expectation is that even the partially tolerant bacteria will be killed. As long as it takes more than one evolutionary step to result in complete tolerance of the antibiotic, the prolonged use of the antibiotic should derail the adaptive process by inhibiting the first step.

The use of a high dose of Bt toxin in crops serves a similar (though not identical) purpose. In all cases studied to date it takes more than one gene, or at least more than a single copy of a gene (heterozygous condition) to confer high tolerance of Bt toxins (Tabashnik 1994; Shelton and Roush 1999). When Bt crops are first commercialized it is estimated that about 1 in 1000 individuals may carry one copy of a gene for tolerance of Bt, and only 1 in 1 million would carry the two copies needed to achieve a high level of tolerance (Gould and others 1997). The high dose approach is set up to ensure that each plant that produces Bt toxin produces enough to kill most of the partially tolerant individuals.

But if the high dose is used by itself, some insects out of the billions that can infest a local area may have two copies of the gene. If they survive and mate, the Bt crops could rapidly lose effectiveness. This is where the refuge part of the "refuge/high dose" approach comes in. All of the current target insects for Bt crops are obligately sexual. That means that they must mate to reproduce, and that their offspring obtain half of their genes from each parent. If a small portion of a farm is planted to a cultivar that does not produce Bt toxin this area serves as a refuge for Bt-susceptible insects. Because the highly tolerant insects are expected to be so rare, they are likely to mate with susceptible insects produced in the refuge. The offspring of these matings will have only one gene for tolerance, and so will be killed if they feed on a Bt-producing plant. By combining the refuge and the high dose, this strategy derails the evolutionary process as long as more than one gene copy is required to survive the high dose. Pests can eventually adapt to such a strategy but the time period required can be 10 to 100 times longer than expected if this strategy is not implemented.

The 1998 EPA Scientific Advisory Panel was clear about what constitutes a high dose and what constitutes an effective refuge. They defined a high dose as 25 times the amount of toxin needed to kill susceptible target insects. They concluded that an effective refuge existed when for every insect with a resistance gene produced in the Bt crop there would be 500 susceptible insects produced that could mate with the resistant insects. These are stringent requirements and they work in concert. If a crop does not quite produce a high dose, the expected number of insects with at least one resistance gene increases. This results in the need for a larger refuge to produce the 1:500 ratio.

How do these recommendations line up with Bt crops that are now on the market in the United States? With Bt potato the data indicate that there is a high dose for the target pest, Colorado potato beetle (Perlak and others 1993). However, it is not confirmed that farmers are planting effective refuges. With corn, most cultivars produce a high dose for the European corn borer, but not for the corn earworm (Andow and Hutchison 1998). Refuges currently appear large enough for the European corn borer, in part because of lack of full adoption of Bt corn, but the refuges may sometimes be too far from the Bt corn to allow insects from the refuge to cross-mate with insects from the Bt crops. In cotton there is a high dose for the tobacco budworm (a major cotton pest) but not for the corn earworm (also called the cotton bollworm in cotton) (Gould and Tabashnik 1998). Proposed refuges of about 10 percent are expected to be sufficient for the tobacco budworm, but may not be sufficient for the cotton bollworm. There appears to be a high dose in cotton for the pink bollworm, but this has not been completely confirmed. There is certainly room for improvements when the producers of Bt crops present their new resistance management plans to the US-EPA in 2000.

Implications for Developing Countries

If the United States is struggling to meet the requirements for resistance management plans, what does this mean for developing countries? Monsanto has already entered joint ventures in China to produce Bt cotton. At a recent USDA/EPA workshop (August 1999, Memphis, TN), there was debate as to whether similar resistance management strategies would be required in China. The expert statement was conditioned on the assumption that no Bt corn was grown in China. If that assumption held then the targeted Chinese pest on Bt cotton, *Helicoverpa armigera*, could utilize non-Bt corn to produce the Bt-susceptible insects. It appears that there now will be Bt corn grown in China, and the Bt cotton that is being planted in China does not have a high dose for the target insect. This is not the kind of scenario that is likely to retard the evolution of adapted pests. If Chinese farmers and administrators come to rely on Bt corn and cotton in the next few years using the current technologies and risk management, there is a clear risk that yields will show variation over time. (It is important to note that one reason that Chinese farmers need

Bt cotton is the fact that the target insect pest, *Helicoverpa armigera,* has adapted to conventional insecticides and can not be effectively controlled.)

There is economic pressure in many developing countries to adopt Bt crops that were developed to control U.S. pests. If these crops are sold as "second hand" cultivars to these countries, it is hard to imagine that they will usually be effective at thwarting pest adaptation. Unless there are careful contingency plans to deal with the eventual failure of these cultivars, their adoption by developing countries could lead to higher than necessary yield variation. For example, it has been argued that situations such as that in Andra Pradesh demonstrate the urgent need for the release of Bt cotton in India. Two kinds of Bt cotton have been field-tested in India: one from the Monsanto Company and one produced by an Indian research institute. Many farmers will be eager to adopt Bt cotton, which can help to control *S. litura* and *H. armigera*. The availability of Bt cotton may also attract many new farmers to invest in growing cotton. However, if a carefully designed resistance management plan is not implemented, the farmers may suffer another severe setback in a few years should the pests adapt to the Bt cotton. In desperation, these farmers may again turn to highly toxic insecticides, repeating a tragic cycle.

It is often said that by the time insect pests adapt to Bt crops, biotechnology will develop replacements. If it was easy to develop replacements, competitive market pressures in the U.S. cotton and corn seed trade would have already resulted in alternative toxins being produced. The only even marginally novel toxin in corn is the Cry9C Bt toxin that AgrEvo has marketed, but because of health concerns, the US-EPA has approved its use only in corn grown for livestock feed. It has been said that the people with the most to lose from pest adaptation to Bt toxins are those who own the companies that own the genetically engineered seeds, but the aggressive stances of some companies against implementation of resistance management plans recommended by US crop scientists does not, however, indicate sincere concern. An explanation for this discrepancy could be that as with the pesticide market, most of the important profits from Bt crops are expected to come in the first years of widespread use, and resistance management could interfere with these early profits. Public and commercial interests are therefore expected to classh.

Bt Resistance Management in Rice

International agricultural research centers such as IRRI (International Rice Research Institute) have devoted significant resources into development of resistance management strategies. At IRRI, research has led to a much better understanding of the type of Bt rices and cultivar deployment strategies that will be needed to arrest adaptation to Bt rices by two major stem- boring pests (Cohen and others 1997). It is clear from this research that even if high dose plants can be developed, it will be difficult to institute effective refuge systems in subsistence, rice growing systems. Seed mixtures of a Bt and non-Bt varieties will be easier for farmers to establish, but studies of the biology of the target pests indicate that field-to-field refuges will be more effective (Cohen et al. 1997; A. Dirie, N.L. Cuong, M.B. Cohen, and F. Gould, unpublished data). In some industrial countries, it has been possible to legislate and enforce the use of refuge fields by farmers growing Bt corn and Bt cotton (Andow and Hutchinson 1998, Gould and Tabashnik 1998). It will presumably be quite difficult to implement the use of refuges by farmers in developing countries, where farm sizes are small, the numbers of farmers is very large, and there is limited communication with farmers through extension agents or other means.

The best way to get around the problem of less than optimal refuges is to build reinforced high-dose cultivars. So far, the best way to do this seems to be by producing cultivars with high doses of two types of toxins that each require a different adaptive mechanism in the insect pest (Gould 1991; Roush 1997). For an insect to survive on such a plant, it would need to carry mutations at two genetic loci, one conferring resistance to each toxin. Insects with two copies (homozygous) of the mutations at both loci will be rare in pest populations that have had limited or no previous exposure to the toxins. Thus smaller refuges would suffice to prevent mating between two resistant individuals. For example, with a variety that produces two toxins it might be sufficient for a village to have 5 percent of its fields planted to non-Bt varieties, compared to the 25 percent refuge that might be necessary to provide good resistance management for a Bt variety that produced only one toxin.

For varieties genetically engineered with two toxins, it would be ideal if one toxin was a Bt delta-endotoxin (the class of toxin used in all Bt crops produced so far), and the second was from an unrelated class of toxins. Unfortunately, as noted above, additional classes of toxins that have all of the advantages of delta-endotoxins have been difficult to find. The best that can be done at present is to select pairs of delta-endotoxins that are highly dissimilar in amino acid sequence (some pairs of toxins sharing as little as 20% amino acid similarity, Feitelson, Payne, and Kim 1992) and that have been shown to bind to different target proteins in the midgut of the insect pest (Van Rie 1991; Gould 1991). Such combinations of toxins have been identified for several important pests (Gould 1998). Unfortunately, in at least two pest species, strains have been identified that have broad-spectrum resistance to widely divergent delta-endotoxins (Gould and others 1992; Moar and others 1995). In addition, given that industrial countries are having difficulty in developing alternative toxins, this will certainly be a high hurdle for international research centers and national agricultural research systems, unless assistance is received from industrial countries in the form of substantially increased research funding or donation of patented technology

Regulatory Requirements

The development and implementation of any resistance management plan in developing countries will require action by national biosafety committees, departments of agriculture, or other regulatory bodies. National biosafety committees in developing countries have made impressive progress in drafting and implementing biosafety regulations for the importation and testing of transgenic crops. For example, within the past 10 years regulations for field testing have been established by China, India, Thailand, and the Philippines. Regulators in developing countries have shown an awareness of the importance of resistance management, but have not yet faced the challenge of producing a specific plan for a specific Bt crop. As Bt crops begin to approach commercialization in developing countries, it is important that international organizations such as ISNAR (International Service for National Agricultural Research) and others, which have helped to train national biosafety committee members, expand coverage of the resistance problem in their training courses and workshops.

Conclusion

In the above discussion we have only touched on some of the problems inherent in developing pest-resistant cultivars that can be expected to sustainably decrease yield variation. While it will not be difficult to spread pest resistant cultivars around the world in the next few years, it will be difficult to do this in a way that increases long-term food security and thereby decreases environmental risks. We must soon decide if sustainable pest-protected crops will be a priority in international agricultural research.

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Potential Health Risks of Genetically Modified Organisms: How Can Allergens be Assessed and Minimized?

Samuel B. Lehrer

Allergies to foods are a significant public health concern throughout the world. Nearly 2 percent of adults and 4-6 percent of children suffer from food allergies, which are defined as an adverse immunologically mediated reaction to antigenic molecules present in foods. The allergic response is mediated by the interaction of cell-bound immunoglobulin E (IgE), a class of antibody molecules uniquely involved in allergic reactions with allergen (Sampson and Metcalfe 1991; Metcalfe, Sampson, and Simon 1996). Antigenic molecules, or allergens, typically are proteins that stimulate allergen-specific IgE production in certain individuals through as yet undetermined mechanisms (Lehrer, Horner, and Reese 1996; Taylor and Lehrer 1996). Inheritance and exposure to allergens are two factors that contribute to the development of allergy. The pathophysiological mechanisms of food allergies are distinct from other food intolerances such as gluten sensitive enteropathy (celiac disease) that are due to nontoxic, nonimmune reactions to foods even though symptoms may resemble those of "true" food allergies. Food allergy symptoms can range from mild discomfort to life-threatening anaphylactic shock (Sampson and Metcalfe 1991; Metcalfe, Sampson, and Simon 1996).

More than 90 percent of the allergic reactions observed in children and adults can be attributed to exposure to eight foods or food groups. These include eggs, fish, shellfish, milk, peanuts, soy beans, tree nuts, and wheat (Taylor and Lehrer 1996). Virtually all allergens are proteins; yet of the enormous numbers of proteins occurring in foods, only a very few are allergenic and only in certain people. Most characterized food allergens, with some exceptions, are stable to digestion and processing, and many of the major allergens are generally proteins that are present in large amounts in allergenic foods. The primary structure of food allergens has been determined by molecular cloning and sequencing (Taylor and Lehrer 1996; Bush and Hefle 1996; Lehrer and others 1997; Reese and Lehrer 1998).

Usually, food allergy develops as follows. An allergen or an immunologically active fragment of that particular allergen crosses from the lumen of the gut through the mucosal membrane barrier; this molecule or its fragment can stimulate different types of lymphocytes that ultimately result in the production of allergen-specific IgE antibodies. These IgE antibodies also have the unique ability to bind to surface receptors on mast cells and basophils; upon a second or subsequent exposure, allergen may bridge cell-bound IgE antibodies. The cross-linking of cell-bound IgE antibodies will lead to the release of both preformed mediators, such as histamine and newly synthesized mediators such as protaglandins, that cause smooth muscle contraction, vasodilation, bronchial constriction, and cell infiltration, which in effect cause symptoms of allergic reactions (Sampson and Metcalfe 1991).

Food Allergens

Generally, food allergens seem to share several common properties; they are proteins or glycoproteins with an acidic isoelectric point (pI), and usually are in the molecular weight range of 10,000 to 80,000 daltons. Most food allergens are fairly resistant to industrial processing, heating, and cooking, as well as showing some resistance to the digestive enzymes of the gut (Lehrer, Horner, and Reese 1996). These properties may aid in the allergenicity of those molecules. These properties are not, however, necessarily unique for food allergens since they can also occur in nonallergenic molecules (Lehrer, Horner, and Reese 1996; Lehrer and others 1997). Substantial in vitro cross-reactivity (sharing similar immunochemical structures) can occur among foods and between foods and other substances (Reese and Lehrer 1998). This can occur within closely related food groups such as crustacea and legumes; however, such in vitro cross-reactivity is not always reflected by clinical cross-sensitivity (Metcalfe, Sampson, and Simon 1996). In addition, foods and seemingly unrelated substances have been shown to cross-react. For example, grass and tree pollens as well as latex allergens cross-react with a variety of fruits and vegetables, oysters have been shown to have common allergens with crustacea and insects and shrimp share allergens with dust mite and cockroaches. The precise nature of cross-reactivity of such unrelated substances is not entirely known but may be due to the presence of common structural or functional proteins (Lehrer and others 1997; Reese and Lehrer 1998). Food allergens that have been characterized are summarized in Table 1. Because many food proteins have been studied for reasons other than their allergenicity (that is, because they are important storage, structural, and functional proteins), it is often possible to identify a food allergen by searching protein databases using only a small part of its entire amino acid sequence (Reese and Lehrer 1998).

Genetically Modified Crops: Allergenicity Risk Assessment

Modern biotechnology provides methods for the identification and selection of genes encoding for specific proteins. A gene from any source (for example, microorganism, plant, or animal) that confers a specific trait can be selectively and precisely introduced or transferred into the genome of another organism where the expression of the transferred gene will confer that desired trait on the host organism. This type of genetic engineering has been used to introduce genes into various microorganisms and plants that are sources of foods and food components. Introduced traits include insect and virus resistance, herbicide tolerance, and changes in composition or nutritional content. Typically the amount of protein expressed by the introduced gene is small and, in some cases, inactivation of a native gene that results in the absence of a specific protein yields the desired trait (for example, the tomato genetically engineered to delay ripening). This technology has also been used to reduce the expression of a major allergen found in rice (Matsuda and others 1993).

Genetically modified crops, now grown on some 40 million hectares around the world, are changing modern agricultural methods. Supporters of this approach believe that genetic engineering is crucial in developing healthy, productive crops that are essential to feed the world's growing populations. Thus, although these methods are being used primarily in the industrial countries, this approach is also important in developing countries. In contrast, critics of GM foods raised concerns because of the unusual methods used to breed these crops; some fear that the genetic variants produced could introduce foreign substances into the food supply with unanticipated negative effects on human health and the environment (Schmidt 2000). A major concern is that a protein encoded by an introduced gene may be allergenic and cause allergic reactions in exposed populations.

Until recently, genetically improved crops that were introduced in a number of industrial countries were favorably received by both domestic and international regulatory bodies; a number of new crop varieties have been successfully marketed to farmers in the United States, China, Argentina, Canada, Australia, and Mexico, amongst others. However, public attitudes toward GM crops have recently diminished, particularly in Europe (Schmidt 2000).

When addressing the potential health risks of GM crops in developing countries, two questions must be considered. First, what are the risks and how can these risks be assessed and minimized? Second, how do these risks relate to benefits for

Table 1 Identified and characterized major food allergens (Lehrer and others 1997, modified). [1]References for partial (P) or complete (C) sequence data

Allergen Source	*Allergens (Systematic and original names)*	*MW (kDa)*	*Sequence Data*	*References*[1]
Gadus callaria (cod)	Gad c 1; allergen M	12	C	Elsayed and Bennich 1975
Gallus domesticus (chicken)	Gal d 1; ovomucoid	28	C	Hoffman 1983
	Gal d 2; ovalbumin	44	C	Langeland 1983b
	Gal d 3; conalbumin (Ag22)	78	C	Williams et al. 1982
	Gal d 4; lysozyme	14	C	Blake et al. 1965
Penaeus aztecus (brown shrimp)	Pen a 1; tropomyosin	36	P	Daul et al. 1993, 1994
Penaeus indicus (indian shrimp)	Pen i 1; tropomyosin	34	P	Shanti et al. 1993
Metapenaeus enis (greasyback shrimp)	Met e 1; tropomyosin	34	C	Leung et al. 1994
Brassica juncea (oriental mustard)	Bra j 1; 25S albumin	14	C	Monslave et al. 1993
Hordeum vulgare (barley)	Hor v 1; BMAI-1	15	C	Mena et al. 1993
Sinapis alba (yellow mustard)	Sin a 1; 25S albumin	14	C	Menendez-Arias et al. 1988
Arachis hypogaea (peanut)	Ara h 1	63.5	C	Burks et al. 1995a,1995b, 1995c
	Ara h 2	17.5	C	Stanley et al. 1997
Malus domestica (apple)	Mal d 1	17.7	C	Vanek-Krebitz et al. 1995
Apium graveolens (celery)	Api g 1	16.2	C	Breiteneder et al. 1995

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the exposed populations? In most industrial countries, where a number of genetically improved crops have been marketed, the public concerns of allergy may be somewhat greater than those of developing countries with emerging economies, where allergy is a less pressing issue among their public health and nutrition concerns. Thus allergy, a disease more frequent among the middle and upper classes of industrial countries, may be considered less of a risk in developing countries as compared to industrial countries.

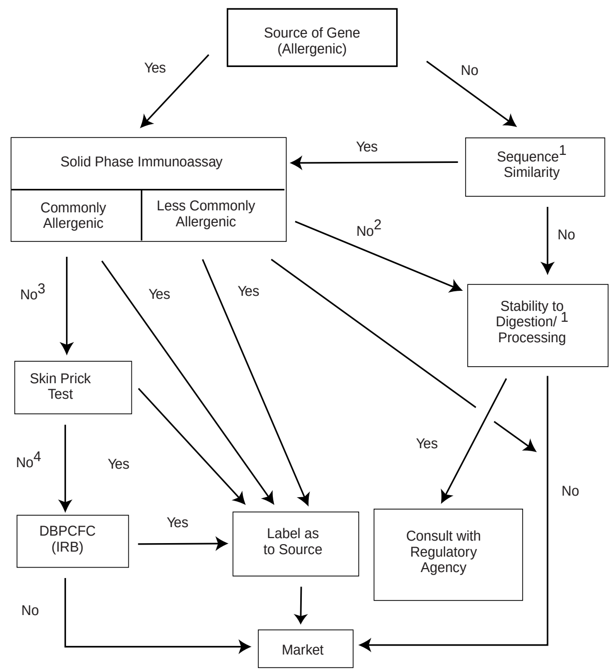
Theoretically, there are two ways in which genetic modification may alter the allergenicity of a food. First, the level of endogenous proteins within a particular crop may be altered by genetic manipulation, potentially raising the level of endogenous allergens. Second, the expression of a new gene in this crop could introduce new allergens normally not present in this particular crop. Thus, there can be an effect on known allergens or unknown allergens. If the endogenous proteins or the newly introduced protein are from known sources of allergens, then assessing the allergens within the GI food is relatively straightforward. However, a more difficult issue is if the allergenicity of the source of the protein is unknown; this generally relates only to new proteins being introduced into GM foods from sources that have ordinarily not been used as human food. The dilemma is that there is no available body of knowledge about the allergenicity of these proteins, and thus one would have to rely on other criteria with which to assess their potential activity.

The ILSI Allergy and Immunology Institute and the International Food Biotechnology Council convened an expert panel of scientists to develop scientific approaches to assess the allergic potential of foods derived from GM crop plants. This initiative resulted in the development of a published project report (Metcalfe and others 1996). This report addressed the cell biology, symptoms, and treatment of food allergy; developed a catalog of allergenic foods; and characterized major food allergens from the perspective of the plants and methods used to genetically modify food crops. This information served as the background for the development of a decision tree for assessing the allergic potential of foods derived from genetically engineered plants (Figure 1).

Eight commonly allergenic foods and more than 160 less commonly allergenic foods were identified. Based on this information, the report concluded that food biotechnologists should avoid the transfer of known food allergens. Genes transferred from sources known to be allergenic should be assumed to encode for an allergen, until proven otherwise. In addition, the allergenic potential of all introduced proteins should be assessed. For genetically improved foods entering the marketplace, consumers should be informed by appropriate labeling that the food contains known or suspected allergens (Metcalfe and others 1996).

The safety assessment decision tree (Figure 1) begins with the characterization of the source of the introduced gene. Is it from a commonly allergenic or less commonly allergenic source or does the source have no history of allergenicity? If there is no history of allergenicity associated with the gene source, its protein product should be subjected to amino acid sequence analysis. The sequence should be compared with those of the more than 180 known allergens that have been deposited into various electronic databases (for example, GenBank, EMBL, SwissProt, PIR). Available software can evaluate for amino acid sequence homologies, structural similarities, and epitope mapping based on eight contiguous amino acids (that is, the suggested minimum size of allergenic epitopes). If this evaluation fails to provide evidence suggesting allergenic potential, the protein should then be subject to physical/chemical testing to establish its stability to digestion and processing. Proteins that are labile to digestion are unlikely to be allergenic. A food containing a protein for which there is no concern based on amino acid sequence or on chemi-

Figure 1 Decision tree for assessment of the allergenic potential of foods derived from genetically engineered food crops.



Notes:

1. It is recommended that an assessment for amino acid sequence similarity to all known allergens and an assessment of stability to digestion be performed for all gene products.
2. Solid phase immunoassay tests depend on availability of sera. Ideally, 14 sera should be used. However, if less than 5 sera are used, then proceed to stability box if results are negative and consult with the appropriate regulatory agency.
3. In the case of equivocal results or suspected false positives, proceed to skin prick tests.
4. DBPCFCs are performed on food products in which there is no evidence of allergenicity based upon solid phase immunoassays and skin prick tests. To assure lack of allergenicity, DBPCFCs should be performed following IRB approval.

Source: This figure was reproduced from an article by Metcalfe and colleagues in *Critical Reviews in Food Science and Nutrition* 1996;36(Suppl):S167. Reprinted by permission of CRC Press, Inc., Pearl River, NY.

cal analysis would not be considered to have allergenic potential (Metcalfe and others 1996).

If the protein originates from a known allergenic source or its amino acid sequence analysis raises concern about the allergenic potential of the molecule, the protein is then evaluated to determine whether it is recognized by serum from individuals with known food allergies (Lehrer, Horner, and Reese 1996; Metcalfe and others 1996; Lehrer and Reese 1997a). Standard statistical methods can be used to estimate the number of sera samples that need to be tested to have a high probability (95.5-99.9 percent) of detecting both major and minor allergens. Equivocal results would necessitate conducting stability testing of the protein, whereas negative results would indicate that the allergenic potential of the protein is negligible. If the protein product of an introduced gene exhibits similarities to known allergens and/or yields positive results in serological analysis, the appropriate regulatory authority should be consulted to determine if and what further testing might be performed (Metcalfe and others 1996).

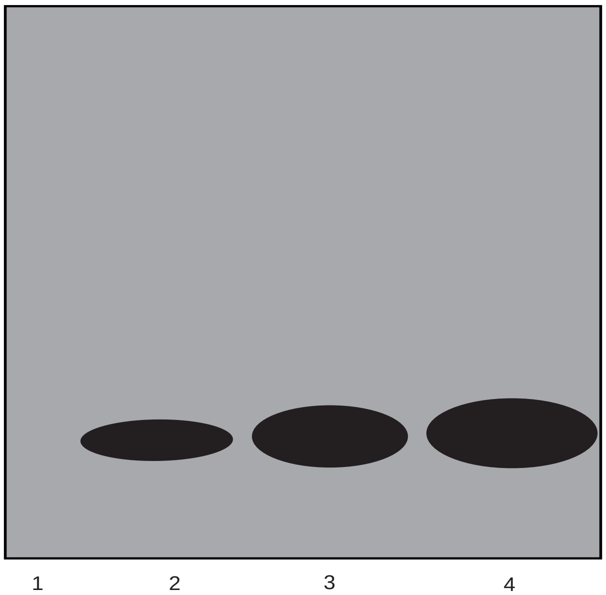
Genetically modified foods containing those proteins that test positive in the serologic analysis should be labeled as to the source of the protein. In addition, for proteins considered to be commonly allergenic based on the serological analysis, confirmatory skin prick testing is recommended. If these tests are positive, double-blind placebo-controlled food challenge testing should be conducted in accord with Institutional Review Board-approved protocols for the use of human subjects. Foods containing proteins confirmed as allergenic in the skin prick and/or food challenge studies could be brought to market with appropriate labeling, although foods confirmed to be allergenic by challenge testing would likely have only a very limited place in the market (Metcalfe and others 1996).

The major challenge for the food industry is testing the source of the gene from which there is no history of allergenic activity, since there is theoretically no known sera available from allergic subjects to test the product (Lehrer, Horner, and Reese 1996; Metcalfe and others 1996; Lehrer and Reese 1997a; 1998). The recommended approach is to compare the amino acid sequence of the protein with that of known allergens as described previously. Any sequence similarity with a particular allergen suggests the sera can be used to screen the product by immunochemical procedures described earlier. If there is no amino acid sequence homology, the stability of the protein to enzymatic digestion and processing can be assessed. If the molecule is easily digested or unstable then there should not be a problem with marketing the product. If, however, the molecule is stable to digestion and processing, then one would need to consult with regulatory authorities (Lehrer, Horner, and Reese 1996; Metcalfe and others 1996; Lehrer and Reese 1997a; 1998).

An actual case study that considers the introduction of a gene for a known allergen in a GM crop is the expression of a Brazil nut protein in soybean (Nordlee and others 1996). Because soybeans are deficient in essential sulfur-containing amino acids such as methionine and Brazil nuts are rich in this substance, food biotechnologists introduced a gene encoding a Brazil nut methionine-rich seed storage protein into soybean. Brazil nuts are known to be allergenic, however, raising concern whether the product of the transferred gene would increase the allergenic potential of the soybean. Because the protein is from a known allergenic source, serological evaluation of the protein was performed. In this case, pooled serum from nine Brazil nut-sensitive individuals recognized the protein, and eight of the nine sera bound to the protein in an immunoblotting assay (Figure 2). Skin prick tests with three of these individuals confirmed the presence of the allergen (Nordlee and others 1996). Based on these findings, development of this product was discontinued.

Another case study, in which allergenicity was not altered, is the high oleic acid soybeans developed by genetic modification. Soybeans were genetically engineered to enhance their oleic acid content, a property considered to produce healthier soybean oil. This genetic modification elevated the levels of several proteins. When the allergen content of the transgenic soybean was compared to the wild-type parental strain, there appeared to be no significant differences in activity based on RAST inhibition assays (Figure 3) as well as immunoblotting methods (Lehrer and Reese 1997b). Thus, qualitatively and quantitatively, the transgenic strain appeared to be allergenically the same as the parental wild-type (Lehrer and Reese 1997b). This indicates that IgE

Figure 2 Reactivity of Brazil nut allergenic serum to a 2 S albumin Brazil nut allergen



Notes: Lane 1: nontransgenic soybean; lane 2: transgenic soybean; lane 3: Brazil nut extract; lane 4: 9 kD 2S albumin Brazil nut allergen.
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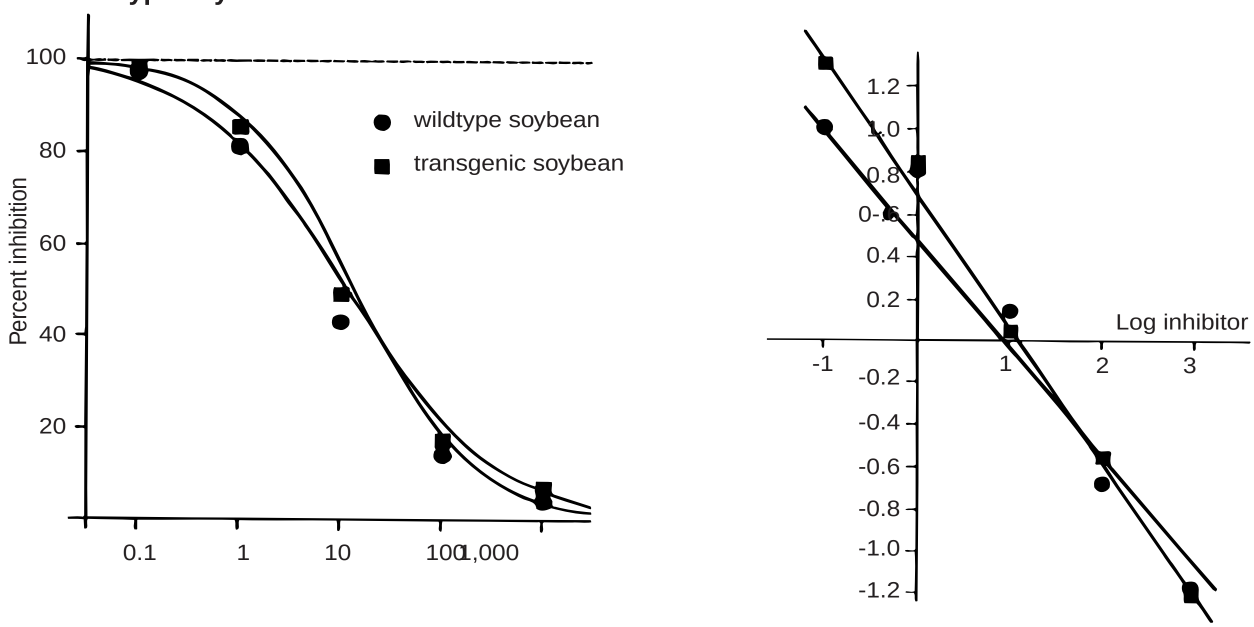
antibody-based assays used to test products developed from sources of known allergens can document no substantial change in the allergenic content. Thus, the probability that an introduced protein will be allergenic is low, and definitive methods are available to detect known allergens.

Conclusion

The assessment of the allergenicity of proteins from unknown allergen sources continues to be a challenge to the food industry. All evidence suggests there is no cause for concern about allergenic potential for proteins introduced into foods from sources with no history of allergenicity, that have no amino acid sequence similarities to known food allergens, that are rapidly digested, and that are expressed at low levels relative to the expression of major allergens. The recommended approach by amino acid sequence comparison and enzymatic digestion resistance is based on current technology available. Future efforts must be directed at refining this technology. This can be achieved through (a) continued allergen identification and amino acid sequence characterization to increase the number of aller-

Figure 3 Inhibition curves and logit-log transformation of the wild-type soy RAST with transgenic and wild-type soy extracts



Note: Statistical analysis showed that both the slopes and the *y*-axis intercepts are statistically identical indicating that the allergen contents and compositions of both soy extracts are identical.
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genic sequences in the data bank; (b) identification of the amino acid sequence properties that define allergenic epitopes to develop more precise sequence screening criteria; and (c) development of an animal model that can recognize food allergens in a manner similar to that which occurs in human disease. In spite of the fact that the technology thus far used to assess the allergenicity of GM foods can be improved, it still serves us very well in identifying potentially allergenic products that may be developed. Thus, it is possible to identify potential risks for allergenicity and minimize their effect on exposed populations.

Last but not least, the risk-to-benefit ratio of these new technologies must be considered. A number of serological assays are being used to reduce the risk as stated above. The benefits derived from GM crops must be considered against these risks, which may vary from country to country. Allergy is a high priority among the middle and upper classes of industrial countries where any added risk in an already well-fed population may be a concern. However, in countries with emerging economies, where allergy is a lower priority than nutrition, the increased productivity benefits of GM crops may far outweigh any potential risk of allergic reactions.

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Modern Biotechnology for Food and Agriculture: Risks and Opportunities for the Poor

Per Pinstrup-Andersen and Marc J. Cohen

The current debate about the potential utility of modern biotechnology for food and agriculture, and the associated potential risks and opportunities, is focused on the initial applications of such biotechnology in industrial country agriculture. The debate is also intertwined with other concerns such as food safety, animal welfare, industrialized agriculture, and the role of private-sector corporations. At present, there is very little commercial utilization of results from modern biotechnology research in developing countries. As a result, the potential contributions of biotechnology to poverty alleviation and enhanced food security and nutrition in developing countries has received little attention, beyond blanket statements of support or opposition.

A debate based on the best available empirical evidence relevant for poor people in developing countries is urgently needed, to identify the most appropriate ways that molecular biology-based research might contribute to the solution of poor people's problems. These problems and the socioeconomic context in which they occur are so different from the problems and context of the countries where most of the biotechnology debate currently takes place that the positions and conclusions from the current debate are largely irrelevant for poor farmers and poor consumers in developing countries. Despite this, many of the arguments in the current debate are extrapolated to conclusions about the potential utility for poor countries and poor people. We will attempt to provide input into a more focused debate on the role of modern agricultural biotechnology in developing countries, a debate that should and will be led by people from developing countries themselves.

The Problem

Small-scale farmers in developing countries are faced with many problems and constraints. Pre- and postharvest crop losses due to insects, diseases, weeds, and droughts result in low and fluctuating yields, as well as risks and fluctuations in incomes and food availability. Low soil fertility and lack of access to reasonably priced plant nutrients, along with acid, salinated, and waterlogged soils and other abiotic factors, contribute to low yields, production risks, and degradation of natural resources as poor farmers try to eke out a living. They are often forced to clear forest or farm ever more marginal land to cultivate crops. Poor infrastructure and poorly functioning markets for inputs and outputs together with lack of access to credit and technical assistance add to the impediments facing these farmers.

These farmers and other rural and urban poor people suffer from food insecurity and poor nutrition, caused in large measure by poverty and lack of nutritional balance in the diet they can afford. About 1.2 billion people, or one of every five humans, live in a state of absolute poverty, on the equivalent of US$1/day or less (World Bank 1999). About 800 million people are food insecure (FAO 1999a), and 160 million preschool children suffer from energy-protein malnutrition, which results in the death of over 5 million children under the age of five each year (ACC/SCN and IFPRI 1999). A much larger number of people suffer from deficiencies of micronutrients such as iron and vitamin A. For example, 2 billion people (one of every three) are anemic, usually as a result of iron deficiency. Food insecurity and malnutrition result in serious public health problems and lost human potential in developing countries.

Around 70 percent of poor and food-insecure people reside in rural areas, although poverty and food insecurity appear to be growing in urban areas as urbanization proceeds apace in developing countries. The World Bank forecasts that poverty's center of gravity will remain rural in the early decades of the 21st century (McCalla and Ayers 1997).

Most rural poor people depend directly or indirectly on agriculture for their livelihood. Poor people in rural or urban areas spend as much as 50–70 percent of their incomes on food (Deaton 1997). Low productivity in agriculture is a major cause of poverty, food insecurity, and poor nutrition in low-income developing countries. This is true for urban and rural poor people alike. Low productivity means low incomes for farmers and farm workers, little demand for goods and services produced by poor nonagricultural households in the rural areas, and unemployment and underemployment in urban areas. It also means high unit costs for food, which translate into reduced consumer purchasing power. High food prices are a serious matter for households that spend a large share of their budget on food. In low-income developing countries, agriculture is the driving force for broad-based economic growth and poverty alleviation. A healthy agricultural economy offers farmers incentives for sound management of the natural resource base upon which their livelihood depends.

These relationships are borne out not only by research but also by history in both developing and industrial nations. Productivity increases in European and U.S. agriculture were extremely important to broad-based economic growth during earlier periods of development. More recently, productivity increases in agriculture, led by agricultural research — the Green Revolution — formed the locomotive of rapid broad-based economic growth and poverty reduction in many Asian countries, including China, Indonesia, South Korea, and India. Recent IFPRI research in four African countries found similar strong linkages between agricultural productivity growth and general economic growth (Delgado and others 1998).

Productivity gains are essential not only for economic growth and poverty alleviation, but to assure that food supplies remain adequate for a growing world population. According to United Nations projections, world population will increase by 25 percent to 7.5 billion in 2020. On average, 73 million people will be added annually. Over 97 percent of the projected growth will take place in developing countries (United Nations Population Division 1998).

Public Investment Critical to Food Security

Agriculture must figure prominently in poverty alleviation strategies of developing countries. Accelerated public investments are needed to facilitate agricultural and rural growth through:

- Yield-increasing crop varieties, including those that are drought and salt tolerant and pest resistant, and improved livestock
- Yield-increasing and environmentally friendly production technology
- Reliable, timely, and reasonably priced access to appropriate inputs such as tools, fertilizer, and, when needed, pesticides, as well as the credit often needed to purchase them
- Strong extension services and technical assistance to communicate timely information and developments in technology and sustainable resource management to farmers and to relay farmer concerns to researchers
- Improved rural infrastructure and effective markets
- Particular attention to the needs of women farmers, who grow much of the locally produced food in many developing countries
- Primary education and health care, clean water, safe sanitation, and good nutrition for all.

These investments need to be supported by good governance and an enabling policy environment, including trade, macroeconomic, and sectoral policies that do not discriminate against agriculture, and policies that provide appropriate incentives for the sustainable management of natural resources, such as secure property rights for small farmers. Development efforts must engage poor farmers and other low-income people as active participants, not passive recipients; unless the affected people have a sense of ownership, development schemes have little likelihood of success.

Developing countries must reverse present declining levels of public investment in agriculture. On average, they devote 7.5 percent of government spending to agriculture (and just 7 percent in Sub-Saharan Africa) (FAO 1996). For their part, donor countries must redress the precipitous decline in aid to agriculture and rural development, which plunged by nearly 50 percent in real terms between 1986 and 1996 (FAO 1998). Overall development aid has also fallen in recent years (Michel 1999). Ironically, our research has found that aid to developing country agriculture not only is effective in promoting sustainable development and poverty alleviation, but it leads to increased export opportunities for industrial countries as well, including, paradoxically, increased agricultural exports (Pinstrup-Andersen, Lundberg, and Garrett 1995; Pinstrup-Andersen and Cohen 1998). Donors must also rethink their rather inflexible emphasis of the past two decades on less government and a smaller public sector, which has contributed to public disinvestment in agriculture in the developing countries (FAO 1996).

Agricultural Research is Essential

Public investment in agricultural research is of particular importance for achieving food security in developing countries. The private sector is unlikely to undertake much of the research needed by small farmers because it cannot expect sufficient returns to cover costs. IFPRI research has shown that the annual rates of return to agricultural research and development are, on average, 73 percent (Alston and others 1998). Benefits to society from agricultural research can be extremely large but will not be obtained without public investments. We have also found that even minor increases in aid to agricultural research for developing countries can significantly accelerate food supplies, while relatively small cuts could have serious negative effects (Rosegrant, Agcaoili-Sombilla, and Perez 1995).

Despite this evidence, low-income developing countries grossly underinvest in agricultural research: less than 0.5 percent of the value of their agricultural production, compared to 2 percent in higher-income countries. Sub-Saharan Africa, which desperately needs productivity increases in agriculture, has only 42 agricultural researchers per million economically active persons in agriculture, compared with 2,458 in industrial countries (Pardey and Alston 1996).

Efforts to improve longer-term productivity on small-scale farms, with an emphasis on staple food crops, must be accelerated. Research and policies are also needed to help farmers, communities, and governments better cope with risks resulting from such factors as poor market integration, poorly functioning markets, and climatic fluctuations. More research must be directed to the development of appropriate technology for sustainable intensification of agriculture in resource-poor areas, where a high percentage of poor people live, and where environmental risks are severe. The needed research must join all appropriate scientific tools together, with better use of the insights of traditional indigenous knowledge.

Research and technology alone will not drive agricultural growth. The full and beneficial effects of agricultural research and technological change will materialize only if government policies are conducive to and supportive of poverty alleviation and sustainable management of natural resources.

Agricultural Biotechnology and Food Security

Can molecular biology-based research contribute to the solution of the problems outlined earlier? Are the potential social and economic benefits likely to exceed potential risks or costs? If these questions are answered in the affirmative, issues related to the design of the technology and the needed policies and institutions must be tackled.

Although conventional applications of biotechnology, such as tissue culture and fermentation amongst others, is under way in several developing countries, little genetically improved (transgenic) seed material has been grown in the poorer developing countries to date so ex post assessment is virtually impossible. A great deal is known, however, about the social and economic risks and benefits associated with traditional Mendelian plant breeding as exemplified by the Green Revolution. The analysis, therefore, begins with the identification of similarities and differences between the Green Revolution and modern biotechnology, and an attempt is made to draw lessons from the Green Revolution and to look at the difference between that technology package and modern biotechnology to try to assess the likely social and economic risks and benefits of modern agricultural biotechnology ex ante.

Comparing the Green Revolution and Modern Biotechnology

Shift to private sector research. There are three differences of particular importance for an assessment of social and economic risks and benefits. The research leading to the Green Revolution was undertaken by the public sector and the improved seed was usually freely available for seed multiplication and distribution. Although breeders' rights may permit an initial charge for the improved materials, the intellectual property rights (IPR) did not extend beyond the initial release. Having acquired the seed, farmers could reuse it without further payment, although reuse of hybrid seed would drastically reduce the yield advantage. This is in keeping with the principle of "farmers' rights" included in the 1983 International Undertaking on Plant Genetic Resources (Wright 1996; FAO 1999b).

In contrast, the bulk of modern agricultural biotechnology research is undertaken by private sector firms, which protect IPRs through patents that extend beyond the first release. Farmers, therefore, cannot legally plant or sell for planting the crop produced with the patented seed without the permission of the patent holder. Patent holders, currently seeking ways to enforce their rights, are considering approaches such as legal agreements and technologies that will activate and deactivate specific genes. However, monitoring and enforcing contracts that prohibit large numbers of small farmers from using the crops they produce as seed would be expensive and difficult.

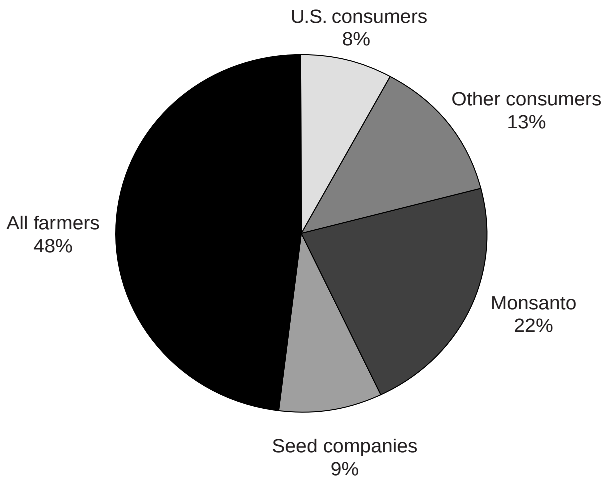
The so-called terminator gene is the first patented technology aimed at biological IPR protection. It is not appropriate for small farmers in developing countries because existing infrastructure and production processes may not be able to keep fertile and infertile seeds apart. Small farmers could face severe consequences if they planted infertile seeds by mistake. Commercialization of the terminator gene now seems unlikely in the short term.

Research is under way on other biological approaches to IPR protection that would not impose such risk on small farmers. These include, for example, genetically engineered seeds that contain desired traits, such as pest resistance or drought tolerance, but in which these are activated only through chemical treatment. Otherwise, the seed would maintain its normal characteristics. Thus, if a farmer planted an improved seed, the offspring would not be sterile; rather they would revert to normal seeds, without the improved traits. The farmer would have the choice of planting the seed and doing no more, or activating the improved traits by applying the chemical. This approach complies with the principle of doing no harm.

It is important to note that even when patents permit a private company to enjoy monopoly or near-monopoly rights over a product it has developed, the firm is unlikely to capture 100 percent of the economic benefits. A recent study of the distribution of the economic benefits generated by the use of herbicide-tolerant soybean seed in the United States in 1997 found that the company, Monsanto, received 22 percent, while seed companies gained 9 percent. Consumers of soybean and soybean products in the United States and other countries reaped a 21 percent share, whereas farmers worldwide obtained 48 percent (Figure 1). The share of U.S. farmers was actually 51 percent of the benefits, but farmers elsewhere experienced net losses of 3 percent (Falck-Zepeda, Traxler, and Nelson 1999).

Rise of proprietary research processes and technologies. A second, and related, difference between the Green and Gene revolutions involves the patenting of processes as well as products. The main

Figure 1 Distribution of 1997 economic surplus from U.S. use of Roundup Ready™ soybean seed (total US$360 million)



(*Source:* Falck-Zepeda and others 1999).

process behind the Green Revolution was conventional plant breeding technology, which lies in the public domain, carried out by public institutions. Today, the processes used in modern agricultural biotechnology are increasingly subjected to IPR protection, along with the products that result.

This means that public sector research institutions may not be able to gain access to basic but proprietary knowledge and processes needed in research, including research on the so-called orphan crops such as cassava and millet. These are critical staples in the diets of many poor people, but they do not offer promising economic returns to private sector R&D efforts, so efforts to develop disease-resistant cassava or drought-tolerant millet, whether through genetic modification or conventional breeding, must come from the public sector. Some firms have agreed to transfer proprietary technologies, without charging royalties, to developing countries where there are few potential commercial prospects. Monsanto, for example, has entered into agreements with Kenyan and Mexican government agricultural research institutes to develop virus-resistant crops (see Lewis, this volume). Arrangements such as these are few and generally involve the philanthropic arms of the private firms (Serageldin 1999).

Enlightened adaptation vs. direct transfer. A third difference involves the adaptation of industrial country agricultural research to developing country conditions. Although based on earlier research in industrial countries, the Green Revolution was focused on solving specific problems in developing countries. Current application of modern biotechnology is focused on industrial country agriculture.

Industrial country research institutions had begun working on development of higher yielding crop varieties in the late 19th century. For example, in Japan, rice breeding under the auspices of the Ministry of Agriculture and public universities led to large yield gains in the early part of the 20th century, with a second wave of major gains after 1945.

During the early decades of Soviet history, under the leadership of geneticist Nikolai Ivanovich Vavilov, the government carried out extensive crop improvement programs and established one of the world's largest germplasm collections. In the United States, hybrid maize research began in the 1920s. Much of the basic research was done by public institutions, such as land grant universities, state experiment stations, and the U.S. Department of Agriculture (USDA). Applications to particular farming conditions and the mass marketing of the new varieties were, in turn, handled by private seed firms such as Pioneer Hi-Bred and DeKalb. The research focused not only on developing higher yielding seeds to bolster food supplies for domestic consumption (which was a critical U.S. concern up to the 1940s), but also on animal feed and production for export.

This research could not simply be transferred to poorer developing countries, where the need was for improved varieties of locally-consumed staples. The research that led to the Green Revolution involved further adaptation to the agroecological conditions of tropical and semitropical areas. It also focused on rice, wheat, maize, root and tuber crops, and tropical fruits and vegetables. The public sector role was, if anything, even more prominent, with international agricultural research centers (IARCs) and national agricultural research systems (NARS),particularly in Asia and Latin America, playing a prominent role. Financial support came from donors of official development assistance and large private foundations, such as Ford, Rockefeller, and Kellogg.

In contrast, modern agricultural biotechnology is still in an early phase, and the focus is overwhelmingly on production on industrial country farms and for industrial country markets. In 1998, 85 percent of the land planted to genetically improved (GI) crops was in just five developed countries (Australia, Canada, France, Spain, and the United States), with the United States alone accounting for about 75 percent of the area. Argentina, China, Mexico, and South Africa cultivated the remaining 15 percent, and the countries other than China include a substantial number of large-scale, capital-intensive farms that produce primarily for industrial country markets. Among the crops produced in these four developing countries are insect-resistant cotton and maize, herbicide-resistant soybean, and tomatoes with a long shelf life. Globally, herbicide-resistant soybean, insect-resistant maize, and genetically improved cotton (containing insect resistance and/or herbicide tolerance genes) account for 85 percent of all plantings. Both the area planted to genetically improved crops and the value of the harvests grew dramatically between 1995 and 1999: from less than 1 million hectares to 28 million in 1998 and approximately 40 million in 1999, and from US$75 million in 1995 to US$1.64 billion in 1998 (James 1999; James and Krattiger 1999; Juma and Gupta 1999).

Private industry has dominated research (there are a few exceptions: for example, Rockefeller Foundation support for research on rice, USDA's role in developing the terminator technology, and modest programs at IARCs). Consolidation of the industry has proceeded rapidly since 1996, with more than 25 major acquisitions and alliances worth US$15 billion.

Little private-sector agricultural biotechnology research so far has focused on developing country food crops other than maize. Moreover, little adaptation of the research to developing country crops and conditions has occurred through the "enlightened" (that is, not for profit, public goods oriented) public and philanthropic channels prominent in the Green Revolution of the developing countries. Some of the exciting international and regional programs are described by Cohen (1999). A program directed at public/private sector linkages is that of the International Service for the Acquisition of Agri-biotech Applications (ISAAA), which transfers and delivers appropriate biotechnology applications to developing countries and builds partnerships amongst institutions.

Relatively little biotechnology research currently focuses on the productivity and nutrition of poor people. The Rockefeller Foundation's agriculture program is one example; in 1998, it provided about US$7.4 million for biotechnology research relevant to developing countries, mainly through IARCs and NARS in developing countries, with a major emphasis on rice. This sum pales by comparison with Monsanto's 1998 R&D budget of US$1.3 billion, much of which funded agricultural biotechnology research (Rockefeller 1999; Monsanto 1999).

As with the Green Revolution, the challenge is to move from the scientific foundation established by industrial country-oriented research efforts to research focused on the needs of poor farmers and consumers in developing countries. Direct transfers of the fruits of agricultural biotechnology research to the developing countries will not work, in most cases. More appropriate research for the developing world might focus on biotechnology and conventional breeding to develop alternative forms of weed resistance, such as leafier rice that denies weeds sunlight rather than incorporating herbicide tolerance into rice. The West Africa Rice Development Association (WARDA), a public IARC in Côte d'Ivoire, has used a combination of conventional plant breeding and tissue culture to develop such rice (WARDA 1999).

Insect-resistant crops would have great potential value for poor farmers. So far, however, the development of crops containing genes from the *Bacillus thuringiensis* (Bt) bacterium, which produces a natural pesticide, has focused largely on the crops and cropping environments of North America. The new crop varieties containing the Bt gene require extremely knowledge-intensive cultivation. They might well be transferable to larger scale operations in some developing countries such as Argentina. The potential usefulness of this application in crops grown by small farmers is open to question. There is considerable debate about risks of the development of resistance in pests, harm to beneficial insects, and cross-pollination of wild and weedy plants with the novel gene. The evidence on these issues is still inconclusive and warrants careful monitoring before the application of Bt is tried on a large scale in crops grown by subsistence farmers.

Research on crops and problems of relevance to small farmers in developing countries will require the allocation of additional public resources to agricultural research, including biotechnology research, that promises large social benefits. There is no reason to believe that this research will offer lower rates of return than other agricultural research and development.

Private-sector agricultural research currently accounts for a small share of agricultural research in most developing countries. The public sector can expand private-sector research for poor people by converting some of the social benefits to private gains, for example, by offering to buy exclusive rights to newly developed technology and make it available either for free or for a nominal charge to small farmers. The private research agency would bear the risks, as it does when developing technology for the market. IARCs have an important role to play as intermediaries in facilitating such arrangements.

Without more enlightened adaptation, continued expansion of genetically improved crop production in the industrial countries may well have a negative impact on small farmers in developing countries. Some developing country consumers would benefit, but those consumers who also farm could experience net losses. In addition, the development of industrial substitutes for developing country export crops, such as cocoa (which in many developing countries is produced by small farmers) could have a devastating impact on developing country farmers' livelihoods.

In sum, the biggest risk of modern biotechnology for developing countries is that technological development will bypass poor farmers and poor consumers because of a lack of enlightened adaptation. It is not that biotechnology is irrelevant, but that research needs to focus on the problems of small farmers and poor consumers in developing countries. Private sector research is unlikely to take on such a focus, given the lack of future profits. Without a stronger public sector role, a form of "scientific *apartheid*" may well develop, in which cutting edge science becomes oriented exclusively toward industrial countries and large-scale farming (Serageldin 1999).

Lessons from the Green Revolution. The outcomes of the Green Revolution offer some guideposts for assessing the likely risks and benefits of agricultural biotechnology for developing countries. Risks and benefits may be inherent in a given technology, or they may transcend the technology (Leisinger 1999). The policy environment into which a technology is introduced is critical. For example, IFPRI research has found that in Tamil Nadu State in India, the adoption of high-yielding grain varieties meant not only increased yields and cheaper, more abundant food for consumers, but income gains for small and larger-scale farmers alike, as well as for nonfarm poor rural households. Increased rural incomes contributed to nutrition gains for these households (Hazell and Ramasamy 1991). Because the Tamil Nadu state government has pursued active poverty alleviation strategies, including extensive social safety net programs and investment in agriculture, rural development, and a fair measure of equity in access to resources such as land and credit, the benefits were widely shared. Where increased inequality followed the adoption of Green Revolution technology, it was not because of factors inherent to the technology, but rather a result of policies that did not promote equitable access to resources. And even in these areas, rural landless laborers usually found new job opportunities as a consequence of increased agricultural productivity, particularly where appropriate physical infrastructure and markets developed.

Successful adoption of Green Revolution technology, however, depended on access to water, fertilizer, and pesticides. Thus, inequality between well-endowed and resource-poor areas increased because of the properties of the technology itself. Likewise, excessive or improper use of chemical inputs led to adverse environmental impacts in some instances. This problem was offset, to some extent, by characteristics that were also inherent in the technology: by allowing yield gains without expanding cultivated area, the technology kept cultivators from clearing forests and moving onto wild and marginal lands.

Overall, the Green Revolution was extremely successful in enhancing productivity in rice, wheat and maize; in increasing incomes and reducing poverty; and in preserving forests and marginal lands by improving yields within existing cultivated areas. By reducing unit costs and prices for food, it greatly benefited poor consumers, and by boosting farmers' incomes, it contributed to gains in nutrition. Would agricultural biotechnology produce similar results in developing countries? The answer depends on whether the research is relevant to poor people and on its ownership, that is, the nature of the intellectual property rights arrangements.

Weighing Risks and Benefits of Biotechnology

Modern biotechnology is not a silver bullet for achieving food security, but, used in conjunction with traditional or conventional agricultural research methods, it may be a powerful tool in the fight against poverty that should be made available to poor farmers and consumers. It has the potential to help enhance agricultural productivity in developing countries in a way that further reduces poverty, improves food security and nutrition, and promotes sustainable use of natural resources. Solutions to the problems facing small farmers in developing countries will benefit both farmers and consumers.

The benefits of new genetically improved food to consumers are likely to vary according to how they earn their income and how much of their income they spend on food. Consumers outnumber farmers by a factor of more than 20 in the European Union, and Europeans spend only a tiny fraction of their incomes on food. Similarly, in the United States, farms account for less than 2 percent of all households, and the average consumer spends less than 12 percent of income on food (U.S. Bureau of Labor Statistics 1999; U.S. Census Bureau 1998; U.S. National Agricultural Statistics Service 1998). In the industrial countries, consumers can afford to pay more for food, increase subsidies to agriculture, and give up opportunities for better-tasting and better-looking food. In developing countries, poor consumers depend heavily on agriculture for their livelihoods and spend the bulk of their income on food.

Strong opposition to GI foods in the European Union has resulted in restrictions on modern agricultural biotechnology in some countries. The opposition is driven in part by perceived lack of consumer benefits, uncertainty about possible negative health and environmental effects, widespread perception that a few large corporations will be the primary beneficiaries, and ethical concerns.

Potential benefits. There are many potential benefits for poor people in developing countries. Biotechnology may help achieve the productivity gains needed to feed a growing global population, introduce resistance to pests and diseases without costly purchased inputs, heighten crops' tolerance to adverse weather and soil conditions, improve the nutritional value of some foods, and enhance the durability of products during harvesting or shipping. New crop varieties and biocontrol agents may reduce reliance on pesticides, thereby reducing farmers' crop protection costs and benefiting both the environment and public health. Biotechnology research could aid the development of drought-tolerant maize and insect-resistant cassava, to the benefit of small farmers and poor consumers. Research on genetic modification to achieve appropriate weed control can increase farm incomes and reduce the time women farmers spend weeding, allowing more time for the child care that is essential for good nutrition. Biotechnology may offer cost-effective solutions to micronutrient malnutrition, such as vitamin A- and iron-rich crops.

Research focused on how to reduce the need for inputs and increase the efficiency of input use could lead to the development of crops that use water more efficiently and extract phosphate from the soil more effectively. The development of cereal plants capable of capturing nitrogen from the air could contribute greatly to plant nutrition, helping poor farmers who often cannot afford fertilizers.

By raising productivity in food production, agricultural biotechnology could help further reduce the need to cultivate new lands and help conserve biodiversity and protect fragile ecosystems. Productivity gains could have the same poverty-reducing impact as those of the Green Revolution if the appropriate policies are in place.

Policies must expand and guide research and technology development to solve problems of importance to poor people. Research should focus on crops relevant to small farmers and poor consumers in developing countries, such as banana, cassava, yam, sweet potato, rice, maize, wheat, and millet, along with livestock.

Health and environmental risks. Genetically improved (GI) foods are not intrinsically good or bad for human health. Their health effect depends on their specific content. GI foods with a higher iron content are likely to benefit iron-deficient consumers. But the transfer of genes from one species to another may also transfer characteristics that cause allergic reactions. Thus, GI foods need to be tested for allergy transfers before they are commercialized. Such testing avoided the possible commercialization of soybeans with a Brazil nut gene. GI foods with possible allergy risks should be fully labeled. Labeling may also be needed to identify content for cultural and religious reasons or simply because consumers want to know what their food contains and how it was produced. While the public sector must design and enforce safety standards as well as any labeling required to protect the public from health risks, other labeling might best be left to the private sector in accordance with consumer demands for knowledge.

Failure to remove antibiotic-resistant marker genes used in research before a GI food is commercialized presents a potential although unproven health risk. Recent legislation in the European Union requires that these genes be removed before a GI food is deemed safe.

Risks and opportunities associated with GI foods should be integrated into the general food safety regulations of a country. International agencies and donors may need to assist some developing countries build the capacity to develop appropriate regulatory arrangements. These regulatory systems are needed to govern food safety and assess any environmental risks, monitor compliance, and enforce such regulations. The regulatory arrangements should be country-specific and reflect relevant risk factors. Progress on achieving a global agreement on biosafety standards is urgently needed (Juma and Gupta 1999). The development of a public global regulatory capacity has lagged far behind the pace of economic globalization.

The ecological risks policymakers and regulators need to assess include the potential for spread of traits such as herbicide resistance from genetically improved plants to unmodified plants (including weeds), the buildup of resistance in insect populations, and the potential threat to biodiversity posed by widespread monoculture of genetically improved crops. Seeds that allow farmers the option of "turning off" genetic characteristics, mentioned earlier, offer great promise for assuring that new traits do not spread through cross-pollination.

Both food safety and biosafety regulations should reflect international agreements and a given society's acceptable risk levels, including the risks associated with not using biotechnology to achieve desired goals. Poor people should be included directly in the debate and decisionmaking about technological change, the risks of that change, and the consequences of no change or alternative kinds of change.

Socioeconomic risks. Unless developing countries have policies in place to ensure that small farmers have access to delivery systems, extension services, productive resources, markets, and infrastructure, there is considerable risk that the introduction of agricultural biotechnology could lead to increased inequality of income and wealth. In such a case, larger farmers are likely to capture most of the benefits through early adoption of the technology, expanded production, and reduced unit costs (Leisinger 1999).

Growing concentration among companies engaged in agricultural biotechnology research may lead to reduced competition, monopoly or oligopoly profits, exploitation of small farmers and consumers, and extraction of special favors from governments. Effective antitrust legislation and enforcement institutions are needed, particularly in small developing countries where one or only a few seed companies operate. Global standards regarding industrial concentration must also be developed; international public policies in this area have not kept pace with economic globalization. Effective legislation is also required to enforce IPRs, including those of farmers to germplasm, along the lines agreed to within the WTO and the Convention on Biological Diversity.

Ethical questions. A major ethical concern is that genetic engineering and "life patents" accelerate the reduction of plants, animals, and microorganisms to mere commercial commodities, bereft of any sacred character. This is far from a trivial consideration. However, all agricultural activities constitute human intervention into natural systems and processes, and all efforts to improve crops and livestock involve a degree of genetic manipulation. Continued human survival depends on precisely such interventions.

Conclusion

Expanded enlightened adaptive research on agricultural biotechnology can contribute to food security in developing countries, provided that it focuses on the needs of poor farmers and consumers in those countries, identified in consultation with poor people themselves. It is also critical that biotechnology be viewed as one part of a comprehensive sustainable poverty alleviation strategy, not a technological quick-fix for world hunger. Biotechnology needs to go hand in hand with investment in broad-based agricultural growth. There is considerable potential for biotechnology to contribute to improved yields and reduced risks for poor farmers, as well as more plentiful, affordable, and nutritious food for poor consumers. It is not, as some critics have charged, "a solution looking for a problem." The problems are genuine and momentous. Public sector research, particularly through IARCs and NARS, is essential for ensuring that molecular biology-based science serves the needs of poor people. It is also urgent that internationally accepted biosafety standards and local regulatory capacity be strengthened within developing countries.

Evaluation of genetically improved crops needs to increase in developing countries; at present, about 90 percent of the field testing occurs in industrial countries. Without field testing, it is virtually impossible to assess potential environmental and health risks. Hence, destruction of test plots by anti-GI activists should cease. Open debate about the issues involved is essential, but physical attacks on research and testing efforts contribute little to the free exchange of ideas or the formulation of policies that will advance food security.

If the appropriate steps, including those outlined above, are not taken, modern biotechnology could bypass poor people. Opportunities for reducing poverty, food insecurity, child malnutrition, and natural resource degradation will be missed, and the productivity gap between developing and industrial country agriculture will widen. Such an outcome would be unethical indeed.

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Ethical Challenges of Agricultural Biotechnology for Developing Countries

Klaus M. Leisinger

Morality is not just some desideratum of the weak for their protection, or an instrument of the strong for tethering the weak, but a factor of utmost importance for society as a whole and its welfare.

The words morals and ethics are used to mean roughly the same thing, even though they do not. By morals we mean broadly accepted norms that govern practical behavior primarily toward our fellow humans—wherever and whenever they live. In its modern definition, morals includes norms also with respect to nature. The discipline of ethics, on the other hand, is moral philosophy—that is, describing the subject as well as comparing and critically reflecting different moralities.

Reflecting philosophically on ethics is a fulfilling and spiritually demanding concern. But ethics—including the ethics of biotechnology and genetic engineering—must be brought down from the lofty heights of ideas or values and placed into the reality of everyday life. To deal responsibly means always and above all to *deal intelligently*—to weigh the consequences of our actions or nonactions according to the benefits and the harm they can provoke.

Intelligent action is acting in one's *enlightened self-interest* and is thus compatible with the selfish tendencies in some of our societies. To assume that altruism and a holistic world-view are predominant human characteristics would be unrealistic.

Because the issue is complex, I will try to touch on some essentials only, and will present a number of propositions under four main categories:

- Ethical challenges in discussion and with semantics
- Ethical challenges of decision processes
- Ethical challenges with regard to solidarity
- The challenge of time.

Discussion and Semantics

Separation of Issues

My first proposition is that we must separate out what has to be separated, and we must discuss issues under the appropriate heading. Discussions about ethics ought to strive for consistency and coherence, so certain rules for discussing the ethical challenges are pertinent. First, we must separate the ethical challenges of biotechnology and genetic engineering in the context of human beings from those of animals and of plants. This paper focuses on plant context, or to "green biotechnology."

Second, we must respect the professional ethics of different disciplines. This means that we need to have biologists assess the biological implications, legal experts assess the legal implications, and so on for economists, sociologists, political scientists, and others. Once professional experts have established the facts, we can call upon the ethicist to assist us in our assessment of the facts. What should not happen—but what happens all the time—is that ethicists or theologians discuss plant biological specificities and second-guess the facts provided by the specialists of that discipline.

At the end of the 20th century, we should see people who have different convictions and opinions as fellow human beings with a diverging view of the world. A more humanist attitude amongst those with differing views will also affect the language we use: Wherever managers of multinational corporations or bureaucrats at research institutes dismiss calls for caution or precaution as stupidity or old-style communist rhetoric, they lack not only style but also wisdom. On the other side of the debate, with due respect for the need for campaign topics and for bogeymen to secure public attention, the preoccupations, prejudice, and distortions of fact may become an end in themselves. The result of such marketing aimed to spur donations to interest groups might well be the end of support for public research, the results of which are likely to be needed in 10-15 years. Some observers fear that today a small minority of radical environmentalists are manipulating the public politically, in a way that may deny poorer nations access to a technology that could help them produce more and better food.

In some European countries, the debate has become one among people whose minds are already made up and who do not want to be bothered by facts, but only need a scapegoat from a multinational corporation. You cannot have responsible discourse under such conditions.

A kind of bio-McCarthyism is taking place, leading to slandering and vilification of anybody who sees genetic engineering and green biotechnology as anything but a nail in the coffin of modern society. But I also want to go on record as noting that those who argue that these technologies are the silver bullets to save the world from starvation should also restrain themselves. Complex problems have no simple solutions. The discussion about the contribution of green biotechnology to food security would gain in quality and power of conviction if all who participated were more balanced in their interventions.

Transparency of Interests

My second proposition is that we need to make our valuations explicit and our interests transparent. Assessing the contribution of genetic engineering to fighting hunger in developing countries is not simply an academic task involving facts and figures and rational evaluation. The interpretation of data is subject to the interests and value judgments of a variety of stakeholders. Because we live in a world of heterogeneous social systems, with a multitude of value judgments and pluralism of interest, identical information leads to diverging verdicts.

Whereas some people consider genetic engineering something unnatural and inherently nasty and a threat to development in poor countries, others see a compelling moral imperative to develop genetically improved crops to combat poverty and ensure food security. The notion that there is no such thing as one objective reality but a multitude of subjective realities seems prevalent in discussions of biotechnology, as it does in discussions of all major social issues.

As Streeten once pointed out, no one can be objective, pragmatic, and idealistic all at the same time. Individual values and interests always exert an enormous influence on the assessment of facts. There is an assumption that science is neutral and objective. What objectivity means here is that the scientist should provide disinterested information about facts, and not permit an intrusion of his or her subjective values. Disinterested sciences have never existed, and never will. It is impossible to avoid having personal valuations affect our judgment, so we should at least make them explicit and give transparency to what we define as desirable and undesirable.

The discussion also gains in clarity if the interests behind arguments are revealed and made transparent. The private sector is often accused of having profit interests. That is true if after investing billions of dollars in research, you hope to find something that is attractive enough that clients will buy it for a good price. Is that a reason for blame in democratic and market-oriented societies, providing the pursuit of commercial interests is based on law and enlightened self-interest?

What are the interests of those opposing biotechnology? For many observers, large international nongovernment organizations are self-styled Robin Hoods interested in saving the world. This may be true, or it may not be so simple. It would certainly be interesting to shed more light on the necessity of opinion marketing for the generation of funds for NGOs. Some of the NGOs are also adept in using their power in media and voter terms. As the media are more likely to take up wild stories about the creation of monsters than stories about slow but steady progress toward better crop varieties for resource-poor farmers, a certain kind of semantics and argumentation has direct relevance for the acquisition of funds. Could it be that in some instances scientific fact in the argumentation is sacrificed for a place in the market of worries?

Although any set of personal values can be legitimate from the perspective of its holders, personal values should not necessarily be imposed on others in the sense of prescriptive ethics. This holds especially true for the competition of anthropocentric and biocentric values.

Differences of values and convictions start at a very fundamental level: There are people who oppose genetic engineering for the fundamental reason that human beings should not do what they perceive as playing God. Others give the biosphere as such specific rights—that is, that species boundaries are not to be violated. I will not deal with this argument other than on the same fundamental level: If God created humans as intelligent creatures, it should be compatible with God's intentions that they use their intelligence to improve living conditions. The ambivalence of technological progress and the fact that a technological innovation can be used for good as well as for ill is neither new nor confined to genetic engineering and biotechnology.

Whether you see biotechnology as a threat or as a blessing depends in part on where you position human beings in the biosphere. If you consider them as the "crown of the creation" in the spirit of Genesis 1.28, you will argue differently if you see human beings as brothers and sisters of animals and plants. Again, while I have high personal regard for those who think in the tradition of Saint Francis of Assisi or Albert Schweitzer, I do not share their convictions. To put it bluntly: If I have to sacrifice larvae of the monarch butterfly in order to save children from blindness or women from anemia, I would regret the sacrifice and do as much as I can to minimize the damage, but in the end I would not hesitate to do it.

Why do I mention this example? Because the Federal Institute of Technology in Zurich informed the world in March 1999 of a sensational achievement. It became possible to genetically modify rice so that it contains vitamin A and iron. This, of course, is of immense benefit to about 250 million poor, malnourished people who are forced to subsist on rice. The consequences of this restricted diet are well known: 180 million people are Vitamin A-deficient, each year 2 million of them die, hundreds of thousands of children turn blind, and millions of women suffer from anemia, which is one of the main killers of women of childbearing age. In my judgment, this achievement makes the research team led by Ingo Potrykus potential candidates for the Nobel Prize for Peace. But did the Swiss, German, or any other media react? Not until at least four months later, and then in a rather low-key manner.

The media treatment and hence public perception was very different when news broke in July 1999 that larvae of the monarch butterfly were damaged in a genetically improved crop experiment that was not representative of natural conditions. This time the story was picked up immediately by the media and taken as clear evidence that genetic engineering may cause incalculable harm to biodiversity. The fact that in 1999—the year of the mass release of GI corn in the United States—the population of the monarch butterfly increased had no impact on the credibility of the stories told. One consequence of this biased press reporting is a selective public perception of genetic engineering.

Disentangling Risks

My third proposition regarding ethical challenges in discussions is that we need to disentangle risks. Current public debate about the Gene Revolution often suffers from the same fate as discussions on the Green Revolution—not differentiating between risks inherent in a technology and those that transcend it. This distinction is of utmost importance in any attempt to reason out the risks arising from biotechnology. Whether this new technology promises to be the key technological paradigm in the fight for food security and reducing poverty depends on how its risks are perceived, disentangled, and accordingly addressed.

Technology Inherent Risks

For genetically improved organisms, the risks classified as inherent in the technology are frequently summarized as biosafety risks. There is a wealth of scientific literature on the deliberate release of living modified organisms into either new environments or areas where they could prove particularly harmful. Until today, no severe biosafety risks have become known. The same is true for genetically altered food: Thousands of scientific papers have demonstrated the safety of the technology and no scientifically reputable test has produced so far any hint that genetically improved food could be in any way toxic.

There is a broad consensus amongst most scientists that serious concerns about the release of living modified organisms are unwarranted. In 1999, nearly 41 million hectares around the world were planted commercially with new genetically improved crops, and no serious issue arose. It is particularly cynical that field trials that could prove the ongoing validity of the scientific consensus on safety in the environment are being vandalized, thus preventing the accumulation of further evidence of the behavior of the new varieties.

Most countries with biotechnological-based industries have sophisticated legislation in place intended to ensure the safe transfer, handling, use, and disposal of such organisms and their products. But even with the best procedures and regulations in place, some risks will remain. Risks—calculable risks—must be taken, otherwise technological progress becomes impossible. There is always the possibility, no matter how slim, that something could go wrong. But science deals in probabilities, while the public has little appreciation for P values, so the few studies discussing specific risks have received disproportionate media play.

Technology Transcending Risks

Technology-transcending risks, as opposed to technology-inherent risks, emanate from the political and social context in which a technology is used (Leisinger 1999). In developing countries, these risks spring from both the course the global economy takes and country-specific political and social circumstances. The most critical risks have to do with three issues: aggravation of the prosperity gap between industrial and developing countries, growth in the disparity in income and wealth distribution within poor societies, and loss of biodiversity. This is not the place to go into a detailed discussion of these issues. What has to be stressed again, however, is the necessity to disentangle risks.

Where there is war, civil strife, and harsh political regimes, there will be hunger. Food insecurity is one of the most terrible manifestations of human deprivation and is inextricably linked to every other facet of development. Poverty is one of the major causes of food insecurity, and sustainable progress in poverty alleviation is critical to improved access to food. Poverty is linked not only to poor national economic performance but also to a political structure that renders poor people powerless. So policy matters of a general nature, and in particular good governance, are of overriding importance for food security. Progress toward food security also requires a proper macroeconomic framework, and the elements that have been most important for success on the poverty front are known today (see Pinstrup-Andersen and Cohen, this volume).

Technology-transcending risks mostly materialize because a gap opens between human scientific technical ability and human willingness to shoulder moral and political responsibility. Today, the risks most likely to inhibit development lie in the political, economic, and social milieu in which technology is applied.

Decision Processes

This is my second category of ethical challenges. In his masterpiece on *Politics as Profession*, Max Weber reminds us that we have to be clear in our mind that every ethically oriented course of action can rest on two altogether different and opposing maxims: It can be oriented to either an *ethic of conviction* or an *ethic of accountability*. The ethic of conviction is not synonymous with irresponsibility or the ethic of accountability with lack of conviction. There is, however, a profound difference between acting in accordance with the ethic of conviction and acting according to ethics of accountability, and hence feeling responsible for the (foreseeable) consequences of what you have done or omitted to do.

The two types of ethical-mindedness that Weber contrasts so absolutely obviously correspond at best to an ideal construct. In reality, people live in both force-fields and have to make decisions with both points of reference. Yet the extent of the ethics practiced by anyone dealing with genetic engineering and biotechnology is measured not only by the quality of the moral will behind it, but by the practical results of what they have decided to do.

This much, however, can be said: The decision for or against genetic engineering and biotechnology cannot be based solely on the ethics of conviction. It cannot be genetic engineering for the sake of genetic engineering—there is more to it. All technological decisions must be the result of a scientific weighing of arguments and be based on a sober and disinterested benefit-risk analysis in a specific situation and within a wider technological portfolio—that is, they have to be decisions based on the ethic of accountability.

Using one of the many methodological approaches for reaching an ethical decision, or at least a *moral determination*, we can ask the following questions:

- What is the perception of the problem?
- How do we analyze the situation?
- What are the practical options?
- What norms, qualities, and perspectives should we use?
- Can we verify a binding applicability of our judgment or norms?
- What is the result of our evaluation?

Ethics of Accountability

At the moment there are more than 800 million people—mostly women and children—living with chronic malnutrition. In addition, hundreds of millions of people more face food shortages during some part of the year. World population will grow by at least another 3 billion over the next 50 years, with virtually all of the increase in developing countries. Researchers at the International Food Policy Research Institute (IFPRI) say that food production in developing countries will have to be doubled in the next 50 years if a major food security crisis is to be prevented.

During that same 50 years, water will become increasingly scarce and what is left will be more polluted. Arable land is shrinking and what is left will be less productive. In addition, Earth is getting warmer, and no one knows what this is going to mean for the ability of poor countries to produce sufficient food. There is one last scary development: Over the past decades, cereal yields per hectare have deteriorated by one-third. Many food experts expect that this downward trend will continue and that conventional breeding might not be able to reverse it.

In this situation, I consider it not only a question of international responsibility and political wisdom to look for new economic, social, political, and technical possibilities for food production, but also an ethical imperative. To turn a blind eye to a problem that today claims the lives of 40,000 children every day is cause for moral outrage.

The spectrum of potential benefits from the application of genetic engineering and biotechnology to food crops in developing countries ranges from diagnostic aids, for example to accelerate the finding of plant and animal diseases, to gene mapping, which allows speedier identification of interesting and useful genetic material for every kind of plant usable in agriculture. The main objective of R&D for food security is to find improved seed varieties that enable reliable high yields at the same or lower tillage costs through qualities such as resistance to or tolerance of diseases and pests as well as to stress factors. Equally important objectives are the transfer of genes with nitrogen-fixing capacity onto grains, and the improvement of food quality by overcoming vitamin or mineral deficiencies.

There is a wealth of serious analyses that see a great potential for genetically improved crops to contribute to human well-being, particularly in developing countries. The possibilities of higher yields from new genetically improved crops plus their capability to cope with soil toxicity may also help prevent the farming of ecologically fragile areas, or the clearing of tropical forests for agricultural purposes. As natural biodiversity in such areas is particularly high, tremendous positive effects for biodiversity would result.

Case studies show that over the past years biotechnology and—so far only to a lesser extent—genetic engineering have allowed marked concrete advances in the direction of higher food security, be it through resistance to fungal and viral diseases in major food crops or through improved plant properties (Flavell 1999). Of course, new agricultural technologies can only contribute one stone to the complex mosaic of agricultural development. Policies must ensure that a development-friendly environment exists and that technological progress is oriented toward the needs of the poor, particularly smallholders.

All serious analyses admit concerns with regard to human health, environmental safety, and intellectual property rights (IPR), but the majority conclude that—with a proper regulatory regimen enforced—benefits are likely to greatly outstrip concerns, so that ethically there should be every effort to realize these benefits. Continued research on all aspects of genetic engineering and biotechnology is necessary to maximize benefits and minimize risks. Whatever helps to address public concerns and regain public confidence for genetic engineering and biotechnology must be done, because in the end, in pluralistic democratic societies, it is social acceptance that makes success feasible.

Ethical Dilemmas

Ethical dilemmas are predicaments that force us to decide between two or more alternative courses of action, each of which is more or less fraught with guilt. Tragic situations illustrative of this quandary abound—situations involving life-and-death decisions and, with them, inevitable suffering and grief. Ethical dilemmas, then, are not situations that confront us with a choice between an ethically enjoined or a forbidden course of action, but rather ones where we are offered a choice between two or more undesirable courses of action. Not doing anything or putting up with a problematic situation can also be a choice, though not an ethically admissible one because it sidesteps the real point at issue: having to decide on which is the *lesser* evil.

Solutions to ethical dilemmas often demand compromises. Many people feel vaguely uncomfortable with this because of the negative connotations attached to the word compromise—as in an uneasy or a shoddy compromise. But qualms bring us no closer to a solution. In pluralistic societies, it is virtually impossible not to enter into compromises. So a few pointers to working towards possibly good compromises may be in order. First, it is important to affirm with all due care a scale of values so as to be clear about which values rank highest. With a scale of priorities to go by, a lesser good can be waived for the sake of a greater one. Compromises done in this vein are unproblematic. To sacrifice higher values to a lower one, in contrast, is ethically not acceptable.

Legal entitlements have certain limits; ethical claims do not. The law defines merely the ethical minimum. How minimal this is can be seen in the manifest inadequacy of the legal framework in many developing countries, for example, where as a result of institutional deficiencies or the paramount presence of political violence, the law is overridden. So even if the law does not expressly compel it, knowing better imposes the obligation to accept responsibility beyond the letter of the law. Concretely, if a developing country has no biosafety regulation or has one but does not enforce it, it might be legal to introduce genetically improved crops, because it is not forbidden. It cannot be legitimate, however, as it would not happen with the informed consent of the authorities and farmers in the countries concerned.

Over and above innumerable examples of the ineffectiveness of laws, there also exists a clear difference between juridical and ethical accountability. Whereas the juridical is contained within precisely defined bounds, a concern for the whole enjoins that ethical responsibility should not be equally confined. In ethical perspective, not everything that is legal is desirable, and not everything that is desirable is a legal obligation.

What does this mean for our subject? With the transfer of biotechnology to developing countries we must apply the Golden Rule—the best technical practices and highest safety standards, even if present local laws or regulations do not require such stringency.

Human Solidarity

The third category of ethical challenges concerns solidarity with our fellow human beings. It is true that in the past 50 years poverty has fallen more than in the previous 500. For the first time, long-cherished hopes of eradicating poverty seem attainable, provided that concerted political will is brought to bear. Since 1980 there has been a dramatic surge in economic growth in many developing countries, bringing rapidly rising incomes to more than 1.5 billion people. But these economic improvements came at a price.

The world has become more economically polarized both between and within countries: The richest 20 percent of the world saw its share of global income rise from 70 to 85 percent, while the share belonging to the poorest 20 dropped from 2.3 to a mere 1.4 percent. The gap in per capita income between industrial and developing countries more than tripled between 1960 and 1995, from US$5,700 to US$16,168.

Will the new technologies deepen these unacceptable inequalities or will they help to reduce them? Looking back at the lessons of the Green Revolution, it seems that the rich got richer, but the poor got less poor. A new analysis points to the employment and hence income effects of the Green Revolution varieties that eventually raised family income. As there are social differences, such as land ownership and access to credit as well as to irrigation, seed varieties with a higher productivity are likely to increase the income of those who have earlier and better access to the modern inputs. This is why *green biotechnology* also can only yield social results in line with the social conditions of those who use it. This is regrettable from an equity point of view—but it is a good governance issue, not a biological one.

An improvement of today's poverty situation in developing countries requires not only good governance but also more solidarity from the industrial countries with poor people in poor nations. Through appropriate allocation of resources, international development assistance can help civil society in developing countries to do better. In addition, new and more effective technologies are needed along with research that helps develop such technologies in developing countries. One of the most effective ways of furthering agricultural and hence rural development was and will continue to be bringing cutting-edge research to resource-poor farmers.

Public and Private Roles in Biotechnology

Genetic engineering and biotechnology are cutting-edge technologies, and where they are appropriate, they can be of great benefit to resource-poor farmers. There is, however, a problem. Many concerned citizens worry that more and more biotechnological research is concentrated in the private sector, and that its results are patented and hence may prove to be too sophisticated or expensive for resource-poor farmers. The worry is justified: When research priorities are determined by the financial return on investment, the needs of those who have the purchasing power are likely to have higher priority than the poverty eradication needs of small farmers. For this reason *public research* must be strengthened, because its fruits can be passed on to small farmers at cost or, via government channels, even free of charge. This cannot be done with the results of research sponsored by private enterprise.

The Consultative Group on International Agricultural Research (CGIAR), with its focus on the needs of the developing countries, has to continue to play a conspicuous role in such an effort—and international financial support for CGIAR therefore ought to remain high. But there must also be more and more intensive cooperation between the private and public sectors. The special knowledge and know-how and the different experience—and patented intellectual property—at the disposal of the private sector, but used only selectively for lucrative markets in industrial countries could be passed on via donated transfers or favorable licensing terms to public research institutes in developing countries. The feasibility of this has already been demonstrated by a number of concrete examples.

As far as the compensation issue for the use of genetic material from developing countries is concerned, solutions are also within reach. Fair arrangements here are not so much a matter of solidarity but justice. Suppose, for example, that a private seeds company discovered a trait in an Ethiopian barley strain that made it resistant to certain plant diseases, and then genetically transferred this property to a wheat variety that would afterwards be commercialized in Ethiopia. Obviously, the farmers in Ethiopia have contributed something by selecting and preserving this variety over a long period of time. It is also obvious that without the R&D work of the seed company, the trait would not have been used outside Ethiopia or in food grains other than the native barley. So both parties—the farmers of Ethiopia and the seed company—have contributed to the new wheat variety, and therefore both have some kind of an intellectual property right and a right to compensation.

The basic question of whether remuneration is due was clearly answered in Article 19 of the Convention on Biological Diversity, and is the consensus of the agencies engaged in development. Yet the technical details of how it should be handled in specific nations are still unclear. As a possible approach to the much needed regulation in this area, I would recommend the following:

WHO shall compensate?	Those who benefit from access to the genes and from their transfer.
What should be compensated?	Genetic material of varieties and species that have been cultivated and preserved by active agriculture.
How much?	Let us look at this issue in terms of license agreements and leave the price to the market mechanism.

From a development policy point of view, funds that result from compensation of genetic material should support the people who over centuries helped preserve the varieties in question.

Action Without Delay

Last, but not least, of the categories of ethical challenges is the challenge of time. As I noted earlier, we face the challenge of meeting the needs of another 3 billion people by 2050, with a shrinking agricultural base and increasingly scarce fresh water. We have an ethical imperative not only to keep the technological portfolio open to biotechnology and genetic engineering, but also not to lose time: Let us not forget, as the Club of Rome pointed out in 1991, that "*every minute lost, every decision delayed, means more deaths from starvation and malnutrition, and means the evolution to irreversibility of phenomena in the environment. No one will ever know for sure the human and financial cost of lost time.*"

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Evolving Role of the Public and Private Sector in Agricultural Biotechnology for Developing Countries

Gerard Barry and Robert Horsch

Most agricultural biotechnology products to date have been developed by the private sector. The process involves a number of steps, including the initial invention of transformation technologies and the identification of genes for plant improvement. Large-scale production of transformed plants for field testing and intensive agronomic evaluation are required, followed by the detailed guiding of the plants and plant products through national and international registration and regulatory processes. After (or during) these first developmental stages, a relationship was established in the United States between the private sector entities and all of those elements of the agriculture and seed industry (private and public) that were needed to commercialize these new crop products. These partnerships have taken many forms, driven largely by the nature of the seed systems and of the products to be commercialized, and by national and commercial considerations. The public sector participants have included national seed companies, universities and other research entities, and provincial, state and national governments. These partnerships and the shared experiences of the private and public sectors, while largely in more industrialized countries so far, have been repeated to a lesser extent in some developing countries, and support the probability that equally productive interactions will continue in these newer areas.

Adoption of Genetically Improved Crops

By 1998, improved crops derived from agricultural biotechnology had been widely adopted by farmers in the United States and Canada, and new genetically improved GI varieties made up to 25 percent of the U.S. corn, 40 percent of the U.S. soybean, 45 percent of the U.S. cotton, 35 percent of the North American canola, and a smaller percentage of the North American potato crops. The new traits included herbicide tolerance, insect protection, virus protection, and hybridization technology. In 1999, the adoption of these improved crops expanded. In some cases expansion was limited only by seed availability.

Adoption and expansion has also occurred elsewhere, with significant acreage of GI crops being grown in China, Australia, and Argentina. About 28 million hectares were planted worldwide in 1998 and 40 million hectares in 1999 (James 1998, 1999). In most cases, the crops developed outside of North America were extensions (by breeding) into locally adapted germplasm of products already produced in North America. This has not always been the case, and as can be seen from the growing development of products specific or exclusive to developing countries, this could be expected to become the exception over time.

The development of these improved crops has taken many years and has required many technological breakthroughs. The early phase, up to first commercialization in 1995-96, probably took close to 20 years. The ability to transform plants, beginning with petunia and tobacco, and later moving to cotton, potato, tomato, soybean, and corn, and still later to wheat and rice, was often discovered and developed by private and public sector researchers, working together or separately. Not inconsequentially, the early recognition of the promise of biotechnology for the improvement of agriculture was evident by the high level of funding for such research in both sectors in many industrial countries, and in the rapid development and dissemination of technology in this area.

The product development phase, characterized by the often large-scale production of transformed crop plants and the initial evaluation in field tests, was carried out almost entirely by the private sector.

The next product development phase, including the larger-scale field evaluations and the beginning of the introgression or backcrossing of the trait into a broad germplasm base, was usually a collaboration between private and public sectors and with other private sector entities. For efficiency, most crops use a limited number of genotypes for genetic transformation, but to serve the farmers, and to remain competitive with other aspects of seed research, the successful trait is quickly bred into all appropriate germplasm. No market was served fully at the outset, but within a very few years, the improved traits have been bred into almost all widely used germplasm, and the diversity of availability of these traits is often equal to that of other agriculturally important traits. RR (herbicide tolerant) soybean, for example, was initially launched in the first year, with a small number of seed companies in varieties in a few maturity groups, but very shortly thereafter was available in the germplasm of over 350 seed companies and germplasm providers.

The later stages, including varietal registration trials or other official evaluations, involved the public sector to a large extent. At this point, the private sector, and with seed partners, entered the new crop lines into the appropriate approval processes that are used to evaluate any new seed or plant. In addition, the added regulatory process and registrations involved the public sector entities not only as approval agents, but also in some cases in the production of the appropriate data to support these approvals.

The final stages, including commercialization, advanced demonstration plots, and continued refinement of product use, involved the private and public sectors and often reflected the existing participants in the seed and or processing industries.

The interactions that have been tried so far include collaboratiing with extension services and agricultural universities, testing the improved crops in national seed certification and varietal registration systems, licensing the crop trait (and often codevelopment of these) to national breeding programs or to local seed companies, and involving national, provincial, or state governments to ensure that the needs of their constituents are met.

Expansion into Developing Countries

The continued expansion of agricultural biotechnology products into new areas, and the development of such products that are specific or exclusive to developing countries, are planned and under way. In some cases, direct adoption of already developed traits, such as insect resistance or herbicide tolerance, is planned following breeding into local germplasm and the completion of relevant registration and approvals processes. These phases also require extensive testing under local conditions and refinement of the use of the technologies to maximize their effectiveness in a new environment. This kind of development was also undertaken for the initial launch areas. There is a growing interest and activity in the study and testing of new biotechnology traits that are required to mimic or complement the traits already developed in other areas of the world. Examples of these include the screening and testing of new *Bacillus thuringiensis* (Bt) proteins that may be used to control the different insect pests found in other areas, or that may be used to extend the range and value of other existing approaches Additional areas of research include improvement of efficiencies of genetic transformation in crop subspecies or in new species. This new wave of research is being carried out by public and private sector entities from industrial or developing countries, and may involve partnerships between such entities and regions.

It is possible that very few new forms of interactions may be needed between the private and public sectors for the successful deployment of existing or new products over those already experienced in industrial countries, although there would be differences in degree. These interactions will, as before, reflect the realities of the participation of different private and public sector entities in the development and in the businesses of seeds and agriculture and the most effective combinations that ensure the best delivery of the products to the farmers. In many cases, involvement with national agricultural research systems (NARS) is expected to be productive. Direct involvement with the CGIAR system is a possibility, but is more likely to occur with specific CGIAR centers.

Other models have been used to foster the availability of important products and technologies to those that need them. In some cases, this has involved the transfer of proven technology for crops in developing countries, including technology for virus protection for potato (Mexico), virus protection for sweet potato (East Africa), virus protection for papaya (Southeast Asia), and Pro-VitA for oilseeds (India). The transfers have been accomplished through partnerships of technology holders and parties interested in jointly providing these to new areas.

Conclusion

The possibility of growing interactions between the private and public sectors has been based on a number of experiences and changes that have occurred over the course of the early phases of the plant biotechnology work. A confidence in, and a fuller understanding of, the different technologies has been gained over time in the development of the earlier commercial products and over a growing geographic base.

Regulatory processes have become clearer in many countries, and the private and public sectors have shown commitments to training and other support, and support for local regulatory system development. Most importantly, the movement of agricultural technologies beyond the purview of the private pector originators has often been driven and encouraged by responsible partners, who recognized the need for these technologies for the people and areas that they were committed to serving.

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Genomics Research: Prospects for Improving Livestock Productivity

Vishvanath Nene, Subhash Morzaria, Lyden Baker, Agnes Odonyo, Ed Rege, Ercole Zerbini, and Richard Bishop

Following the "Green Revolution" that increased cereal production in some developing countries, a more holistic "doubly green revolution" has been prescribed for agriculture in the 21st Century if the global community is to both sustain the growing human population and its demand for food in a manner that conserves natural resources (Conway, 1997).

An important component of the approaches to improving productivity in the agricultural sector involves the use of biotechnology. The tools of molecular biology already contribute to the characterization of animal, plant, and microbial genetic resources. Molecular techniques have been employed to isolate genes for the diagnosis of disease and its prevention by development of safe and efficacious subunit vaccines and to capture desirable production traits in plants and animals. However, genomics research is undergoing a revolution of its own, where the emphasis is shifting from a study of single genes to a systems approach involving a study of all the genes or groups of genes that occur within an organism. This has become possible due to development of large-scale DNA sequencing strategies together with computer infrastructure and software capacity to manage the process and analyze the data produced. Bioinformatics research in combination with microarray or "DNA chip" technologies and other high throughput screening strategies herald new approaches to analyzing biological systems in the context of whole genome sequences (McKusick 1997).

The discipline of genomics offers fresh perspectives on research problems and the private sector has positioned itself to take advantage of these developments, as the return on investment is high. The international agricultural research centers of the Consultative Group on International Agricultural Research (CGIAR) must do likewise or the gap in science addressing the needs of the poor in developing countries will grow wider. In this review we highlight four project activities where the tools of biotechnology are being used at ILRI, and outline major developments occurring in genomics as these will impact on future research activities. Research partnerships are crucial for accessing some of the genomics technologies, and ILRI has formed one such linkage to address a constraint to vaccine development against a lethal disease of cattle that occurs in sub-Saharan Africa.

Constraints to Livestock Productivity in Developing Countries

There is evidence for a rapidly increasing demand for livestock products in developing countries as a result of population and income growth and urbanization leading to a shift of dietary preference away from cereal-based foods and "the next food revolution" (Delgado and others 1999). Milk and meat consumption has grown by about 3 and 5 percent per year, respectively, and is expected to increase even more by 2020. Thus, the increase in livestock production is being demand-driven although it is not evenly spread among developing countries. Livestock agriculture usually accounts for 25-30 percent of the agricultural GDP of developing countries and is thus an important component in their economies.

Most smallholder farming systems, the priority target group of the CGIAR, rear animals in a mixed crop-livestock system and livestock play an integral role in the lives and livelihood of these resource-poor farmers. Meat and milk are high-calorie foods that also provide micronutrients and are essential for improvement and maintenance of human health. Livestock are an important source of draft power and traction, activities that would otherwise be performed primarily by women and children. Livestock are able to convert otherwise indigestible crop residues into food that is fit for human consumption, and in a synergistic relationship livestock manure plays an important role in nutrient recycling that helps to sustain crop production. Manure can also provide cheap and affordable domestic fuel in certain circumstances. The sale of farm products, such as milk, can provide a daily income for the rural poor and this usually benefits women who tend to be the managers of smallholder systems. In addition, because of their high value, livestock contribute to asset building and constitute a form of social security.

There are differing constraints to increasing livestock productivity in developing countries depending on prevailing agroecological conditions. Perhaps most importantly, increase in livestock performance and productivity can be gained by changes in diet and feeding practice, from improvements in farm management strategies and disease control. Livestock with relevant productivity and disease resistance traits can also contribute to maximizing the efficiency of animal agriculture. ILRI recently re-examined the critical issues affecting livestock productivity and identified seven key areas under which most research relating to productivity enhancement and sustainability would fall:

- Improvement of livestock feeds and nutrition
- Management of natural resources as it relates to the livestock sector
- Improvement of animal health
- Characterization and utilization of livestock genetic potential
- Livestock policy analysis
- Systems analysis and impact assessment
- Strengthening livestock research capacity of the national agricultural research systems (NARS) of developing countries.

Biotechnology Research at ILRI

The tools of molecular biology are being used in five of the seven key researchable areas outlined above. Thus, there is clearly much scope for the application of biotechnology in alleviating constraints to livestock productivity. Four activities that will benefit from the developing science of genomics are outlined below.

Selection of Dual-Purpose Crops for Improved Yield

Conventional crop breeding programs tend to concentrate on selecting varieties that have high grain yield for human consumption, with less value placed on crop residues, such as leaves and stems, for animal feed. Crop residues, also called stover, tend to have poor nutritional value and efforts have been made to improve this by chemical and biological means. However, there has been little adoption of these techniques by smallholder farmers for a variety of social and economic reasons. An alternative, more environmentally friendly and practical strategy would be to increase the nutritive value of crop residues through genetic enhancement.

A collaborative project between the International Crops Research Institute for the Semi-Arid Tropics (ICRISAT), ILRI, and NARS in India aims to identify improved dual-purpose crop varieties of sorghum and millet. Crop residues play a major role in animal feed in the smallholder mixed crop-livestock farming systems in India's semi-arid tropics. Improved digestibility of crop residues as feed for ruminants will result in an increased conversion of crop material into valuable animal products such as meat, milk, manure and animal draft power. A feed simulation model estimates that as little as 1 percent increase in digestibility of crop residues would result in a 6-8 percent increase in animal products and traction capacity (Kristjanson and Zerbini 1999).

The ongoing research ranges from participatory rural appraisals of crop varieties at the farm level (Chambers 1990) to the identification of quantitative trait loci (QTLs) for residue quantity and quality (Hash and Breese 1999; Hash and

Witcombe 1994). The project addresses four major research issues:

- farmer perceptions of quality and productivity traits in crop residues
- relative importance of genetic (G) and environmental (E) variation and G x E interactions in nutritive value
- opportunities for indirect selection for stover quality in selected genotypes, based on observable morphological or agronomic characters
- application of existing and novel DNA markers to identify QTLs that contribute significantly to the observed genetic variation in digestibility traits.

Identifying the desirable heritable traits for improved stover quality and defining the existing genotypes that carry these characters will enable a final selection to be made in multilocational trials on station and on farm. These selected genotypes will then be available for the future development of new dual-purpose cultivars by conventional and marker assisted breeding techniques and ultimately through biotechnology.

Improvement of Rumen Fermentation

Molecular techniques have great potential for enhancing rumen function by allowing the introduction of new or improved fermentation activities thereby improving the utilization of poor quality feeds or expanding forage resources. Current rumen microbiology research at ILRI focuses on two major areas: detoxification of plant toxins which constitute anti-nutritional factors; and enhancement of the rate of degradation of fiber to improve the utilization of poor quality feeds.

The rumen microbes of wild ruminants are of particular interest because they survive in areas where feeds contain high concentrations of fiber and factors that are toxic for domesticated ruminants. For example, *Bison bison* have a superior ability to digest low quality forages when compared to *Bos taurus* (Varel and Dehority 1989).

Alteration of rumen function could occur via genetic manipulation of rumen organisms or by using defined microbes to supplement the rumen flora. For example, the transfer and establishment of an exotic rumen microbe in the rumen of naive animals has been described, allowing previously susceptible livestock to successfully utilize toxic *Leucaena leucocephala* as feed (Jones and Megarrity 1986). A gene from the soil bacterium *Moraxella* that allows detoxification of the plant toxin fluoroacetate has been successfully expressed in the rumen bacterium *Butyrivibrio fibrisolvens* (Gregg and others 1994) and shown to protect sheep from fluoroacetate poisoning (Gregg and others 1998). Rumen cellulolytic microbial genes have also been transferred to several noncellulolytic rumen bacteria, but it has not always been possible to alter the phenotype of genetically altered bacteria (Cheng and others 1992), indicating that there is much to be learned.

Little is known about the diversity of rumen microbes. Thus, application of molecular techniques including denaturing gradient gel electrophoresis (Muyzer and Smalla 1998), competitive PCR (Reilly and Attwood 1998), group specific hybridization probes (Zhang and others 1997) and shotgun sequence analysis of 16S ribosomal RNA genes, to characterize rumen microbial communities, will contribute much to an understanding of the ecology of rumen organisms. By linking these data with animal diets and in vitro analyses it may be possible to define key microbes and their role in the detoxification of phytotoxins and fiber degradation. Such information should lay the foundations for the manipulation of specific organisms for the benefit of domesticated ruminants.

Livestock Genetic Resources and Genetics of Disease Resistance

Over the centuries, livestock farming under different environmental conditions has resulted in breeds with traits such as heat tolerance and disease resistance, which favor their survival under these stresses. Farmers have also been breeding for a variety of attributes with a major focus on productivity traits such as increased milk and meat yields. As a result of such selective forces there exists a variety of breeds with different potential to benefit farming systems in different environments, the relative importance of one trait over another being dictated by farming conditions.

Livestock genetics research at ILRI focuses primarily on cattle, sheep, and goats, and is divided into two major activities: characterization, conservation, and use of tropical indigenous animal genetic resources; and genetics of disease resistance.

Basic breed information and indigenous knowledge of animal husbandry is being collated to contribute to breed biodiversity information in a database, and to help guide decisions on use of breeds. Molecular characterization is being used to analyze the population genetics of African ruminant livestock. This study, the first, covering the whole of sub-Saharan Africa, has provided a basis for a comprehensive examination of the origin and classification of African cattle, and has identified a possible new center of cattle domestication in Africa (Bradley and others 1996; Hanotte and others 1999). The second area of research is currently directed at the development of DNA markers to identify the QTLs or genes that bestow disease resistance to trypanosomosis in cattle and helminthosis in sheep.

Trypanosomosis is the most important livestock disease in Africa, constituting a major constraint to livestock production, with annual losses estimated at US$1340 million without including indirect losses such as manure and traction (Kristjanson and others 1999). Conventional methods of control, such as vaccination, chemotherapy, and vector control are unavailable, expensive or difficult to sustain. The N'Dama breed of cattle, native to the tsetse-infested areas, is known to be tolerant to infection with *Trypanosoma congolense* (d'Ieteren and others 1998). Research focuses on this breed, and central to this project was the establishment of an F2 population of cattle in which the tolerance trait is segregating. Correlation of animal genotype with phenotype has lead to the identification of five chromosomal regions controlling resistance to trypanosomosis (Hanotte, O. and others, personal communication).

Helminthosis, or gastrointestinal worm infection, constitutes one of the most important animal health constraints to sheep and goat production in both tropical and temperate regions of the world (Gill and LeJambre 1996). Current control methods in industrial countries focus on anthelmintic treatment or controlled grazing. In the tropics, these control methods are limited by the high cost of anthelmintics, their uncertain availability, increasing frequency of drug resistance and limited scope for controlled grazing. There is evidence for genetic resistance among certain indigenous tropical small ruminant breeds, for example, the East African Red Maasai sheep (Baker and others 1998). Similar breeding programs and activities to that described above for trypanotolerance in cattle are under way to identify genetic markers linked to QTLs controlling resistance to helminthosis in sheep.

The ruminant research is being supported by sophisticated mouse studies where genetically resistant and susceptible strains and advanced inter-cross lines are being used as surrogate models for trypanosomosis and helminthosis research (Kemp and others 1997). Using comparative rodent and ruminant genomics, it is expected that the time to discovery of important genes that are relevant in ruminants will be considerably shortened. The products of this research will be molecular probes as markers for disease resistance. These could be used for more efficient selection in conventional breeding programs for improved performance in extant indigenous livestock breeds endowed with innate disease resistance. Alternatively marker-assisted introgression approaches could be used for development of new, productive livestock types through efficiently combining disease resistance genes with genes for enhanced productivity that already exist in many breeds in areas where the diseases of concern do not occur. By understanding the molecular basis of resistance to these diseases it may also be possible to develop novel alternative disease control strategies.

Animal Health Improvement by Vaccine Development

Vaccination offers one of the most effective and sustainable methods of disease control (Kurstak 1999; McKeever and Morrison 1998; Morrison 1999). The considerable potential of vaccine for effective disease control can be gauged by the eradication of smallpox and the global vaccines programs of the World Health Organiation. Veterinary vaccines against a number of livestock and poultry diseases have already played a critical role in increasing livestock productivity under disease challenge (Mowat and Rweyemamu 1997). ILRI's vaccine research program concentrates on two major diseases that affect ruminant livestock in Africa: trypanosomosis caused by

Trypanosoma congolense and *T. vivax*; and East Coast fever caused by *Theileria parva*.

Vaccine development against an infectious organism is more likely to succeed when there is clear evidence of acquired immunity to infection. It is then possible to define immune responses that contribute to immunity and to use screening systems based on this knowledge to identify pathogen molecules that are the targets of protective immune responses, and to incorporate these into experimental vaccines. Another effective method of disease control involves reducing the pathological effects of infection rather than parasite burden itself (Playfair, Taverne, and Bate 1991). This approach holds promise in trypanosomosis vaccine research where study of the pathogen and host-parasite interaction has so far not revealed any obvious clues for vaccine development against the organism itself. As will be described below, genomics research offers new opportunities in combating infection and disease by understanding the biology of pathogens and their hosts in greater detail.

Developments in Genomics Research

Genomics is setting new paradigms in research approaches within biological sciences, and will be a major force in enhancing the rate of progress in understanding biological systems and exploiting them for development of products. The rapid rates of progress in this field are based on high throughput technologies in the area of structural and functional genomics (McKusick 1997). Data derived from such research have the potential to significantly decrease the time frame for problem solving and to initiate novel research activities. The purpose of this section is to make the reader aware of the changes taking place in genomics. It is not intended to be an exhaustive list of the full range of methods that have been developed or those that are being developed as a consequence of the huge increase in genome sequence data. What is pertinent is that these technologies allow novel approaches to address biological problems, and because some of them currently require very specialized resources and expertise, the only way to access them is through research partnership.

A series of new platform technologies have been developed that have resulted in rapid advances in three areas that are interlinked. When taken together the area of genomics has become an incredible growth industry during 1995-99, and it is widely believed that these research areas and the immense amount of new data that they generate will fundamentally change approaches to asking and answering questions in biology. What are the changes that have occurred and what are the consequences?

First, developments in DNA sequencing have made the acquisition of whole genome sequences a reality and it is now almost routine to sequence microbial genomes. Such data, when interpreted using bioinformatics gives a complete listing of all the genes present in an organism, the genetic "blueprint" of an organism. The first genome sequence of an organism more complex than a virus was published in 1995 (Fleischmann and others 1995). Twenty-three genome sequences are now available in a public database held at the National Center for Biotechnology Information, and numerous genome sequencing projects of a wide variety of organisms, including plants and mammals, are under way

Second, a number of different types of technologies have been developed for genome analysis allowing rapid genotyping and genome expression studies using microarray technology (Lander 1999). What puts this technology into a different league is that with the growing list of whole genome sequence data available, it will be possible to scan the genomes of different organisms rapidly and to develop a systematic approach for mapping genetic traits (Brown and Botstein 1999; Chakravarti 1999).

Third, developments in computational biology or bioinformatics, which were essential in underpinning the advances in DNA sequencing and genome analysis, will increasingly allow the prediction of gene function from gene sequence (Burks 1999). Although there are currently considerable gaps in this knowledge base, it is nevertheless possible to build a theoretical framework of the biology of an organism from the listing of its genes. This forms a very powerful base for hypothesis-driven experimentation. In addition, by comparing physical and genetic maps across different organisms it is possible to significantly reduce the time frame for the identification of important genes (Bevan and Murphy 1999). The genome sequences of several microbes are already available and soon the annotated genomes sequence of a plant (*Arabidopsis thaliania*), the fruit fly (*Drosophila melanogaster*), mouse, and humans will become available. These resources will define a new era in comparative genomics research and the biological sciences.

Relevance of *T. parva* Genome Sequence for ECF

East Coast fever (ECF) is a usually fatal disease of cattle, and approximately 24 million cattle in 11 countries in eastern, central and southern Africa are at risk (Norval, Perry, and Young 1992). ECF is characterized as a lymphoproliferative disorder and is caused by an intracellular protozoan that induces a reversible cancer-like phenotype of parasite infected white blood cells (Irvin and others 1975; ole-MoiYoi 1989). The levels of morbidity and mortality particularly in improved exotic cattle breeds are extremely high. Estimates of annual economic losses of US$168 million establish that effective and sustained control of the tick-transmitted causative agent of ECF, *Theileria parva*, would have a high impact (Mukhebi, Perry, and Kruska 1992). Conservative *ex ante* impact analysis indicates that investment in research to develop improved vaccines against ECF has a potential cost-benefit ratio of 15:1 (Kristjanson 1997). The current methods of disease control include use of acaricides to prevent tick infestation and live vaccines that rely on infection with potentially lethal parasites, followed by treatment (Radley 1981). The disadvantage of acaricide use includes cost and development of tick resistance to the treatment. Additional problems, with broader implications, include pollution of the environment and toxic residues in animal products. The disadvantages of live vaccines include strain-specific immunity, high cost, requirement for drug treatment (oxytetracycline), and a possibility of causing severe disease due to incorrect vaccine administration and requirement for a cold chain to deliver the vaccine.

It has been demonstrated that antibodies against surface components of sporozoites, the infective stage of *T. parva*, introduced into the mammalian host by feeding ticks, will inhibit their capacity to gain entry into host cells to establish infection (Musoke and others 1982). By analyzing the mechanism of immunity engendered by infection and treatment it has been demonstrated that a subset of T cells called cytotoxic T lymphocytes (CTLs) play a major role in the clearance of pathogenic, schizont-infected cells (Morrison and others 1987). Thus, antigens from two lifecycle stages of the parasite that are the targets of protective immune responses, are desirable components of a vaccine against ECF. ILRI is currently evaluating a recombinant form of p67 (Musoke, Nene, and Morizaria 1993), the major surface antigen of sporozoites, as an antisporozoite vaccine because, under laboratory conditions, p67 routinely induces immunity in about 70 percent of immunized cattle. This molecule is a promising vaccine antigen and is undergoing development to improve protective efficacy. The search for schizont vaccine antigens is complicated by the cell biology of antigen processing and CTL recognition of parasite infected cells. The specificity of CTLs is likely to be determined by interaction of a receptor on the T cell with a peptide 8 to 11 amino acid residues long that is associated with host MHC class I molecules (Collins and Frelinger 1998). Consideration of molecular mechanisms in cell biology indicates that schizont molecules must gain access to the host cell cytoplasm, and from there into the host cell MHC class I antigen processing pathway. Conventional methods to identify such peptide antigens are technically demanding, and genomics research offers an alternative approach to vaccine antigen identification.

As described previously, from the genome sequence of an organism it is possible to predict all the genes encoded within it. Schizont molecules that access the host cell cytoplasm are likely to be either secreted or shed from the cell surface. Again cell biology dictates that these types of parasite molecules will be processed by the classical secretory pathway and will contain N-terminal peptides with conserved features that can be identified from gene sequences in a high percentage of cases (Nielsen and others 1997). Thus from the complete listing of *T. parva* genes it will be possible to identify a subset of genes that contain most if not all candidate vaccine antigens, thereby overcoming the current constraint in identifying antigens recognized by cytotoxic T cells. This set of parasite genes would have to undergo further screening to identify which ones are suitable for cattle experiments (see Nene and others 1999 for more details).

The genome sequence would also underpin other research on the parasite. It will be possible to build a hypothetical framework if the biology of the parasite and, for example, its biochemical capacity. Very little is known about the latter, and much could be inferred from the complement of parasite genes. From such information it may be possible to define novel drug targets, an approach that has already stimulated new research in chemotherapy of malaria and toxoplasmosis (Waller and others 1998; Jomaa and others 1999). It may also be possible to gain insight at the molecular level of host-parasite interaction that ultimately results in ECF. A unique aspect of the schizont, referred to earlier, is that it causes infected cells to behave like cancer cells. The schizont induces host cells to proliferate and it divides in synchrony with the host cell resulting in huge increases in schizont parasitemia (Carrington and others 1995). By understanding this phenomenon and the molecules that mediate the process, new methods of disease intervention may be developed. This research potentially has implications for human medicine, particularly leukemia research. The genome sequence would allow valuable comparative analysis of related pathogens that cause disease in livestock (*T. annulata*, *Babesia*, and *Eimeria*) or which cause debilitating diseases in humans (*Plasmodium* and *Toxoplasma*).

Partnership in Sequencing *T. parva*

To determine the genome sequence of *T. parva*, ILRI has formed a collaborative partnership with the Institute for Genomic Research (TIGR), a private but not-for-profit research institute based in the United States. TIGR is a world leader in the large-scale acquisition of DNA sequences, and pioneered the "shotgun" DNA sequencing approaches that are now being used to assemble whole genome sequences. Although this process has been used primarily with microbial genomes and purified eukaryotic chromosomes, it is believed that it can be extended to assemble the genome sequence of complex eukaryotes (Venter, Smith, and Hood 1996). TIGR also has considerable expertise in bioinformatics and microarray technology, and both will be essential in analyzing and prioritizing parasite genes for further study.

The genome sequencing project will build on the considerable data already acquired (Nene and others 1999), and has two additional collaborating institutes, which like ILRI wish to make use of the *T. parva* genome sequence data. The first is the Institute of Molecular and Cell Biology-Africa (IMCB-A), which has been recently established in Nairobi under the auspices of UNESCO. IMCB-A has a particular interest in the human-veterinary interface that *T. parva* research offers as a model system for vaccine and cancer research. The second is the Department of Infectious Diseases at the University of Hokkaido, Japan, which plans to use the *T. parva* data in comparative analysis with a related *Theileria* parasite, *T. sergentii,* that infects cattle in Southeast Asia and Japan (Uilenberg 1981).

Constraints to Delivery

Although genomics research offers new avenues leading to potential solutions of constraints to livestock agriculture, it must be recognized that the commercial implication of products resulting from such research means that intellectual property rights (IPR) must be exercised. This might seem contrary to the philosophy of the CGIAR that products developed by the CGIAR are for the public good, and to the funding sources that pledge public funds for research. It is envisaged that biotechnology product manufacture and marketing would occur through the private sector, and it is not likely that a commercial company would undertake such an activity in the absence of a framework that legally protects its investment. Thus, patents and other forms of IPR are necessary and can be used to ensure that products reach the intended client and at reasonable cost.

The issue of IPRs resulting from the genome sequence of *T. parva* has been resolved, because TIGR as a not-for-profit institute is aware of the public good that would accrue from this research. However, many problems face the commercialization of experimental vaccines. Because of the nature of the product being developed, for example, it often occupies a niche market for poor farmers in developing countries. This is not a lucrative market for the commercial sector in the industrial countries, economic principles making it difficult to justify incurring the research and development costs. A number of the technologies in vaccine development are held by the private sector, and additional constraints may arise in a lack of freedom to operate. Licensing requirements of third party intellectual property could result in increased costs or even prohibit product development. Such constraints in the discovery to delivery pathway require novel solutions or the benefits of science will not be realized.

Conclusion

The discipline of genomics will accelerate the acquisition of fundamental knowledge about biological systems. The outputs of genomics research will change our approach to solving biological problems, and result in novel uses of biotechnology to develop and improve products for crop and livestock agriculture. The CGIAR must position itself, as has the commercial sector, to exploit the rapid advances being made and to adopt genomic technologies. This will support the strategic role of the CGIAR in global agricultural partnerships, and strengthen its ability to contribute to the principles of poverty eradication, food security, and protection of the environment.

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Leveraging Partnerships Between the Public and Private Sector – Experience of USAID's Agricultural Biotechnology Program

Josette Lewis

When the U.S. Agency for International Development (USAID) was designing a new program in agricultural biotechnology in 1990, a number of factors framed the Agency's thinking about involvement of the private sector in collaboration with U.S., international, and developing country public research institutions. Primary among these was, and still is, the predominant role of the private sector in biotechnology research. By 1990, private sector investment in agricultural biotechnology research exceeded public research through universities and government research laboratories. Considering this large private investment and commercial interest in biotechnology, collaboration with the private sector suggested a means of accessing both research tools developed by the private sector and of accessing specific technical expertise. Additionally, as part of its planning process, USAID called upon the National Research Council of the U.S. National Academy of Sciences for assistance in identifying broad priorities for consideration in an international biotechnology development program. Among the recommendations, the NRC panel placed equal weight on addressing institutional management issues, particularly the capacity to address issues of intellectual property rights (IPRs) and biosafety, as on research and technology development. Building on this recommendation, USAID designed a program that integrated aspects associated with the dissemination and application of biotechnology, particularly management and technology transfer issues, with biotechnology research and training. Partnership with the private sector, which approaches research management with a commercial or application orientation, could contribute to achieving this goal of closing the gap between research and technology application. Finally, at this time USAID had already gained experience in public-private sector collaboration through its support of the Monsanto-Kenyan Agricultural Research Institute (KARI) program for development of disease-resistant sweet potato. This program illustrated the value of such partnerships in gaining access to technical expertise, as well as to proprietary technologies.

Despite the potential benefits of involving the private sector in international development, it is important to clarify that the private sector will not replace the role of the public sector in research generally, nor in facilitating broad application of biotechnology in developing countries in particular. Further, the goal of such partnerships is not to remake fully public sector research institutions in the mold of the private sector. USAID continues to recognize the strong record and primary objective of public universities in the area of research and training. USAID also recognizes that the private sector will not deliver biotechnology applications for many crops, such as some minor or food security crops, will not address all biotic and abiotic production constraints important in developing countries, nor will it realize commercial markets in all developing countries. The role of public sector research to filling these gaps remains vital. The goal of USAID in supporting collaborations with the private sector is to leverage additional funding and expertise to complement the role of the public sector.

Finally, in discussing the rationale for public-private sector collaboration, one should consider the private sector perspective on partnership with USAID and developing countries. In many cases, philanthropy and good public relations is a factor. In one instance USAID has funded a partnership that holds potential commercial value to the company, involving the characterization of potentially novel Bt strains from Egypt. But generally, short-term commercial benefit is not the principal factor. Companies may, however, have longer-term interests in developing a market relationship with a particular country for other biotechnology-based products. Collaborative research partnerships may assist the private sector in building relationships or an understanding of pathways for market access. Another potential motivation for the private sector is access to genetic resources such as in the aforementioned collaboration in Egypt to characterize potentially novel strains of Bt. This particular collaboration was significant in that the ownership of IPR-related to these Bt strains belonged to the Egyptian partner, and were made available to the company under the terms of a contractual agreement. Whatever the motivation behind private sector participation in such research partnerships, the role of seed funding from USAID appears significant to defraying some of the financial risk for the private sector partner, and encouraging their involvement in the development of biotechnology applications for developing countries.

Examples of Direct Public-Private Collaboration

During the 1990s, USAID has directly supported several public-private sector collaborative research programs, largely through the Agricultural Biotechnology Support Program (ABSP). Led by Michigan State University (MSU), ABSP represents partnerships between a number of U.S. universities, U.S. and developing country companies, the international agricultural research centers (IARCs), and developing country public research institutions (NARS or national agricultural research systems). The project is described in detail by Ives, Maredia, and Erbisch 1999).

The public-private sector partnerships USAID has supported include:

Monsanto Company and the Kenyan Agricultural Research Institute (KARI)

- This was the first USAID biotechnology-related public-private partnership
- Research aimed at development of virus-resistant sweet potato
- Monsanto donated (through a royalty-free license) virus-resistance technology to Kenya and other African countries for application in sweet potato
- Monsanto provided training to several KARI scientists in their laboratories for one to two years
- KARI-Monsanto partnership has continued long beyond direct USAID support or funding.

DNA Plant Technologies and Costa Rican and Indonesian-Owned Tissue Culture Companies

- A private sector-led research project was part of the original USAID program design, and this grant to DNAP was co-awarded and integrated into ABSP along with the Michigan State University-led program
- Research on development of commercial-scale micropropagation systems for tropical crops (banana, pineapple, coffee)
- Costa Rican company and DNA Plant Technologies have continued to work as business partners though USAID funding ended several years ago.

ICI Seeds and Central Research Institute for Food Crops (CRIFC)/Indonesia

- Focused on development of insect-resistant (Bt) tropical corn
- Included training of CRIFC scientists at ICI Seeds (that later became Zeneca) in use of proprietary transformation technologies
- Ultimately faced difficulty in negotiating technology transfer agreements for proprietary technologies.

Pioneer Hi-Bred and Egyptian Agricultural Genetic Engineering Research Institute (AGERI)

- Characterization of potentially novel strains of Bt isolated by AGERI in Egypt
- Application of Bt technology to development of insect-resistant corn

- Training of AGERI scientists in characterization of Bt and corn transformation technologies
- U.S. and Egyptian patents on strains are owned by AGERI; AGERI pursuing commercialization in Egypt and Pioneer has license in the United States.

Institutional Capacity Building

Complementing these examples of research collaboration has been ABSP's institutional capacity-building activities in the areas of IPR, technology transfer, and biosafety. Biosafety regulatory and management capacity has been conducted primarily in support of the application of public sector biotechnology research in developing countries. This will not be discussed further here. IPR issues, however, remain associated with the private sector for most developing countries, particularly the private sector in the United States and Europe. Developing awareness and understanding of IPR plays an increasingly important part to facilitating collaborations with the private sector where proprietary research materials or germplasm is involved.

ABSP's efforts in IPR have covered both plant variety protection and patent forms of IPR, with the principal aim of increased understanding of and capacity to manage the exchange of proprietary materials, in the context of collaboration with biotechnology or seed companies. This has been approached through workshops, courses, and internships with offices of technology transfer at two ABSP partner universities. To date under the ABSP program, MSU has served as the contractual intermediate on most research agreements between companies and public research institutions in developing countries. In this role, MSU assists both parties in establishing mutually beneficial research terms. However, the long-term goal is to develop the capacity among developing country institutions to negotiate and manage the terms of research agreements independently with the private sector. The role of MSU as an intermediate in the short term, and capacity building efforts in the area of IPR and technology transfer in the longer-term have helped increase the confidence of companies to engage in collaborative research that will involve the exchange of proprietary materials with developing countries. It has also helped developing countries protect their own interests when they contribute germplasm to the collaboration, such as in the Bt work between Egypt and Pioneer Hi-Bred.

Taking a step beyond an understanding of IPR, some of ABSP's public sector partners are pursuing an institutional model for technology transfer similar to that used by U.S. universities to promote a range of relationships with the private sector. Particularly notable is the interest in transfer of technologies to the local private sector, including seed companies and growers. Both Ministries of Agriculture in Egypt and Indonesia are developing offices of technology transfer to serve as the focal point for handling collaborative research agreements, licensing, and dissemination of technologies for large-scale testing or commercialization. These offices will serve as a means of strengthening the institutional capacity of the ministries' agricultural research system to manage IPR associated with collaboration with the private sector. It will also broaden avenues for dissemination of technologies, beginning to close the gap between research and technology application. ABSP has provided support to development of such offices through training programs, workshops, and the sharing of sample documents and agreements used by MSU's Office of Intellectual Property.

Constraints to Implementing Public-Private Partnerships

Although research collaboration with the private sector has been a valuable complement to USAID's public sector research and training in biotechnology, these new partnerships present challenges to all parties: USAID, NARS, and private sector partners in the United States. The most significant constraint surrounds IPR, due both to the lack of awareness and management capacity among public institutions as well as dissimilarities in the extent of protection afforded by national laws. ABSP's capacity-building efforts to address the former constraint have improved the level of confidence among all parties in the exchange of proprietary materials. However, the absence of patent protection does mean that some companies will not transfer certain technologies or certain crop applications, which might compromise significant commercial interests. This was the case, for example, with an ABSP collaboration between CRIFC in Indonesia and ICI Seeds (Zeneca). Ultimately, an agreement with ICI Seeds (Zeneca) for transfer of the Bt genes or maize transformation technology to CRIFC, for use in Indonesia, could not be reached due to the lack of patent protection and the level of proprietary interest by the company in those technologies. Based on that early experience, ABSP and USAID have taken steps to address IPR concerns up front, and use the resolution of IPR issues as criterion for establishment of such public-private sector collaborations.

Beyond IPR constraints, the three partners - USAID, developing countries, and companies - come together with different cultural perspectives and unfamiliarity with differing institutional approaches. Public research institutions in developing countries may be unaccustomed to negotiating with the private sector, and companies are unfamiliar with the bureaucratic processes and government contractual requirements associated with USAID funding. USAID must also recognize that the goals of the private sector differ from its traditional development partners in the university and nonprofit community. An important factor in resolving some of these differences and in building confidence has been the role of MSU in management of ABSP's public-private sector partnerships. MSU assists in bridging the three cultures. The university has had long experience in dealing both with USAID and with developing country partners. Since U.S. government policy changes in the mid 1980s, MSU, like most U.S. universities, has also worked with the private sector through their domestic technology transfer activities. For the private sector, MSU's management and experience defrays some of the risk associated with the unfamiliar partnership. For both USAID and the developing country partners, MSU maintains development objectives and interests at the forefront.

Benefits from the ABSP Experience

The rapid scientific and commercial development of biotechnology poses new challenges to international development organizations. Not only did biotechnology come along at a time of shrinking international agricultural research budgets, providing the challenge of expanding the research agenda without reducing existing priorities, but it also presents new policy challenges and a reflection on the role of the public sector. USAID has approached these challenges in part through pursuit of partnerships between developing countries and the private sector. Although the role of the private sector will not replace that of the public sector in realizing the benefits of biotechnology to developing countries, partnerships between the public and private sectors bring broader resources to bear on this goal. Under the ABSP program, developing country scientists have gained access to short- and long-term technical training in company laboratories. It is this access to technical expertise and biotechnology tools that has been the primary benefit of such partnerships. Not inconsequential, however, has been the financial support with which the private sector has matched USAID seed funding. In most cases, USAID funding has gone exclusively to support the expenses of travel and the costs of developing country scientists and not for research costs of the company. While no USAID collaborative projects have been a fully philanthropic exercise for the private sector, as for-profit institutions, they have deeper pockets from which they continue support of research which USAID helped initiate.

Finally, an indirect benefit of public-private sector partnership has been the introduction of a new management and institutional culture to public sector research (NARS) in developing countries. This is a new culture with greater focus on the outcome of research, on technology dissemination, and on working through a diverse set of partners, including the private sector, to extend the application of new technologies to farmers.

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Intellectual Property Protection: Who Needs It?

David L Richer

The world is faced with an unprecedented explosion in technology. Not all of this is universally welcomed – the irritation of mobile telephones on public transport comes immediately to mind – but the new technologies affect every area of our lives. Nowhere is this more true than in agriculture.

Changes in farming proceeded slowly but steadily for thousands of years, but accelerated during the last two centuries as scientists and other observers came to understand the farming process, the need for particular nutrients and rotations, and the nature of pests and diseases. Further acceleration followed after the 1950s with increased mechanization and the introduction of effective pesticides, herbicides, and fungicides. Biotechnology has accelerated the pace of change once again throughout the 1990s.

Biotechnology provides a major opportunity to meet the nutritional needs of an expanding world population, with finite land resources. It offers a new approach to the control of pests and diseases, it will provide crops of improved nutritional quality; and it will bring about increased yields.

Biotechnology is unlikely to be a complete solution to our agricultural problems, but it will play a key role in a sustainable agriculture that also uses integrated pest management and plant breeding techniques. That is the expectation in industrial countries, but it is only a hope for many others. There is a pressing need for the agricultural revolution to spread throughout the world, but to achieve it, we must provide an incentive to the innovators and owners of the new crop production technologies to share them.

There are many forms of encouragement - from argument to finance - and one of these is the subject of this paper. The process of technology exchange will be encouraged and facilitated by a strengthening of intellectual property laws, especially those of the developing countries. Unfortunately, like modern biotechnology, intellectual property rights (IPR) are controversial and often misunderstood.

This paper addresses some of these misunderstandings, and indicates how strengthening intellectual property rights will enable farmers throughout the world to receive the latest developments in crop production.

Intellectual Property

Intellectual property is a broad term used to cover patents, designs, trademarks, plant breeders' rights, copyright, and trade secrets. All of these have a part to play in the development and commercialization of plant production products. However, the three most important IPRs in this context are patents, plant breeders' rights, and trade secrets. None of these creates as much argument as patents.

A patent is a monopoly of limited scope, granted to the owner of an invention, for a limited period of up to 20 years. It is a right that is effective *only* in the country that grants the patent. While it is in force, a patent enables the owner to exclude others from using the invention commercially in that country.

A patent provides the innovator with a limited period within which he/she has the opportunity to recoup his/her investment in the research and development (R&D) of the invention. In return, the inventor discloses the invention to the public, and that disclosure enables other scientists and interested parties to use the invention in their own research. In due course, that research may lead to further innovation, and society will benefit. It is no coincidence that those countries with strong research-based industries are also those countries with strong intellectual property laws.

IPR is national in character, and like other national laws they vary from country to country. Attempts to bring some harmonization into this area have succeeded in the Agreement on Trade Related Aspects of Intellectual Property Rights, generally referred to as TRIPs. TRIPs, which entered into force in 1995, applies to all members of the World Trade Organization (WTO). TRIPs, however, is not a complete remedy for inadequate laws since it lays down only minimum levels of protection, rather than providing for the optimum. Nevertheless these levels are important, none more so than the basis for a patent set out in Article 27. Article 27 provides that patents shall be available for any inventions, whether products or processes, in all fields of technology, provided that they are *new, involve an inventive step, and are capable of industrial application.*

Patent rights are of little use if they cannot be enforced, and TRIPs also provides that member countries shall ensure that enforcement procedures are available under national law, so as to permit effective action against any act of infringement of an IPR. Enforcement is a particular concern in the field of biotechnology, where the capability of biological materials carrying genetic information to self-reproduce makes the copying of an invention and the infringement of patent rights all too easy.

The implementation of TRIPs will undoubtedly strengthen IPR in many parts of the world, but implementation is unlikely in the short term. Developing countries are permitted a transitional period, until 2005, within which to bring their intellectual property laws into compliance with the minimum standards laid down in TRIPs. Unfortunately, many developing countries lack the means rather than the will to take the necessary steps.

Objectives of IP Laws

The objectives of intellectual property law are stated succinctly in TRIPs: The protection and enforcement of intellectual property rights should contribute to the promotion of technological innovation and to the transfer and dissemination of technology. It is useful to consider these two aspects separately.

Promotion of Technological Innovation

The cost of developing a new plant protection chemical is over US$150 million; the cost of developing a new transgenic plant commercially is comparable. The investment in R&D must be recovered, and the monopoly period - provided first by patents and second by protection of the confidential data supplied in regulatory packages - is essential to provide the innovator with sufficient time and opportunity to make that recovery. Without IP protection, research-based companies would be unable to bear the risk of the major investment in R&D required to bring those technologies to the market.

The incentive effect of patents for developing countries is sometimes questioned on the grounds that these countries have little private sector research, and may produce few inventions. It is certainly true that inventors in those countries file few patents domestically or abroad, but without adequate IPRs, there is little incentive for local companies to set up their own research departments, nor for foreign companies to bring their technology and their research capabilities to the countries. It is left to the public sector to be the major fund provider of this research. That funding is vital, but it is not sufficient.

Technology Transfer

Farmers must have the opportunity to obtain modern crop production products at a reasonable price. Local research organizations need access to the latest technologies in the form of transfer of materials and know-how to further their own research, research which is often necessary to provide solutions to peculiarly local problems. These requirements can be met partially in developing countries by means of technology transfer.

The importance and benefits of technology transfer are widely recognized, and it is consequently a cause for concern and regret that in the field of crop production, technology transfer proceeds so slowly. While part of the problem lies in funding, another factor results from the two sides – the technology providers and the technology receivers – viewing each other and the technology transfer process with suspicion.

The private sector, potentially the major provider of new technology, ought to be eager to provide technology that will lead to the development of new markets. Companies are worried, however, that providing their know-how, whether by sales or by licensing, is tantamount to giving the technology away, unless it has the protection of enforceable IPR. In the case of biotechnology, where reproduction of plant material is relatively simple, companies may be powerless to prevent their technology from being copied and their markets destroyed or undermined by those who have not incurred the expenses of developing the technology.

The developing countries that want and need the technology fear the technology provider's demands for stronger IPRs which, they believe, will lead to higher prices and a drain on currency reserves. These concerns are real - and are discussed later - but there is clear evidence that strengthening IP laws leads to an increase in technology transfer to the benefit of both the provider and the recipient.

In the recent past, as an example, companies in industrial countries were reluctant to bring their products into the Chinese markets. There was inadequate patent and data protection, and once companies had established their market, generic manufacturers rapidly appeared to reap the benefit. These local manufacturers also exported the products to neighboring states where there was either weak or no patent protection, or where enforcing patents required a long and uncertain litigation process. As a consequence, China was deprived of the latest plant production products.

China has recently strengthened its patent law, and although it still needs improvement in its enforcement procedures, companies are now not only prepared to collaborate with Chinese companies, they are actively seeking collaboration.

Apprehensions

There are many concerns surrounding intellectual property law, and although these are often based on misunderstanding, they remain a barrier to progress. It is essential that those who believe that strengthening IPRs will be beneficial, should listen and inform. As a contribution to this process, I would like to consider four specific issues: prices, local development of technology, theft of resources, and ethics and morality. This is by no means an exhaustive list of possible topics.

Prices

It is argued that IPRs lead to an increase in prices. While it is true that products containing new technology will generally be sold at higher prices, that is not the same thing as a general increase in prices. The old technologies remain; indeed the introduction of new technologies may well make the old ones cheaper.

New genetically improved seeds are more costly to develop and produce, and those increased costs must be recovered. Farmers expect to pay a higher price for seed which will bring added value, but no farmer will pay more for the benefit than the increase in value which it will provide. Producers have little choice but to price their products so as to share the added value with the farmer.

Such arguments will be of little interest to poor and subsistence farmers. In order to receive the benefits of the new technology, they must first acquire the seed. Intellectual property will not be of much help to them. They will require the assistance and support of government agencies and international organizations such as the World Bank (Lele, Lesser, and Horstkotte-Wesseler 1999).

It is also argued that without IPRs, local companies would be able to copy the products and bring them to the local markets at much cheaper prices. That may be true but the advantages - such as they are - are short term, and serve to delay the introduction of new products. Moreover, if the originator ceases to act as product steward for the products, the result is often a flow of substandard products with inadequate instructions for their use, and which are ineffective.

Local Development of Technology

Some opponents of intellectual property claim that patents inhibit local research, and interfere with the work of local companies and research organizations.

The freedom to carry out research is safeguarded under patent law; experimental use for research purposes is not an infringement of the rights of the patent owner. Scientists are free to take the invention, to modify it, and to incorporate it into their own research programs. Dissemination and use of knowledge in this way is a fundamental part of the original contract between the owner of the patent and the state granting the right. It results in the faster development of the technology, and the introduction of new products and processes.

Public funding of research in developing countries plays an essential role in addressing local problems, but it will not be sufficient. There are always other demands on the available money. Local companies and research organizations need inward investment, in finance and in the form of materials and know-how. Yet again, however, it has to be acknowledged that these materials and know-how have a value to the private sector which will be unwilling to supply them if it feels that in doing so, it will lose control over them.

Publicly funded research organizations themselves do not always make the best use of the intellectual property protection that is available. The International Agricultural Research Centres of the CGIAR, for example, have tended to favor not seeking intellectual property protection, a position thatwas noted in the 1996 OECD Survey "Intellectual Property Technology Transfer and Genetic Resources": "[The] Centres have to operate in a changed research and funding environment and to collaborate with organisations for which intellectual property is a necessary counterpart to their willingness to invest in development. This has long been true of industrial organisations, and academic and public sector organisations are also now taking a more positive attitude towards protecting innovations resulting from their research. The International Agricultural Research Centres may therefore wish to review their own positions in this respect." The recent CGIAR center statements on genetic resources, intellectual property rights, and biotechnology reflect the evolution of the centers' thinking on these issues (CGIAR 1999).

Patenting the results of this research would not prevent the IARCs from making them available, but it will give them the option of entering into cross-licensing agreements or collaborations with companies holding other intellectual property of interest. Patents become bargaining chips that can be traded to further the research aims of the IARCs.

Theft of Resources

A recent attack on the private sector is that companies in industrial countries are stealing the resources and know-how of local populations, patenting these resources, and then denying the use of the technology to the population who had used it, often for centuries. The case of the Indian neem tree is often quoted.

Indian farmers have used the seeds of the neem tree for pest control for centuries. The American company, W R Grace, discovered a process for extracting the oil from the seeds, and applied for patents. Alarmists spread the story that the Grace patents would prevent farmers from continuing to use their traditional methods of pest control. The story created understandable consternation amongst Indian farmers and a worldwide outcry against big business. The story is nonsense.

Patents are granted only for inventions that are new and not obvious, and the use of the neem seeds in pest control fell into neither of these categories when Grace applied for its patent. Grace could not monopolize the use, nor could a patent give Grace ownership of the neem tree or its seeds (Grace buys seed on the open market). And finally, no patent can stop anyone from doing something which he was doing before the patent application was filed.

Similar stories are now circulating concerning the so-called theft of genes by the industrial world. If this does occur, then it will be illegal under the provisions of the Convention on Biological Diversity.

In any event, it is worth stressing again IPRs extend only to the new inventions created from the isolation and transference of the gene. The identification of a gene with a useful trait in a local plant, and the transference of that gene into a different crop plant, may entitle the discoverer to patent the use of that gene in the transformed plant, and perhaps to the transformed plant itself. However, the patent will give the innovator no rights over the original plants, which can continue to grow or be grown without reference to the patentee.

Ethics and Morality

TRIPs provides that inventions may be excluded from patentability if their exploitation should be prevented in order to protect *ordre public* or morality. It is important to note that it is the exploitation of the invention that is of concern here, not the invention itself. This distinction has been missed by many, and has resulted in the morality arguments being extended from the use of biotechnology to biotechnology itself, and from there to biotechnological patents. Parties who believe that biotechnology is immoral also argue that patenting biotechnological inventions – or, more emotively, patenting life – is immoral. Many patents, particularly in Europe, are presently being attacked on these grounds.

The consequences of attacking patents on moral grounds may not lead to the results which opponents of biotechnology hope, a point noted by Jefferson (1999) in his expert paper prepared for the Secretariat advising the Convention on Biological Diversity. The paper is an exhaustive review of the so-called "terminator" genes, referred to in his paper as "genetic use restriction technologies" and abbreviated to GURTs.

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

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

In less elegant words, what has been invented cannot be uninvented. Even if a patent is cancelled on the grounds that the invention is immoral, the inventor is still able to use the invention. Indeed, everyone is free to use it. Patent law is not the route to regulating the use of biotechnology (see also Leisinger, This volume).

The Way Forward

The case for strengthening IPRs in developing countries is, I believe, overwhelming, and the need to strengthen these rights is urgent. Countries should evaluate their positions without delay, and should be encouraged to implement TRIPs – or better, to improve upon TRIPs – as soon as possible. That said, the modification of intellectual property laws requires money and skilled advisers, both of which may be in short supply in some developing countries.

Funding and other technical assistance is available. The World Intellectual Property Organization (WIPO) has an agreement with the World Trade Organization (WTO) to provide assistance to developing countries to meet their TRIPs commitments, to provide technical assistance in drafting, and to train staff and provide software. However, the limited resources of WIPO and WTO remain a constraint and could mean that some countries are unable to meet their commitments, even by the 2005 deadline.

The World Bank and other international development agencies could certainly help by providing resources to the WTO or directly to developing countries for this purpose. Such funding would not only increase the number of countries meeting their TRIPs obligations by the deadline or even earlier, it would also promote open and constructive discussion of TRIPs in the next WTO round.

There is a further and additional approach which could save both time and resources. There is little logic in many different nations, each having similar standards and economic goals, to examine and grant patents for the same invention. The most efficient and economic approach is a regional organization, such as the African Regional Intellectual Property Office (ARIPO), the

African Intellectual Property Organisation (OAPI) or the European Patent Convention, which centralize the examination and granting of patents for all member countries into one office.

Conclusion

Enforceable and strong IPRs are essential to encourage the transfer of the latest technologies to developing countries, and for stimulating research in these same new technologies. They are vital for the modernization of crop production in developing countries.

Weak intellectual property laws and the inability to enforce intellectual property rights will limit the access of developing countries to the new technology, which is so important for the development of their agriculture and the saving of valuable environmental resources. Weak laws will inhibit much-needed inward investment.

Each country must evaluate its own intellectual property laws and needs carefully, but I would urge all developing countries to strengthen these rights as soon as possible, and for the World Bank and other international development agencies to assist them in this endeavor. I am confident that the benefits – the access to the new technologies and inward investment - will follow.

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Managing Intellectual Property – Challenges and Responses for Agricultural Research Institutes

Joel I. Cohen

Agricultural development has benefited from a long history of public sector/public good investment. However, public good investments in agriculture face an uncertain future because of (1) increased emphasis on market mechanisms forcing publicly funded organizations to respond to broader economic opportunities; (2) tendencies to limit freely germplasm for national agricultural research; and (3) changes brought about by the introduction of intellectual property rights (IPR).

The Changing Context for Intellectual Property

External forces are affecting agricultural research in developing countries and exerting pressure for change. These forces include the *integration of markets, growing activities of the private sector (including but not limited to multinational companies), and innovations in national and international legal and regulatory regimes*. Changes in research management and management of intellectual property are occurring in response to these global trends, each having the potential to redefine how agricultural research organizations will provide public goods to meet their country's food and agricultural needs.

In adjusting to these external forces and changing the management of IPR, a national agricultural research organization (NARO) must take into account (1) the policy framework guiding its mission, objectives and programs, (2) its stakeholders, and (3) its research scientists. Given these various interests, and as the management of intellectual property (IP) attached to agricultural biotechnology is a relatively new phenomenon, developing, implementing and managing such a dynamic system can present formidable challenges and complications. The primary purpose of intellectual property ownership by NAROs, however, is to promote the fundamental research mission of the institute, keeping in mind the development of products available for use by small- and medium-scale farmers.

Clarification of ownership of assets and freedom to operate have important roles to play in this regard. Assets include research inputs, including patent rights for a gene sequence or for a laboratory or industrial process, and outputs. Copyrights and trade secrets may govern access to and use of experimental techniques and laboratory notes. Patents for research outputs may be sought for novel processes and products, while plant variety protection is sought for new crop varieties. Management needs to ensure that (1) ownership of intellectual property used by a research organization is respected by all who use the property, and (2) organizations are in a position to identify, secure, manage, and exploit the intellectual property that they generate.

Managing IP at the Institute Level

Various consultations, studies and related workshops have highlighted complexities regarding management of IP for NAROs, including several sponsored by the International Service for National Agricultural Research (ISNAR), and reported in Cohen (1999). They have led to the identification of five tasks and associated responsibilities that help institutes structure responses to the challenges facing them with regard to the management of IP. The five tasks proposed here include the following:

1. *Clarifying institutional roles*

- Relating legal status of the institute to relevant legal frameworks, regulatory regimes and stakeholders
- Defining institutional policies for assembling and using an IP portfolio, including how research is conducted, and its publication and disclosure
- Clarifying opportunities available for scientists between research financed for/by commercial sector versus that disseminated as public goods
- Develop cost calculations and records for IP.

2. *Identifying IP*

- Promoting general awareness and understanding of the importance of IPRs
- Conducting an inventory of IP used in the institute
- Disclosing IP generated to the research liaison office.

3. *Securing ownership*

- Introducing IP rules as a part of contracts for research staff and visitors
- Obliging the disclosure of IP generated by researchers
- Attending to the registration of IPRs.

4. *Managing IP*

- Liaison with IP suppliers
- Policing licensed IPRs
- Integrating IP policy with institute's mission to benefit expected end-users
- Instructing researchers as "expert witnesses" in cases of infringement or other inquiries.

5. *Technology transfer and marketing IP*

- IP evaluation
- Liaison with IP exploiters (industry and commerce)
- Developing IP agreements (licenses and material transfer agreements-MTAs)
- Formulating a remuneration strategy.

Institutional Responses – Selected Examples

Research, case studies, and examples from national and international organizations have been selected to highlight challenges and responses regarding the management of IP. They also illustrate various aspects of the proposed tasks for IP management

Use of Proprietary Technolgy: Conducting Institutional Inventories

One of the changes affecting agricultural biotechnology research is the successful development of new tools and inputs from the private sector. These technologies and materials are finding wide utility in global agricultural research. IPRs protect most of these inputs.

Proprietary technologies and materials are those that are privately owned, managed, or protected through some sort of IPRs. Developers of such materials and technologies may place restrictions on their use during the research stage or in a later stage, when products derived from the protected materials are ready for wide dissemination. A growing number of research inputs are protected as intellectual property. This section focuses on the use of such protected or proprietary materials and technologies among seven CGIAR centers and from five countries in Latin America. It documents the difficult and often confusing situation that institutions face regarding the use and dissemination of products resulting from proprietary science where others hold IP rights.

The studies aimed to (1) assess the extent to which proprietary applications of biotechnology (technologies and materials) are being used in NAROs and CGIAR centers, (2) present potential legal implications regarding use of the identified proprietary technologies and materials, and

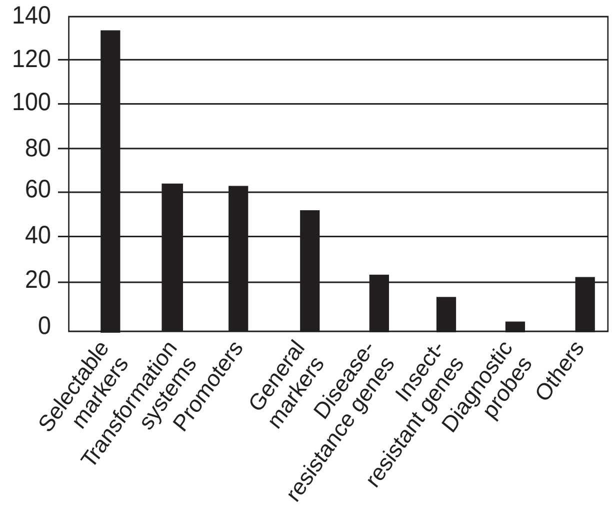
(3) synthesize findings and recommendations to stimulate further discussion.

CGIAR study. Every center responding to the survey currently uses proprietary inputs (technologies and materials) for biotechnology research. In total, 46 discrete technologies and materials were reported, covering eight technology categories. These included transformation systems, selectable markers, promoters, genetic markers, disease resistance genes, insect resistance genes, diagnostic probes, and other technologies or materials. As most centers apply these technologies and materials in several commodities, we recorded 166 specific applications of proprietary research inputs. Of the eight technology categories surveyed, selectable marker genes, promoters, and transformation systems show the broadest utility across centers, indicating the role that proprietary technologies and materials have assumed in research at the international agricultural research centers (IARCs), as is true for advanced research centers globally. Most, but not all, centers are using proprietary genetic markers, a set of disease- and insect-resistance genes. Some centers have integrated these technologies more than others across their research portfolio (Cohen and others 1998).

NARO study. In 1998, ISNAR conducted a similar survey among NAROs in Brazil, Chile, Colombia, Costa Rica, and Mexico. At the time of the study, none of the institutions that were surveyed had suitable institutional or legal frameworks for related IPR topics. With the exception of two research centers, none of the institutions had an office or person responsible for assisting the researchers in issues of intellectual property, access to adapted technologies, technology transfer, or ways to protect their own inventions. The researchers were functioning without the institutional support needed to address these issues for their research.

The range of proprietary technologies and materials used by the research organizations and the number of applications reported in each category are summarized in Figure 1. In total 34 different technologies and materials as well as 386 specific applications of proprietary research inputs were reported. While not all proprietary inputs pose difficulties regarding intellectual property ownership and the dissemination and use of resulting products, this study has helped research organizations explore areas where potential difficulties may occur.

Figure 1 Proprietary technologies and materials covered in Latin American study



With regard to proprietary technologies and their permission for use, the Latin American study found that MTAs accounted for 25 percent of acquisitions, being the most common means, as is true for the CGIAR centers. This study highlighted the importance of international collaboration and purchase of proprietary technologies, totaling 35 percent of acquisitions. Other applications either lacked formal written agreements or information was not available (35 percent). The use of licenses, as another form of technology transfer, was very limited, accounting for only 5 percent.

IPR and proprietary science

As demonstrated by these studies, international and national organizations using biotechnology for agricultural development are operating in a complex environment, reflecting a transition from earlier periods where products and processes for research resided in the public domain. The increasing acquisition of proprietary technologies, their use in research serving the public good, and the vast array of developing countries where such use occurs, raises questions regarding appropriate IPR arrangements. However, for many scientists and institutions, such concerns are overwhelming. Yet their work continues, trusting that as final products are developed, no legal instruments will block the dissemination of improved materials to their clients.

Adopting a more proactive strategy requires significant time and investment in taking steps to find institutional mechanisms to address these complex challenges. Such advancements are being made by both the CGIAR centers and by larger national research organizations in developing countries. National and international institutions are exploring whether they should invest in IP management or adopt a "wait and see" approach. They realize that no one clear position has been given by commercial biotechnology providers, as owners of much of the IPR for applications identified, regarding the use of third-party IP used for or with developing countries.

Practitioners Workshop in Costa Rica

Institutional inventories, such as those described for selected CGIAR centers and Latin American agricultural research organizations, present a first approximation regarding use of proprietary inputs. They provide a source of common information, allowing for analysis that is more detailed and formal IPR audits, and serve as a foundation for work regarding the institutional management of IP.

The data from the Latin American study were reviewed and verified before presentation to a workshop held by ISNAR in Costa Rica, in September 1999, of key individuals having institutional responsibilities for IPR (Falconi and Salazar 1999). Participants included senior research scientists and program coordinators from five NAROs. The purpose of the workshop was to discuss and analyze the results of the survey of proprietary technologies among selected Latin American research organizations, and to identify management needs. The specific objectives were to:

1. Review in detail the study's findings and recommendations
2. Assess the legal implications of related IPR developments
3. Assess individual and institutional needs with regard to study findings
4. Identify future case studies in the management of IPR and review the case study approach.

Identifying practitioner and organizational needs

Practitioner needs refer to knowledge that scientists need to help address the problems identified in the study. These needs are classified as either technical (acquisition of skills and abilities) or those that are related to management and policy. Priorities emerged with regard to managerial/policy needs to:

1. Promote/support the creation of institutional IP units
2. Promote/motivate the development of institutional IP policy/strategy
3. Promote IP management parameters during research planning
4. Promote negotiation needed for licensing proprietary assets at institute level
5. Introduce new criteria for the management of information related to proprietary technologies in research institutes (for example, confidentiality, timing of publication).

Identifying organizational constraints

After analyzing and prioritizing individual practitioner needs, participants were asked to identify organizational restrictions regarding the management of IP at the institutional level. These included the following:

1. Lack or limited development of an IP unit to handle technology transfer, licensing, institutional negotiations, training, protection of assets/cultivars, processes and products of research
2. Lack of clear policies related to internal and external use of proprietary assets
3. Lack of economic studies to support the licensing in or the protection of technologies and products
4. Lack of clarity in present legislation, such as TRIPs requirements and definitions of terms such as natural process, discovery and invention, and part of the total plant.

Institutional Responses – Selected Examples

Embrapa, Brazil

Since 1995, the Brazilian Agricultural Research Corporation (Embrapa) has developed and begun to implement a new internal policy for intellectual property protection. Embrapa has given high priority to its responsibility for protecting intellectual innovations, thereby helping to ensure that they become institutional assets. Its institutional IP policy published in 1996 states the following basic principles:

- Embrapa has to maximize its capacity to use intellectual property rights to facilitate the transfer or the licensing of technology, processes, and products without sacrificing its social mission
- Embrapa has to seek legal protection for the technologies, processes, and products derived from its research program, giving credit to employees as inventors
- Embrapa may authorize the use of its protected assets through a royalty-free license only when its social commitments are at risk and only after approval from its Intellectual Property Committee
- Embrapa research centers cannot release a new cultivar or disclose any process or product without previous analyses by the designated committee of the possibility, convenience, and opportunity for protection.

Following implementation of the policy, the institute began to discuss necessary internal changes by considering the economic and social consequences of forthcoming policy changes (Sampaio, This volume; Sampaio and Brito da Cunha 1999). The following challenges regarding intellectual property protection were identified:

1. *Implementing an internal intellectual property policy that requires legal support.* Embrapa has been implementing an internal policy, in conjunction with Congress approving the necessary legal framework.
2. *Raising awareness of intellectual property.* The institute has launched an internal awareness-raising campaign through lectures, courses, and workshops to promote and diffuse the new intellectual property policy. This campaign would also help researchers understand that they should have their research results prescreened for possible intellectual property protection before publication.
3. *Creating assets from intellectual property.* Embrapa should protect all assets coming from its research programs. Thus, revenues can be obtained through licensing, or the institute can allow a third (resource-poor) party to use an asset free.
4. *Establishing regulatory infrastructure.* Embrapa hired and trained personnel to manage the implementation of its policies and intellectual property laws. It took into account that this includes a learning curve for preparing and filing patents and negotiating and licensing a protected technology.
5. *Modifying licensing system.* Embrapa is in the process of modifying its cultivar licensing system and its basic seed production program to suit the IPR legislation and the growing presence of a much stronger and competitive private seed industry in the country.

AARD, Indonesia

Similar developments have occurred in the Agency for Agricultural Research and Development (AARD) of Indonesia. Here, a new office for intellectual property and technology transfer was established (KIAT), in July 1999. The overall task of KIAT is to manage IPR resulting from AARD center's research and to transfer technology to the private sector (T. Subagyo, pers. comm., 1999). The office has three main tasks:

1. Provide information and services for technology in agriculture
2. Serve as a "one stop" service for agribusiness and the private sector
3. Provide guidance on intellectual property rights protection.

With regard to the first task, that of providing information, KIAT searches and prepares research results from AARD centers that would indicate products ready for commercialization. Certain products arising from AARD research efforts have been patented and sold, such as *Rhizoplus*, a fertilizer for soybeans containing Rhizobia and several other microbes. KIAT functions in this way across the seven research centers that comprise AARD.

With regard to relations with agribusiness, KIAT hopes to better address services sought by the private sector and other investors, beginning by preparing feasibility studies and moving to marketing. Working in collaboration with the

Director of IPR in the Department of Justice, IP is sought for research results coming from the individual centers.

Regulatory Regimes and IP Challenges facing the IARCs

Preparing responses to specific regulatory regimes has also been important for the IARCs of the CGIAR. These have included responses to the CBD, FAO agreements on germplasm, and awareness regarding potential national responses to WTO, UPOV and TRIPS agreements (Hawtin and Reeves 1998). In this context, the centers have put forward *Guiding Principles for the Consultative Group on International Agricultural Research Centers on Intellectual Property and Genetic Resources*, which was adopted as an interim working paper by the CGIAR in 1996 (CGIAR 1999).

The CGIAR Panel on Proprietary Science and Technology reviewed these guiding principles in 1998. Most of the panel members were satisfied with the Guidelines, but it was felt that some changes were needed, particularly the use of clear mission-based guidelines when seeking IP protection, and some changes in emphasis (TAC 1998).

In addition, the Panel commented on the desirability of strengthening CGIAR and IARC capacity for managing IPR. An organizational plan was presented that could contribute toward an effective intellectual property management program. There would be two aspects of such a program, one helping with problems regarding access to proprietary science owned by others, and the second regarding protection of new developments made by CGIAR centers themselves. The report stated that, "any program developed would begin with a centralized resource center and would require a local liaison at each center."

Following the Panel's report, several developments have occurred to enhance center management of intellectual property and related issues. These have included implementing the Central Advisory Service (CAS) for Proprietary Technology for the CGIAR,based at ISNAR, The Hague (ISNAR 1999), individual centers undertaking formal IP audits, focused technology development and related IPR protection undertaken in association with CAMBIA, Canberra, Australia, and the beginnings of "Intellectual Property Management Units" among selected centers.

Institute Responses and the Five Management Tasks

The previous examples, taken from NAROs and CGIAR centers, illustrate IP management challenges and responses, and their relation to the five management tasks identified earlier. An essential aspect for each example has to do with *clarification of institutional roles*. In taking on these actions, particularly in relation to legal frameworks, various cases cited stressed the need for their research organizations to make decisions regarding IP management and protection more transparent and responsive to stakeholders.

This includes the need to clarify the range of opportunities available to scientists. This becomes increasingly important as NAROs and the CGIAR centers explore strategic partnerships with the private sector, and the receipt of funds from a broader range of investors. Scientists seek clarity as to how and if they should enter these agreements, and how to balance such research with those targeting equity or sustainability objectives.

Management of IP means that there are increasing costs for research. This is true whether such management occurs in an ad hoc manner through consultations, a centralized service, or decentralized systems with research liaison officers at each center. Cost effectiveness of providing IP management is in need of study and clarification. Institutional needs for IP offices and professional staff, as well as the support required for associated actions, means that costs must be carefully considered and justified against other needs.

Issues regarding tasks 2 and 3 (*identifying and securing ownership of IP*) were explored in earlier sections, as to how institutional inventories mobilize more detailed analysis of IP, including formal IP audits, as well as provide educational opportunities for staff involved. However, resolving ownership and operational freedom will require further concerted action.

With regard to responsibilities described as *managing IP*, among developing country institutes, there are few examples as to how they will evaluate and protect IP arising from their scientist's efforts. However, there are examples of subsidiaries or advanced research institutes that provide such evaluation services. Additional actions have not been discussed, including monitoring and enforcing relevant IPRs and the integration of IP policy with a given institutional mission.

Technology transfer and marketing IP has been mentioned in many of the cases cited. Institutions are exploring ways in which enhanced management of IP and institutional assets can facilitate technology transfer. Here, special attention will be needed to ensure that such transfer occurs not only to commercially able partners, but also to providers or suppliers that can address institutional needs for providing products addressing equity and sustainability.

NAROs and IARCs: Differing Needs, Different Responses

Responses with regard to IP management and the proposed five tasks will differ between NAROs and CGIAR centers. For example, there are greater expectations to patent inventions by the NAROs than by the international centers, especially given the intention that center patents, if needed at all, may be essentially defensive in nature, and not sought as an additional mechanism for finance.

Furthermore, these two systems, one national and one international, each have different policies and reasons for assembling and using IP portfolios. For the CGIAR centers, an emphasis has been placed on managing IP to achieve bargaining chips, in seeking to gain access to protected technologies and as a means to secure freedom to operate, not to obtain financial returns from public investments. As seen in the case of Embrapa and AARD, expectations regarding IP assets appear quite different, especially with regard to facilitating greater access to the private sector for commercialization and expectations of remuneration from technology that is commercialized.

Decentralized Research and IP Management

Developments cited in this paper describe advisory services for management of intellectual property conducted through centralized IP offices serving decentralized research systems. While development programs strengthening national agricultural research increasingly emphasize greater decentralization, with regional and local decisionmaking, when it comes to providing IP expertise, a centralized office or service may be more economical and viable.

The centralized offices described in our case studies provide agricultural research organizations with an economy of scale by investing in one unit to work with designated counterparts at their local research centers, as is the case for Embrapa and AARD. The effectiveness of such arrangements will depend on the services that the centralized facility provides, its availability and responsiveness to the needs of the local client centers, and the ability to effect decisions taking into account both local and strategic needs. Similar considerations have been given to a centralized advisory service for IPR from the CGIAR centers (Reeves 1999).

Centralized offices assisting with IP management do not take over research functions. They exist to address specific responsibilities highlighted among the five tasks identified earlier, relieving local institutes, centers and scientists from the full burden of these responsibilities. The centralized facility can also undertake studies with regard to topics such as benefit sharing and alternative mechanisms to protection. Over time, a balance of responsibilities can be envisioned, moving from advisory services on the one hand, to more focused and centralized management practices on the other.

Such centralized offices will not replace the need for staff trained in IP issues at local institutions, but rather reinforce the need for communication between the local research institutions and the centralized offices. Agreement on a division of labor could be achieved by allocation of responsibilities based on the five tasks. Recently, the CGIAR's Central Advisory Service (CAS)(ISNAR 1999), reviewed such services for the CGIAR centers. The centralized services could provide for the following:

- Educational programs
- Organizing information and policy development workshops
- Maintaining a registry of expertise and an information base on new patents and IP developments

- Research on topics of system-wide importance
- Designing a system-wide patent disclosure form specific to CGIAR
- Assisting in negotiations with IP holders to protect a center's freedom of action
- Providing principles for strategic alliances with private sector.

As experience grows, the CAS may also begin to advise the NAROs on IP management in ways that would facilitate interactions with the international centers.

Enhancing Capacity for Scientists, Managers and Policymakers

Challenges lie ahead as institutes either begin or continue to define the means by which they will manage IP. Continued and expanded education opportunities are needed to address these challenges over the long term; addressing not only sweeping institutional changes, but also the new skills needed by individuals faced with such daunting challenges and responsibilities. The need for capacity and competency in the area of IP management is one of the new frontiers that agricultural scientists, managers and policymakers will face in the coming century.

The Scientific Challenge

Agricultural scientists are clearly affected by globalization trends and intellectual property regimes. For many, this means becoming more strategic and systematic in their collaborative research programs, and seeking clearer understanding of the institutional implications of their work. There are also many administrative matters to attend to, including the way in which laboratory or research notebooks are handled, and knowing when and how to make public presentations or disclosures of research results (Crespi 1998).

The Management Challenge

In many of the case studies cited, researchers function without the type of institutional support needed to properly manage IP. The examples provided from the NAROs, CGIAR centers, and universities illustrate the growing importance that such management has for research organizations responsive to emerging IPR regimes and cognizant of the potential significance of their own assets. In this regard, gaps exist between scientists and institute directors, between directors and clients, and between institutions and policymaking bodies where modifications of IPR regulations are needed.

Serious attention is needed to address these management gaps to ensure that the primary purpose of intellectual property ownership by NAROs promotes their fundamental research mission. With regard to individual institutes, the opportunity to provide research liaison officers or contact points for the centralized service should be considered (Blakeney 1999). The research liaison officer can improve the understanding of legal rights given for protecting creative effort and will help to further the institution's research mission. Most importantly, this means protecting and maintaining the IP assets of the institute and developing awareness and appreciation of the use of patent documents and registered plant variety data as research resources.

The Policy Challenge

The previous examples have given indications of how national and international research systems are considering policy matters with regard to IPR. However, many questions are still left unanswered regarding *a research system's ability to provide public goods while working in the context of the three global trends*: market integration, emerging private sector, and changing legal and regulatory regimes. Further studies addressing the provision of public goods by national and international research organizations, in relation to globalization trends, are urgently needed. Such studies can help define modalities or scenarios for agricultural research and explore means for appropriate benefit sharing among stakeholders, including alternative treaties to UPOV and opportunities for implementing "farmers' rights" as well as "breeders rights" (CoFaB 1998).

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Communicating About Biotechnology and Addressing Public Concerns

(Editors' Note A special session on communications included a panel of science interpretive writers with international experience in industrial countries, developing countries, the biotechnology industry, and nongovernmental organizations. Panel members were asked to address the central question of how controversial topics such as genetically improved organisms are handled from their perspective. Other issues included the role of the research community, the role of science writers in educating the public (without telling them how to think), and how science writers can do a better job explaining how science goes about finding answers. The following session report provides some useful insights.)

Background

Rick Weiss

How do science writers report the news of a global scare, such as the controversy over genetically improved organisms (GIOs) in Europe, without escalating the scare? Most important, how do we decide whether there is something to be afraid of in the first place?

Many scientists and international development experts probably have a polarized view of the media's role in the ongoing debate over GIOs. Many probably believe that the press has only served to fan the flames of panic. Perhaps seen from the other side, some may think that the proper job of the media is to convince the public that science is the key to a happier future.

The truth is somewhere in between those two extremes. Most media people do not want to foment panic, but they are paid to be skeptical. It is a long tradition in journalism to be skeptical, and for reporters to see themselves as watchdogs for the public good. And in this sense, the press, at least in the United States, is sympathetic to the precautionary principle, words that are well-known in Europe but somewhat new in North America. Most science writers do not feel it is their job to sell the public on science. We must however, continue to explain how science goes about finding answers, which after all is an elegant way of getting at the truth.

At the same time, science writers like to think of themselves as rational voices, and are happy to pass on to the public whatever enthusiasm and promise that scientists may be able to rationally engender in them. It has become an accepted part of a science writer's job to help educate a public who are generally poorly informed about science. To make a story understandable to the public, it is often necessary for a science writer to use valuable column space to define technical jargon or interpret what the scientist is trying to convey.

That is a difficult job, of course, and it is especially so in social issues such as the one affecting GIOs, because the job of keeping the public informed about itself and its feelings is, by definition, a circular one. The media influences public opinion by what journalists write, and then they write about what public opinion is. We take polls to take the pulse of the public, and when we publish the results of those polls we in turn influence public opinion, and then we write about how public opinion is changing.

If you polled people in the United States about whether they want genetically improved foods labeled, most would say yes. Pose another question: Do you want them labeled if the FDA has said they are safe and it is going to cost you an additional five cents for every product that has a new label? Just about everyone will say no. How the question is asked makes a big difference.

Industrial Country Perspective

Carola Kaps

Why is public opinion in Germany so negative against genetic engineering? Europe has been plagued by many food scandals (for example, the BSE scandal in the UK and the foodstuffs scandal in Belgium). These were not handled very well by the public sector institutions. There is a severe case of mistrust in the public mind, and people generally do not trust regulators.

We have a regulatory system that is not sufficiently effective, which is one reason why Germans are not eager to have GIOs. Some companies in the food distribution area have publicly stated they will not carry GIO products on their shelves.

There is also a subtle anti-Americanism as well because of the hormone beef issue, and consolidation in the seed sector by mostly American companies.

A third issue was that the first generation of the GIOs, which are mostly in the bulk area of agricultural products, really did not have a major benefit that could be explained to the consumer. It was more industry- and productivity-driven. We lost the chance to explain to consumers and influence public opinion that it is not only an industry affair, that it is not only multinational, that it is not only American and American trade interests, but that there is really something to be gained for everybody.

Many people in industrial countries take a negative view of GIOs, which is an arrogant attitude taken in the context of local food surpluses, and a generally high standard of living. Can we then dictate to developing country farmers who urgently need to increase their productivity just to feed their families? Developing country people, including farmers, can decide whether they want to use this new technology, but they need markets for their products. It would, therefore, be better to have everyone convinced that biotechnology is a good thing.

Why do I think the battle is not lost? Europeans, and Germans in particular, do have a heart for the developing countries. The goodwill of the people is there.

If a message could be sent that this is really something that helps the developing countries from a development point of view, from an income point of view, from a poverty alleviation point of view, I do believe that public opinion could be swayed.

Because of this subtle antagonism against multinationals, I believe that the public institutions and the CGIAR System have a mission that is geared toward development and toward the developing countries. You are not afraid to become partners.

This conference is a positive step, though I would have liked to see such a forum organized much earlier. The CGIAR system must do more in terms of public relations, to be more proactive, to share success stories that are interesting and that will catch the attention of science journalists. A good example was the CGIAR system hairy potato story, which received international coverage of a new potato variety able to resist insects.

In the mid 1990s, there was a big issue about Bt rice being introduced at the International Rice Research Institute. There was considerable local and foreign NGO activity trying to prevent this. This should have been a wake-up call for the System to say: let's get together, let's be proactive. You may have had a success like Jubilee 2000, and public opinion would not be—at least in some industrial countries—so negative toward biotechnology issues.

Developing Country Perspective

Govindan Venkataramani

I will describe briefly how science, particularly agriculture, is being covered in the Indian media. I fully endorse the view that the task of science journalists is to understand science before teaching or informing others.

The media plays the role of watchdog in a civil society, besides having a role in educating the public. The responsible journalist always takes a balanced view when covering a scientific breakthrough

In essence, media provides an active platform for a meaningful dialogue and discussion between the scientific community and the general public.

Several benign biotechnologies that are noncontroversial have been well reported in the media. The relevance of the biotechnology revolution in meeting the food challenges in the future is also being widely acknowledged.

The media in India has extensively covered success stories of biotechnology innovations in the fields of agriculture, horticulture, livestock production, medicine, and forestry. The tissue culture technology, for instance, has been hailed as a boon for horticulturists and foresters. It has also been advocated as the technology to conserve plant genetic resources for future generations.

Similarly, embryo transfer technology and the wide range of new veterinary pharmaceuticals and vaccines have been welcomed with enthusiasm. Many such environmentally benign biotechnologies that would foster sustainable agriculture have been received with warmth.

The ecotechnology revolution that blends the time-honored farmers' wisdom and the environmentally benign frontier technology continues to get attention in the media. Energy- and space-saving biotechnologies are needed that will maximize productivity per unit of land, use of water and other inputs.

The media also focuses on safety and ethical issues regarding modern biotechnology, particularly the use of GMOs in agriculture.

The views of the scientists about the safety of the products of genetically improved plants and other organisms have also been given equal space in the media. In the last few years, some specific issues that jeopardize the environment, food security, and human nutrition have been extensively discussed, and the media has espoused this cause.

Various viewpoints and the fears of the public and farmers have been well reported by the Indian media, and this awakening among the public has led to some welcome policy changes by biotechnological firms. A recent public outcry about the genetic use restrictions technologies (the so-called "terminator" gene and "verminator" gene) has caused a multinational company to initiate a series of public awareness campaigns, including the development of a Web page and publishing biotechnology updates.

The company has just come out with a public statement that it did not intend to commercialize this kind of technology that would prevent farmers reusing seed. The pressure groups and the wide media attention brought about this important development.

Other hot issues related to biotechnological research in recent years are bio-piracy and intellectual property rights. Some unscrupulous firms have violated ethics and safety issues, and the NGOs and farmers associations are challenging them.

Historical varieties in a region and the time-honored technology or knowledge of traditional communities are also well documented in the media. These reports, such as the Basmati rice developed at least 250 years ago in India and Pakistan, support the cause against the patenting of such traditional material.

At a recent International Conference on Genetically Modified Plants: Implications for Environment, Food Security and Human Nutrition, organized at the M.S. Swaminathan Research Foundation, some participants felt that the existing regulatory mechanisms in India governing the field-testing of GMOs are not adequate and do not instill a necessary degree of public or media confidence in bioethics and biosafety in India.

We need a better understanding of the issues and greater interaction amongst the public and private sector scientists, NGOs, media, policy groups, and the judiciary. Interactive workshops and dialogues could resolve conflicts that arise.

The most important recommendation from the recent international conference in India is the need for information empowerment and education at all levels, starting with the farming community. This is essential in taking the benefits of biotechnology to promote sustainable agriculture. The media should use its strength of ethics, integrity, and transparency to support the cause of taking the benefits of environmentally benign biotechnologies to usher in an evergreen revolution.

An Industry Perspective

Walter von Wartburg

I believe biotechnology, in whatever form or field, will eventually be socially accepted. I also believe it will take quite some time for what I call the societal gestation of this new technology. How long will depend on good corporate behavior and how well communication is handled.

Communicators must pinpoint the field of biotechnological application, narrowing down to interesting stories, such as the one on the hairy potato from Centro Internacional de la Papa (CIP).

Science journalists should also consider that the fears and public anxieties are quite different in different areas of biotechnology. When one considers genetically improved microorganism, the fear often is for public health and safety. Are we going to have a catastrophe that may not be reversible?

If you consider genetically improved plants, it becomes an issue of ecological damage, possibly irreversible ecological damage. For genetically altered animals, the issue is the integrity of creation.

If we look at human areas of biotechnology application, the issues are human rights, individuality, and ethical freedom.

The topics and the concerns change depending on the technology you use. For developing countries, the considerations are often quite different, and reporting must be tailored for this audience.

Over the years I have identified what I call attitudinal sins, the things researchers and research administrators should not do.

- The first is the wait-and-see attitude. If you receive criticism, you do not react because you think science is self-explanatory, and people will find out one day how marvelous this all is.
- Second, if you receive criticism and the criticism is mounting, you adopt a belittling attitude, as if the problem does not exist. This can result in reduced credibility of future work.
- The third one is the "everything under control" attitude. People know what happened in the atomic energy industry. Is the mad cow disease under control? It is well to remember that not everything is under control.
- The next one is the "we know best" attitude, because we developed the technology. The difference between knowing best and knowing better is sometimes quite important.
- "You have to believe me." Nobody has the absolute truth or the absolute trust. Trust is a matter of experience and trust has to be earned.
- Another attitudinal sin is "freedom works best," because a system of total freedom has always produced the best possible economic output. This is probably not true, because people want to have at least some level of control. Government control over biotechnology makes much more sense in the long run, in my view.
- The last one is the "discredit the critics" attitude. This one is self-explanatory.

We should all take opposing views seriously. If this message is all you take away from the conference, I will have made my point. Opposing views are part of the problem-solving process in a mature society, so you have to take them seriously, and deal with them.

- Establish an ongoing stakeholder dialogue. Do not think that once you have written that marvelous booklet that your communication work is complete. Communication only has value if it affects perceptions.
- People want more choice, not more education. People want to know all the arguments for or against, then they can make choices.
- The concept of benefit/risk management should be explained fully. Explain what you mean by benefits: social benefits, individual benefits, and the distribution of benefits, and do the same regarding risks.
- Integrate different scientific disciplines: it is not just toxicity or genetics. It is all the disciplines, all the "ologies" of science, from toxicology to pharmacology to sociology and so on.

Trust is the ultimate element on which you can base communication. If you are trusted, what you tell people will change perceptions, or will at least affect perceptions. If you are not trusted, communication fails.

If people believe that something is self-explanatory, especially when it is as complex as biotechnology, they will lose out. We must communicate to change perceptions, to convince that elusive 51 percent of the key people that biotechnology is a good thing. Social acceptance will follow.

An NGO Perspective

Jagdish Patel

The UK Food Group is a network of 30 organizations concerned about worldwide food security. The network includes Oxfam, Action Aid, Save the Children, and Christian Aid. My views on genetically improved foods are personal, and do not necessarily reflect those of the network members. My presentation is generally based on research that has been undertaken in the U.K.

Government officials, politicians, and scientists frequently express frustration at so-called inaccurate and emotional reactions of the public in the GI debate. And often the campaign groups and the media are singled out as villains, guilty of spreading hysteria through stories that are based on half-truths or unproven speculation.

A recent report published in the U.K. ("The Politics of GI Food") demonstrates that many ordinary people have a thorough grasp of issues such as uncertainty. And if anything, the public in the U.K. are ahead of many scientists and policy advisors in their instinctive feeling for a need to act in a precautionary manner. I will be drawing heavily in my presentation on this report.

I believe the public is not ignorant of the broad issues, that the public trust has been lost, that the issues that concern the public have not been addressed by the regulatory bodies, and that we need greater public involvement in the policy decisions on GI food and crops.

The reactions of the public in the U.K. and some parts of Europe have been formed to a considerable extent by the BSE, or mad cow disease, incident as well as the farce that was the BSE crisis. Uppermost in people's minds is the unreliability of the scientific reassurance in the BSE case. Subsequent scientific assurances are still not sufficient to convince the French government or the public that that beef is safe.

In the case of GI foods, the public did not need to know about genetics to judge Monsanto when it attempted to introduce GI foods by mixing GI and non-GI soya into the food chain. To make matters worse, an advertising campaign launched to educate the British public was banned by the U.K. advertising standards agency because it was judged to be misleading.

Supermarkets also initially said that you could not label GI foods, that it would reduce customer choice. Now, as we know, most supermarket chains do label GI foods, and most, in fact, have said that they would be discontinuing their use in own brands where they can. But this kind of inconsistent advice does not foster trust.

Most people are not able to assess the risks themselves, and rely on a regulatory system to assess food safety issues. The U.K. government's strong pro-GI stance undermined its independence.

Monsanto's research found that when people were told that GI crops were regulated by government, people's level of mistrust increased. The Center for the Study of Environmental Change at Lancaster University found that the public perceived the government and regulators to be the same thing.

The crucial issues here are independence and trust. Both were, and perhaps still are, lacking in the U.K. context, and these have become key issues in determining people's attitudes to GI crops and new agricultural technology. While these factors may create a certain perspective for the public, research at Lancaster University shows that the public is open-minded in discussing the potential benefits attached to genetic engineering.

Many issues of public concern have not been addressed by any part of the regulatory system, and people want to know the need for GI foods and the social benefits envisaged; the potential for indirect, cumulative, synergistic, ecological, or health effects; and the wider impacts on agriculture and the countryside. They want to know how to compare the significance of risks and uncertainties, such as for human health, biodiversity, and pesticide use that are attached to different agricultural strategies.

They also want to know the degree of public control and international pluralism that might be desirable and possible in a global system dominated by a small number of large companies. They also want to know if GI foods can eliminate hunger. They also want to have a systematic and transparent way for a regulatory appraisal to take account of different values and interests in society.

To put all that more simply, is the technology needed, who stands to gain and lose, and how are the ethical issues considered?

Going back to the regulatory system in the U.K. and to the questions I raised, the system was not structured in a way to respond to those questions. The questions are, however, at the heart of public concern, although there is little government sponsored debate around them.

Some people may feel these ethical questions are not grounded in science. The GI foods issue is inherently ethical in nature, rather than purely scientific. I would also add in this context that not all NGOs are the same. The NGO debate is multifaceted, and complex. A number of NGOs that are involved, certainly those in the U.K., come from very different perspectives, and have very different approaches on how GI crops and agriculture should proceed.

Some of them have banded together in what is called the "Five-Year Freeze" to say: we do not know enough about this technology so let's have a five-year breathing space.

How then do we communicate about biotechnology and address public concerns? The research in the U.K. argues for a switch from the narrow focus on scientific and technical issues to deal with the political, legal, and ethical difficulties of handling the uncertain effects of new technologies. They argue for greater public involvement. This would build legitimacy and accountability of political decisions on GI foods through a more participatory style of decision making in which a far wider range of options is considered.

Only by involving the public can governments and scientists hope to rebuild the trust that has been lost.

I have two recommendations that could be relevant to the CGIAR system. One is to have a conference in all the countries concerned, involving all stakeholders including farmers and the NGOs. It is in civil society where the constructive debate needs to take place.

There is concern about the time being lost as we put in place— or as we ponder the future of GI technology and the structures that need to be put in place—the biosafety regulations and antitrust laws. There have also been a number of emotional statements about people going hungry while we dither.

My second recommendation is that we should look at other agricultural strategies and other options, as well as looking for what has been described as the "silver bullet" of biotechnology.

Conclusions

Rick Weiss

What are the main take-home points from this session of the Conference? The group of international writers above clearly make the point that biotechnology is a complicated story, in part because it is a science story, an economic story, and a story about politics and international trade, topics that are part of the biotechnology puzzle.

Biotechnology is also about intellectual property rights, and about ethics and democracy. We should, therefore, not feel bad that the story has evolved in such an erratic fashion. Perhaps nothing more could be expected of a story that has so many facets that connect in so many different ways, and which we are all trying to struggle to get through.

The point has been made that, as complicated as the subject is, the problem of coming to a final public decision about the risks or benefits of this technology has been exacerbated in part because, in the United States at least, we are not used to thinking about questions of agriculture and farmers' concerns. These are not usually high on the list of news items or things that people are clamoring to hear more about.

And rational discussion has been undermined by previous food safety scandals, such as BSE, and the general public mistrust of regulators, especially in Europe, and mistrust of the government. The idea that money and business concerns have percolated deeply into biotechnological science suggests that there is reason to think twice about whether you should believe what you hear.

Education is important, whether it is for reporters or the general public. The public needs and deserves to be educated better about these issues.

The public is not as ignorant as we sometimes expect, and people are developing a basic understanding of how to analyze how much risk they want to have in their lives, and where they want to have that risk. Their opinions probably deserve a little more attention than we have been willing to give them.

The debate over GI foods and crops is really part of a much larger area of science, of biotechnology generally, and these areas of science all have their own particular constellations of risk and benefits that deserve to be addressed independently. It behooves those who communicate about these issues to make those distinctions clear.

Perhaps there are some subcategories where the benefits clearly exceed the risks, and we ought to be moving forward more quickly without being dragged back by the debate over foods. Perhaps there are some areas, such as environmental or health concerns relating to some of these foods, for which that benefit:cost ratio is not so attractive, and for which more time could be spent doing research to see where we should go with it.

The extent to which this technology is accepted, or the extent to which its developers hope to see it accepted, will depend on the corporate response to concerns that people have. Reasonable or not, the concerns are there, and we already know some of the ways corporations can get it wrong.

The theme of this session is to communicate. Perhaps if we do enough of it, the truth will come out. There are various ways to do this—news media, corporate types of newsletters, Web outlets, and citizens' juries.

We must not forget that there are alternatives to these new technologies. In fact, the CGIAR has been developing those kinds of alternatives for a long time, and there is no reason to stop supporting progress in all the different areas of plant breeding and traditional ways of helping people who need help, and who may someday benefit from modern technology.

Contributors

Papers

Moh'd M. Ajlouni, National Center for Agricultural Research and Technology Transfer, P.O. Box 639, Baga 19381 Jordan

Ariel Alvarez-Morales, CINVESTAV-IRAPUATO, Apdo Postal 629, Irapuato, Gto. CP 36500, Mexico

Lyden Baker, International Livestock Research Institute, P.O. Box 30709, Nairobi, Kenya

Gerard Barry, Rice Team, Monsanto, 700 Chesterfield Parkway North, Chesterfield, MO 63017 USA

Richard Bishop, International Livestock Research Institute, P.O. Box 30709, Nairobi, Kenya

Lynn R. Brown, World Bank, 1818 H. Street N.W., Washington, D.C. 20433 USA

Christopher J. Chetsanga, Biotechnology Research Institute, 1574 Alpes Road, Hatcliffe, P.O. Box 6640, Harare, Zimbabwe

Joel I. Cohen, Information and New Technologies, ISNAR, P.O. Box 93375, 2509 AJ The Hague, The Netherlands

Marc J. Cohen, International Food Policy Research Institute, 2033 K Street N.W., Washington, D.C. 20006 USA

Michael B. Cohen, International Rice Research Institute, MCPO Box 3127, Makati City,1271, Philippines

R. James Cook, Washington State University, P.O. Box 646430, Pullman, WA 99164-6430 USA

Reynaldo E. de la Cruz, National Institutes of Molecular Biology and Biotechnology (BIOTECH, University of the Philippines, Los Banos, Philippines

Ana Mercedes Espinoza, Centro de Investigacion en Biologia Celular y Molecular, Universidad de Costa Rica, San Jose, Costa Rica

Behzad Ghareyazie, Agricultural Research Institute of Iran, Seed and Plant Improvement Campus, Mard-Abad Road, Karaj, Islamic Republic of Iran

Fred Gould, Department of Entomology, North Carolina State University, Raleigh, NC 27695-7634

Robert Horsch, Rice Team, Monsanto, 700 Chesterfield Parkway North, Chesterfield, MO 63017 USA

Brian Johnson, Biotechnology Advisory Unit, c/o English Nature, Roughmoor, Bishop's Hull, Taunton TA1 5AA, UK

Samuel B. Lehrer, Tulane University Medical Center, 1700 Perdido Street, Room 321 (SL-57), New Orleans, LA 70112 USA

Klaus M. Leisinger, Novartis Foundation for Sustainable Development, WRO-1002 11 59m /xg-4002 Basel, Switzerland

Josette Lewis, Biotechnology Adviser, U.S. Agency for International Development, Ronald Reagan Building, 1300 Pennsylvania Avenue, Washington, D.C. 20523-2110 USA

Magdy Madkour, Agricultural Genetic Engineering Research Institute, Gaioa Street, Giza 12619, Cairo, Egypt

H. Malkawi, National Center for Agricultural Research and Technology Transfer, P.O. Box 639, Baga 19381, Jordan

Alexander McCalla, Rural Development Division, World Bank, 1818 H Street N.W., Washington, D.C. 20433 USA

Subash Morzaria, International Livestock Research Institute, P.O. Box 30709, Nairobi, Kenya

Miguel Munos, Centro de Investigacion en Biologia Celular y Molecular, Universidad de Costa Rica, San Jose, Costa Rica

Cyrus G. Ndiritu, Kenya Agricultural Research Institute, P.O. Box 57811, Nairobi, Kenya

Vish Nene, International Livestock Research Institute, P.O. Box 30709, Nairobi, Kenya

Bongiwe Njobe-Mbuli, National Department of Agriculture, Private Bag x250, Pretoria 0001, Republic of South Africa

Agnes Odonyo, International Livestock Research Institute, P.O. Box 5689, Addis Ababa, Ethiopia

Gabrielle J. Persley, Rural Development Department, World Bank, 1818 H Street N.W., Washington, D.C. 20433 USA

Per Pinstrup-Andersen, International Food Policy Research Institute, 2033 K Street, N.W., Washington, D.C. 20006 USA

Ed Rege, International Livestock Research Institute, P.O. Box 5689, Addis Ababa, Ethiopia

David L. Richer, AgrEvo U.K. Ltd., Chesterford Park, Saffron Walden, Essex CB10 1XL, England

Maria Jose Amstalden Sampaio, Embrapa, U.S. Plant, Soil and Nutrition Lab-ARS/USDA, Tower Road, Ithaca, NY 14853-2901 USA

Ismail Serageldin, Vice President, World Bank, 1818 H Street N.W., Washington, D.C. 20433 USA

Manju Sharma, Department of Biotechnology, Ministry of Science and Technology, Block 2 (7th floor), CGO Complex, Lodi Road, New Delhi, 110 003, India

Ana Sittenfeld, Centro de Investigacion en Biologia Celular y Molecular, Universidad de Costa Rica, San Jose, Costa Rica

M.S. Swaminathan, M.S. Swaminathan Research Foundation, Taramani, Chennai 600 113, India

Morakot Tanticharoen, National Center for Genetic Engineering and Biotechnology, 73/1 Rama 6 Road, Ratchadevi, Bangkok 10400, Thailand

Alejandro Zamora, Centro de Investigacion en Biologia Celular y Molecular, Universidad de Costa Rica, San Jose, Costa Rica

Ercole Zerbini, International Livestock Research Institute South Asia Project at the International Crops Research Institute for the Semi-Arid Tropics, Patancheru, 502 324 AP, India

Qifa Zhang, Huazhongh Agricultural University, National Key Laboratory of Crop Genetic Improvement, Wuhan 430070, China

Session Chairs:

Donald Winkelmann, CGIAR Technical Advisory Committee, Washington, D.C. USA

Ronald Cantrell, International Rice Research Institute, Los Banos, Philippines

Ruben Echeverria, Inter-American Development Bank, Washington, D.C., USA

Kanayo Nwanze, West Africa Rice Development Association, Cote d'Ivoire

Adel El-Beltagy, International Center for Agricultural Research in the Dry Areas, Aleppo, Syria

Nina Federoff, Life Science Consortium and Biotechnology Institute, Pennsylvania State University, USA

Indra K. Vasil, Biotechnology Action Council, Unesco, and University of Florida, USA

Joel E. Cohen, Rockefeller University, USA

Calestous Juma, Center for International Development, Harvard University, USA

R. S. Paroda, Indian Council of Agricultural Research, India

Louise Fresco, Research, Extension and Training Division, FAO, Italy

Wanda Collins, Centro Internacional de la Papa, Peru

Rick Weiss, Science Reporter, The Washington Post, Washington, D.C., USA

Discussants:

Ana Sittenfeld, Universidad de Costa Rica, San Jose, Costa Rica

Val Giddings, Biotechnology Industry Organization, USA

Miguel Altieri, University of California, Berkeley, USA

Jean Halloran, Consumer Policy Institute, USA

James Maryanski, US Food and Drug Administration, USA

Bongiwe Njobe-Mbuli, Department of Agriculture, South Africa

Alain de Janvry, University of California, Berkeley, USA

Jean Marc von der Weid, Assessoria e Servicos a Projetos em Agricultura Alternativa, Brazil

Mark Sagoff, University of Maryland, USA

Geoffrey Hawtin, International Plant Genetic Resources Institute, Italy

Villoo Morawala-Patell, University of Agricultural Sciences, Bangalore, India

Sam Dryden, Emergent Genetics, Inc., USA

Francisco Reifschneider, Embrapa, Brazil

Timothy Reeves, Centro Internacional de Mejoramiento de Maiz y Trigo, Mexico

Hope Shand, Rural Advancement Foundation International, USA

Carola Kaps, Frankfurter Allgemeine Zeitung, Germany

G. Venkataramani, The Hindu, India

Walter P. von Wartburg, former Head of Corporate Communications, Novartis, Switzerland

Jagdish Patel, UK Food Group, UK

Rapporteurs:

Villoo Morawala-Patell, University of Agricultural Sciences, Bangalore, India

Francisco Reifschneider, Embrapa, Brazil

Joseph Mukiibi, NARO, Uganda

Mohamed Roozitalab, Ministry of Agriculture, Iran

William Padolina, International Rice Research Institute, Philippines

Richard R. Harwood, Michigan State University, USA

Derek Byerlee, World Bank, Washington, D.C. USA

Selcuk Ozgediz, CGIAR Secretariat, Washington, D.C. USA

John Dodds, International Center for Agricultural Research in the Dry Areas, Syria

Gesa Horstkotte-Wesseler, World Bank, Washington, D.C. USA

Conference Rapporteur:

Charlotte Kirk Baer, National Resarch Council/National Academy of Sciences, USA

Gabrielle J. Persley, World Bank, Washington, D.C. USA

Acronyms and Abbreviations

ARIPO	African Regional Intellectual Property Office
BIO	Biotechnology Industry Association
Bt	*Bacillus thuringiensis*
CBD	Convention on Biological Diversity
CGIAR	Consultative Group on International Agricultural Research
CIAT	Centro Internacional de Agri-cultura Tropical (CGIAR)
CSIR	Council of Scientific and Industrial Research (India)
DST	Department of Science and Technology (India)
FAO	Food and Agriculture Organization of the U.N.
GFAR	Global Forum on Agricultural Research
GIO	Genetically improved organism
GPS	Geographic positioning system
GURT	Genetic use restriction technology
IARC	International agricultural research center
ICAR	Indian Council of Agricultural Research
ICMR	Indian Council of Medical Research
ICRISAT	International Crops Research Institute for the Semi-Arid Tropics (CGIAR)
ICSU	International Council for Science
IFAD	International Fund for Agricultural Development
IFPRI	International Food Policy Research Institute (CGIAR)
ILRI	International Livestock Research Institute (CGIAR)
IPR	Intellectual property rights
IRRI	International Rice Research Institute (CGIAR)
KARI	Kenyan Agricultural Research Institute
MTA	Material transfer agreement
NARO	National agricultural research organization
NARS	National agricultural research system
NAS	U.S. National Academy of Science
OAPI	Organisation Africaine de la Propriete Intellectuelle (Yaounde)
OECD	Organization for Economic Cooperation and Development
PCR	Polymerase chain reaction
R&D	Research and development
RFLP	Restriction fragment length polymorphism
SADCC	Southern African Development Coordination Conference
TAC	Technical Advisory Committee (of the CGIAR)
TCDC	Technical Cooperation Among Developing Countries
TRIPs	Trade-Related Aspects of Intellectual Property Rights

TWAS Third World Academy of Sciences
UNDP United Nations Development Programme
UNEP United Nations Environment Programme
UNESCO United Nations Educational, Scientific and Cultural Organization
UNIDO United Nations Industrial Development Organization
UPLB University of the Philippines at Los Banos
UPOV Union Internationale pour la Protection des Obtentions Vegetales (Union for the Protection of New Varieties of Crops)
USAID U.S. Agency for International Development
USC Union of Concerned Scientists
WARDA West Africa Rice Development Association
WIPO World Intellectual Property Organization
WTO World Trade Organization

Secretariat
Consultative Group on International Agricultural Research
The World Bank
1818 H Street, N.W., Washington, D.C. 20433, USA
Telephone: 202.473.8951 Fax: 202.473.8110
www.cgiar.org