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# Biotechnology and Sustainable Agriculture

## ICSU Series on Science for Sustainable Development

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# Biotechnology and Sustainable Agriculture

by  
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Experimentation and Biotechnology  
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## Preface

One of the issues for consideration at the World Summit on Sustainable Development (WSSD) is the identification of ways to access the results and benefits arising from the applications of biotechnology for sustainable development, while ensuring ethical standards and safety of their use.

To address this issue, ICSU's Advisory Committee on Genetic Experimentation and Biotechnology (ACOGEB) commissioned an analysis of the present status of the applications of biotechnology to agriculture, the emerging scientific trends, and their contributions and consequences for human health, biodiversity and other components of the environment.

The ACOGEB members who initiated the study were Drs Richard Roberts (former ACOGEB Chair), Oscar Grau, Anne McLaren, Jim Peacock, and Marc van Montagu (current ACOGEB Chair). This report is completed by an ACOGEB-commissioned meta review of some twenty science-based reviews of the issues involved in genetically

modified foods and crops, which have been undertaken by various national, international and private agencies over the past few years. The meta-review will be published in September 2002 ([www.icsu.org](http://www.icsu.org)).

Dr Gabrielle Persley, and the UK-based Doyle Foundation, has taken the responsibility for the coordination and preparation of this report and the meta review. We thank also Drs Per Pinstrup Andersen, Andrew Bennett, Sylvia Burssens, Marc Cohen, Cuberto Gaza, Brian Johnson, Larry Kohler, Reginald MacIntyre and John Komen for their contributions of key source documents and their helpful comments during the preparation of this report. The technical assistance of Margaret Macdonald-Levy and John Schiller in bringing the report to completion is gratefully acknowledged.

We trust that this report will make a helpful contribution to the discussion on ways to improve the interactions amongst science, society and the natural world.

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## Executive Summary

The focus of the 2002 World Summit on Sustainable Development is on improving the relationship between human society and the natural environment. This document discusses the contributions and consequences of current and future applications of gene technology in agriculture, and the ways that these may affect human health and the environment.

### Present contributions of gene technology to agriculture

The contributions of gene technology to today's agriculture are already substantial. Discoveries in gene technology have led to:

- Better understanding of how plants function, and how they respond to the environment.
- More targeted selection objectives in breeding programs to improve the performance and productivity of crops, trees, livestock and fish, and post harvest quality of food.
- Use of molecular (DNA) markers for smarter breeding, by enabling early generation selection for key traits, thus reducing the need for extensive field selection.
- Molecular tools for the characterization, conservation and use of genetic resources
- Powerful molecular diagnostics, to assist in the improved diagnosis and management of parasites, pests and pathogens.
- Vaccines to protect livestock and fish against lethal diseases.

It seems likely that in most countries the applications of gene technology to agriculture will be a two-stage process. Firstly, there are many applications of gene technology that can be used to improve the management and efficiency of present agricultural practices. Secondly, there are options for the targeted introduction of transgenic strains, genetically modified for one or more specific traits. Although transgenic strains of various species of crops, trees, livestock and fish have been developed experimentally, only transgenic crop varieties are in widespread commercial use in agriculture today.

### Commercial cultivation of transgenic crops

Broadly, the first wave of genetically modified crops, which are in commercial use, address production traits; the second wave, which are mainly under development, address quality and nutritional traits; and the third wave address complex stress response traits and novel products able to be produced in plants. The scientific basis of dealing with each of these groups of traits is increasingly complex.

The production traits targeted in the first wave of transgenic crop varieties specifically addressed the economic and environmental costs of chemical management in large-scale agriculture. An important factor in the initial choice of production traits was the fact that the major early private investors in plant biotechnology were several multinational chemical companies. This arose because the long-term viability of chemically based agriculture was being questioned. In regard to the development of novel genetic approaches for specific production traits, a combination of new scientific possibilities, business opportunities and decreasing viability of chemically-based agriculture led to the targeting of particular production traits (particularly insect resistance and herbicide tolerance) and their subsequent commercial development into new transgenic crop varieties.

The first transgenic plant was produced experimentally in 1983. The first commercial cultivation was in 1995. By 2001, there were almost 53 million hectares of genetically modified crops growing in thirteen countries. These crops are mainly soybean, corn, cotton and oil seed rape, with resistance to certain insects and/or herbicide tolerance. Many other crops and traits are under investigation but most have yet to be taken through to practical use.

### Trait selection

The developers of the first generation of genetically modified organisms faced a number of technical limitations that influen-

ced the choice of species and traits that have been taken through to full product development. The constraints include:

- The *availability of genes* controlling traits that could be manipulated. Initially only traits controlled by single genes could be manipulated. Most characteristics of food, yield, and responses to stress are complex traits, controlled by several genes.
- The *efficiency of the methods* to produce genetically modified organisms that express the desired trait consistently under field conditions;
- The need to meet *evolving regulatory requirements* for new crop varieties and other living modified organisms (LMOs) containing genes from outside their normal range of hybridization.

*Management of single gene production traits:* The careful targeting and correct management of single gene traits is critical for their successful use in agriculture, so as to avoid the boom/bust cycles typical of single gene resistance. In the deployment of new transgenic varieties of *Bt*-crops, such as cotton and corn, in broad scale agriculture, much effort has gone into devising and implementing specific crop management arrangements that lessen the pressure for the evolution of resistance in the target pest. These crop cultivation regimes include leaving some of the field as non-transgenic, susceptible crops (providing refugia for the insects) or to include in the plant two or more different genes for pest resistance (*gene stacking*).

## Dealing with complex traits

Emerging scientific developments are enabling complex traits to be addressed, with the intention of developing new products of potential value for agriculture, human health and the environment. The attractiveness of the new targets is tempered by the fact that they are technically difficult, requiring the expression and control of multiple genes, often involved in different biochemical pathways. The new targets include traits for:

*Increasing sustainable agricultural production*, by the cultivation of crops that are better able to tolerate biotic stresses (pests, diseases and weeds) and abiotic stresses (drought, salinity, and temperature stress).

*Delivering health benefits* through more nutritionally beneficial foods, with higher content of essential vitamins and minerals, especially in staple crops; and reducing allergenic, carcinogenic and/or toxic compounds in certain plants.

*Using plants for pharmaceutical production:* More economical and efficient production of vaccines against human diseases, and other pharmaceuticals in plants.

*Using plants for production of products for industrial purposes:* including novel compounds such as biodegradable plastics and industrial strength fibers.

*Environmental benefits:* Using plants (and microbes) to mitigate the effects of industrial pollution (*bioremediation*), by increasing their ability to remove and/or break down toxic compounds in the soil.

## Emerging scientific discoveries

Recent scientific developments confer the ability to study the structure and function of all the genes within an organism simultaneously (through *genomics*), as well as the protein products they code for (through *proteomics*). It is also possible to study the role of all the chemical compounds in the metabolism of the cell (through *metabolomics*). These emerging scientific developments are being greatly assisted by powerful computing and statistical techniques that enable the assembly, interrogation and interpretation of large databases (through *bioinformatics*). New terms are being coined to describe these rapidly evolving branches of science and the techniques on which they are based.

The emerging scientific possibilities also pose new challenges in the assessments of the risks and benefits of potential new products to human health and the environment. Some of the potential products are meant for food or feed use, while others are intended for use as pharmaceuticals, and others as compounds for industrial uses. Some will require inter-specific transfer and control of multiple genes. Others will rely on switching on (or off) and better regulating genes that are already present in the organism but not usually expressed.

The new scientific developments also offer potential means to overcome some of the perceived risks in the cultivation of genetically modified crops. These include limiting the unintentional movement of genes out of the target crop (through *gene containment*); better food safety assessments of unintended changes in the composition of foods by assessments of the content of whole foods (through *metabolomics*); and the removal of antibiotic resistant, selectable markers from GM foods.



The challenge is to define how emerging scientific discoveries, such as those in the rapidly evolving fields of *genomics*, *proteomics* and *metabolomics*, amongst others, can be translated into safe applications of biotechnology that will lead to new varieties of crops, novel foods and new products that deliver benefits for society. These new applications and their risks and benefits will differ in different parts of the world. *Careful thought needs to be given to identifying the most suitable targets and desirable traits for future research and development efforts, in different countries and environments.*

### **New understanding of plant and animal genes through genomics**

*Genomics* refers to the processes used in identifying the location and function of all the genes contained in an organism. This new knowledge will change the future of breeding for improved strains of all domesticated species of crops, livestock, fish, and tree species.

*Twelve crops, five livestock and two fish species provide over 90% of the world's food.* For these staple species, national and international public sector research has made a large investment in genetic resources and breeding materials, and has an understanding of their behavior in different environments. These scientific and biological resources will become increasingly important in gaining knowledge about the function of genes, in developing molecular markers and other means to assist in the breeding of improved strains.

The first plant genome that has been completely sequenced is a small, model species, *Arabidopsis thaliana*. The genomic sequencing of economically important crops is also being undertaken. The most advanced are the several public and private gene sequencing projects on rice, all of which are now in the public domain. A maize genome-sequencing project is also in progress. Rice, maize and other cereals share a large number of common genes. Other genome sequencing projects of at least 120 different plant species are in progress.

### **Understanding the role of proteins through proteomics**

Most cellular functions are carried out by multi-protein complexes. New techniques are enabling these complexes to be unravelled, and the functions of individual proteins

understood. These techniques allow the identification and quantification of proteins expressed in a particular tissue or in a specific developmental or environmental condition, such as in response to stress.

### **Understanding what happens in the cell through metabolomics**

Information on metabolite levels in the cell is critical to obtaining an overview of a biological process. Examining changes in metabolic profiles is an important part of assessing gene function and relationships of phenotypes. Modern high-resolution techniques allow the establishment of a profile of all metabolites present in a specific plant tissue. A variety of previously unidentified biochemical pathways can now be understood. Metabolomics can also provide information on metabolic network regulation in response to genetic and environmental perturbations, leading to a better understanding of plant responses to stress. Extensive databases of quantitative information are being developed about the degree to which each gene responds to environmental stimuli, such as biotic and abiotic stresses. These databases will provide insights into the set of genes that control complex responses and will create powerful opportunities to assign functional information to genes of otherwise unknown function

*Metabolic engineering:* Metabolic engineering is the *in vivo* manipulation of biochemistry to enable plants to produce non-protein products or to alter cellular properties. The products may be native to the plant or novel (expressed after the introduction of genes from another source). Recent research shows that it is technically possible to produce the following products in plants at the experimental level: Vitamin A precursors; essential oils; medicinally important alkaloids; biodegradable plastics; vaccines. Several of these products are now in development phase and are coming forward for regulatory approval.

### **Understanding risks and benefits of gene technology**

The rapid increase in the use of new techniques for understanding and modifying the genetics of living organisms has led to greatly increased interest and investments in biotechnology. These developments have been accompanied by

public concerns as to the power of the new technologies and the safety and ethics of their use for improving human health, agriculture and the environment.

Public concerns about the applications of biotechnology lie in four major areas: (1) Ethical issues; (2) Socio-economic effects; (3) Food safety and human health; and (4) Impact on biodiversity and the environment. In agriculture, these concerns relate particularly to the release of living modified organisms (LMOs) for agricultural purposes. These organisms may be plants, trees, livestock, fish and/or microorganisms.

The *ethical issues* relate to moral and social concerns about the nature of gene technology itself and the consequences of its use in specific situations. There are concerns about the appropriateness of the use of intellectual property rights in relation to living organisms, and means to ensure the equitable sharing of benefits by holders of genetic resources, owners of indigenous knowledge and inventors.

*Socio-economic effects* are concerned with the economic risks and benefits in the use of new biotechnology applications, the implications of intellectual property management on agriculture in different countries and in identifying who gains and who loses from the use of new technologies in various circumstances.

In relation to *food safety and human health*, there are concerns as to assessing the risks of genetically modified foods to human health, in the short and long term; identifying specific nutritional benefits of genetically modified foods developed for this purpose; and searching for any unintended effects of genetic modifications on food.

In relation to *impact on biodiversity* and other possible *environmental effects*, the concerns relate to assessing the risks and benefits of releasing living modified organisms into the environment, and the effects such releases may have on the environment. These effects may be through *direct effects* on the environment, including potential impact on biodiversity, and/ or *indirect effects* through changing agricultural practices that affect the environment.

Consideration of all these issues, on a case by case basis, provides a basis for choices on the merits and safety of the applications of new biotechnologies to address particular problems, relative to existing agricultural technologies and other technology options. All these issues are important in making choices on the use of gene technology to address particular aspects of sustainable development. This document addresses specifically the emerging scientific trends;

the scientific basis of assessing the effects of gene technology on food safety and human health; and the impact of gene technology on biodiversity and the environment.

## Conclusion

Achieving the potential benefits of modern molecular science will require substantial private and public investments, and a wide range of scientific skills. These required skills lie not only in gene technology, but also in the related fields of plant breeding, agronomy and physiology, food and nutrition and in natural resources management. There also needs to be greatly improved linkages amongst the social, scientific, industrial and environmental communities, so as to better define the ways in which science can benefit society and to design new technologies in ways that are socially and environmentally acceptable and beneficial in different countries and communities.

New developments in science and technology, including the continuing discoveries in gene technology, can contribute to achieving strategies for sustainable development, if they are:

- Directed at clearly defined targets that affect poverty reduction, food security, environmental conservation and/or trade competitiveness;
- Accompanied by political will, supportive public policies, and public and private investments in both science and technology and product development and delivery;
- Implemented under the auspices of transparent regulatory frameworks that generate public trust and confidence in the safety and ethical use of new biological products and processes for human health, agriculture and the environment.

This overview document will be complemented by a meta-review commissioned by ICSU that is analysing the key findings of some twenty reviews on GM foods and crops that have been conducted by various national, international and private agencies within the past three years. Particular attention is being given to identifying the areas of commonality amongst the reviews, identifying any areas of differing perspective, and highlighting those areas where there are gaps in knowledge that may be able to be addressed through additional well targeted research. The meta review will be published by ICSU in September 2002, at the time of the ICSU General Assembly in Rio de Janeiro, Brazil, and will be available at [www.icsu.org](http://www.icsu.org).

# 1. Overview

The focus of the 2002 World Summit on Sustainable Development in Johannesburg is on improving the relationship between human society and the natural environment. The United Nations Secretary General has identified five specific areas for action. These are:

- *Water and sanitation*, including improving the efficiency of water use in agriculture. Agriculture is the largest consumer of water, an increasingly scarce natural resource;
- *Energy*, including increasing the use of renewable energy sources;
- *Health*, including the link between the environment and human health, and diseases such as malaria that disproportionately affects poor people;
- *Agricultural productivity*, including the effects of declining agricultural productivity, land degradation and the impact of human activity on forests, grasslands and wetlands;
- *Biodiversity and ecosystem management*, including the impact of human activity on tropical rainforests, mangroves, marine fisheries and coral reefs.

This document discusses the contributions and consequences of current and future applications of gene technology in agriculture, and the ways that these may affect human health and the environment.

## Role of Science and Technology in Food Security and Poverty Reduction

Science and technology have underpinned social and economic gains from agriculture. From 1960 to 2000, increases in global food production more than kept pace with population growth. Over this period, world cereal production doubled, *per capita* food production increased 37%, calories supplied increased by 35% and food prices fell by almost 50% (Pinstrup Andersen et al 1999). Most of the agricultural productivity gains were due to yield increases, parti-

cularly those resulting from the discovery of dwarfing and other genes that conveyed useful traits into new, high yielding wheat and rice varieties. These and other scientific discoveries, when combined with a mix of supportive public policies, appropriate institutions, political commitment, public and private investments in rural areas (particularly for irrigation, credit and inputs), led to halving the numbers of people living in poverty, and largely achieving food self sufficiency, especially in Asia. However, the overall achievements mask significant variations in agricultural performance across regions. For example, the productivity gains across much of Asia have not been matched by similar productivity increases in Africa, in either crops or livestock.

Despite the increasing global availability of food, some 850 million people lack access to sufficient nutritious food at affordable prices. Approximately 60% of these people live in South and East Asia, while 25% live in sub-Saharan Africa (Pinstrup-Andersen and Cohen 2000).

World population projections predict that about 73 million people will be added to the world's population every year from 2002 to 2020. Most will be living in the developing world. Meeting the food needs of this growing and increasingly urbanized population will require increases in agricultural productivity and matching these increases to rising incomes and consequent dietary changes, especially the increasing demand for livestock and fish. World food and feed grain production will need to increase by 40% and roots and tubers by 58% in order to meet projected world food demand in 2020 (Pinstrup-Andersen et al 1999). Livestock production will need to double by 2020 in order to meet the expected demand for milk and meat (Delgado et al 1999). Improving the livelihoods and incomes of people in rural and urban areas is also critical to food security, since people's access to food depends on income. These production increases will have to be achieved through sustainable increases in agricultural production per unit of land and water, in order to conserve natural resources, and reverse some of the damaging effects of past agricultural practices.

## Environmental Trends

- The intensification of agriculture in favorable areas has come at the cost of damage to the environment, with increasing salinity problems in irrigated areas, and damage to human health, ecology and wildlife due to misuse of pesticides.
- Other agricultural-associated practices, including deforestation, overgrazing, over fishing and water pollution also threaten the sustainable use of natural resources.
- Decreasing water availability for agriculture is one of the most important trends. There is a need for more efficient use of water in agriculture, including the development of drought tolerant crop varieties.
- Pressure on agricultural land for urbanization and industrialization increases. There are limited prospects for expanding the land available for agriculture, except by moving into forests, or marginal areas with poor soils and little water.
- Deforestation and loss of biodiversity by the clearing of land for agriculture is occurring in areas of mega-terrestrial biodiversity. The use of modern plant varieties also threatens the loss of land races of crops.
- Natural disasters pose a continuing threat to agriculture, and the long-term effects of climate change are unknown.

## Future Food Security Strategies

Strategies to achieve the needed increases in the quantity and quality of global food supplies and ensuring that there is sufficient food available at affordable prices in the developing world include:

- Achieving sustainable productivity increases in food, feed, and fiber crops in both irrigated and rain-fed areas
- Improve nutrient content of diets, especially for women and children
- Reducing chemical inputs of fertilizers and pesticides and replacing these with biologically based products.
- Integrating soil, water, and nutrient management.
- Conserving, characterizing and using agriculturally related biodiversity
- Improving the nutrition and productivity of livestock and controlling livestock diseases
- Achieving environmentally sustainable increases in marine fisheries and aquaculture production.

- Increasing trade and competitiveness in global markets, especially for products from developing countries.

Developments in science and technology, including the continuing discoveries in gene technology, can contribute to the above strategies for achieving food security, if they are:

- Directed at clearly defined targets that affect poverty reduction, food security, environmental conservation and/or trade competitiveness;
- Accompanied by political will, supportive public policies, and public and private investments in both science and technology and product development and delivery;
- Implemented under the auspices of regulatory frameworks that generate public trust and confidence in the safety and ethical use of new biological products and processes for human health and the environment.

## Developments in Modern Science

Modern science encompasses new developments in the biological, physical and social sciences. In the biological sciences, recent discoveries allow much greater understanding of the structure and function of human, animal and plant genes and the proteins and other biochemical products they produce. Discoveries in the physical sciences underpin the revolution in information and communications technologies. These branches of science come together in the field of *bioinformatics*, whereby large amounts of biological data can be assembled and analysed.

There are also new developments in the social sciences that underpin community participation in technology development and evaluation. Participatory methods can help understand the problems and identify the researchable issues, particularly of small farmers operating in marginal environments. These participatory approaches may also help to clarify the concerns of people in rural and urban communities in regard to the deployment of new technologies, including the products of biotechnology. They may also assist in the integration of modern science and traditional knowledge, in order to develop knowledge-intensive solutions to specific problems that are technically feasible and socially and ethically acceptable, in various rural and urban communities (CGIAR 2002; Serageldin and Persley 2000).

## Scope of Biotechnology

*Biotechnology*, broadly defined, refers to any technique that uses living organisms or substances from these organisms to make or modify a product, improve plants, trees or animals or develop microorganisms for specific uses. The applications of biotechnology consist of a suite of evolving technologies that are based on scientific discoveries that are rapidly increasing understanding of the structure and function of genes and their behavior in the environment. A chro-

nology of the key developments in the science of genetics is given in Table 1.1.

The present applications of biotechnology important for agriculture and the environment include:

- *Microbial fermentation*, used, for example, to develop new agents for biocontrol of pests and diseases and new bio-fertilizers;
- *New diagnostics and vaccines*, based on molecular characterization of parasites, pathogens and pests;

**Table 1.1:** Chronology of key developments in the science of genetics.

1866	Mendel postulates a set of rules to explain the inheritance of biological characteristics in living organisms.	1982	First successful transfer of a gene from one animal species to another (a transgenic mouse carrying the gene for rat growth hormone). First transgenic plant produced, using an agrobacterium transformation system.
1900	Mendelian law rediscovered after independent experimental evidence confirms Mendel's basic principles.	1983	First successful transfer of a plant gene from one species to another.
1903	Sutton postulates that genes are located on chromosomes.	1985	US Patent Office extends patent protection to genetically engineered plants.
1910	Morgan's experiments prove genes are located on chromosomes.	1986	Transgenic pigs produced carrying the gene for human growth hormone.
1911	Johannsen devises the term "gene", and distinguishes genotypes (determined by genetic composition) and phenotypes (influenced by environment).	1987	First field trials in USA of transgenic plants (tomatoes with a gene for insect resistance). First field trials in USA of genetically engineered microorganism.
1922	Morgan and colleagues develop gene mapping techniques and prepare gene map of fruit fly chromosomes, ultimately containing over 2000 genes.	1988	US Patent Office extends patent protection to genetically engineered animals. First GMO approved. Human genome mapping project initiated.
1944	Avery, MacLeod and McCarty demonstrated that genes are composed of DNA rather than protein.	1989	Plant genome mapping projects initiated (for cereals and <i>Arabidopsis</i> ).
1952	Hershey and Chase confirm role of DNA as the basic genetic material.	1996	First commercial cultivation of genetically modified (transgenic) crops.
1953	Watson and Crick discover the double-helix structure of DNA.	1998	First successful cloning of a mammalian species (Dolly, the sheep).
1960	Genetic code deciphered.	2000	Human genome map completed
1971	Cohen and Boyer develop initial techniques for rDNA technology, to allow transfer of genetic material from one organism to another.	2000	Plant genome mapping projects for rice and <i>Arabidopsis</i> completed.
1973	First gene (for insulin production) cloned, using rDNA technology.	2001	52 million hectares of land planted to genetically modified crops in 13 countries.
1974	First expression in bacteria of a gene cloned from a different species.		
1976	First new biotechnology firm established to exploit rDNA technology (Genentech USA).		
1980	USA Supreme Court rules that microorganisms can be patented under existing law (Diamond v. Chakrabarty).		
1982	First rDNA animal vaccine approved for sale in Europe (colibacillosis). First rDNA pharmaceutical (insulin) approved for sale in USA and UK.		

DNA = deoxyribonucleic acid, GMO = genetically modified organism.  
rDNA = recombinant DNA, UK = United Kingdom, USA = United States of America.  
Sources: Persley, 1990; ADB, 2001

- *Tissue culture and micro-propagation*, for multiplying high-quality planting material;
- *Molecular markers*, used for *marker assisted selection* (MAS) of desirable traits in plant, animal, fish and tree breeding;
- *Genetic engineering* used to identify and transfer one or more genes within and between species, resulting in *transgenic (genetically modified)* organisms;
- *Genomics*, the study of all the genes present in the genome of an organism, including their structure (*structural genomics*), understanding their function (*functional genomics*), and comparing the molecular basis of similarities and differences between organisms (*comparative genomics*).
- *Proteomics* involves large-scale studies on gene expression at the protein level, including the purification, identification, and quantification of proteins and the determination of their localization, modifications, interactions and activities.
- *Metabolomics* relates to the analysis of all cellular metabolites.
- *Bioinformatics* is the acquisition, collation and interrogation of large collections of complex biological data.
- Molecular (DNA) markers for smarter breeding, by enabling early generation selection for key traits, thus reducing the need for extensive field selection.
- Powerful molecular diagnostics, to assist in the improved diagnosis and management of parasites, pests and pathogens.
- Development of vaccines for the control of livestock and fish diseases.

In terms of crops, applications of gene technology are used widely in present day agriculture for the development of new (conventional) crop varieties, through marker assisted selection. They also provide important tools for the characterization, conservation and use of genetic resources (Platais and Persley 2002).

Several large corporations have made major investments to adapt the new discoveries in the biological sciences for commercial purposes. A large proportion of this investment has been directed towards the development of new plant varieties for large-scale commercial agriculture in temperate zones. Private industry has dominated this research, accounting for approximately 80% of all R&D in agricultural biotechnology (James 2001a).

In 2001, it is estimated that approximately 52.6 million hectares of land were planted in 13 countries with transgenic varieties of over 20 plant species (James 2001b,c). The most commercially important of these genetically modified crops are soybean, corn, cotton and canola (oil seed rape), with resistance to certain insects and/or tolerance to selected herbicides. These new varieties are being grown primarily in the USA, Argentina, Canada and China. The value of the global market in transgenic crops grew from US\$75 million in 1995 to approximately US\$ 2 billion in 2000. These trends are illustrated in Figure 1.1, and Tables 1.2 and 1.3.

The traits these new plant varieties contain include insect resistance (corn, cotton), herbicide resistance (corn, soybean), delayed fruit ripening (tomato) and virus resistance (papaya). The benefits of these new crops come from better weed and insect control, with less use of chemical pesticides and herbicides; higher productivity, and more flexible crop management. These benefits accrue primarily to farmers and agribusinesses, although there are also some economic benefits accruing to consumers in terms of maintaining food production at low prices (Carpenter et al 2002; James 2001a).

## Commercial Applications of Biotechnology in Agriculture

The increasing specificity in the handling of genes has meant that inventors can protect their discoveries by means of patents and other forms of intellectual property rights. This has led to substantial private investment in the biosciences, leading to what has been called a *biotechnology revolution*. Most modern biotechnology applications are in health care, where biotechnology-based processes are now used routinely as the basis for the discovery and production of most new medicines, diagnostic tools, and medical therapies.

The contributions of gene technology to today's agriculture are also substantial. Discoveries based on the continuing rapid developments in gene technology have led to:

- Better understanding of how plants function, and how they respond to the environment.
- More targeted selection objectives in breeding programs to improve the performance and productivity of crops, livestock and fish and post harvest quality of food.

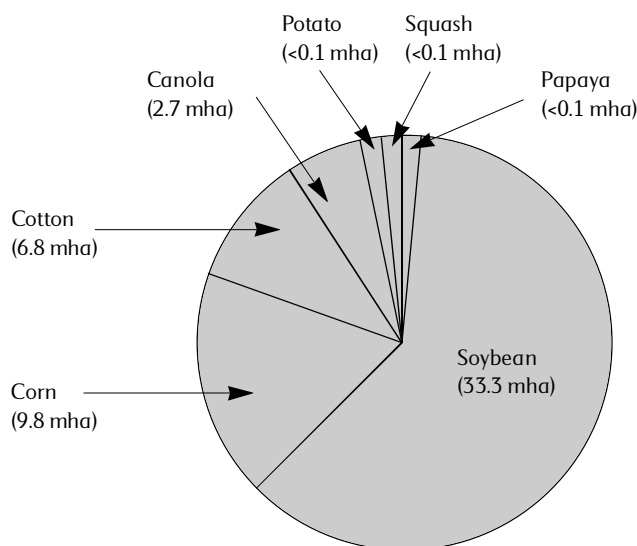
### Applications of Biotechnology to Achieve International Development Goals

Several emerging economies are making major investments of human and financial resources in biotechnology with the aim of using these new developments in science and technology to reduce poverty, improve food security, conserve the environment and/or improve trade competitiveness. This matrix of international development objectives and the ways biotechnology may be used to address them is illustrated in Tables 1.4 and 1.5 (ADB 2000; Persley and Lantin 2000; Persley and MacIntyre 2001).

Present applications of biotechnology in emerging economies include increasing use of marker-assisted selection to give more precise and rapid development of new strains of crops, livestock, fish and trees. Other biotechnology applications such as tissue culture and micro-propagation are being used for the rapid multiplication of clean planting material for horticultural crops and trees. New diagnostics and vaccines are being adopted for the diagnosis, prevention and control of fish and livestock diseases (Tables 1.4 and 1.5).

**Figure 1.1. Commercial cultivated genetically modified crops in 2001.**

Source: James 2001c.



**Table 1.2. Countries planting GM crops in 2000 and 2001.**

Country	2000 (million hectares)	2001 (million hectares)
USA	30.3	35.7
Argentina	10.0	11.8
Canada	3.0	3.2
China	0.5	1.5
South Africa	0.2	0.2
Australia	0.2	0.2
Romania	<0.1	<0.1
Mexico	<0.1	<0.1
Bulgaria	<0.1	<0.1
Spain	<0.1	<0.1
Germany	<0.1	<0.1
France	<0.1	-
Uruguay	<0.1	<0.1
<b>TOTAL</b>	<b>44.2 m ha</b>	<b>52.6 m ha</b>

Source: James 2001c.

**Table 1.3. Predominant GM crops and traits, 2001.**

Crop	million hectares ( m ha)
Herbicide-tolerant soybean	33.3
Bt Corn	5.9
Herbicide-tolerant canola	5.7
Herbicide-tolerant corn	2.1
Herbicide tolerant cotton	2.5
Bt / Herbicide-tolerant cotton	2.4
Bt cotton	1.9
Bt / Herbicide-tolerant corn	1.8
<b>TOTAL</b>	<b>52.6 m ha</b>

Source: James 2001c.

The most widespread new transgenic crop varieties being grown in emerging economies are new cotton varieties containing one or more genes from the bacterium, *Bacillus thuringiensis* (Bt), for insect resistance. These varieties were grown by some 4 million farmers on at least 1.5 million hectares of land in China in 2001. The resulting socio-economic benefits identified in China are reduced pesticide use, improved profitability of cotton for farmers, and reduced ill effects due to pesticide misuse on human health and the environment (Pray et al 2000). New insect resistant (Bt) cotton varieties are also being grown in South Africa.

### Emerging Scientific Trends

Applications of biotechnology in agriculture are in their infancy. Most current genetically engineered plant varieties are modified only for a single trait, such as herbicide tolerance or

pest resistance. The rapid progress being made in plant sciences is expected to enhance plant breeding as the functions of more genes and how they control particular traits are identified. These developments may enable more successful breeding for complex traits such as drought tolerance. This may be of particular benefit to those farming in marginal and rainfed lands worldwide since breeding for such difficult traits has had limited success with conventional breeding of the major staple food crops.

Further scientific advances may result in crops with a wider range of traits, some of which are likely to be of more direct interest to consumers. For example, new crop varieties may have traits that confer improved nutritional quality to food, potentially beneficial to people affected by malnutrition and vitamin and mineral deficiencies. For example, genes have been identified that can modify and enhance the composition of oils, proteins, carbohydrates, and starch in food/feed grains and root crops. A gene encoding beta carotene/vitamin A formation has been incorporated experimentally in rice.

**Table 1.4. Illustrative applications of biotechnology to the goal of poverty reduction**

Biotechnology applications (1-6)									
Poverty reduction objective	Constraint	Target	1 Microbial fermentation/ bio-control/ bio-fertilizers	2 New diagnostics/ vaccines	3 Tissue culture/ micropropagation	4 Molecular markers and MAS	5 Genetic engineering/ transgenics	6 Functional genomics	Specific global examples
Increasing rural incomes	Lack of clean seed/ Planting material	Vegetative crops and trees	Bio-pesticides	Plant disease diagnostics	Cardamom Potato Banana				India Vietnam Kenya
Sustainable production in resource poor areas	Drought Pests Acid soils	Cereals Maize Al tolerance				Maize Insect Resistance Al tolerance.		Drought tolerance in cereals	AMBIONET / CIMMYT
More nutritious food for poor	Vitamins Micro-nutrients	Rice Rice				Iron	Vitamin. A Rice		IRRI India China

1. Traditional biotechnology applications such as microbial and food fermentation.
2. New diagnostics and vaccines based on molecular applications.
3. New methods for tissue culture and micropropagation of planting material.
4. Use of molecular markers in marker-assisted selection (MAS) in conventional plant and animal breeding.
5. Genetic engineering to produce transgenic plant/and/or animal strains, containing new specific gene(s) controlling a particular trait.
6. Genomics: understanding the physical structure of the genome, and in functional genomics, the function of specific genes.

AMBIONET - Asian Maize Biotechnology Network  
 CIMMYT - International Maize and Wheat Improvement Center  
 IRRI - International Rice Research Institute

Source: Persley, G.J. 2001. Agricultural Biotechnology: Global Challenges and Emerging Science. In: Persley, G.J., and MacIntyre, L.R. (eds.) *Agricultural Biotechnology: Country Case Studies—A Decade of Development*. CAB Publishing, Wallingford, U.K.



## NEW UNDERSTANDING OF PLANT AND ANIMAL GENES

*Genomics* refers to the processes used in identifying the location and function of all the genes contained in an organism. This new knowledge is changing the future of breeding for improved strains of crops, livestock, fish, and tree species. Although much of the discussion about biotechnology today is focused on the opportunities and risks associated with inter-specific gene transfer, the same scientific discoveries brings new tools to assist breeders to identify and transfer genes through conventional breeding within a particular species. In many environments, future gains in productivity will depend upon manipulation of complex traits, such as

drought or heat tolerance or tolerance to parasites. These traits are often difficult to identify and utilize in conventional breeding programs without the additional help of modern science.

*Twelve crops, five livestock and two fish species provide over 90% of the world's food.* For these staple species, national and international public sector research has made a large investment in genetic resources and breeding materials, and has led to an understanding of their behavior in different environments. These scientific and biological resources will become increasingly important in gaining knowledge about the function of genes and in developing molecular markers to assist in the breeding of improved strains.

**Table 1.5. Illustrative applications of biotechnology to the goal of food security**

Biotechnology applications (1-6)									
Food security objective	Constraint	Target	1 Microbial fermentation/ bio-control/ bio-fertilizers	2 New diagnostics/ vaccines	3 Tissue culture/ micropropagation	4 Molecular markers and MAS	5 Genetic engineering/transgenics	6 Functional genomics	Specific global examples
Meeting demand predictions for staples	Pests/diseases  Abiotic stresses	Rice  Salinity/drought tolerance in cereals	Rice Integrated pest management			Cereals/ Drought tolerance	Bacterial blight (Xa1 gene) Salinity tolerant genes	Rice genome Cereals	ARBN/ IRRI China India China ICRISAT CIMMYT
Increasing livestock	Diseases  Production	Cattle/pigs/sheep. Dairy cattle		Foot and mouth disease (FMD)	Embryo technology				Thailand  India
Increasing fish/aquac.	Diseases	Shrimp viruses		Molecular diagnostics					Thailand
Increasing vegetables	Pests/diseases	Tomato/potato	Bacterial wilt biocontrol agent		Potato (Vietnam)	Bacterial wilt resistant varieties			AVRDC Vietnam

1. Traditional biotechnology applications such as microbial and food fermentation.
2. New diagnostics and vaccines based on molecular applications.
3. New methods for tissue culture and micropropagation of planting material.
4. Use of molecular markers in marker-assisted selection (MAS) in conventional plant and animal breeding.
5. Genetic engineering to produce transgenic plant/and/or animal strains, containing new specific gene(s) controlling a particular trait.
6. Genomics: understanding the physical structure of the genome, and in functional genomics, the function of specific genes. ARBN - Asian Rice Biotechnology Network

AVRDC - Asian Vegetable Research and Development Center  
 CIMMYT - International Maize and Wheat Improvement Center  
 ICRISAT - International Crops Research Institute for the Semi-Arid Tropics  
 IRRI - International Rice Research Institute

Source: Persley, G.J. 2001. Agricultural Biotechnology: Global Challenges and Emerging Science. In: Persley, G.J., and MacIntyre, L.R. (eds.) *Agricultural Biotechnology: Country Case Studies—A Decade of Development*. CAB Publishing, Wallingford, U.K.

Strategic research is required in order to understand the genetic basis of the agriculturally important crops, livestock and fish, to identify potentially useful genes to address important constraints, and to understand how the gene products (proteins and other metabolites) function in the cells of the living organism. Scientific developments in emerging areas offer promise of new ways to deal with previously intractable problems in crop and livestock production, forestry and fisheries and contribute to sustainable development. To achieve this promise, they will need to be combined with other skills in areas such as nutrition, biochemistry, immunology, ecology and risk management, as well as understanding and addressing community concerns about gene technology itself.

## Understanding Risks and Benefits of Gene Technology

The rapid increase in the use of new techniques for understanding and modifying the genetics of living organisms has led to greatly increased interest and investments in biotechnology. These developments have been accompanied by increasing public concerns as to the power of the new technologies and the safety and ethics of their use for improving human health, agriculture and the environment.

Public concerns about the applications of biotechnology lie in four major areas:

- Ethical issues;
- Socio-economic effects;
- Food safety and human health; and
- Impact on biodiversity and the environment.

The *ethical issues* relate to moral and social concerns about the nature of gene technology itself and the consequences of its use in specific situations. There are concerns about the appropriateness of the use of intellectual property

rights in relation to living organisms, and means to ensure the equitable sharing of benefits by holders of genetic resources, owners of indigenous knowledge and inventors.

*Socio-economic effects* are concerned with the economic risks and benefits in the use of new biotechnology applications, the implications of intellectual property management on agriculture in different countries and in identifying who gains and who loses from the use of new technologies in various circumstances. These issues are addressed in detail by Pardey et al (2001).

In relation to *food safety and human health*, there are concerns as to assessing the risks of genetically modified foods to human health, in the short and long term; identifying specific nutritional benefits of genetically modified foods developed for this purpose; and searching for any unintended effects of genetic modifications on food.

In relation to *impact on biodiversity* and other possible *environmental effects*, the concerns relate to assessing the risks and benefits of releasing living modified organisms into the environment, and the effects such releases may have on the environment. These effects may be through *direct effects* on the environment, including potential impact on biodiversity, and/ or *indirect effects* through changing agricultural practices that affect the environment.

Consideration of these issues, on a case by case basis, provides a basis for choices on the merits and safety of the applications of new biotechnologies to address particular problems, relative to existing agricultural technologies and other technology options. While acknowledging the importance of all these issues in making choices on the use of gene technology to address particular aspects of sustainable development, subsequent chapters of this document address: The emerging scientific trends (Chapter 2); the scientific basis of assessing the effects of gene technology on food safety and human health (Chapter 3); and the impact of gene technology on biodiversity and the environment (Chapter 4).

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## 2. Emerging Scientific Trends

The contributions of gene technology to today's agriculture are already substantial. Discoveries in gene technology have led to:

- Better understanding of how plants function, and how they respond to the environment.
- More targeted selection objectives in breeding programs to improve the performance and productivity of crops, trees, livestock and fish, and post harvest quality of food.
- Use of molecular (DNA) markers for smarter breeding, by enabling early generation selection for key traits, thus reducing the need for extensive field selection.
- Molecular tools for the characterization, conservation and use of genetic resources
- Powerful molecular diagnostics, to assist in the improved diagnosis and management of parasites, pests and pathogens.
- Vaccines to protect livestock and fish against lethal diseases.

In crop agriculture, applications of gene technology are making major contributions to present day agriculture by the development of new (conventional) crop varieties, through the use of marker assisted selection. The other important application of gene technology in agriculture is in the development of novel, transgenic plant varieties. Here new genetic instructions are introduced into the crop by laboratory-based molecular methods, leading to new plant varieties that have been genetically modified for a specific trait.

It seems likely that in most countries the applications of gene technology to agriculture will be a two-stage process. Firstly, there are many applications of gene technology that can be used to improve the management and efficiency of present agricultural practices. These include the use of molecular markers in smarter breeding, new diagnostics and vaccines. Secondly, there are options for the targeted introduction of transgenic strains, genetically modified for one or more specific traits. Although transgenic strains of various species of crops, trees, livestock and fish have been developed experimentally, only transgenic crop varieties are in widespread commercial use in agriculture.

### Commercial cultivation of transgenic crops

Broadly, the first wave of genetically modified crops, which are in commercial use, address production traits; the second wave, which are mainly under development, address quality and nutritional traits; and the third wave for the future address complex stress response traits and novel products able to be produced in plants. The scientific basis of dealing with each of these three groups of traits is increasingly complex.

The production traits targeted in the first wave of transgenic plant varieties specifically addressed the economic and environmental costs of chemical management in large-scale agriculture. An important factor in the initial choice of production traits was the fact that the major early private investors in plant biotechnology were several multinational chemical companies. The long-term viability of chemically based agriculture was being questioned as potentially:

- damaging to human health;
- damaging to the environment, due to chemical damage to living organisms, and excess chemical run off into water courses;
- less effective, due to the build-up of pesticide tolerance in target pests and diseases, thus shortening the economic life of agri-chemicals;
- less feasible due to the difficulty in discovering new agri-chemical compounds.

Biologically based management strategies were been sought, not only to reduce chemical use in agriculture but also to find more powerful ways to increase sustainable productivity and improve quality. Strategies for integrated pest management and later integrated crop management were developed in some areas. These strategies aimed to reduce inputs of chemical pesticides, herbicides and fertilisers, maximise the effectiveness of natural enemies for pest control and make judicious use of host-plant resistance for disease and pest control.

In regard to the development of novel genetic approaches for specific production traits, a combination of new scientific possibilities, business opportunities, and decreasing viability of chemically-based agriculture led to the targeting of particular production traits (insect resistance and herbicide tolerance) and their subsequent commercial development into new transgenic crop varieties.

The first transgenic plant was produced experimentally in 1983. The first commercial cultivation was in 1995. By 2001, there were almost 53 million hectares of genetically modified crops growing in 13 countries (James, 2001). The most commercially important of these crops are soybean, corn, cotton and canola (oil seed rape). The traits these new plant varieties contain are mainly insect resistance (corn, cotton), herbicide resistance (corn, soybean), delayed fruit ripening (tomato) and virus resistance (papaya) (Figure 1.1, Tables 1.2, 1.3). Many other crops and traits are under investigation but most have yet to be taken through to practical use.

## Trait Selection

### SINGLE GENE PRODUCTION TRAITS

The developers of the first generation of genetically modified (transgenic) crops faced a number of technical limitations that constrained the choice of crops and traits that have been taken through to full product development. These constraints included:

- The *availability of genes* controlling traits that could be manipulated. Initially, only traits controlled by single genes could be manipulated; and single genes control only a limited number of traits.
- The *efficiency of the methods* to produce genetically modified plants that express the desired trait consistently under field conditions;
- The need to meet *evolving regulatory requirements* for new crop varieties (and other genetically modified organisms) containing genes from outside their normal range of hybridization.

#### *Choice of single gene traits*

Initially, only certain traits that were controlled by a single gene could be genetically manipulated for the development

of transgenic crops. Thus, single genes that conveyed resistance to certain species of insects (*Lepidoptora*) by producing a toxin, were derived from a soil-borne bacterium (*Bacillus thuringiensis*) and transferred to several plant species. This discovery led ultimately to the commercial production of *Bt* cotton and *Bt* corn. Similarly, various single genes that conferred tolerance to selected herbicides were transferred to soybean, canola and corn. In some instances, these two traits have been combined, to produce insect and herbicide tolerant corn and cotton. These applications have led to reductions in the amount of pesticide being used for insect control in cotton and corn (Carpenter et al 2002; James 2001).

#### *Management of single gene traits*

The careful targeting and correct management of single gene traits is critical for their successful use in agriculture. The management of single gene traits is important so as to avoid the boom/bust cycles typical of single gene resistance when used previously in agriculture.

For example, when single gene traits are being manipulated to enhance pest or disease resistance in a plant, there is a risk that the pest or pathogen will evolve so as to overcome this host resistance. This occurs with conventionally bred plant varieties, which are usually replaced after a number of years as the pest or pathogen evolves (eg wheat varieties with rust resistance). Yet, there are also instances where conventionally bred plant varieties with single-gene based disease resistance has been stable over many years, especially for bacterial and virus diseases.

In the deployment of new transgenic varieties of *Bt*-crops, such as cotton and corn, in broad scale agriculture, much effort has gone into devising and implementing specific crop management arrangements that mitigate against the evolution of resistance in the target pest. These crop cultivation regimes include leaving some of the field as non-transgenic, susceptible crops (refugia for the insects), which reduces the evolutionary pressure on the pest to evolve to overcome the pest resistance in the plant (Gould, 1996; Rousch, 1996).

Another strategy is to include in the plant two different genes for pest resistance (eg two different *Bt* genes). This *gene stacking strategy* makes it more difficult for the pest to evolve, as it has to overcome two or more resistance genes with different modes of action.

## DEALING WITH COMPLEX TRAITS

Most characteristics of food are controlled by more than one gene. Thus taste, aroma, color, nutritional composition and other aspects of food quality are the result of complex biochemical reactions within the plant before and after harvest. Crop yield is also a complex characteristic, with many genes involved in plant development, flowering, and yield components.

Crop responses to stress during cultivation are often controlled by many genes, which stimulate complex biochemical pathways within individual plant cells. For example, many genes control plant responses to fungal infections. Similarly, some plants have developed means to respond to environmental stresses such as drought by changing their metabolism to accommodate having less water available (eg sorghum).

### New targets

Emerging scientific developments are enabling complex traits to be addressed, with the intention of developing new products of potential value for agriculture, human health and the environment (Table 2.1). These include traits in the following categories:

*Increasing sustainable agricultural production*, by the cultivation of crops that are better able to tolerate biotic stresses (pests, diseases and weeds) and abiotic stresses (drought, salinity, and temperature stress).

*Delivering health benefits* through more nutritionally beneficial foods, with higher content of essential vitamins and minerals, especially in staple crops such as rice. Reducing allergenic, carcinogenic and/or toxic compounds in certain plants may also be possible, so that they are safer sources of food. (eg reduced cyanide content in cassava; removing allergenic content of nuts; modifying oil content of certain plants to produce more long chain, poly-unsaturated fatty acids).

*Using plants for pharmaceutical production*: Certain plants may provide a platform (bioreactor) for the more economical and efficient production of specific proteins, such as vaccines against human diseases, and other pharmaceuticals. This approach is being used successfully in microbes and transge-

**Table 2.1.** Complex traits being addressed through emerging scientific developments in plant biotechnology

Target	Trait	Illustrative crops
Improved productivity	Drought tolerance Salinity tolerance Aluminum tolerance Disease resistance	corn rice tobacco rice
Health benefits	Vitamin A content Iron content Reduced toxins	rice, mustard rice cassava
Value added traits	Colour changes Flavour changes	flowers tomato
Plants for medicinal purposes	Vaccine production	banana , potato tomato, tobacco
Plants for industrial purposes	Biodegradable plastic production Starch production Alcohol production	corn  corn sugarcane
“Self regulating” plants	Limiting gene flow to related and/or wild species	oilseed rape
Removing toxic compounds from the environment (bioremediation)	Mercury pollution  Cadmium contamination	<i>Arabidopsis thaliana</i>  tobacco

nic animals that have been genetically engineered to produce certain high value pharmaceuticals (eg insulin in microbes; blood clotting factor in sheep). (Larrick and Thomas, 2001).

*Using plants for production of products for industrial purposes*: These compounds may include novel compounds such as biodegradable plastics and industrial strength fibers, as well as the more efficient production of common plant products such as starch and alcohol used for industrial purposes.

*Environmental benefits*: Using plants (and microbes) to mitigate the effects of industrial pollution (bioremediation), by increasing their ability to remove and/or break down toxic compounds in the soil. Recent demonstrations include trans-

genic plants changing mercury into a less toxic form (Bizily *et al.*, 2000); plants with improved abilities of Cd accumulation (Cobbett, 2000); and plants degrading industrial waste and harmful substances (Hannink *et al.*, 2001).

## From promises to reality

The attractiveness of the new targets amongst complex traits is tempered by the fact that they are technically difficult, requiring the expression and control of multiple genes, often involved in different biochemical pathways.

Recent scientific developments confer the ability to study the structure and function of all the genes within an organism simultaneously (through *genomics*), as well as the protein products they code for (through *proteomics*). It is also possible to study the role of all the chemical compounds in the metabolism of the cell (through *metabolomics*). These emerging scientific developments are being greatly assisted by powerful computing and statistical techniques that enable the assembly, interrogation and interpretation of large databases (through *bioinformatics*). New terms are being coined to describe these rapidly evolving branches of science and the techniques on which they are based (Boxes 2.1-2.3).

These new fields of science are using a series of sophisticated techniques to locate and characterize genes, proteins and other compounds, understand their functions and the means to manipulate them for new purposes. Most importantly, several methodologies have been developed that permit the study of genes, proteins and other metabolites collectively rather than individually (Box 2.4).

The emerging scientific possibilities also pose new challenges in the assessments of the risks and benefits of potential new products to human health and the environment. Some of these potential products are meant for food or feed use, while others are intended for use as pharmaceuticals, and others as compounds for industrial uses. Some will require inter-specific transfer and control of multiple genes. Others will rely on switching on (or off) and better regulating genes that are already present in the organism but not usually expressed.

New scientific developments also offer potential means to overcome some of the risks involved in the cultivation of genetically modified crops. These include limiting the unintentional

### Box 2.1: Components of biotechnology

*Biotechnology is any technique that uses living organisms or parts thereof to make or modify a product, improve plants or animals, or develop microorganisms for specific uses.*

All the characteristics of any given organism are encoded within its *genetic material*, which consists of the collection of *deoxyribonucleic acid* (DNA) molecules that exist in each cell of the organism. The complete set of DNA molecules in an organism comprises its *genome*. The genome is divided into a series of functional units, called genes. The genome contains two copies of each gene, one having been received from each parent. The collection of *traits* displayed by any organism (*phenotype*) depends on which genes are present in its genome (*genotype*). The appearance of any specific phenotypic trait also will depend on many other factors, including: whether the genetic information responsible for the trait [*i.e.* the specific gene(s) associated with it] is turned on (*expressed*) or off, the specific cells within which the genes are expressed, and how the genes, their expression, and the gene products interact with environmental factors (genotype x environment effects).

### Box 2.2: Recombinant DNA Technologies

In the 1970s, a series of complementary advances in the field of molecular biology provided scientists with the ability to readily move DNA between close and more distantly related organisms. Today, this *recombinant DNA technology* has reached a stage where a piece of DNA containing one or more specific genes can be taken from nearly any organism, including plants, animals, bacteria, or viruses, and introduced into any other organism. This process is known as *transformation*. The application of recombinant DNA technology has been termed *genetic engineering*. An organism that has been improved, or *transformed*, using modern techniques of genetic exchange is commonly referred to as a *genetically improved organism* or a *living modified organism*.

The offspring of any traditional cross between two organisms also are *genetically improved* relative to the genotype of either of the contributing parents. Strains that have been genetically improved using recombinant DNA technology to introduce a gene from either the same or a different species also are known as *transgenic strains* and the specific gene transferred is known as a *transgene*. Not all genetically improved organisms involve the use of cross-species genetic exchange. Recombinant DNA technology also can be used to transfer a gene between different varieties of the same species or to modify the expression of one or more of a given plant's own genes, such as the ability to amplify the expression of a gene for disease resistance.

nal movement of genes out of the target crop (through *gene containment*), where such movement may pose a risk to biodiversity or to the environment. Better food safety assessments of any unintended changes in the composition of foods may be undertaken by assessments of the content of whole foods (through *metabolomics*).

The challenge is to identify how emerging scientific discoveries, such as those in the rapidly evolving fields of *genomics*, *proteomics* and *metabolomics*, amongst others, can be translated into safe applications of biotechnology that will lead to new varieties of crops, novel foods and new products that deliver benefits for society. These new applications and their risks and benefits will differ in different parts of the world. Careful thought needs to be given to identifying the most suitable targets and desirable traits for future research and development efforts, in different countries and environments.

## Understanding Plant and Animal Genes

The past decade has 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 invested substantial public and private resources into the development of new technologies, skills and equipment to work with human genes. The same technologies are directly applicable to all other organisms, including plants, animals, insects, and microbes. Thus, the new scientific discipline of *genomics* has arisen, which has contributed to powerful new approaches to identify the functions of genes and their applications in agriculture, medicine, and industry.

*Genomics* refers to means of determining the DNA sequence and identifying the location and function of all the genes contained in the genome of an organism. The advent of large-scale sequencing of entire genomes of organisms as diverse as bacteria, fungi, plants, and animals, is leading to the identification of the complete complement of genes found in many different organisms. This is dramatically enhancing the rate at which an understanding of the function of different genes is being achieved. This new knowledge is changing the ways of developing future improved strains of crops, trees, livestock and fish.

## Platform technologies

Rapid technical advances are occurring in three major areas: (1) DNA sequencing; (2) genome analysis, and (3) computational biology (bioinformatics). Firstly, developments in DNA sequencing have made the acquisition of whole genome sequences possible. These data, when interpreted with the assistance of *bioinformatics*, can provide a complete listing of all the genes present in an organism, (its *genetic blueprint*). The first genome sequence of a higher organism was published in 1996. More than 23 genome sequences are available, and some 60 or more genome sequencing projects of a wide variety of organisms, including plants, animals, parasites, and microbes, are under way (more details on structural genomic projects are available on The Institute for Genomic Research-TIGR- web site, <http://www.tigr.org/>).

Secondly, different types of technologies have been developed for genome analysis, which speed up the process. What puts this type of genome analysis into a different league is that, with the immense increase in the amount of DNA sequence data available, it is possible to scan whole genomes rapidly and to develop a systems approach for mapping genetic traits.

### Box 2.3: New terms in biotechnology

- *Genomics* is the discovery and study of many genes simultaneously on a genome-wide scale. The three-inter-related strands of genomics are structural, functional and comparative genomics:
- *Structural genomics* is concerned with the determination of genome structure at the sequence level.
- *Comparative genomics* involves understanding the molecular basis of similarities and differences between the genomes of organisms.
- *Functional genomics* focuses on understanding the function of specific genes.
- *Proteomics* involves large-scale studies on gene expression at the protein level, including the purification, identification, and quantification of proteins and the determination of their localization, modifications, interactions and activities in the organism.
- *Metabolomics* relates to the analysis of all cellular metabolites, so as to understand all the compounds working in a cell, and the biochemical pathways by which they act.
- *Bioinformatics* is the use of computers for the acquisition, collation, interrogation and interpretation of large collections of complex biological data.



There are continuing improvements in molecular techniques so as to reduce their costs and increase their speed and efficiency in dealing with large numbers of genes. Particularly important are cDNA microarray techniques. These are used in functional genomics to identify how each gene responds to a specific environmental stress. Similar techniques are being developed for the study of proteins, through proteins arrays.

For example, in microarray analysis, when all the genes in a plant (about 25,000 in *Arabidopsis thaliana*) are placed on a glass slide and subjected to a sequence of environmental stresses, it is possible to determine the several genes that are most important in the organism's overall response to stress. These genes will be those that react to all the stresses. This small number of genes can then be studied in more detail for their specific functions and potential use in the development of stress-tolerant plant varieties.

New developments in the molecular tools for gene, protein and metabolite studies have been reviewed recently by van Montagu and Burssens (2002). The molecular tools presently available and their uses are summarized in Box 2.4.

## Bioinformatics

It is possible to use the developments in *bioinformatics* to understand the complex genetic interactions involved in growth, development, and environmental responses. Developments in bioinformatics are allowing the prediction of gene function from gene sequence. Thus from genome sequences of DNA it is possible to build a theoretical framework of the biology of an organism (Flavell, 1999). This forms a powerful base for further experimentation. In addition, as the numbers of physical and genetic maps of different species increase, it becomes possible to compare these across different organisms (through *comparative genomics*), be they microbes, plants or animals, and to significantly reduce the time required identifying important genes. Some of these genes are conserved (shared) between organisms. These technologies allow novel approaches to addressing biological problems.

The results of the early genome mapping projects have shown that many genes are conserved (shared) amongst organisms as diverse as humans, animals, plants, fish and microbes.

### Box 2.4: New Biotechnology Methodologies at Gene, Protein, and Metabolite level

Technology	Methodologies
<b>Genomics</b>	
<i>Structural Genomics</i>	Genomic sequencing: whole genome shot gun sequencing and by low cost shot gun sequencing of enriched genic regions. Expressed sequence tags (EST) sequencing. AFLP, SNP technology.
<i>Functional Genomics</i>	cDNA microarrays AFLP expression profiling High-throughput phenotyping of transgenic plants and temperature sensitive mutants Post transcriptional gene silencing (RNA interference) Chemical genetics
<b>Proteomics</b>	2D gel analysis Gel free protein separation + MALDI-TOF Protein microarrays Twohybrid screen Peptide aptamers
<b>Metabolomics</b>	Liquid/Gas chromatography combined with mass spectrometry (HPLC-MS; HPGC-MS) Capillary electrophoresis (HPCE-MS; CEC)
Source: van Montagu and Burssens 2002	

## Plant genome mapping (structural genomics)

Much research in plant sciences is done on model plants such as *Arabidopsis thaliana*, a small crucifer plant belonging to the *Brassicaceae*. Plant genomes vary greatly in size, ploidy, and chromosome number. *Arabidopsis thaliana* was chosen as the preferred model plant for genomic and related biological studies because of its small genome and short generation time. The knowledge acquired on model plants has spill over benefits to economically important crops in the development of novel traits.

The first plant genome that has been completely sequenced is *Arabidopsis thaliana*, as a result of the international *Arabidopsis* Genome Initiative, which commenced in 1996. The *Arabidopsis* genome sequencing shows both structural features of the genome and gives information about the function of several genes. The total genome holds about

25,500 genes. About half of these genes appear to be specific to plants.

The genomic sequencing of economically important crops is also being undertaken. The most advanced are the several sequencing projects on rice, to map the *indica* (*Oryza sativa* var *indica*) and *japonica* (*Oryza sativa* var *japonica*) rice types. Some of these projects are being undertaken by public consortia, led by scientists from China, Japan and the international rice genome sequencing project, for *indica* rice (Yu et al; 2002). Others are being undertaken by private companies, for *japonica* rice (Goff et al, 2002). Almost half the genes so far identified in rice are similar to genes that occur in *Arabidopsis thaliana*. A maize genome-sequencing project is also in progress. It appears likely that rice, maize and other cereals share a large number of common genes.

There are also many other genome sequencing projects, for over 100 plant species, based on the use of expressed sequence tags (ESTs). These species include soybean, oilseed rape, sugar cane, amongst others (see <http://www.nature.com/genomics>).

### Functional genomics for trait discovery

The purpose of functional genomics is to understand the role that a particular gene plays in the life of a plant. Several techniques have been developed to assist in the identification of gene function. These include knock-out techniques (whereby an individual genes is disrupted and the resulting mutant phenotype compared with the wild type to identify any changes in phenotype). This technique is being used in rice to identify the function of all the genes in rice.

A completely sequenced plant genome such as rice, for example, will provide a pool of genetic markers and genes for rice improvement through marker-assisted selection or genetic transformation. To fully exploit the wealth of molecular data it is necessary to understand the specific biological functions encoded by DNA sequence through detailed genetic and phenotypic analyses. Thus unlike genome sequencing (structural genomics), functional genomics requires diversity of scientific expertise as well as genetic resources for evaluation. In many important food crops, national and international public sector research has a large investment in genetic resources and breeding materials, and a long history of understanding biological function and genotype x environ-

ment interactions. These scientific and biological resources will become increasingly important in gaining knowledge about the function of genes and in developing molecular markers to assist the breeding process (Fischer et al 2000).

### Proteomics

Most cellular functions are carried out by multi-protein complexes. New techniques are enabling these complexes to be unravelled, and the functions of individual proteins understood. Techniques for large-scale protein separation, combined with precise approaches that analyze, identify, and characterize the separated proteins, are enabling researchers to investigate cellular function at the protein level.

*Proteomics* has been enabled by the accumulation of both DNA and protein sequence databases, improvements in mass spectrometry, and the development of computer algorithms for database searching (van Montagu and Burssens 2002).

New techniques allow the identification and quantification of proteins expressed in a particular tissue or in a specific developmental or environmental condition, such as in response to stress. These techniques include 2-Dimensional - protein gel electrophoresis combined with mass spectrometry (*Box 2.4*). Recent improvements are making the techniques more sensitive so that they can detect small amounts of proteins (Mann 2001).

The recent development of protein arrays will be a powerful method to link genomics with proteomics. In this system, fully active proteins are spotted onto membranes to study protein interactions, protein-nucleic acid interactions or protein-ligand interactions (Ge, 2000).

### Metabolomics

Besides the integration of data on protein function and activity, information on metabolite levels in the cell is critical to obtaining a holistic view on a biological process and its functional biocomplexity. Examining changes in metabolic profiles (through *metabolomics*), can be an important part of an integrative approach for assessing gene function and relationships of phenotypes (van Montagu and Burssens, 2002).

Modern high-resolution techniques allow the establishment of a profile of all the metabolites present in a specific

plant tissue. By use of improved tools for analytical chemistry a variety of previously unidentified biochemical pathways can now be understood.

Metabolomics can provide information on metabolic network regulation in response to genetic and environmental perturbations, leading to a better understanding of plant responses to stress. Genes encoding the biosynthetic enzymes can also be more easily identified and consequently the production of secondary and intermediary metabolites in crop plants can be envisaged. The study of secondary metabolites is of particular interest to the pharmaceutical industry, since most drugs are based on plant derived products.

By exploring the three levels of genomic analysis (transcriptome, proteome and metabolome), extensive databases of quantitative information are being developed about the degree to which each gene responds to environmental stimuli. These stimuli may come from biotic and abiotic stresses such as pathogens, pests, drought, salt; from chemicals such as phytohormones, growth regulators, herbicides and pesticides; or from changes in developmental processes such as germination and flowering. These databases will provide insights into the set of genes that control complex responses and will create powerful opportunities to assign functional information to genes of otherwise unknown function (van Montagu and Bursens, 2002).

### Improving Enabling Technologies for Gene Manipulation

The essential tools of gene technology are the techniques that enable one or more genes that control a particular trait to be transferred within or between species, switched on, and made to express themselves in the right place, at the right time and in the right amount. Thus several enabling technologies are required to facilitate the detection, transfer, and expression of genes (Box 2.5).

Initially, only a limited number of plant species and sometimes only a small number of strains within a species could be transformed and regenerated. Much current research is directed at improving the enabling techniques for gene technology, so that the techniques become faster, more precise, less expensive and more widely applicable to all plant species. For example, improved techniques are being developed to enable the introduction and simultaneous expression of

multiple genes that control a particular trait. Other techniques being developed are concerned with new ways to manipulate the plant's own genes, by switching them on and off, perhaps in response to particular environmental stimuli.

### Potential Applications from Emerging Scientific Developments

#### NEW APPROACHES FOR DISEASE RESISTANCE AND STRESS TOLERANCE

Examples of the current approaches that are being used to develop new crop varieties with tolerance to plant diseases are described in Box 2.6. New approaches to dealing with the complex traits associated with abiotic stress tolerance in the environment are summarised in Box 2.7.

#### METABOLIC ENGINEERING FOR PRODUCING SPECIFIC COMPOUNDS IN PLANTS

Metabolic engineering is the *in vivo* manipulation of biochemistry to produce non-protein products or to alter cellular properties (Elborough and Hanley, 2002). The products may be native to the plant or novel (expressed after the introduction of genes from another source). The non-protein products able to be produced by plants include:

- alkaloids such as quinine,
- lipids such as long-chain polyunsaturated fatty acids,
- polyterpenes such as rubber,
- structural components such as lignin,
- osmoprotectants such as glycine betaine,
- aroma compounds such as S-linalool in tomatoes,
- pigments such as blue delphinidin in flowers,
- vitamins such as folic acid,
- biodegradable plastics such as polyhydroxyalkanoates.

Recent research shows that the following applications of metabolic engineering are technically possible in plants at the experimental level: increasing vitamin A content (Ye et al 2000); increasing essential oil production (Mahmoud and Croteau, 2001); decreasing lignin deposition (Abbott et al 2002); stimulating the bioconversion of secondary metabolites to medicinally important alkaloids (Van der Fits and Memelink, 2000); improving tomato flavor (Wang et al 2001)

and producing biodegradable plastics in plants (Bohmert et al, 2000). Several of these products are now in development phase and are likely to be coming forward for regulatory approval over the next several years.

## Meeting Evolving Regulatory Requirements

The revolutionary nature of the discoveries in gene technology has also raised concerns as to the safety of genetically modified foods for human consumption and the potential impact of genetically modified crops and other living modified organisms (LMOs) on the environment. These concerns arise largely because the first generation of genetically modified crops have been produced by the introduction into plants of genes from other phyla, with whom the plants would not normally cross in nature.

Regulatory/risk issues that are being addressed through new research developments include:

- *Limiting gene flow* to related and wild species, by *gene containment*;
- Control of *trait expression* and movement, to minimise impact on non-target species; for example, by limiting transgene expression to specific plant parts and times in the life cycle;
- *Removal of DNA from selectable markers and promoters*, especially when these are derived from bacteria or viruses.

*Selectable markers* are used to demonstrate that a transformation event has occurred and to select these transformed individual plants in the laboratory. These selectable markers have often been genes for antibiotic resistance derived from bacteria. The use of *antibiotic resistance markers* especially has raised some concerns that these may contribute to the further development of antibiotic resistance in humans, by horizontal gene transfer of DNA from genetically modified foods and crops to humans and animal pathogens. The likelihood of this happening is remote. Nevertheless, new selectable markers such as those conveying a green fluorescent pigment are replacing these antibiotic resistant selectable markers. Another approach is to remove the selectable marker after the transformed plants have been selected in the laboratory but before they move into field testing and product development (Hare and Chau, 2002).

### Box 2.5: Gene Transfer Technologies

Two primary methods currently exist for introducing new transgenic genetic material into plant genomes in a functional manner. For plants known as dicots (broad-leaved plants such as soybean, tomato, and cotton), transformation is usually brought about by use of the bacterium, *Agrobacterium tumefaciens*. *Agrobacterium* naturally infects a wide range of plants by inserting some of its own DNA directly into the DNA of the plant. By taking out the undesirable traits associated with *Agrobacterium* infection and inserting a gene of interest into the *Agrobacterium* DNA that will ultimately be incorporated into the plant's DNA, any desired gene can be transferred into a dicot's DNA following bacterial infection. The cells containing the new gene subsequently can be identified (with the aid of selectable markers) and grown (using plant cell culture techniques) into a whole plant that now contains the new transgene incorporated into its DNA.

Plants known as monocots (including cereals such as maize, wheat, and rice) are not readily infected by *Agrobacterium*. The external DNA that is to be transferred into the plant's genome is coated on the surface of small tungsten balls and the balls are physically shot into plant cells (the biolistic method, using a gene gun). Some of the DNA comes off the balls and is incorporated into the DNA of the recipient plant. These transformed cells can similarly be identified and grown via cell culture into a whole plant that contains the foreign DNA. In the case of *Agrobacterium*-mediated gene transfer, its success varies with the plant species, and even between strains within the one species. There are continuing efforts to increase the efficiency of transformation techniques, for example by the selection of particular strains of *Agrobacterium*.

#### Improving gene control

In the early transformation efforts, genes were inserted at random into the genome. The location at which the gene was placed randomly on the plant chromosome has been shown to affect the level of gene expression. (because chromosomal proteins modulated gene expression). For various reasons, an introduced gene may not express itself properly, for example if multiple copies of the gene are inserted into the plant (a feature termed *gene silencing*). Much research effort is going into improving gene control and regulation, so as to increase the precision of the transformation process. Ideally, a single copy of a gene will be able to be inserted into a particular part of the genome. Such improvements in gene control will allow precise gene placement and possibly also gene replacement.

#### Multiple gene control

Where multiple genes are required to produce a desired plant type (phenotype), an important prerequisite is to be able to switch on all the required genes simultaneously and to a similar degree. Yet coordinating the expression of more than one gene has proved difficult. Two types of strategies are employed when introducing multiple genetic modifications. These are *simultaneous* or *sequential transformation*. In *simultaneous transformation*, several genes are either collected into one transforming molecule and introduced into the target plant, or they may be simultaneously inserted while on different transforming molecules. In *sequential transformation*, a transgenic plant is re-transformed with a second gene, or two plant lines receive one transgene each and their progeny are crossed and the resulting double transformant selected from amongst the next generation progeny.

Sources: Van Montague and Bursenns 2002; Elborough & Hanley, 2002

### **Box 2.6: New Approaches to Plant Disease Resistance**

The new developments in genomics offer means for the more targeted development of host resistance to pathogens, based on understanding of the genomic make up of the host and its pathogens, and their interactions in different environments.

In developing new resistant cultivars of crop plants, a desired approach is where disease resistance genes control pathogens at low metabolic cost by inducing defense responses only in those cells that are challenged by the pathogen, thus minimizing any yield penalty in the cultivated crop. Genomic approaches are increasing understanding of the genetic basis of plant disease resistance, through greater understanding of resistance genes themselves and other genes and the pathways that they regulate in the plant.

For example, through *structural genomics*, large-scale sequencing is being used to reveal the detailed organization of resistance gene clusters and the genetic mechanisms involved in generating new resistance to specific pathogens. Global functional analysis is being used to understand the complex regulatory networks and the diversity of proteins involved in resistance and susceptibility in plants.

*Comparative genomics*: Early studies are showing that significant blocks of genetic material are shared among genomes of related species (eg cereals). As the genomes of more plant species are sequenced and compared, it may become possible to predict the position of some genes in various parts of the genome. A few studies are looking at the sharing (*synteny*) of resistance genes within cereals, grasses, and Solanaceous species (potato, tomato). Early results suggest that there is relatively little sharing of disease resistance genes even amongst related species.

*Functional genomics*: It is anticipated that catalogues of genes expressed under a range of different conditions, in different organs, or in different individuals, will become available. The global analysis of plant gene expression is still in its infancy and its full potential is far from being realised. Genes that have altered expression in compatible and incompatible plant-pathogen interactions are being characterised, through *microarray* analysis. For example, in maize, over 100 genes may be involved in the response to a single fungus.

These genes need to be further examined on a gene by gene basis to determine which genes produce proteins that are important in causing resistance in the plant to the pathogen. This may be done by various techniques (such as viral-induced gene silencing, viral over-expression, gene knock-out and promoter-trap strategies). In addition to testing the function of individual genes, these strategies can also be used with libraries of unknown sequences for *gene discovery*. It is likely that each of these approaches will be able to demonstrate the function of some but not all genes, and a combination of strategies will be required.

*Discovery and cloning of disease resistance genes*: About twenty disease resistance genes have now been cloned. This has required expensive map-based cloning or transposon-tagging of individual genes. Resistance gene discovery will become much faster when resistant phenotypes are matched to candidate sequences identified by genomic sequencing. The present limiting step in the discovery of disease resistance genes is the confirmation of the function of individual genes. New approaches are speeding up the introduction and evaluation of individual genes in crops, for example through the use of viral vectors to directly introduce candidate genes into the target plant for evaluation, rather than introducing the genes through a time-consuming transformation and regeneration process.

Source: Michelmore 2000

### **Box 2.7: New Approaches to Plant Stress Tolerance**

Past efforts to improve plant tolerance to drought, high salinity and temperature stress through conventional plant breeding and/or genetic engineering have had limited success, largely due to the complexity of stress responses. More rapid progress is now expected through comparative genomic studies of a diverse set of model organisms, and through the use of new techniques. The latter include techniques such as high-throughput analysis of expressed sequence tags (ESTs), large scale parallel analysis of gene expression, targeted or random mutagenesis and gain-of-function or mutant complementation. The discovery of novel genes, determination of their expression patterns in response to abiotic stress, and an improved understanding of their roles in stress adaptation (through functional genomic studies and proteomics), will provide the basis of new strategies to improve stress tolerance in crops.

#### **Genetic engineering of abiotic stress tolerance traits**

Genetic engineering offers the possibility of the direct introduction into a target plant of a small number of genes. In regard to improving tolerance to abiotic stresses, experimental strategies rely on the transfer of one or more genes that encode either biochemical pathways or endpoints of signaling pathways that are controlled by a constitutively active promoter. These gene products protect the plant, either directly or indirectly, against

environmental stresses. A lack of understanding of metabolic flux, and the interrelationship of osmotic, desiccation and temperature tolerance mechanisms, and their corresponding signaling pathways have limited the success of these transgenic approaches in plants. It is anticipated that new developments in genomics and proteomics will offer more information and new strategies for managing abiotic stress in plants.

#### **Genomic analysis for abiotic stress tolerance**

Studies (using EST and genomic sequencing and cDNA microarray analysis) are seeking to identify the complement of genes essential for tolerance to osmotic potential, desiccation, or temperature stress, respectively. The large data sets being assembled will be integrated and compared with plant species naturally tolerant to these stresses in order to identify tolerance mechanisms that are conserved across species.

Approaches with proteomics will also be necessary to assess the protein modifications that are relevant to stress tolerant phenotypes. The functional determination of all genes that participate in stress adaptation or tolerance is expected to provide an understanding of the biochemical and physiological basis of stress responses in plants. With this information derived from model plants such as *Arabidopsis*, it should become possible to manipulate and optimise stress tolerance traits for improved crop productivity.

Source: Cushman and Bohnert 2000

## EMERGING REGULATORY ISSUES FROM NEW APPLICATIONS AND NOVEL PRODUCTS

There are also some additional regulatory issues emerging from the new applications of plant biotechnology. These issues include:

- Ensuring that when plants are used to produce products for industrial uses, these products do not inadvertently enter the food chain;
- Inter-action with pharmaceutical regulations, where plants are used to produce vaccines and other medicinal products;
- Identifying the extent of regulation required for nutritionally modified foods (*nutriceuticals*), to ensure that these foods meet their makers' claims for improving nutritional quality, for example by the expression of nutritionally significant levels of essential vitamins and minerals;
- Identifying where crops with modifications to genes normally present in the crop species may need to be regulated differently from those containing transgenes from other phyla;
- Identifying where crops with complex traits regulated by several genes may have a reduced likelihood of transferring these complex traits to related species and wild relatives, than transgenic crops carrying single gene traits, and

any differences in regulation and safety assessments that may be required.

Regulatory systems need to be sufficiently flexible to be able to respond to emerging scientific developments, both in terms of encouraging their use to address risks associated with current applications of gene technology, and in recognizing any new issues likely to arise when new scientific opportunities are applied to agriculture.

## Conclusion

Achieving any of the new applications of plant science will require substantial private and public investments, and a wide range of scientific and communication skills. The required scientific skills lie not only in gene technology, but also in the related fields of plant breeding, agronomy and physiology, food and nutrition and in natural resources management. There also needs to be greatly improved linkages amongst the social, scientific, industrial and environmental communities, so as to better define the ways in which science can benefit society and to design new technologies in ways that are socially and environmentally acceptable and beneficial in different countries and communities.

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## Web sites

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- [www.genomicglossaries.com](http://www.genomicglossaries.com)
- [www.irri.org/genomics/irsg.proj/html/\(rice genomic information\)](http://www.irri.org/genomics/irsg.proj/html/(rice_genomic_information))
- [www.agron.missouri.edu/\(maize genome information\)](http://www.agron.missouri.edu/(maize_genome_information))
- [www.nsf.gov/bio/pubs/awards/genome98.htm](http://www.nsf.gov/bio/pubs/awards/genome98.htm)
- [www.nsf.gov/bio/pubs/awards/genome99.htm](http://www.nsf.gov/bio/pubs/awards/genome99.htm)

### 3. Agricultural Biotechnology, Food Safety and Human Health

The applications of modern biotechnology to agriculture, particularly the development of genetically modified foods and other living modified organisms (LMOs), are the subject of widespread public debate as to the safety and efficacy of the new products, and the ethical and socio-economic issues surrounding their development and use. Public concerns about gene technology lie in four major areas:

- Ethical issues
- Socio-economic effects
- Food safety and human health,
- Impact on biodiversity and the environment.

This chapter deals with the scientific issues associated with assessing the risks and benefits of genetically modified foods to human health.

#### Risks to Human Health

There are several areas of public concern in regard to potential human health risks of genetically modified (GM) foods. These concerns relate to understanding the potential of proteins and/or other molecules in GM foods to cause allergic reactions, to act as toxins or carcinogens, and/or to cause food intolerance reactions. Other concerns relate to the use of antibiotic-resistant markers in crops and the potential for their transfer to human pathogens. There are also concerns about possible unintended effects of gene technology.

The risks to be assessed include the need to be aware of possible unintended effects of all new foods, including those produced by the applications of gene technology. The possible unintended consequences of gene technology and the risks that these represent in GM foods include unanticipated compositional changes in food. Such effects are known to occur occasionally in conventional plant breeding, and may also occur during biotechnology-based crop improvement.

Methods to test and evaluate these types of risks are being applied to GM foods to detect any increased risks associated

with particular foods. These methodologies are kept under continuing review and updating through a series of consultations organized by the Food and Agriculture Organization (FAO) and the World Health Organization. The 2000 consultation (FAO/WHO 2000) concluded that “*the Consultation was satisfied with the approach used to assess the safety of the genetically modified foods that have been approved for commercial use.*”

There are no instances known of harmful effects on human health resulting from the consumption of presently available GM foods (OECD 2000). However, this does not mean that risks do not exist as new foods are developed with novel characteristics. GM foods need to be assessed on a case-by-case basis, using scientifically robust techniques, to ensure that those foods that are brought to market are safe for consumers.

#### Benefits to Human Health

The risks in genetically modified foods need to be weighed against the benefits. Future genetically modified foods that are being developed include a number of functional foods that may offer some nutritional benefits to consumers in both industrial and developing countries. Human health benefits of genetically modified foods lie in the potential for introducing traits that convey factors such as:

- Improved nutritional quality of foods (eg higher vitamin and mineral content, lower fat content)
- Reduced toxic compounds in food (eg cassava with lower levels of cyanide)
- Pest tolerant crops able to be grown with lower levels of chemical pesticides
- Disease resistant crops with lower levels of potentially carcinogenic mycotoxins.



## The Scientific Basis of Risk Assessment of Genetically Modified Foods

Several international scientific unions have undertaken a joint review of the scientific basis for assessing the risks and benefits of genetically modified foods and crops, in relation to their impact on human health and nutrition. The findings of this study in regard to the scientific basis of regulation and risk assessment are summarised here, based on the review by Kuiper (2002).

Safety assessment of GM foods is carried out on a case-by-case basis, taking the specific genetic modifications into account, and comparing the properties of the new food with those of the traditional counterpart. This comparative approach, applying the principle of *substantial equivalence*, is based on the assumption that conventional foods are generally considered as safe for consumption, based on a history of safe use. Any identified differences between the GM food and its conventional counterpart are assessed with respect to their safety and nutritional implications for the consumer. The concept of *substantial equivalence*, as developed by the OECD and endorsed by the United Nations Food and Agricultural Organization and the World Health Organization, is a starting point for safety evaluation and contributes to an adequate food safety assessment strategy (Kuiper 2002).

The comparative safety assessment approach should be followed for the next generation of GM foods in order to establish the degree of equivalence with presently available foods. The unmodified host organism may function as the relevant comparison for testing the degree of equivalence, but in some instances a safety assessment of the new food per se will be necessary. The latter may be required for GM crops with extensive modification of existing metabolic pathways or addition of new ones, or for GM plants with decreased levels of naturally occurring toxins, which previously could not be used as food sources. Food safety assessment strategies should be designed on a case-by-case basis (Kuiper 2002). Guidelines for the safety assessments of foods derived from recombinant DNA plants have been developed by FAO/Codex (FAO 2002).

### New methods for safety assessment of whole foods

Safety testing of whole foods is difficult. New approaches for safety assessment of whole foods, taking advantage of modern molecular, biological, toxicological and analytical

methods, are possible. Present approaches for detecting expected and unexpected changes in the composition of GM food crops are primarily based on measurements of a limited selection of single compounds (*targeted approach*). In order to increase the possibility of detecting any unintended effects, new profiling methods (using gene expression technologies, proteomics and metabolomics) should be further developed and validated, for a *non-targeted approach*.

Such new profiling techniques should enable increasingly comprehensive assessments of compositional changes in food. The principal problems associated with advanced technologies for the determination of compositional changes in food lie not in the compositional analyses themselves, but in assessing the significance of the results of those analyses (Kuiper 2002).

New approaches to food safety testing are of particular interest for assessing the safety and nutritional significance of future GM foods and crops that are being developed for potential improvements in their nutritional qualities, such as increased vitamin or mineral content or modified oil content.

### Post market monitoring of foods

The usefulness of post-marketing surveillance as an instrument to gain additional information on long-term effects of foods or food ingredients, either GMO-derived or traditional, should not be overestimated, given the multifactorial origin of many food-related diseases and the variability in genetic predisposition of the human population. Routine application in the food sector may yield limited information, and would be costly. Only in cases with specific biological end-points, for example identifying allergenicity or food intolerance, or when exposure assessment is hampered by insufficient insight into the diets of specific consumer groups, do post-marketing surveillance strategies seem to be useful. Pre-market safety assessment of GM foods will need to provide sufficient safety assurance for consumers (Kuiper, 2002).

### Assessing Risks of Allergic Reactions from GM foods

*Allergenicity* may be raised in foods by raising the level of a naturally occurring (endogenous) allergen or by introducing a new allergen. Any protein that has been added to a food

should be assessed for its potential *allergenicity*, whether it is added by genetic engineering techniques or by other manufacturing processes. More than 90 percent of the food allergens that affect 2 percent of adults and 4 to 6 percent of children are associated with eight food groups, particularly crustacea, eggs, fish, peanuts, soybean, tree nuts and wheat. These foods merit close attention when examining GM foods for the potential for any increased risk of allergenicity (Lehrer 2000).

Genetic modification may alter the allergenicity of a food in different ways. First, the level of naturally occurring (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 the 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 GM food is relatively straightforward. A more difficult issue is if the allergenicity of the source of the protein is unknown. This 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 the need to rely on other criteria with which to assess their potential activity (Lehrer 2000).

A Panel convened by the International Life Sciences Institute (ILSI) Allergy and Immunology Institute and the International Food Biotechnology Council (IFBC) developed scientific approaches to assess the allergic potential of foods derived from GM crop plants. Their report (Metcalf et al 1996) addressed the cell biology, symptoms and treatment of food allergy; developed a catalog of allergenic foods; and characterized major food allergens from the perspectives of the methods used to genetically modify food crops. The Panel also developed a decision tree to provide a framework for assessing the allergic potential of foods derived from genetically modified plants. The decision tree used the following risk assessment criteria: 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.

Genes transferred from sources known to be allergenic should be assumed to encode for that allergen, until proven

otherwise. This transfer of allergenicity was demonstrated when a gene was transferred experimentally from Brazil nut to soybean, with the intention of enhancing production of sulfur-containing amino acids in soybean (Box 3.1).

In the Joint FAO/WHO 2000 consultation *on safety aspects of genetically modified foods of plant origin*, the issue of the allergenicity of genetically modified foods was addressed. The IFBC/ILSI decision-tree approach was adapted for the evaluation of novel proteins introduced into genetically modified foods (Figure 3.1). The Consultation concluded “*that if a genetically modified food contains the product of a gene from a source with known allergenic effects, the gene product should be assumed to be allergenic unless proven otherwise. The transfer of genes from commonly allergenic foods should be discouraged unless it can be documented that the gene transferred does not code for an allergen*” (FAO/WHO 2000).

The FAO/WHO 2000 Consultation also concluded that additional criteria should be considered when the source of the genetic material is not known to be allergenic. The level and site of expression of the novel protein and the functional properties of the novel protein are two such criteria.

The FAO/WHO 2001 Consultation developed a new decision tree (Figure 3.2) that builds upon previous approaches to examining allergenicity but also encompasses several additional strategies. In contrast to previous decision-tree strategies, the FAO/WHO 2001 decision tree makes no distinction between commonly and less commonly allergenic source

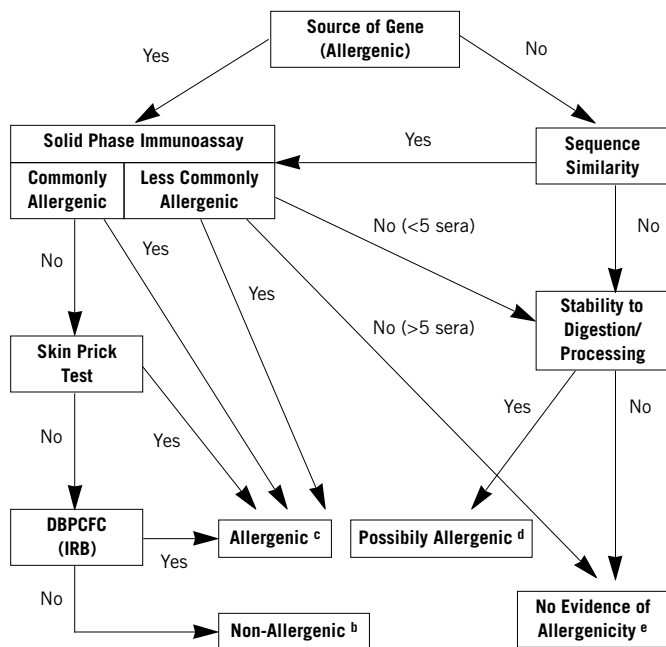
**Box 3.1. Case study of Brazil nut protein gene expressed in soybean**

Soybeans are deficient in essential sulfur-containing amino acids such as methionine and Brazil nuts are rich in this substance. A gene encoding a Brazil nut methionine-rich seed storage protein was introduced into soybean in a experimental approach to develop improved animal feed. Brazil nuts are known to be allergenic, raising concern as to 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 novel protein in soybean. Skin prick tests with three of these individuals confirmed the presence of the allergen in soybean. Based on these findings, further product development was discontinued, in case the modified animal feed inadvertently entered the human food chain.

Source: (Nordlee and others 1996).

**Figure 3.1. Assessment of the allergenic potential of foods derived from genetically modified crop plants.**

Source: FAO/WHO 2000



a. Figure 3.1 was adapted from the decision-tree approach developed by International Food Biotechnology Council and Allergy Immunology Institute of the International Life Sciences Institute (Metcalfe *et al.*, 1996)

b. The combination of tests involving allergic human subjects or blood serum from such subjects would provide a high level of confidence that no major allergens were transferred. The only remaining uncertainty would be the likelihood of a minor allergen affecting a small percentage of the population allergic to the source material.

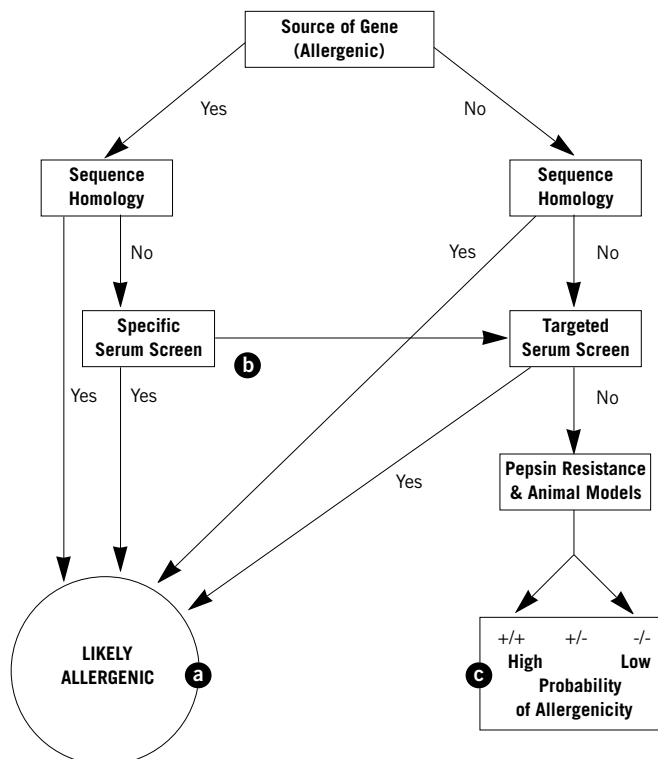
c. Any positive results obtained in tests involving allergic human subjects or blood serum from such subjects would provide a high level of confidence that the novel protein was a potential allergen. Foods containing such novel proteins would need to be labelled to protect allergic consumers.

d. A novel protein with either no sequence similarity to known allergens or derived from a less commonly allergenic source with no evidence of binding to IgE from the blood serum of a few allergic individuals (<5), but that is stable to digestion and processing should be considered a possible allergen. Further evaluation would be necessary to address this uncertainty. The nature of the tests would be determined on a case-by-case basis.

e. A novel protein with no sequence similarity to known allergens and that was not stable to digestion and processing would have no evidence of allergenicity. Similarly, a novel protein expressed by a gene obtained from a less commonly allergenic source and demonstrated to have no binding with IgE from the blood serum of a small number of allergic individuals (>5 but <14) provides no evidence of allergenicity. Stability testing may be included in these cases. However, the level of confidence based on only two decision criteria is modest. The FAO/WHO 2000 Consultation suggested that other criteria should also be considered such as the level of expression of the novel protein.

**Figure 3.2. Assessment of the Allergenic Potential of Foods Derived from Biotechnology.**

Source: FAO/WHO 2001



a. Any positive results obtained from sequence homology comparisons to the sequences of known allergens in existing allergen databases or from serum screening protocols, indicate that the expressed protein is possibly allergenic.

b. The degree of confidence in negative results obtained in the specific serum screen is enhanced by the examination of larger numbers of individual sera. Conducting the specific serum screen with small numbers of individual sera when large numbers of such sera are readily available should be discouraged.

c. When positive results are obtained in both the pepsin resistance and animal model protocols, the expressed protein has a high probability to become an allergen. When negative results are obtained in both protocols, the expressed protein is unlikely to become an allergen. When different results are obtained in the pepsin resistance and animal model protocols, the probability of allergenicity is intermediate.

Source: FAO/WHO 2001

materials with respect to specific serum screening. Thus, specific serum screening is undertaken irrespective of the relative frequency of allergy to the source material in question, provided sera are available.

The 2001 Consultation accepted that the current decision tree (Figure 3.2) will require future modifications as a result of the rapidly expanding scientific base in the allergy and biotechnology fields, but concluded that this decision tree is appropriate now, based on present knowledge. One issue for future consideration is the potential risk associated with inhaling (as distinct from ingesting) allergens from GM crops.

The major challenge is testing the source of the gene from which there is no history of allergenic activity, since there are theoretically no known sera available from allergic subjects to test the product. The presently recommended approach is to compare the amino acid sequence of the protein with that of known allergens. Any sequence similarity with a particular allergen suggests the sera can be used to screen the product by immunochemical procedures. 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 the risk of allergenicity is low and there should not be a problem with marketing the product. If, however, the molecule is stable to digestion and processing, then regulatory authorities need to consider the risks it may pose to some members of the population as a source of possible allergens (Lehrer 2000).

For genetically modified foods entering the marketplace, consumers should be informed by appropriate labeling if the food contains known or suspected allergens, as is the case with other common foods containing nuts or other known allergens (Metcalf et al 1996).

### **Assessing Risks of Antibiotic Resistance Transfer from GM foods**

There are public concerns about the risk that the antibiotic-resistance genes used as selectable markers in developing genetically modified foods may be transferred to microorganisms that are human pathogens, adding to the increasing problem of antibiotic resistance in human pathogens. This problem of decreasing effectiveness of antibiotics has arisen largely as a result of widespread overuse of antibiotics in human and animal health. However it is unlikely that the use

of antibiotic markers in GM foods is a component of the problem. Studies by the OECD, FAO and WHO have assessed the risk of transfer of an antibiotic marker from a GM food to a human pathogen as being remote. (FAO/WHO, 2000). This would entail the horizontal transfer of a gene across widely dispersed species, a rare event. Nevertheless, the use of these antibiotic markers as selectable markers in GM foods is being phased out.

Selectable marker genes are required to ensure the efficient genetic modification of crops. Selectable markers used to identify transformed plants in the development phase confer resistance either to antibiotics, herbicide or metabolic inhibitors. Once the transformed plants have been identified, these markers are no longer required. Several strategies (site specific recombination, homologous recombination, transposition, and co-transformation) have been developed to eliminate these genes from the genome after they have fulfilled their purpose. Chemically inducible, site-specific recombinase systems are also emerging as valuable tools for efficiently regulating the excision of marker transgenes when their expression is no longer required (Hare and Chau 2002).

### **Labeling of Genetically Modified Foods**

A key concern of consumers is being able to identify those foods that may contain allergens and other potentially harmful substances, so that people who have allergic or food intolerant reactions to particular foods can avoid them. Others may wish to avoid certain foods on health, ethical or religious grounds. Informative food labeling could provide information about the composition of specific products and enable consumers to make choices about their use, after assessing their risks and potential beneficial effects.

Informative labeling of GM foods requires that the nutrient content of the food is disclosed, in relation to similar foods produced by conventional techniques of crop improvement and cultivation, as well as any additional protein (or other) content resulting from the specific transgene modification. Labeling of food as *GM* or *non GM* indicates the use of modern molecular plant breeding and other production techniques involving gene technology. It conveys no information to consumers as to the nutritional content or safety of particular foods.

## Food Safety Standards

One result of public concerns about the safety of GM foods is that GM foods are now required to meet higher standards of safety than foods produced either by conventional agriculture or by organic agriculture.

Given increasing global concerns about food safety broadly, all countries need to have in place food safety regulations and

human and institutional capacity to be able to set and apply food safety standards. Food safety standards are required to ensure the quality of food supplies both for local consumption in the country of origin and to meet increasingly stringent export standards set by importing countries. Achieving internationally agreed food safety standards for GM foods that guarantee safety of products, and are not perceived to be non-tariff barriers to trade is a challenge to the international community.

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- [www.vib.be](http://www.vib.be)
- [www.who.int/fsf](http://www.who.int/fsf)

## 4. Agricultural Biotechnology, Biodiversity and the Environment

Public concerns about the risks and benefits of living modified organisms (LMOs) in the environment are based on the premise that when such organisms contain genes introduced from outside their normal range of sexual compatibility, these organisms may present new risks to the environment. Present gene technology enables new and potentially useful traits to be introduced into plants, trees, microorganisms, livestock and fish. Although new strains of all have been developed experimentally, only genetically modified (transgenic) crops are in widespread commercial cultivation in the environment.

In 2001, approximately 52.6 million ha of genetically modified crops were cultivated commercially by some 5.5 million farmers in 13 countries (James 2001). These crops were mainly genetically modified corn, cotton, oil seed rape and soybean, modified with new genes for insect resistance and/or herbicide tolerance. (Figure 1.1; Tables 1.2, 1.3).

### Environmental Impact Issues

The issues about the impact of living modified organisms (LMOs) on the environment are about the risks and benefits of *direct ecological effects and indirect environmental effects* (Johnson 2000). Amongst direct effects, most concern is about the potential impact of LMOs on biodiversity, including their direct impact on non-target species. Amongst indirect effects, these effects may be the result of changing agricultural management practices, particularly those brought about by the use of transgenic crops in intensive crop management systems. There are also beneficial effects of genetically modified crops in the environment, when compared to present agricultural practices and other technology options (Carpenter et al 2002). These benefits also need to be taken into account when undertaking risk/benefit analysis of specific applications in particular environments.

In terms of international obligations, the Cartagena Biosafety Protocol of the Convention on Biological Diversity was

agreed in January 1999 by over 100 countries. The Protocol states that nations have the right and responsibility to determine if the applications of modern biotechnology, in particular living modified organisms (LMOs), will have any impact on biodiversity.

### Direct ecological effects of genetically modified plants in the environment

In addressing the risks posed by the cultivation of plants in the environment, five environmentally related safety issues need to be considered. These issues are the potential for:

- *Gene transfer*, meaning the movement of genes from a crop through outcrossing with wild relatives to form new hybrid plants.
- *Weediness*, meaning the tendency of a plant to spread beyond the field where first planted and establish itself as a weed or invasive species.
- *Trait effects*, meaning effects of traits that are potentially harmful to non target organisms.
- *Genetic and phenotypic variability* meaning the tendency of the plant to exhibit unexpected characteristics.
- *Expression of genetic material from pathogens*, such as the risk of genetic recombinations following mixed virus infections.

*Gene flow and transfer of traits to other species:* Gene transfer may be an issue when crops are being grown in areas close to their wild relatives with whom they are able to cross naturally to form inter-specific hybrids. Natural hybridization occurs within 12 of the world's 13 most important food crops and their wild relatives (the exception being banana since cultivated banana is infertile). Wild relatives occur mainly in the centers of diversity of these crops. (Table 4.1).

Natural hybridization may occur at low frequency when pollen blows or is otherwise transported from crops to wild relatives in the vicinity. Recent research confirms that genes

introduced into some genetically modified crops may move into related native species at low frequency. The difference from natural hybridization is that genes inserted into GM crops are often derived from other phyla, giving traits that have not been present in wild plant populations. The ecological concern is that these genes may change the fitness and population dynamics of hybrids formed between native plants and related GM crops, eventually backcrossing genes into the native species. The importance of pollen transfer from GM crops to wild relatives is not that it occurs but whether the resulting hybrids survive and reproduce and introgress genes back into the native population and, if so, whether these have any negative environmental impacts. The issue is not so much the rate of gene flow, rather the impact that this might have on agriculture and the environment (Johnson 2000).

**Weediness:** There are concerns that GM plants could have negative impacts on natural ecosystems by increasing weediness by two routes. Firstly, the GM plants could establish self-sustaining populations outside cultivation themselves. The concern is that these plants may become invasive weeds that out compete wild populations and thus lead to further decreases in biodiversity in native plant habitats. Weeds having

tolerance to a range of herbicides could also emerge. Secondly, novel genes from GM crops could be introduced into their wild relatives by pollen spread and the survival and reproduction of the resulting hybrids. This may have negative impact on the wild plant population if new genes are introgressed back into the wild plant population. For this to happen, the new genes must increase the plants' fitness to survive and reproduce in the wild.

Transfer of certain genes, such as resistance to insects, fungi and viruses may increase fitness (ability to reproduce) of any resulting hybrids. If hybrids acquired insect resistance from GM crops, they could damage food chains dependent on insects feeding on previously nontoxic wild plants. It is possible that "foreign" genes introduced accidentally from GM crops to crop/native plant hybrids would decrease their fitness in the wild, leading to rapid selection of these genes out of the population.

**Trait effects:** Trait effects are the effects of traits that may be harmful to non-target organisms. For example, plants modified to produce pesticidal proteins such as *Bt* toxins may have both direct and indirect effects on populations of non-target species. One group of *Bt* toxins primarily targets *Lepidoptera*

**Table 4.1:** Centers of diversity of the world's major food crops and their wild relatives

Food Crop	Scientific Name	Center of Origin	First Domestication
Corn	<i>Zea mays</i>	México	Mexico
Beans	<i>Phaseolus spp.</i>	Central and South America	Central America and South America for <i>P. vulgaris</i> and <i>P. lunatus</i> ; Central America for <i>P. coccineus</i> and <i>P. acutifolius</i>
Potato	<i>Solanum tuberosum</i>	High plateau of Bolivia-Peru	High plateau of Bolivia-Peru
Sweet Potato	<i>Ipomoea batatas</i>	Western South America, especially Peru and possibly Mexico	Western South America
Cassava	<i>Manihot esculenta</i>	Central and South America	Central and South America
Groundnut	<i>Arachis hypogaea</i>	Peru (earliest archaeological evidence), Southern Bolivia and Northern Argentina	Southern Bolivia and Northern Argentina
Wheat	<i>Triticum spp.</i>	Mediterranean Region and Southwest Asia	Mediterranean Region and Southwest Asia
Barley	<i>Hordeum vulgare</i>	Southwestern Asia	Southwestern Asia
Sorghum	<i>Sorghum bicolor</i>	Africa	Sudan, Chad
Millets	<i>Eleusine coracana</i> and <i>Pennisetum americanum</i>	Africa	Africa
Rice	<i>Oryza sativa</i> and <i>Oryza glaberrima</i>	India or China	Large area including NE India, N Bangladesh, Thailand, Burma, Laos, Vietnam and S. China
Soyabean	<i>Glycine max</i>	Eastern part of northern China	Eastern part of northern China
Banana/Plantain	<i>Musa spp</i>	New Guinea, Malay peninsula for <i>Musa acuminata</i>	New Guinea and the Pacific Islands

Source: *Platais and Persley 2002*

(butterflies and moths, particularly the European corn borer) and the other affects *Coleoptera* (beetles). The effects of *Bt* toxin-producing plants on non-pest species amongst these insect groups may vary widely, depending on the sensitivity of different insect species, the concentration of *Bt* toxin in the transgenic plants and environmental conditions.

For example, laboratory experiments demonstrated that the larvae of Monarch butterflies (a relative of the European corn borer) were susceptible to pollen from *Bt* corn when ingested in large amounts. Subsequent field experiments in several locations in North America found that there were no significant differences between Monarch butterfly survival in areas planted with *Bt* corn and those planted with conventional crops. Ecological studies published by the US National Academies of Science also show that presently cultivated strains of *Bt* corn pose little risk to Monarch butterflies (Zangerl *et al* 2001).

*Genetic and phenotypic variability:* Genetic and phenotypic variability is the tendency of a plant to exhibit unexpected characteristics in addition to the expected characteristics. This trait is well known from conventional breeding, but becomes an identifiable hazard if the variability leads to one of the other biosafety issues, such as greater weediness or greater tendency for outcrossing in the genetically modified organism.

*Expression of genetic material from pathogens:* Another potential hazard is the possibility of recombination of a virus gene expressed by the plant with genes from another virus infecting that plant. This risk is similar to the risk of genetic recombinations following mixed virus infections, which also occur in nature.

## Indirect environmental effects of genetically modified plants

*Genetically modified crops and agricultural intensification: effects on biodiversity:* The management of some genetically modified crops is likely to differ from conventional intensive agriculture or organic farming.

The use of more effective pesticides (including herbicides) over the past 20 years has been a major cause of the decline in farmland birds, arable wild plants, and insects in several European countries. The more widespread use of broad-spectrum herbicides may accelerate this trend. This may be of more concern in Europe where farming, wild landscapes and wildlife habitats are in closer proximity to one another than in

other areas with more broad-scale agriculture, such as North America and Australia (Johnson 2000).

Besides the aesthetic and scientific reasons for conserving biodiversity within and around agricultural crops, there is another important utilitarian reason for doing so. This is the possibility of losing the food chain links between native species and crop systems. This link is vital to preserve the early warning function of biodiversity, whereby damage to feeding species (eg birds) signal warning of dangers in food crops or the chemicals used to manage them. On the other hand, there is evidence accumulating that the use of GM crops with insect resistance is reducing the volume and frequency of pesticide use on cotton, corn and soybean in North America (Carpenter *et al* 2002). Similar transgenic crops are also having demonstrable beneficial effects on human health in China and South Africa (Pray *et al* 2000).

The future development of new crops with improved tolerance to abiotic factors (such as drought, salinity and frost) and the advent of 'pharmed' crops that may be used to produce vaccines and industrial products, may also change crop management practices. These new crops may either increase or decrease demand for arable land in the long term. They may also put further pressure on natural biodiversity when crop cultivation extends into presently marginal lands, or into areas not presently used for agriculture. For example, salt tolerant rice may be able to be cultivated in coastal areas where mangroves presently grow, with resulting ecological changes in land and water use and associated plant and marine life.

Biotechnology can also contribute to the characterization and conservation of biodiversity. Increasing the productivity of crops can reduce pressure on biodiversity by reducing the need for agriculture to move into forests and marginal lands.

## New scientific developments

There are some promising new developments in R&D that may assist in the design of future genetically modified crops that would have clear benefits to the environment and that would mitigate some of the environmentally damaging effects of agricultural intensification (Johnson 2000). Some R&D challenges for the 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.



- Achieving insect resistance by altering physical characteristics of plants, perhaps by increasing hairiness or thickening the plant cuticle.
- Altering the growing characteristics of crops, for example by shortening the growing season or changing the timing of harvests, offers the prospect of allowing more fallow land and less autumn planting.
- Using new discoveries from functional genomics to identify useful genes within species, and understanding how better to regulate them to control useful traits. This approach will place more emphasis on the control of genes already existing within species rather than on inter-specific gene transfers, especially those that require gene movement amongst distantly related species.

The greater understanding of the environmental risks and benefits posed by gene technology may lead to the better design of future genetically modified crops. For example, where gene flow is a risk in out-crossing crops growing in their center of diversity, close to wild relatives with which they may cross, it may be possible to include genetic mechanisms of pollen incompatibility to limit the risk of gene flow. Also, where crops are to be used for industrial purposes to produce products such as vaccines, or industrial polymers, the crop of choice should be one with which there is no risk of gene flow to related edible crops or wild species in the area of cultivation (Johnson 2000).

### Future ecological research needs

There is a need for further ecological research and developing agreed standards and protocols to enable the continuing monitoring of the behavior of genetically modified crops after their experimental (small-scale) and commercial (large-scale) releases into the environment. There is a need to set up effective monitoring systems to detect gene transfer and research to assess its ecological impacts. Most of the present research has been undertaken in Europe and North America. Little has been undertaken in tropical environ-

ments, which are the centers of diversity of most of the world's major food crops (Table 4.1).

Such ecological research will require additional support by national governments and international agencies in their efforts to develop methodologies and undertake participatory field studies on the environmental impact of GM crops. These assessments should be undertaken using participatory approaches so as to involve local communities in the evaluation of the risks and benefits of new technologies.

Additional data would then feed back into risk assessments, so as to inform future decisions on the decisions on the appropriate technology choices in addressing specific problems, including the development and management of genetically modified crops for agricultural purposes.

### Future role of the international agricultural research centers

There is a need for greater science-based understanding of the risks and benefits in the applications of biotechnology in agriculture and the environment. The international agricultural research centers supported by the Consultative Group on International Agricultural Research (CGIAR) may have an important role to play here. The centers represent a unique resource in addressing these issues, as they constitute:

- The world's largest collection of plant genetic resources and their wild relatives held in trust by the Centers.
- A geographically dispersed network of research centers, located throughout the world's major agro-ecosystems, and across the centers of diversity of the world's major food crops.
- Data and research capability in the use of geographic information systems that could be used to model and evaluate the likely behavior of living modified organisms in different environments and assess the risks and benefits associated with particular traits in those environments.
- Research capabilities in the applications of gene technology to crops, livestock, forestry and fisheries, and associated socio-economic, policy and management expertise.

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## Web sites

- [www.icsu.org](http://www.icsu.org)
- [www.biodiv.org/biosafety](http://www.biodiv.org/biosafety)
- <http://binas.unido.org/binas>
- [www.checkbiotech.org](http://www.checkbiotech.org)
- [www.doylefoundation.org](http://www.doylefoundation.org)
- [www.iobc.org](http://www.iobc.org)
- [www.unep.org](http://www.unep.org)

# Glossary

## Glossary of Terms

**Bioinformatics:** the assembly of data from genomic analysis into accessible forms. It involves the application of information technology to analyze and manage large data sets resulting from gene sequencing or related techniques.

**Diagnostics:** more accurate and quicker identification of pathogens using new diagnostics based on molecular characterization of the pathogens.

**Functional genomics** is the knowledge that converts the molecular information represented by DNA into an understanding of gene functions and effects: how and why genes behave in certain species and under specific conditions. To address gene function and expression specifically, the recovery and identification of mutant and over-expressed phenotypes can be employed. Functional genomics also entails research on the protein function (proteomics) or, even more broadly, the whole metabolism (metabolomics) of an organism.

**Gene chips** (also called DNA chips) or microarrays. Identified expressed gene sequences of an organism can, as expressed sequence tags or synthesized oligonucleotides, be placed on a matrix. This matrix can be a solid support such as glass. If a sample containing DNA or RNA is added, those molecules that are complementary in sequence will hybridize. By making the added molecules fluorescent, it is possible to detect whether the sample contains DNA or RNA of the respective genetic sequence initially mounted on the matrix.

**Genomics:** the molecular characterization of all the genes in a species.

**High throughput** (HTP) screening makes use of techniques that allow for a fast and simple test on the presence or absence of a desirable structure, such as a specific DNA sequence and the expression patterns of genes in res-

ponse to different stimuli. HTP screening often uses DNA chips or microarrays and automated data processing for large-scale screening, for example to identify new targets for drug development.

**Insertion mutants** are mutants of genes that are obtained by inserting DNA, for instance through mobile DNA sequences, transposons. In plant research, the capacity of the bacterium *Agrobacterium* to introduce DNA into the plant genome is employed to induce mutants. In both cases, mutations lead to lacking or changing gene functions that are revealed by aberrant phenotypes. Insertion mutant isolation, and subsequent identification and analysis are employed in model plants such as *Arabidopsis* and in crop plants such as maize and rice.

**Molecular breeding:** identification and evaluation of useful traits using marker-assisted selection.

**Shotgun genome sequencing** is a sequencing strategy for which parts of DNA are randomly sequenced. The sequences obtained have a considerable overlap and by using appropriate computer software it is possible to compare sequences and align them to build larger units of genetic information. This sequencing strategy can be automated and leads to rapid sequencing information, but it is less precise than a systematic sequencing approach.

**Single nucleotide polymorphisms** (SNPs) are the most common type of genetic variation. SNPs are stable mutations consisting of a change at a single base in a DNA molecule. SNPs can be detected by HTP analyses, for instance with DNA chips, and they are then mapped by DNA sequencing.

**Transformation:** introduction of single genes conferring potentially useful traits.

**Vaccine technology:** using modern immunology to develop recombinant DNA vaccines for improved control of animal and fish disease.

## A genetic “google”: Turning the language of the cell into the book of life

**DNA = Letters:**

Letters of the alphabet (four different *nucleic acids*, abbreviated as G,A,T,C)

**Genes = Words**

A specific string of letters make a word (*gene*) that has a meaning (*function*)

**Genomes = many words**

Different strings of words (*genes*) make up a *genome*

**Genomics = studying words**

Study of all the words (*genes*) in an organism (*genome*)

**Structural genomics**

Dictionary of words (*genes*), without meanings

**Functional genomics**

Identifies meaning (*function*) of the words (*genes*)

**Comparative genomics**

Identifies if same words (*genes*) occur in different dictionaries (*genomes*) (ie. Identify shared *genes amongst different organisms*) that may have the same meaning (*function*)

**Bioinformatics = search engine**

The “google” for genes:

There are computer based programs and data bases to help locate words (*genes*), understand their meaning (*function*) and identify where they are shared amongst different dictionaries (*genomes*)

*This overview document will be complemented by a meta-review that has been commissioned by ICSU and its Advisory Committee on Genetic Engineering and Biotechnology (ACOGEB). This meta review is analysing the key findings of some twenty reviews on GM foods and crops that have been conducted by various national, international and private agencies within the past three years.*

*Several reviews have concentrated on those aspects of gene technology most likely to affect human health, while others were more concerned with the potential impact of gene technology on agriculture and the environment. Some reviews, both national and international, were charged with advising governments on appropriate regulatory frameworks for gene technology.*

*Other reviews have been concerned specifically with the potential impact of gene technology in emerging economies. Several reviews have looked not only at the scientific issues but have also considered the broader context, including the ethics, and values that underpin the interaction between science and societies in different parts of the world. The reviews were*

*mainly those conducted by means of independent panels of experts, usually commissioned by national academies of science or by international agencies, including the United Nations agencies.*

*The content of the reviews is being analysed in the areas of:*

- *Human health -Risks and benefits*
- *Agriculture and the environment*
- *Regulatory frameworks*
- *Emerging issues*
- *Gaps in knowledge*

*Particular attention is given to identifying the areas of commonality amongst the reviews, identifying any areas of differing perspective, and highlighting those areas where there are gaps in knowledge that may be able to be addressed through additional well targeted research.*

*The meta review will be published by ICSU in September 2002, at the time of the ICSU General Assembly in Rio de Janeiro, and will be available at [www.icsu.org](http://www.icsu.org).*

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