Modern food biotechnology, human health and development: an evidence-based study

FOOD SAFETY DEPARTMENT*
WORLD HEALTH ORGANIZATION

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ACRONYMS AND ABBREVIATIONS

Bt	*Bacillus thuringiensis*
CBD	Convention on Biological Diversity
CPB	Cartagena Protocol on Biosafety
DNA	deoxyribonucleic acid
ERA	environmental risk assessment
EU	European Union
FAO	Food and Agriculture Organization of the United Nations
GEF	Global Environment Facility
GM	genetically modified
GMM	genetically modified microorganism
GMO	genetically modified organism
IPR	intellectual property right
MLS	multilateral system of facilitated access and benefit-sharing
NGO	nongovernmental organization
OECD	Organisation for Economic Co-operation and Development
PVP	plant variety protection
R&D	research and development
SPS Agreement	Agreement on the Application of Sanitary and Phytosanitary Measures
TRIPS	Agreement on trade-related aspects of intellectual property rights
UNCED	United Nations Conference on Environment and Development
UNDP	United Nations Development Programme
UNEP	United Nations Environment Programme
WHO	World Health Organization
WTO	World Trade Organization

EXECUTIVE SUMMARY

This study was commissioned by the World Health Organization (WHO) to establish a knowledge base for evaluating the application of modern biotechnology in food production. The study does not seek to address all issues and evidence in detail, but rather aims to place in context the overall impact of this technology on human health and development. The study reviews evidence in several broad areas related to the use of genetically modified (GM) organisms in the food supply (GM foods), including a review of GM food products currently available, the assessment of risks and benefits, the broader impact on societies, and the existing regulatory capacity in countries. The evidence was collected and collated by WHO with the support of a background group of external experts (list of experts - annex 1). Data for the study were gathered through traditional methodology as well as through an open questionnaire and an Internet-based electronic discussion process. Preliminary results were discussed at a broad stakeholder meeting held in 2003 (list of participants - annex 1), informing further data search and revision.

The first GM food (delayed-ripening tomato) was introduced on the US market in the mid-1990s. Since then, GM strains of maize, soybean, rape and cotton have been adopted by a number of countries and marketed internationally. In addition, GM varieties of papaya, potato, rice, squash and sugar beet have been trialed or released. It is estimated that GM crops cover almost 4% of total global arable land.

The development of GM organisms (GMOs) offers the potential for increased agricultural productivity or improved nutritional value that can contribute directly to enhancing human health and development. From a health perspective, there may also be indirect benefits, such as reduced agricultural chemical usage and enhanced farm income, and improved crop sustainability and food security, particularly in developing countries. Contradictory findings for such benefits sometimes reflect different regional or agricultural conditions.

The use of GMOs may also involve potential risks for human health and development. Many genes used in GMOs have not been in the food supply before. While new types of conventional food crops are not usually subject to safety assessment before marketing, assessments of GM foods were undertaken before the first crops were commercialized. To provide international consistency in the assessment of GM foods, principles developed by the Codex Alimentarius Commission (a joint programme of WHO and the Food and Agriculture Organization of the United Nations; FAO) now cover food safety, while the Cartagena Protocol on Biosafety covers environmental safety of GMOs. Many countries have established specific premarket regulatory systems in accordance with this international guidance that require a case-by-case risk assessment of each GM food. Risk assessment methodology undergoes continuous improvements, a fact that is recognized by the Codex principles, including the need for risk assessments to consider both the intended and unintended effects of such foods in the food supply. GM foods currently traded on the international market have passed risk assessments in several countries and are not likely, nor have been shown, to present risks for human health.

Although risk-assessment systems have been in use for some time, the perception of GM food among consumers has not always recognized these assessments. One explanation is that many national food-safety systems have had problems performing good risk communication in this area. In many countries, social and ethical considerations may cause also resistance to modifications which interfere with genes. These conflicts often reflect deeper issues related to the interaction of human society with nature — issues that should be taken seriously in any communication effort. However, while in many regions, food is clearly considered part of historical identity and societal life, scepticism towards GM food is not necessarily linked to traditionalism or to absence of knowledge about this new technology. Investigations of public perception indicate that the sceptical consumer will acknowledge arguments both for and against GM food and, in general, does not demand ‘zero risk’. Likewise, it has been seen that critical attitudes towards GM food are not necessarily linked to a negative attitude towards the use

of biotechnology as such, as demonstrated by a generally positive attitude towards the use of biotechnology in modern medicine. The issue of benefit to society therefore seems to constitute an important aspect related to acceptance of new technology.

Intellectual property rights are an important part of the GM food debate. Problems of assuring equal access to genetic resources, sharing benefits on a global level, and avoiding monopolization exist for GM food as for other uses of gene technology. Related to this are concerns about a growing influence of the chemical industry in seed markets. Sustainable agriculture and biodiversity are likely to benefit most when a rich variety of crops are planted, and a potential exclusive use of certain chemical-resistant GM crops could be seen to create dependency.

Conflicting assessments and incomplete substantiation of the benefits, risks and limitations of GM food have added to existing controversies. During a famine situation in southern Africa in 2002, the reluctance among several recipient countries to receive GM food aid was not primarily linked to health or environment issues, but to socioeconomic, ownership and ethical issues. Such controversies have not only highlighted the wide range of opinions within and between Member States, but also the existing diversity in regulatory frameworks and principles for assessing the benefits and risks of GM food. In addition, many developing countries cannot afford to build the separate capacities required for effective regulation of GM foods, which again underlines the benefits that could be derived from international work for broader evaluations of GM food applications.

At the international level, 15 legally binding instruments and non-binding codes of practice address some aspect of GMO regulation or trade. Such sector-based regulations increase the already overstretched capacity of developing countries, and present challenges to develop a fully coherent policy and regulatory framework for modern biotechnology. This study makes the case for the need for an evidence base to facilitate a more coherent evaluation of the application of modern food biotechnology and the use of GM foods. Such an evidence base should: deal with the assessment of human health and environmental risk as well as benefit; evaluate socioeconomic factors, including intellectual property rights; and consider ethical aspects. International harmonization in all these areas is a prerequisite for the prudent, safe and sustainable development of any new technology, including the use of biotechnology to produce food. Work towards such harmonization can only move forward through inter-sectoral collaboration and would therefore necessarily extend beyond the WHO mandate into the mandates of several other international organizations. This report should be seen as one possible starting point for further inter-sectoral discussions.

1. INTRODUCTION

1.1 Goals and terms of reference

The World Health Organization (WHO) commissioned this study to establish a broad knowledge base for Member States, international standard-setting bodies and other stakeholders, in order to achieve transparent and inclusive consensus on the evaluation and application of modern biotechnology in the production of food. The aim of this study is to determine the significance of the application of modern biotechnology to food production in terms of human health and development. The study does not seek to address all issues and evidence in detail, but rather to place in context the overall impact that modern food biotechnology may have on human health and development. It is intended to serve as a scientific basis for potential discussion by the governing bodies of WHO.

The study reviews evidence in five broad areas:

1. Current use, research and impending development of foods produced through modern biotechnology, and their significance for human health and development.
2. Risk assessments of present and future products of modern biotechnology in relation to food safety, human nutrition and environmental health.
3. The significance of modern food biotechnology for food security, and the impact of intellectual property rights on research.
4. National capacity for risk assessment and management.
5. The impact of modern food biotechnology on civil society, considering social and ethical concerns.

1.2 Methodology

A background group consisting of experts from various Member States (*Annex 1*) established the terms of reference of the study and a guidance document that directed a small team within WHO to gather the evidence. Members of the background group also assisted in data gathering.

Data were gathered using extensive literature and Internet searches, and through a questionnaire supported by approximately 120 responses which was circulated to a broad range of stakeholders in May 2002. The comments received from an electronic stakeholder discussion held between January and April 2003 have also been incorporated. The opinions of participants who attended a stakeholder meeting on 5–6 June 2003 in Geneva, comprising representatives from governments, consumers, industry, research and nongovernmental organizations (NGOs), from developed and developing countries, have also been included.

The focus on including a broad basis of scientific evidence as well as descriptions of opinions from a broad group of stakeholders has resulted in a list of references which includes documentation from many Internet sites. Documentation originating solely from Internet sites should not, in general, be treated or presented as documentation derived from peer-reviewed literature; however, it has been considered necessary in this study to include data and information presented from both sources, with a clear indication of when information is available solely from Internet sources.

1.3 Modern food biotechnology: definition and overview of potential benefits and risks

According to the definition of the Codex Alimentarius Commission (CAC 2001a) (adapted from the Cartagena Protocol on Biosafety — see *Section 3.3*), modern biotechnology is defined as the application of (i) *in vitro* nucleic acid techniques, including recombinant deoxyribonucleic acid (DNA) and direct injection of nucleic acid into cells or organelles, or (ii) fusion of cells beyond the taxonomic

family, that overcome natural physiological reproductive or recombination barriers, and that are not techniques used in traditional breeding and selection.

This study focuses on the application of modern biotechnology (especially recombinant DNA technology) to organisms used to produce food.

The application of modern biotechnology to food production presents new opportunities and challenges for human health and development. Recombinant gene technology, the most well-known modern biotechnology, enables plants, animals and microorganisms to be genetically modified (GM) with novel traits beyond what is possible through traditional breeding and selection technologies. It is recognized that techniques such as cloning, tissue culture and marker-assisted breeding are often regarded as modern biotechnologies, in addition to genetic modification.

The inclusion of novel traits potentially offers increased agricultural productivity, or improved quality and nutritional and processing characteristics, which can contribute directly to enhancing human health and development. From a health perspective, there may also be indirect benefits, such as reduction in agricultural chemical usage, and enhanced farm income, crop sustainability and food security, particularly in developing countries.

The novel traits in genetically modified organisms (GMOs) may also, however, carry potential direct risks to human health and development. Many, but not all, genes and traits used in agricultural GMOs are novel and have no history of safe food use. Several countries have instituted guidelines or legislation for mandatory premarket risk assessment of GM food. At the international level, agreements and standards are available to address these concerns.

GMOs may also affect human health indirectly through detrimental impacts on the environment, or through unfavourable impacts on economic (including trade), social and ethical factors.

These impacts need to be assessed in relation to the benefits and risks that may also arise from foods that have not been genetically modified. For example, new, conventionally bred varieties of a crop plant may also have impacts — both positive and negative — on human health and the environment.

1.4 Recent international controversies and study initiative

Conflicting assessments and incomplete substantiation of the benefits, risks and limitations of GM food organisms by various scientific, commercial, consumer and public organizations have resulted in national and international controversy regarding their safe use as food and safe release into the environment. An example is the debate on food aid that contained GM material offered to countries in southern Africa in 2002, after 13 million people faced famine following failed harvests. This international debate highlighted several important issues, such as health, safety, development, ownership and international trade in GMOs.

Such controversies have not only highlighted the wide range of opinions within and between Member States, but also the existing diversity in regulatory frameworks and principles for assessing benefits and risks of GMOs. In view of this lack of consensus, the Fifty-third World Health Assembly in 2000 adopted resolution WHA53.15 (WHO 2000b), according to which WHO should strengthen its capacity to support Member States to establish the scientific basis for decisions on GM food organisms, and ensure the transparency, excellence and independence of opinions delivered. This study aims to provide an evidence base to assist individual Member States in their consideration of the application of modern food biotechnology and the use of GM foods, and to facilitate greater international harmonization in this regard.

2. CURRENT USE, RESEARCH AND IMPENDING DEVELOPMENT OF FOODS PRODUCED THROUGH MODERN BIOTECHNOLOGY

Foods produced through modern biotechnology can be categorized as follows:

1. Foods consisting of or containing living/viable organisms, e.g. maize.
2. Foods derived from or containing ingredients derived from GMOs, e.g. flour, food protein products, or oil from GM soybeans.
3. Foods containing single ingredients or additives produced by GM microorganisms (GMMs), e.g. colours, vitamins and essential amino acids.
4. Foods containing ingredients processed by enzymes produced through GMMs, e.g. high-fructose corn syrup produced from starch, using the enzyme glucose isomerase (product of a GMM).

This study, however, makes no attempt to discriminate between the various categories, and the discussion that follows describes the current and future applications of modern biotechnology in the production of crops, livestock, fish and microorganisms in food production.

2.1 Crops

2.1.1 Crop breeding and the introduction of GM crops for food production

Conventional breeding, especially of crops, livestock and fish, focuses principally on increased productivity, increased resistance to diseases and pests, and enhanced quality with respect to nutrition and food processing. Advances in cellular genetics and cell biology methods in the 1960s contributed to the so-called 'green revolution' that significantly increased varieties of staple food crops containing traits for higher yield and resistance to diseases and pests in a number of both developed and developing countries (Borlaug 2000). A key driver of the green revolution was to improve the potential to provide sufficient food for all. The intensification and expansion of agriculture brought about by these methods and agricultural systems have, however, also resulted in new forms of health and environmental risks through, for example, increased use of agrochemicals and intensified cultivation resulting in soil erosion.

The development of molecular biology in the 1970s and 1980s introduced more direct methods for the analysis of genetic sequences and allowed the identification of genetic markers for desired traits. Such marker-assisted breeding methods are the basis of some current conventional breeding strategies.

Whereas modern methods of breeding have significantly increased crop yields over the past 50 years, the future potential of these methods is constrained by the limitations in the natural diversity of trait genotype within crop species and sexual-compatibility boundaries between crop types.

To overcome these problems, a number of interested groups (scientists, farmers, governments, agricultural companies) have since the 1980s considered other means to achieve the objectives of improved yields, sustainable agricultural systems, and improvements in human and animal health and the environment. This includes the use of more modern methods to introduce novel traits, such as tolerance to drought, salt, or pests. To achieve these objectives, various public and, more recently, private research programmes have aimed to improve the understanding of and links between crop performance and molecular genetics.

With the development and use of recombinant DNA in the 1980s, a tool to overcome the limitation of species incompatibility was found. Modern biotechnology employs molecular techniques to identify, select and modify DNA sequences for a specific genetic trait (e.g. insect resistance) from a donor organism (microorganism, plant or animal), and transfer the sequence to the recipient organism so that it expresses this trait.

Various transformation methods are used to transfer recombinant DNA into recipient species to produce a GMO. For plants, these include transformation mediated by *Agrobacterium tumefaciens* (a common soil bacterium that contains genetic elements for infection of plants) and biolistics — shooting recombinant DNA placed on microparticles into recipient cells. The methods used in the transformation of various animal species include microinjection, electroporation and germ-line cells (FAO/WHO 2003a). The success rate of transformations in animals tends to be lower than in plants, and to vary from species to species, thus requiring the use of many animals.

Genetic modification is often faster than conventional breeding techniques, as stable expression of a trait is achieved using far fewer breeding generations. It also allows a more precise alteration of an organism than conventional methods of breeding, as it enables the selection and transfer of a specific gene of interest. However, with the present technology, in many cases it leads to random insertion in the host genome, and consequently may have unintended developmental or physiological effects. However, such effects can also occur in conventional breeding and the selection process used in modern biotechnology aims to eliminate such unintended effects to establish a stable and beneficial trait.

It should be noted that conventional breeding programmes directed by the molecular analysis of genetic markers are also of critical importance to modern plant and animal breeding. However, human and environmental health consequences of these techniques are not considered here.

2.1.2 GM crops currently in commercial production

At present, only a few GM crops are permitted for food use and traded on the international food and feed markets. These include herbicide- and insect-resistant maize (*Bt*[1] maize), herbicide-resistant soybean, rape (canola) oilseed, and insect- and herbicide-resistant cotton (primarily a fibre crop, though refined cottonseed oil is used as food). In addition, several government authorities have approved varieties of papaya, potato, rice, squash, sugar beet and tomato for food use and environmental release. The latter crops, however, are currently grown and traded only in a limited number of countries, mainly for domestic consumption.

The regulatory status of GM crops varies among the countries that permit their use and updates can be found on various web-sites, including those of the Organisation for Economic Co-operation and Development (OECD) and the International Centre for Genetic Engineering and Biotechnology (ICGEB).

In 2004, the estimated global area of commercially grown transgenic or GM crops was 81 million hectares, grown by 7 million farmers in 18 developed and developing countries. Seven countries grew 99% of the global transgenic crop area in 2004 (*Table 1*).

[1] Insect-resistant GM crops have been developed by expression of a variety of insecticidal toxins from the bacterium *Bacillus thuringiensis* (*Bt*).

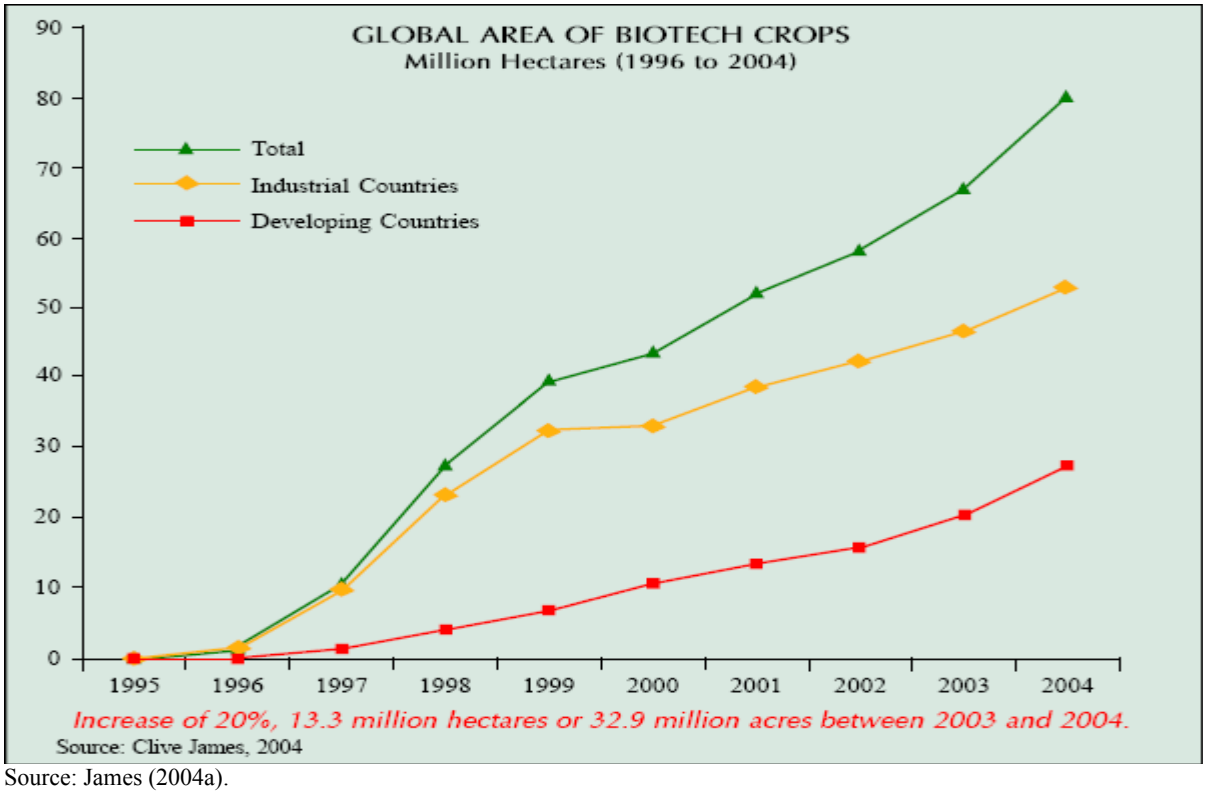
Table 1 Global transgenic crop area, both by area (million hectares) and percentage of global area planted (%)

Country	*2001*		*2002*		*2003*		*2004*	
	ha × 10^6	%	ha × 10^6	%	ha × 10^6	%	ha × 10^6	%
United States of America	35.7	67.9	39.0	66.4	42.8	62.8	47.6	58.8
Argentina	11.8	22.4	13.5	23.0	13.9	20.4	16.2	20.0
Canada	3.2	6.1	3.5	6.0	4.4	6.5	5.4	6.7
Brazil	–	–	–	–	3.0	4.4	5.0	6.2
China	1.5	2.8	2.1	3.6	2.8	4.1	3.7	4.6
Paraguay	–	–	–	–	–	–	1.2	1.5
South Africa	0.2	0.4	0.3	0.5	0.4	0.6	0.5	0.6
Other countries	0.2	0.4	0.3	0.5	0.8	1.2	1.3	1.6
Total (world)	**52.6**	**100**	**58.7**	**100**	**68.1**	**100**	**80.9**	**100**

Source: James (2005). 2004 data (and by extrapolation 2003) are included in this reference.

Figure 1 illustrates the global trends of commercial GM crops planted between 1996 and 2004.

Figure 1 Global transgenic crop growth (million hectares) between 1996 and 2004



Source: James (2004a).

During the nine-year period 1996 to 2004, herbicide tolerance has been the dominant trait introduced to commercial GM crops, with insect resistance second. In 2004, herbicide tolerance present in soybean, maize and cotton accounted for 72%, or 58.5 million hectares, of global GM plantings. Insect-resistant *Bt* crops accounted for 15.7 million hectares (20%), and 'stacked' genes (GM cotton or maize crops with both herbicide tolerance and insect resistance) accounted for 8% or 6.8 million hectares of the global transgenic area (James 2004a). Virus-resistant crops, such as papaya (resistant to ringspot virus), potato (tolerant to potato virus Y and potato leaf roll virus) and yellow crookneck squash (resistant to watermelon mosaic virus) are commercially grown on a very small area in comparison.

The two dominant GM crop/trait combinations in 2004 were: herbicide-tolerant soybean, 48.4 million hectares or 60% of the global total; and *Bt* maize, 11.2 million hectares, equivalent to 14% of the global area planted to transgenic crops.

2.1.3 Future trends in GM crops

The commercial introduction of transgenic crop plants with agronomic traits is often referred to as the first generation of transgenic plants. Further development of GM crops with agronomic traits is continuing, and production of a range of GM crops with enhanced nutritional profiles is also under way (PIFB 2001). Various novel traits are currently being tested in laboratories and field tests in a number of countries. Many of these second-generation GM crops are still in the development stage and are unlikely to enter the market for several years.

The key areas of research and development (R&D) in plants are (i) agronomic traits and (ii) altered nutrition and composition.

2.1.3.1 Agronomic traits

Pest and disease resistance. In the short term, most newly commercialized GM crops will continue to concentrate on agronomic traits, especially herbicide resistance and insect resistance and, indirectly, yield potential (PIFB 2001). R&D in this area aims to:

- introduce herbicide-resistance traits in a broader range of varieties of maize, soybean and canola;
- broaden the range of herbicides that can be used in combination with the transgenic herbicide-resistant crop, such as introduction of tolerance to the herbicides bromoxynil, oxynil and sulfonylurea; and
- stack novel genes for insect resistance in plants, such as novel *Bt* variants containing different toxins.

Virus resistance. Virus resistance could be extremely important to improving agricultural productivity (Thompson 2003). Field tests of the following virus-resistant crops are currently being conducted in various parts of the world: sweet potato (feathery mottle virus); maize (maize streak virus); and African cassava (mosaic virus). These crops may be available for commercialization within the next 3–5 years. Because of its complex genome, work on wheat resistant to the barley yellow-dwarf virus has made little progress and is still undergoing laboratory investigation. Resistance to nematodes (root worms) in a GM potato has also been achieved.

2.1.3.2 Altered nutrition and composition

Vitamin-A-enhanced rice. The best-known example of a GM crop conferring enhanced nutritional properties is rice containing a high level of beta-carotene — a vitamin A precursor (so-called 'golden rice') (Potrykus 2000). Vitamin A is essential for increasing resistance to disease, protecting against visual impairment and blindness, and improving the chances of growth and development. Vitamin A deficiency (WHO/UNICEF 1995) is a public health problem that contributes to severe illness and childhood mortality. This preventable condition increases the burden of disease on the health systems of developing countries. A number of strategies have been suggested for combating vitamin A deficiency, including dietary approaches (e.g. fortification of foods) and supplementation via pills (WHO 2000c). Within the context of improving the supply of vitamin A, the usefulness of vitamin A-enhanced rice has been discussed in various forums, such as an electronic forum coordinated by the Food and Agriculture Organization of the United Nations (FAO) in 2000 (FAO 2000).

Vitamin A-enhanced rice and maize varieties are at present being developed for cultivation in developing countries. Current efforts are aimed at ensuring that vitamin A in rice can be absorbed efficiently in the human gut. Once this is resolved, 300 grams of transgenic rice could make a significant contribution to the daily human requirement for vitamin A.

'High iron' rice. Prevalence of iron deficiency is very high in those parts of the world in which rice is the daily food staple (WHO 2000a). This is because rice has a very low iron content. Transgenic rice seeds with the iron-carrier protein ferritin from soy were found to contain twice as much iron as seeds of non-transformed rice (Gura 1999). Rice has been transformed with three genes which increase iron storage in rice kernels and iron absorption from the digestive tract (Lucca et al. 2002).

Improved protein content. Researchers are also investigating methods that could improve the protein content of staple vegetables, such as cassava, plantain and potato (PIFB 2001). Results from greenhouse trials show that these tubers have 35–45% more protein, and enhanced levels of essential amino acids.

Removing allergens and antinutrients. Cassava roots naturally contain high levels of cyanide. As they are a staple food in tropical Africa, this has led to high blood-cyanide levels which have harmful effects. Application of modern biotechnology to decrease the levels of this toxic chemical in cassava would reduce its preparation time. In potatoes, insertion of an invertase gene from yeast reduces the natural levels of glycoalkaloid toxin (Buchanan et al. 1997).

The allergenic protein in rice has been reduced by modifying its biosynthetic pathway (PIFB 2001). The significance in human allergenicity of these lower levels has not been demonstrated. There is also work to reduce allergenicity in wheat (Buchanan et al. 1997). This work involves inserting a thioredoxin-biosynthesis gene to break the disulfide bonds in the offending protein but without interfering with the functionality of the wheat proteins.

Altered starch and fatty acid profile. In the quest to provide healthier foods, there is an effort to increase the starch content of potatoes so that they absorb less fat during frying (PIFB 2001). To create healthier fats, the fatty-acid composition of soy and canola has been altered to produce oils with reduced levels of saturated fats. R&D is currently focusing on GM soybean, oilseed rape and oil palm (PIFB 2001). Two GM crops of this nature have been approved in the United States of America (USA) for growing and food/feed use — high oleic acid soy and high lauric acid oilseed rape (Agbios 2005). High oleic acid soy is also permitted as food in Australia and Canada. R&D is in the early stages with respect to oils with improved nutritional value.

Increased antioxidant content. The lycopene and lutein contents of tomatoes have been increased as have isoflavones in soy (WHO 2000c). These phytonutrients are known to improve health or prevent disease. Research in this area is at a relatively early stage of development, as knowledge of phytonutrients is limited and not all phytonutrients are beneficial.

Environmental stresses. Tolerance to environmental-stress factors through genetic modification is an area that is in the early stages of R&D (PIFB 2001). Resistance to salinity and drought are being researched intensively. Salinity is estimated to affect 20% of agricultural land and 40% of irrigated land worldwide. Salt and drought tolerance involve numerous genes interacting in a complex manner. Owing to this multigenic character, conventional breeding techniques have had little success in the generation of salt- or drought-tolerant varieties. Salt tolerance may be conferred to sensitive crops by the transfer of multiple genes linked to a relevant pathway from a tolerant crop. The likely time frame for commercialization for such GM crops is unknown.

Tolerance to aluminium (a growth-limiting factor in acid soils) is in the early phase of R&D for several crops, including papaya, tobacco, rice and maize, but they are not expected to be in commercial use for several years.

Attempts have been made to improve the photosynthetic system in plants through genetic modification. Crops such as maize and sugar cane are more efficient in converting energy into sugars than most broadleaf crop plants. By introducing genes for more efficient photosynthesis from one crop to another, efficiency could be improved by 10% with an enhancement in yield. The likely time frame of commercialization is unknown.

Male-sterility traits have been introduced for obtaining 100% hybrid sowing-seed for the purposes of environmental containment of GM crops. Various male-sterile maize varieties have been approved for market introduction in the USA. In addition, various male-sterile rapeseed and canola varieties have been approved for environmental release and food use in the European Union (EU), Canada and the USA. Another strategy for containing gene flow between plants attempts to introduce asexual seed propagation in crops (seed production without the need to pollinate). None of the above-mentioned strategies has proved applicable to all crop species, and a combination of approaches may prove most effective.

2.2 Livestock and fish

In terms of food production, the application of modern biotechnology to livestock falls into two main areas: animal production and human nutrition. Many of the applications discussed below are in the early stages of R&D.

2.2.1 Fish

The projected increasing demand for fish suggests that GM fish may become important in both developed and developing countries. Enhanced-growth Atlantic salmon containing a growth hormone gene from Chinook salmon is likely to be the first GM animal on the food market (FAO/WHO 2003a). These fish grow 3–5 times faster than their non-transgenic counterparts, to reduce production time and increase food availability. At least eight other farmed fish species have been genetically modified for growth enhancement. Other fish in which genes for growth hormones have been experimentally introduced include grass carp, rainbow trout, tilapia and catfish (PIFB 2003; PIFB/FDA 2003). In all cases, the growth-hormone genes are of fish origin.

To address some of the practical problems of aquaculture, research attempts are seeking to improve disease resistance by producing Atlantic salmon with a rainbow trout lysozyme cDNA. Lysozyme has antimicrobial properties against fish pathogens such as *Vibrio*, *Aeromonas* and *Yersinia*. Another type of antimicrobial protein (silk moth cecropin) is under investigation in catfish (Dunham et al. 2002). This would improve catfish resistance to diseases such as enteric septicaemia.

The farming of carnivorous fish species, such as trout and salmon, has led to overfishing of sand eels and capelin. To tackle this problem, research is looking into the possibility of altering the metabolism of these species by improving their digestion of carbohydrates, to enable a shift to a more plant-based diet.

Lack of cold tolerance in warm-water species such as the common carp and tilapia can lead to significant stock losses in winter. The suggestion of work in this area is to alter the molecular conformation of lipids, thus increasing membrane fluidity. To extend the geographical range of fish farming, an antifreeze gene from one fish species is transferred to the species of interest. Although freeze-resistant strains of Atlantic salmon have been produced, the level of antifreeze protein secreted by the salmon was insufficient to have a significant impact on the freezing point of blood (Fletcher et al. 2002).

The issues concerned in the identification of hazards and the assessment of risks that could be associated with the release of GM fish are still being addressed (FAO/WHO 2003a). One of these

aspects involves the production of sterile GM fish to minimize the environmental risk of releasing them into wild populations.

2.2.2 Livestock and poultry

Foods derived from GM livestock and poultry are far from commercial use. Several growth-enhancing novel genes have been introduced into pigs that have also affected the quality of the meat, i.e. the meat is more lean and tender (FAO/WHO 2003a). This research was initiated over a decade ago, but owing to some morphological and physiological effects developed by the pigs, these have not been commercialized.

Many modifications to milk have been proposed that either add new proteins to milk or manipulate endogenous proteins (PIFB 2002b). Recently, researchers from New Zealand developed GM cows that produce milk with increased levels of casein protein. Use of such protein-rich milk would increase the efficiency of cheese production. Other work aims to reduce the lactose content of milk, with the intent of making milk available to the population of milk-intolerant individuals.

Other applications of genetic modification in animal production in the early stages of R&D include improvement of disease resistance, increased birth rates in sheep, altered sex ratio in poultry, increased egg production in poultry by creating two active ovaries, and improved feed conversion in the 'enviropig' (environmentally friendly pigs that excrete less phosphorus). Most of this work is still theoretical and therefore estimates of time frames for possible commercial introductions of any of these applications are unavailable.

2.3 Microorganisms

2.3.1 Microorganisms as foods

Currently, there are no known commercial products containing live genetically modified microorganisms (GMMs) on the market. In the United Kingdom, GM yeast for beer production has been approved since 1993, but the product was never intended to be commercialized (NCBE 2005). Other microorganisms used in foods (which are in the R&D phase) include starter fermentation cultures for various foods (bakery and brewing), and lactic acid bacteria in cheese. R&D is also aimed at minimizing infections by pathogenic microorganisms and improving nutritional value and flavour.

Attempts have been made to genetically modify ruminant microorganisms for protecting livestock from poisonous feed components. Microorganisms improved by modern biotechnology are also under development in the field of probiotics, which are live microorganisms that, when consumed in adequate amounts as part of food, confer a health benefit on the host (FAO/WHO 2001c).

2.3.2 Food ingredients, processing aids, dietary supplements and veterinary chemicals derived from GM microorganisms

Many enzymes used as processing aids in food and feed production are derived through the use of GMMs (European Commission 2004). This means that the GM microorganisms are inactive, degraded or removed from the final product. GM yeasts, fungi and bacteria have been in commercial use for this purpose for over a decade. Examples include: alpha-amylase for bread-making, glucose isomerase for fructose production, and chymosin for cheese-making. Most of the microorganisms modified for food processing are derivatives of microorganisms used in conventional food biotechnology.

GMMs are also permitted in a number of countries for the production of micronutrients, such as vitamins and amino acids used for food or dietary supplement purposes. An example is the production of carotenoids (used as food additives, colourants or dietary supplements) in GM bacterial systems. In

the future, complete metabolic pathways could be integrated in GM microorganisms, enabling them to produce new compounds.

For animal husbandry, veterinary products such as bovine somatropin, used for increasing milk production, have been developed using genetic engineering. Bovine somatropin has been on the market in several countries for over a decade.

The technique of protein engineering aims at altering the genetic, and thus amino acid, sequence of enzymes. Hitherto, protein engineering has not been used extensively in enzyme production. R&D in this area aims to change enzyme characteristics, e.g. improve temperature or pH stability. Enzymatic processing often replaces existing chemical reactions. In many instances, this results in lowered energy consumption and less chemical waste.

2.4 Conclusions

Over the past 50 years, advances in genetics and molecular biology have enabled the development and commercial release of GMOs with traits that transcend the species barrier. The traits borne by GMOs may potentially bring significant benefits to the production of food.

Currently, the most frequently commercialized GMOs are crops of soybean, maize and cotton. GM soybean dominates plantings of GM crops, followed by GM maize and GM cotton. GM crops are estimated to cover almost 4% of total global arable land. Agronomic traits are the most prominent traits introduced in GM crops. In the near future, agronomic traits will continue to dominate new varieties of GM crops. However, over the medium term, a small but increasing proportion of GM crops will contain changes in quality and nutritional traits.

While fast-growing GM salmon and GM cattle expressing increased levels of protein are in an advanced stage of development, most other transgenic animals for food use are still in the early stages of R&D.

Many food-processing aids (enzymes) produced through the use of GM microorganisms have been on the market for over a decade, and are used in a wide variety of processed foods. Hitherto, no live GM food microorganisms as such have been introduced onto the market.

3. RISK OF GMOs AND GM FOODS TO HUMAN HEALTH AND THE ENVIRONMENT

Introduction of a transgene into a recipient organism is not a precisely controlled process, and can result in a variety of outcomes with regard to integration, expression and stability of the transgene in the host (FAO/WHO 2003a).

3.1 History of risk assessment of GMOs

When new foods (crop varieties, animal breeds or microorganisms) are developed by traditional breeding methods, they are usually not subject to specific pre- or postmarket risk or safety assessment by national authorities or through international standards. This is in contrast to requirements introduced for GMOs and GM foods.

The concept of risk assessment of GMOs was first discussed at the Asilomar Conference in 1975 (Fredrickson 1979; Talbot 1983). The discovery of recombinant DNA had raised concerns among researchers regarding the potential creation of recombinant viruses whose escape would threaten public health. Fourteen months after a voluntary moratorium on research involving recombinant DNA techniques, guidelines for the physical and biological containment of riskier experiments were drafted and agreed. These guiding principles were the basis of the USA guidelines for research in modern biotechnology developed in 1976 by the National Institutes of Health Recombinant DNA Advisory Committee. Other countries were soon to follow (OECD 1986).

Early regulatory requirements were intended to prevent the accidental release of microorganisms from research facilities. In continuation of this, regulation for contained use and deliberate release of GMOs was developed, e.g. EU regulations in 1990. These guidelines elaborated a premarket human-health and environmental-safety assessment requirement for all GMOs and GM foods on the basis that they are novel and have no history of safe food or environmental use.

Many countries have since established specific premarket regulatory systems requiring the rigorous assessment of GMOs and GM foods before their release into the environment and/or use in the food supply. A summary of some national and international legislation is available on the OECD Internet site (OECD 2005).

While many national regulatory bodies base their safety assessment of GMOs and GM foods on shared concepts, differences in regulatory systems have led to disagreements and confusion in their deployment. While the terms ‘safety assessment’ and ‘risk assessment’ are often used interchangeably in some literature, these are two clearly different, but interlinked processes. For a further description of typical steps of a safety assessment, see *Section 3.2.1*, and for a schematic overview of the risk-assessment process, see *Figure 2*.

To provide international consistency in risk analysis of GMOs and GM foods which incorporates risk assessment, management and communication components, a number of international regulatory and standard-setting bodies have introduced uniform standards. These include standards for human-health and environmental-safety assessment of GMOs and GM foods, and notification of their movement across national borders. The objective of uniform global standards for risk assessment would be challenging as countries are bound to reach different decisions on the scope of the assessment, particularly the resolution of whether or not to include social or economic aspects.

International regulatory systems covering GM food safety (Codex *Principles*) (CAC 2003b) and environmental safety (Cartagena Protocol on Biosafety) (CBD 2000) came into force in 2003.

The concept that allows for the comparison of a final product with one having an acceptable standard of safety is an important element of a GM food safety assessment. This principle was elaborated by

FAO, WHO and OECD in the early 1990s and referred to as 'substantial equivalence' (FAO/WHO 1990). The principle suggests that GM foods can be considered as safe as conventional foods when key toxicological and nutritional components of the GM food are comparable to the conventional food (within naturally occurring variability), and when the genetic modification itself is considered safe (OECD 1993). However, the concept has been criticized by some researchers (Millstone et al. 1999). At a *Joint FAO/WHO consultation on foods derived from biotechnology* held in 2000, it was acknowledged that the concept of substantial equivalence contributes to a robust safety assessment, but it was also clarified that the concept should represent the starting point used to structure the safety assessment of a GM food relative to its conventional counterpart (FAO/WHO 2000). The consultation concluded that a consideration of compositional changes should not be the sole basis for determining safety, and that safety can only be determined when the results of all aspects under comparison are integrated.

This study does not cover aspects of occupational health which are often addressed in regulations dealing with the safety of work with GMOs in contained areas. It should also be noted that the adventitious presence of non-approved products of modern biotechnology among the approved is not within the scope of this study.

3.2 Assessment of the impact of GM foods on human health

3.2.1 Principles for the safety assessment of GM foods

The Codex Alimentarius Commission[2] (CAC, or Codex) adopted the following texts in July 2003: *Principles for the risk analysis of foods derived from modern biotechnology*; *Guideline for the conduct of food safety assessment of foods derived from recombinant-DNA plants*; and *Guideline for the conduct of food safety assessment of foods produced using recombinant-DNA microorganisms*. The last two texts are based on the *Principles* and describe methodologies for conducting safety assessments for foods derived from recombinant-DNA plants and microorganisms, respectively (CAC 2003b,c,d).

The premise of the *Principles* dictates a premarket assessment, performed on a case-by-case basis and including an evaluation of both direct effects (from the inserted gene) and unintended effects (that may arise as a consequence of insertion of the new gene). The Codex safety assessment principles for GM foods require investigation of:

(a) direct health effects (toxicity);

(b) tendency to provoke allergic reactions (allergenicity);

(c) specific components thought to have nutritional or toxic properties;

(d) stability of the inserted gene;

(e) nutritional effects associated with the specific genetic modification; and

(f) any unintended effects which could result from the gene insertion.

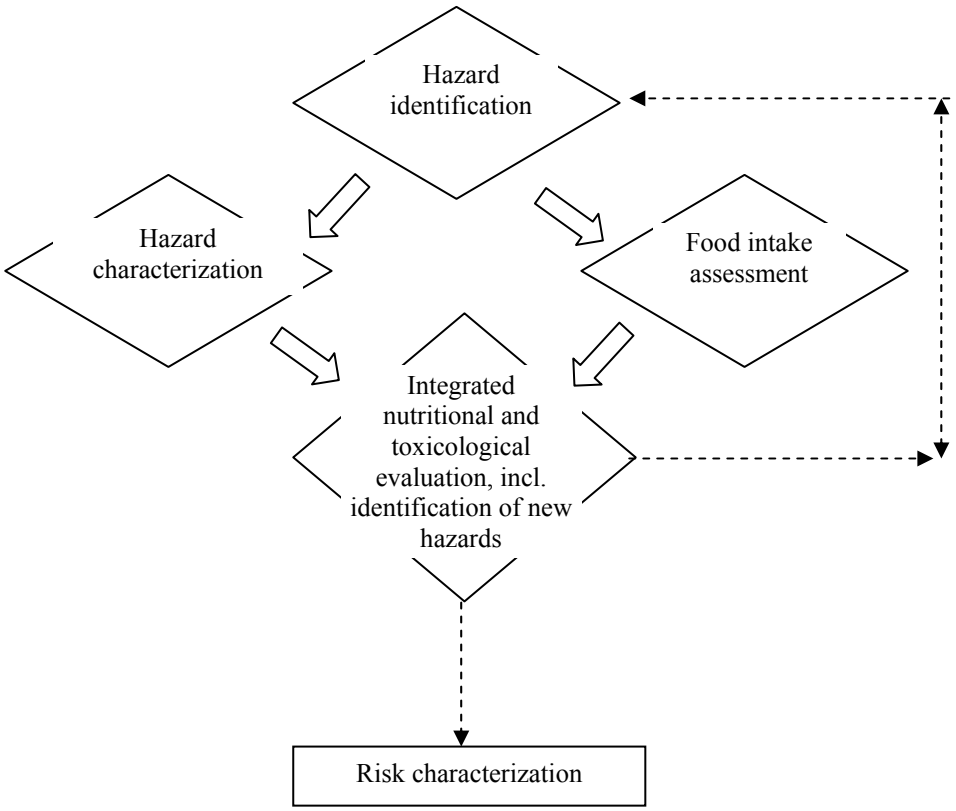
Codex principles do not have a binding effect on national legislation, but are referred to specifically in the *Agreement on the Application of Sanitary and Phytosanitary Measures* of the World Trade Organization (SPS Agreement, see WTO 1995), and are often used as a reference in the case of trade disputes.

The 2003 *Expert consultation on the safety assessment of foods derived from GM animals, including fish* (CAC 2003a) formed the opinion that to further develop the risk-assessment process with current scientific knowledge, integrated toxicological and nutritional evaluations should be conducted in order to identify food-safety issues that may need further investigation (*Figure 2*). Both evaluations

[2] A joint FAO/WHO body responsible for developing the standards, codes of practice, guidelines and recommendations that constitute the *Codex Alimentarius* (the international food code).

combine data from the hazard identification and characterization, and food intake assessment steps. It should be noted that such newly suggested further developments of the risk-assessment process have not yet been considered by Codex, and that the international principles and guidelines for risk analysis and safety assessment of foods derived from biotechnology are as accepted by Codex in 2003 (CAC 2003b,c,d).

Figure 2Schematic overview of a suggested further development of the risk assessment process (FAO/WHO 2003a)



3.2.2 Potential direct effects on human health

The potential direct health effects of GM foods are generally comparable to the known risks associated with conventional foods, and include, for example, the potential for allergenicity and toxicity of components present, and the nutritional quality and microbiological safety of the food.

As mentioned above, many of these issues have not traditionally been specifically assessed for conventional food; but in one area — toxicity of food components — there is ample experience related to the use of animal experiments to test potential toxicity of targeted chemical components. However, the intrinsic difficulty in testing whole foods, as opposed to specific components, in animal feeding experiments have resulted in the development of alternative approaches for the safety assessment of GM foods.

The safety assessment of GM food follows a stepwise process aided by a series of structured questions. Factors taken into account in the safety assessment include:

- identity of gene of interest, including sequence analysis of flanking regions and copy number;
- source of gene of interest;

- composition of GMO;
- protein expression product of the novel DNA;
- potential toxicity;
- potential allergenicity; and
- possible secondary effects from gene expression or the disruption of the host DNA or metabolic pathways, including composition of critical macronutrients, micronutrients, antinutrients, endogenous toxicants, allergens and physiologically active substances.

A series of FAO/WHO expert consultations held in 2000, 2001 and 2003 recognized that animal studies can be of help but that there are practical difficulties in obtaining meaningful information from conventional toxicology testing, especially with whole-food studies in laboratory animals (where the appropriate animal diet is a factor that needs to be assured) (FAO/WHO 2000, 2001b, 2003a). The consultations also noted that very little is known about the potential long-term effects of any foods. At present, there is no conclusive information available on the possible health effects of modifications which would significantly change the nutritional characteristics of any food, such as nutritionally enhanced foods.

3.2.3 Potential unintended effects of GM foods on human health

Unintended effects, such as elevated levels of antinutritional or toxic constituents in food, have on occasion been characterized in conventional breeding methods, e.g. glycoalkaloid levels in potatoes. Organisms derived from conventional breeding methods, including tissue cultures, may have a somewhat enhanced possibility for genetic (and epigenetic — environmentally induced changes that affect the expression of a gene without changing the DNA sequence) instabilities, such as the activity of mobile elements and gene-silencing effects (FAO/WHO 2003a). These effects could increase the probability of unintended pleiotropic effects (affecting more than one phenotypic trait), e.g. increased or decreased expression of constituents or possibly modifications in expressed proteins, as well as epistasis (the interaction of the inserted gene with other genes).

It has been argued that random insertion of genes in GMOs may cause genetic and phenotypic instabilities (Ho 2002) but, as yet, no clear scientific evidence for such effects is available. A better understanding of the impact of natural transposable elements on the eukaryotic genome may shed some light on the random insertion of sequences.

Gene expression in conventional and GM crops is subject to environmental influences. Environmental conditions such as drought or heat can stimulate some genes; turning the expression up or down. The assessment of potential synergistic effects is necessary in the risk assessment of organisms derived from gene stacking, i.e. breeding of GMOs containing genetic constructs with multiple traits (Andow et al. 2004; FIFRA SAP 2004; Kuiper et al. 2004). Internationally agreed procedures for the assessment of such organisms are desirable.

Unintended effects can be classified as insertional effects, i.e. related to the position of insertion of the gene of interest, or as secondary effects, associated with the interaction between the expressed products of the introduced gene and endogenous proteins and metabolites. There is common agreement that targeted approaches, i.e. the measuring of single compounds, is very useful and adequate to detect such effects, as has been done with conventionally bred products. To enhance and improve the identification and analyses of these unintended effects, profiling methods have been suggested. This untargeted approach allows detection of unintended effects at the mRNA (microarray), protein (proteomic) and metabolite (metabolomic) level. It still remains to be seen which of these techniques (once validated) would be useful for routine risk-assessment purposes.

Unintended effects were specifically addressed by the FAO/WHO *Expert consultation on the safety aspects of genetically modified foods of plant origin* (FAO/WHO 2000) and the Codex *Principles for*

the risk analysis of foods derived from modern biotechnology (CAC 2003b). These consultations noted that there is a need to establish the consequences of natural baseline variations, the effects of growing conditions and environmental influences, and the ways to interpret safety-relevant data from profiling techniques. Adequate methods for the assessment of potential, unintended effects need to be evaluated for specific GMOs case by case, where the assessment already aims to consider unintended toxic and antinutritional factors through analysis of proximal constituents and GM characteristics.

As profiling methods are not in use in routine risk assessment, the second step in the comparative safety assessment has been suggested as a measure for identifying and characterizing any unintended effects that may be associated with complex foods.

3.2.4 Potential human-health effects from horizontal gene transfer

Natural genetic transformation has been found to occur in different environments, e.g. in food (Kharazmi et al. 2003). In addition, it has been shown that ingested DNA from food is not completely degraded by digestion, and that small fragments of DNA from GM foods can be found in different parts of the gastrointestinal tract (Schubbert et al. 1997, 1998; Mercer et al. 2001; Heinemann and Traavik 2004; Netherwood et al. 2004; Nielsen and Townsend 2004; van den Eede et al. 2004). As the consequences of horizontal gene transfer (HGT) may be significant in some human-health conditions, the potential for HGT needs to be part of the risk assessment of GM food.

FAO/WHO consultations (FAO/WHO 2001b) have also discussed the potential risks of gene transfer from GM foods to mammalian cells or gut bacteria. These panels have suggested that it may be prudent in a food-safety assessment to assume that DNA fragments survive in the human gastrointestinal tract and can be absorbed by either the gut microflora or somatic cells lining the intestinal tract. It was agreed that the assessment needs to take into account a number of factors including, but not limited to, the specific characteristics encoded by the DNA sequences, the characteristics of the receiving organism, and the selective conditions of the local environment of the receiving organisms.

Some scientists have pointed to the present methodological limitations of a comprehensive scientific evaluation of this problem (mainly because of estimations that only approximately 1% of naturally existing bacteria can be cultured, and therefore analyzed). Discussion also addresses the consequences of a rare probability of a transfer event against the high numbers of bacteria and genes available for transfer.

The DNA construct used to change the genetic composition of a recipient organism should be considered within an assessment, especially if the gene or its promoter (e.g. cytomegalovirus promoter) (Ho et al. 2000) has been derived from a viral source. Sequences unrelated to the target gene could be introduced as part of the construct (FAO/WHO 2003a). Inadvertent introduction of such sequences into the germ-line of a GM animal not only has the potential for creating unintended genetic damage, but can also contribute by recombination to the generation of novel infectious viruses. A well-known example is the generation of a replication-competent murine leukaemia virus during the development of a vector containing a globin gene (Purcell et al. 1996).

The horizontal transfer of recombinant genetic material to microorganisms has demonstrated an enhanced stability of DNA under certain conditions (Lorenz and Wackernagel 1987). Natural transformation of DNA to bacteria involves the active uptake of extracellular DNA by bacteria in a status of competence (Sikorski et al. 1998; Graupner et al. 2000) or in rare, illegitimate recombination events (de Vries and Wackernagel 2002). The probability of such an event occurring appears to be extremely low, and very much related to the genes, constructs and organisms in question.

The FAO/WHO expert panels concluded that horizontal gene transfer is a rare event that cannot be completely discounted, and that the consequences of such transfer should be considered in a safety

assessment. The panels encouraged the use of recombinant DNA without antibiotic-resistance genes (particularly those that could interfere with human or animal therapies), or any other sequences which could stimulate transfer. The panels also discouraged the use of any unnecessary DNA sequences, including marker genes in the genetic construct (FAO/WHO 2001b, 2003a). The safety assessment of a genetic construct should also examine the included marker genes. Commonly used marker genes code for antibiotic resistance. Risk assessment of these selectable genes should focus on gene transfer to microorganisms residing in the gastrointestinal tract of humans or animals. As the potential of this gene transfer cannot be completely ruled out, the safety assessment should also consider information on the role of the antibiotic in human and veterinary medical uses.

3.2.5 Potential immune responses and allergenicity induced by GM foods

Food allergies or hypersensitivities are adverse reactions to foods triggered by the immune system. Within the different types of reactions involved, non-immunological intolerances to food and reactions involving components of the immune system need to be differentiated. The former may invoke reactions such as bloating or other unpleasant reactions, but are thought not to involve the immune system and called 'food intolerances'.

Allergic reactions to traditional foods are well known. The major food allergens are proteins in and derived from eggs, fish, milk, peanuts, shellfish, including crustaceans and molluscs (e.g. clams, mussels and oysters), soy, tree nuts (e.g. almonds, Brazil nuts, cashews, hazelnuts/filberts, macadamia nuts, pecans, pine nuts, pistachios and walnuts) and wheat. Whereas the groups of main allergens are well known and advanced testing methods have been elaborated, traditionally developed foods are not generally tested for allergens before market introduction.

The application of modern biotechnology to crops has the potential to make food less safe if the newly added protein proves to cause an allergic reaction once in the food supply. A well-known case is the transfer of a gene encoding a known allergen, the 2S-Albumin gene from the Brazil nut, to a previously safe soybean variety. When the allergenic properties of the transgenic soybean were tested, sera from patients allergic to Brazil nuts cross-reacted with the transgenic soybean (Nordlee et al. 1996). For this reason, a commercial product was never pursued. On the other hand, the introduction of an entirely new protein that has not been previously found in the food chain represents a different case.

In the first case, guidelines for assessing foods with known allergens are clear. The second case is more difficult to assess because there is no definitive test to determine the potential allergenicity of a novel protein. Instead, several risk factors provide a rough guide as to the likelihood of allergenicity.

Risk-assessment protocols for food allergy examine four elements: (1) allergenicity assessment (is the food or elements in the food a potential allergen); (2) dose response assessment (is there a safe concentration of the allergen); (3) exposure assessment (how likely is it that people will encounter the allergen); and (4) susceptible subpopulations (how do those prone to allergy react to this new food).

Elements of an allergenicity assessment include a comparison of the sequence of the transferred gene (including the flanking regions at the site of insertion) with sequence motifs of allergenic proteins from databanks, an evaluation of the stability of the newly expressed proteins against digestion, and animal and immune tests, as appropriate.

Absence of sequence similarity with allergenic protein epitopes, and low stability under acidic or proteolytic conditions, do not preclude the presence of a potential allergen. There are proven incidents which have contradicted the general rules, e.g. where small modifications in a protein sequence determine allergenicity (Ferreira et al. 1996). Allergenicity prediction using protein-sequence motifs identified from a new allergen database has been proposed as a new and superior strategy for identifying potential allergens (Jank and Haslberger 2003; Stadler and Stadler 2003). Some experts

consider that the use of sera from polysensitized patients is important for the testing of allergenicity. Areas of improvement of risk assessment of allergens include mechanistic studies of animal models and genomic techniques.

FAO/WHO expert panels (FAO/WHO 2001a) have established protocols for evaluating the allergenicity of GM foods on the basis of the weight of evidence. The strategy adopted is applicable to foods containing a gene derived from either a source known to be allergenic or a source not known to be allergenic. The panels have, however, discouraged the transfer of genes from known allergenic foods unless it can be demonstrated that the protein product of the transferred gene is not allergenic. These principles have been applied by many regulatory agencies assessing the safety of GM foods and have provided the basis for Codex guidelines for the safety assessment of foods derived from biotechnology (CAC 2003c,d).

The cellular basis of immune responses is not completely understood, and a better understanding of the interaction of the immune system and foods in general is required in order to decipher whether specific GM foods may have impacts on the immune system apart from allergenicity. The impact of cell-mediated reactions (without involvement of immunoglobulin E antibodies) on hypersensitivity reactions elicited by foods is a matter of current research (Janeway et al. 2001; Walker-Smith 2003).

3.2.6 Safety aspects of food derived from GM animals

Genetically modified animals have mainly been produced for biomedical research purposes. To date, no GM food animals have been introduced onto international markets. But GM food animals such as fish can be expected in the near future. In principle, the assessment of food and feed safety for GM animals follows the general principles of the assessment of GMOs outlined above. However, the specificities of the introduction of transgenes into animals, often using viral constructs for introduction into the germ-line, need distinct consideration. A 2003 report of the Pew Initiative on Food and Biotechnology (PIFB 2003) reviewed techniques for the production, uses and welfare of GM animals, as well as safety aspects.

The risk assessment of foods derived from GM animals needs to be undertaken, as for other GM foods, on a case-by-case basis (CAC 2001a). This includes an assessment of potential recombination of viral vectors used for transformation with wild-type viruses (Mikkelsen and Pedersen 2000), especially in poultry, where potential incomplete digestion could lead to intestinal uptake of orally administered proteins, and an assessment of peptide expression that may have hormonal activity (e.g. in fish).

The FAO/WHO expert consultation on the *Safety assessment of foods derived from GM animals, including fish* held in 2003 addressed the key issues for food safety and evaluated the extent of scientific knowledge with regard to hazard identification and characterization unique to transgenic animals (FAO/WHO 2003a).

Phenotypic analysis. Because of their size, and limitations in the generation process, there will in general be few initial founders for screening of GM animals, meaning that information on the variation range between animals with the same genetic modification will be rather limited. This will make interpretation of differences difficult. Furthermore, a selection of the edible tissues and products to be analyzed has to be made for the different animal species. In specific cases, phenotypic analysis may also be advisable after processing or, for fish, during the various stages of spoilage. For example, adverse biogenic amines can be formed during spoilage in salmon, tuna, herring and other fish species. Similarly, formaldehyde may be produced in spoiled shrimp, cod, hake and many other species.

Compositional analysis. Background data on the natural variation for individual constituents in different tissues need to be generated. Data in existing databases must be evaluated for their quality and value for use in comparative compositional analysis.

3.2.7 Safety aspects of foods derived from or produced with GMMs

The production of food additives or processing aids using GMMs, where the microorganism is not a part of the food, has become an important and generally well-accepted technology, with a significant number of such products on the market (Ross et al. 2002). Experience with the purification of proteins in the biomedical field suggests that well-standardized purification protocols are of central importance for the safety of these products.

Where the GMMs are a part of the food matrix (e.g. starter culture containing live or sterilized microbes), certain criteria were established in 2001 by a *Joint FAO/WHO expert consultation on foods derived from biotechnology* (FAO/WHO 2001b) for assessing the risks that may be associated with the preparation of such foods. These include the genetic constructs (vectors) used in the GM microorganisms, the pathogenic potential of GMM, and the detrimental effects of a potential gene transfer (considering a higher incidence for gene transfer (Salyers et al. 2004) and the various mechanisms involved).

For GMMs used in foods (e.g. in fermented foods or in functional food preparations), the ensuing risk assessment ought to focus on the effects of a possible interaction between the GMM and endogenous intestinal microflora and the potential immune-stimulatory or immunomodulatory effects of the microorganisms in the event the gastrointestinal tract is colonized (FAO/WHO 2001b).

Small regulatory elements derived from viral DNA are commonly used to drive the expression of transgenes in GMOs. Viral-DNA constructs are sometimes used as transgenes to establish resistance against viral pests, as they express viral proteins that confer viral resistance on plants. Some scientists suggest that the potential interaction of GM viral constructs with related wild-type viruses needs to be part of the risk assessment, to evaluate the potential of new viral pest strains evolving through mechanisms of recombination (Mellon and Rissler 1994; Frischmuth and Stanley 1998).

Insertion of viral vectors into functionally important genes of recipient patients in the field of biomedicine has been reported, and whereas such vectors are not commonly used in food production, this evidence indicates the limited understanding of mechanisms directing insertion of genetic constructs (Check 2003).

3.2.8 Safety aspects of foods derived from biopharming

The potential to produce human proteins in animals has resulted in great interest in new possibilities for human health, but also in efforts to establish appropriate risk-assessment methods. The biosafety aspects of molecular ‘farming’ (or ‘pharming’) can be divided into two major groups: the potential spread of transgenes; and the potential negative effects of the expressed protein on the environment and the consumer (PIFB 2002a; Fischer et al. 2004; Mascia and Flavell 2004). Practices and guidelines ensuring effective separation of ‘biopharming’ are being investigated. Experts agree that the risk assessment should ensure that proteins designed to produce pharmaceutical products, e.g. in the animal’s milk, cannot find their way to other parts of the animal’s body, possibly causing adverse effects.

3.2.9 Potential effect of GMOs on human health mediated through environmental impact

Work on environmental-health indicators (von Schirnding 2002) suggests that various agricultural practices have direct and indirect effects on human health and development. Hazards can take many forms — wholly natural in origin, or derived from human activities and interventions. The need to assess indirect effects of the use of GMOs in food production has been emphasized by many countries. Potential environmental-health hazards from the release of GMOs into the environment have been discussed in a report by WHO and the Italian Environment Protection Agency, in which health effects have been analyzed “as an integrating index of ecological and social sustainability” (WHO/EURO–

ANPA 2000). For example, the production of chemicals or enzymes from contained GM microorganisms (e.g. chemicals, pharmaceuticals or food additives) have contributed significantly to decreases in the amount of energy use, toxic and solid wastes in the environment, thereby significantly enhancing human health and development (CBD 2003).

A further example of beneficial human/environmental outcomes of introducing GM crops is the reduction in the use, environmental contamination and human exposure to pesticides demonstrated in some areas. This has occurred especially through the use of pesticide-resistant *Bt* cotton, which has been shown to decrease pesticide poisoning in farm workers (Pray et al. 2002).

Outcrossing of GM plants with conventional crops or wild relatives, as well as the contamination of conventional crops with GM material, can have an indirect effect on food safety and food security by contamination of genetic resources. Although initial concerns about introgression of transgenic DNA into traditional landraces of maize in Mexico arose as a result of the findings of transgenic DNA in such landraces in 2000 (Quist and Chapela 2001, Ag BioTech 2002; Alvarez-Morales 2002) recently published results from samples taken during a broad, systematic survey in 2003 and 2004 in the same region shows no transgenes in these landraces (detection limit approx. 0.01%) (Ortiz-García et al. 2005). Still, the potential for introgression remains a possibility and risk-mitigation measures are being considered.

Both outcrossing and contamination characteristics are dependent on the pollination and distribution characteristics of pollen and seeds of the specific plant. In the USA, GM 'Starlink' maize was not approved for food use, but unintentionally started to appear in maize food products. This example demonstrated the problem of contamination and highlighted the potential for unintended impacts on human health and safety (Taylor and Tick 2001; Macilwain 2005). In the case of Starlink maize, full segregation of GM varieties not intended for food use and other varieties of the same crop species could not be achieved.

Improved molecular methods for containment of the transgenes as well as farm management measures are under discussion, e.g. isolation distances, buffer zones, pollen barriers, control of volunteer plants, crop rotation and planting arrangements for different flowering periods, and monitoring during cultivation, harvest, storage, transport and processing (Daniell 2002; European Commission 2003b; National Research Council 2004).

The likelihood of GM animals entering and persisting in the environment will vary among taxa, production systems, modified traits, and receiving environments. The spread and persistence of GM fish and shellfish — or their transgenes — in the environment could be an indirect route of entry of GM animal products into the human food supply. This is because escaped individuals or their descendents could subsequently be captured in fishing for those species. Similar mechanisms might apply for poultry such as ducks and quail that are subject to sport or subsistence harvest. Live transport and sale of GM fish and poultry pose another route for the escape of GM animals and their entry into the environment.

3.3 GMOs and environmental safety

3.3.1 Principles of environmental risk assessment

In many national regulations, the elements of environmental risk assessment (ERA) for GM organisms include the biological and molecular characterizations of the genetic insert, the nature and environmental context of the recipient organism, the significance of new traits of the GMO for the environment, and information on the geographical and ecological characteristics of the environment in which the introduction will take place. The risk assessment focuses especially on potential consequences for the stability and diversity of ecosystems, including putative invasiveness, vertical or horizontal gene flow, other ecological impacts, effects on biodiversity and the impact of the presence of GM material in other products (Connor et al. 2003).

Different approaches in the ERA regulations of different countries have often resulted in different conclusions on the environmental safety of certain GMOs, especially where the ERA focuses not only on the direct effects of GMOs, but also addresses indirect or long-term effects on ecosystems, e.g. impact of agricultural practices on ecosystems (FAO/WHO 2004).

Internationally, the concept of 'familiarity' was developed also in the concept of environmental safety of transgenic plants. The concept facilitates risk/safety assessments, because to be familiar means having enough information to be able to make a judgement of safety or risk (FAO/WHO 2000). Familiarity can also be used to indicate appropriate management practices, including whether standard agricultural practices are adequate or whether other management practices are needed to manage the risk (FAO/WHO 2000). Familiarity allows the risk assessor to draw on previous knowledge and experience with the introduction of plants and microorganisms into the environment and informs appropriate management practices. As familiarity depends also on knowledge of the environment and its interaction with introduced organisms, the risk/safety assessment in one country may not be applicable in another country.

Currently, the Cartagena Protocol on Biosafety (CPB) of the Convention on Biological Diversity is the only international regulatory instrument which deals specifically with the potential adverse effects of GMOs (known as living modified organisms (LMOs) under the Protocol) on the environment, taking also into account effects on human health (CBD 2000). The Protocol covers transboundary movements of any GM foods that meet the definition of an LMO. Annex III of the Protocol specifies general principles and methodology for risk assessment of LMOs. The Protocol establishes a harmonized set of international rules and procedures designed to ensure that countries are provided with the relevant information, through the information exchange system called the Biosafety Clearing House (CBD 2005c). This Internet-based information system enables countries to make informed decisions before agreeing to the importation of LMOs. It also ensures that LMO shipments are accompanied by appropriate identification documentation. While the Protocol is the key basis for international regulation of LMOs, it does not deal specifically with GM foods, and its scope does not consider GM foods that do not meet the definition of an LMO. Furthermore, the scope of its consideration of human-health issues is limited, given that its primary focus is biodiversity, in line with the scope of the Convention itself. Consequently, the Protocol alone (which entered into force on 11 September 2003) is not sufficient for the international regulation of GM foods.

3.3.2 Potential unintended effects of GMOs on non-target organisms, ecosystems and biodiversity

This study does not focus specifically on the effects that GMOs used in food production may have on the environment. However, these aspects need to be considered in a holistic assessment of GM food production, as environmental effects may indirectly affect human health and development in many ways. Some of the established indirect effects on human health are specifically addressed in *Section 3.2.9*.

Potential risks for the environment include unintended effects on non-target organisms, ecosystems and biodiversity. Insect-resistant GM crops have been developed by expression of a variety of insecticidal toxins from the bacterium *Bacillus thuringiensis* (*Bt*). Detrimental effects on beneficial insects, or a faster induction of resistant insects (depending on the specific characteristics of the *Bt* proteins, expression in pollen and areas of cultivation), have been considered in the ERA of a number of insect-protected GM crops. Studies on the toxicity of *Bt* maize on the monarch butterfly in the USA indicate that for most commercially available hybrids, the *Bt* expression in pollen is low, and laboratory and field studies show that no acute toxic effects at any pollen density would be encountered in the field (Sears et al. 2001). These questions are considered an issue for monitoring strategies and improved pest-resistance management.

Increased doses of herbicide can be applied post-emergence to herbicide-tolerant crops, thus avoiding routine pre-emergence applications and reducing the number of applications needed. Also, the need

for tilling can be reduced under critical soil conditions. In certain agro-ecological situations, such as a high weed pressure, the use of herbicide-tolerant crops has resulted in a reduction in quantity of the herbicides used. However, in other cases, herbicide use has stayed the same or even increased (American Soybean Association 2001; Benbrook 2001, 2003). In other situations, the following have been investigated: potentially detrimental consequences for plant biodiversity, weed shifts to less-sensitive species and development of herbicide resistance, decreased biomass, adverse effects on wildlife such as arthropods or birds, or consequences for agricultural practices, e.g. the use of the ecologically important practice of crop rotation (Watkinson et al. 2000; Dale et al. 2002; Phipps and Park 2002; Hauge Madsen and Streibig 2003).

Outcrossing. Outcrossing of transgenes has been reported from fields of commercially grown GM plants, including oilseed rape and sugar beet, and has been demonstrated in experimental releases for a number of crops, including rice and maize. Outcrossing could result in an undesired transfer of genes such as herbicide-resistance genes to non-target crops or weeds, creating new weed-management problems.

The consequences of outcrossing can be expected in regions where a GM crop has a sympatric distribution and synchronized flowering period that is highly compatible with a weedy or wild relative species, as demonstrated for rice (Ellstrand 2001; Chen et al. 2004). In view of the possible consequences of gene flow from GMOs, the use of molecular techniques to inhibit gene flow has been considered and is under development. Isolation distances or future molecular strategies for transgene confinement in transgenic crops may reduce gene flow (Daniell 2002). Stringent isolation measures may be necessary because of complex dispersal mechanisms for certain crops. Gene confinement techniques, e.g. introducing the transgene in plastids which are not inherited paternally, are either not very effective because of gene flow via seeds (Board on Agriculture and Natural Resources 2004; Snow et al. 2004) or they are still in an early stage of development.

GM animals. The possibility that certain genetically engineered fish and other animals may escape, reproduce in the natural environment and introduce recombinant genes into wild populations is raised in a report of a United States Academy of Science study (Board on Agriculture and Natural Resources 2002). Genetically engineered insects (PIFB 2004), shellfish, fish and other animals that can easily escape, are highly mobile and that form feral populations easily, are of concern, especially if they are more successful at reproduction than their natural counterparts. For example, it is possible that if released into the natural environment, transgenic salmon, with genes engineered to accelerate growth could compete more successfully for food and mates than wild salmon, thus endangering wild populations. The use of sterile, all-female genetically engineered fish could reduce interbreeding between native populations and farmed populations (Muir and Howard 2002), a current problem with the use of non-engineered fish in ocean net-pen farming. Sterility eliminates the potential for spread of transgenes in the environment, but does not eliminate all potential for ecological harm. Monosex triploidy is the best existing method for sterilizing fish and shellfish, although robust triploidy verification procedures are essential (PIFB 2003; FAO/WHO 2003a).

GMMs. Gene transfer from bacteria to bacteria in the soil has been demonstrated in some systems, e.g. for antibiotic-resistance genes (Nwosu 2001), and only a limited number of releases of GMMs (e.g. *Pseudomonas* and *Rhizobium*) has been permitted; mainly to explore the spread and the fate of microorganisms in nature.

Risk assessment in this field is impeded by a number of factors, such as the limited knowledge of microorganisms in the environment (only approximately 1% of soil bacteria are currently described), the existence of natural transfer mechanisms between microorganisms, and the difficulties in controlling their spread.

3.3.3 Status of methods for estimating potential environmental entry

Methods by which to reliably characterize potential environmental entry have not yet been standardized. Net-fitness methodology (Muir and Howard 2002) does provide, however, a systematic and comprehensive approach based on contemporary evolutionary and population biology. It involves a two-step process of (1) measuring fitness-component traits covering the entire life-cycle for GM animals, their conventional counterparts, and crosses between the two; and (2) entering the fitness data from step 1 into a simulation model that predicts the fate of the transgene across multiple generations. There is a need to validate the predictions based on this method. Initial experiments are under way to this end (FAO/WHO 2003a).

3.4 Regional specificity in safety assessments

Contradictory findings for benefits and risks for the same GM crop may reflect that such effects may be a consequence of different agro-ecological localities or regions. For example, the use of herbicide-resistant crops could potentially be detrimental in a small-sized agricultural area which has extensive crop rotation and low levels of pest pressure. Moderate herbicide uses on these GM plants could be beneficial in other agricultural situations (see discussion on herbicide reductions or *Bt* plants).

At present, no conclusive evidence on environmental advantages or costs can be generalized from the use of GM crops. Consequences may vary significantly between different GM traits, crop types and different local conditions including ecological and agro-ecological characteristics (Gianessi et al. 2003; Ammann 2004).

In the USA, the overall difference in herbicide use between GM and conventional soybeans ranged from +7 to –40% (1995–1998), with an average reduction of 10%. These changes have been associated with a number of factors including soil type, weed pressure, farm size, management style, prices of different herbicide programmes, and climate (Hin et al. 2001). Potential advantages of *Bt* maize have been widely attributed to regions with a significant pest pressure from the maize borer (Obrycki et al. 2001).

The consequences of outcrossing can produce highly different characteristics, depending on the potentially different recipient plants in different ecological regions (Snow 2002). These observations suggest that risk assessment needs to reflect the regional specificities of the receiving environments in addition to the characteristics of the GMO.

In 1999, the government of the United Kingdom asked an independent consortium of researchers to investigate how growing GM crops might affect the abundance and diversity of farmland wildlife compared with growing conventional varieties of the same crops (Andow 2003). In the largest-ever field trials of GM crops in the world, the researchers compared three GM crops with their conventional counterparts. The crops were sugar- and fodder-beet (considered as a single crop), spring-sown oilseed rape, and maize. The GM crops had been genetically modified to make them resistant to specific herbicides. Other types of GM crops, such as those engineered to be resistant to certain insect pests, were not included in the study. The team found that there were differences in the abundance of wildlife between GM herbicide-tolerant crop fields and conventional crop fields. Growing conventional beet and spring rape was better for many groups of wildlife than growing GM herbicide-tolerant beet and spring rape. There were more insects, such as butterflies and bees, in and around the conventional crops because there were more weeds to provide food and cover. There were also more weed seeds in conventional beet and spring rape crops than in their GM counterparts. Such seeds are important in the diets of some animals, particularly some birds. In contrast, growing GM herbicide-tolerant maize was better for many groups of wildlife than conventional maize. There were more weeds in and around the GM herbicide-tolerant crops, more butterflies and bees at certain times of the year, and more weed seeds.

The researchers stress that the differences they found do not arise just because the crops have been genetically modified. They arise because these GM crops give farmers new options for weed control. That is, they use different herbicides and apply them differently. The results of this study suggest that growing such GM crops could have implications for wider farmland biodiversity. However, other issues will affect the medium- and long-term impacts, such as the areas and distribution of land involved, how the land is cultivated and how crop rotations are managed. These make it hard for researchers to predict the medium- and large-scale effects of GM cropping with any certainty. In addition, other management decisions taken by farmers growing conventional crops will continue to have an impact on wildlife.

Monitoring of the environmental impacts of GM crops in various regions and from investigation over longer time periods may be necessary to conclude on effects and consequences.

3.5 Monitoring of human health and environmental safety

In the future, GMOs may gain wider approval for environmental release, either with or without approval to enter them in the human food supply. In such situations, it will be important to consider whether or not to apply postmarket monitoring for unexpected environmental spread of the GMOs and their transgenes) that may pose food safety hazards. Methods for detection of such GMOs and their transgenes in the environment are likely to involve application of two well-established bodies of scientific methodologies: (1) diagnostic, DNA-based markers; and (2) sampling protocols that are adequate (in terms of statistical power) and cost-effective. However, there is a need to fully develop appropriate protocols for application of these methods to postmarket detection of environmental spread of GMOs and their transgenes. Monitoring can also be helpful to assure confinement of GMOs during R&D (FAO/WHO 2003a).

Postmarket monitoring (or surveillance) of GM foods with respect to direct human-health impacts has been raised at international conferences (Health Canada 2002) and within the Codex Alimentarius Commission. Opinions regarding such monitoring vary from neither necessary nor feasible, to being essential to support and improve the results of a risk assessment and enable an early detection of uncharacterized and unintended hazards. Some have suggested that monitoring of potential long-term effects of GM foods with significantly altered nutritional composition (Amanor-Boadu and Amanor-Boadu 2002) should be mandatory.

The *Expert consultation on the safety assessment of foods derived from GM animals* held in 2003 (FAO/WHO 2003a) identified a need for postmarket surveillance, and therefore a product-tracing system, for:

- confirmation of the (nutritional) assessments made during the premarket phase;
- assessment of allergenicity or long-term effects; and
- unexpected effects.

The issue of postmarket surveillance is closely related to risk characterization. In general, potential safety issues should be addressed adequately through premarket studies, as the potential of postmarket studies is currently very limited. Postmarket surveillance could be useful in certain instances where clear-cut questions require, for instance, a better estimate of dietary exposure and/or the nutritional consequences of GMO-derived food.

Tools to identity or trace GMOs or products derived from GMOs in the environment or food-chain are a prerequisite for any kind of monitoring. Detection techniques (such as polymerase chain reaction; PCR) are in place in a number of countries to monitor the presence of GMOs in food, to enable the enforcement of GM labelling requirements, and to monitor effects on the environment. Attempts to standardize analytical methods for tracing GMOs have been initiated (European Commission 2002).

3.6 Conclusions

GM foods currently available on the international market have undergone risk assessments and are not likely to present risks for human health any more than their conventional counterparts.

The risk-assessment guidelines specified by CAC are thought to be adequate for the safety assessment of GM foods currently on the international market. Guidelines for environmental risk assessment have been developed under the Convention on Biological Diversity.

The potential risks associated with GMOs and GM foods should be assessed on a case-by-case basis, taking into account the characteristics of the GMO or the GM food and possible differences of the receiving environments.

In the field of potential risks derived from outcrossing or contamination from GM crops, relevant consequences need to be investigated for specific crops, and strategies for risk management need to be explored.

As highlighted in the Codex *Principles for the risk analysis of foods derived from modern biotechnology* (CAC 2003b), the assessment of the potential of GM foods to elicit hypersensitivity reactions should be part of the risk assessment for GM foods. This includes a general analysis of the proteins expressed and assessment of the specific properties of the GM food under consideration to elicit hypersensitivity reactions. A better understanding of the impact and interaction of food with the immune system is required to decipher how and whether conventional and GM foods cause specific health and safety problems.

New methodology for the development of GMOs may significantly reduce potential risks derived from the random integration of transgenes used in current methods.

4. DEVELOPING REGULATORY AND SAFETY SYSTEMS FOR MODERN FOOD BIOTECHNOLOGY: A ROLE FOR CAPACITY BUILDING

4.1 Defining capacity building

The United Nations and international development agencies coined the term 'capacity building' in the early 1990s after an appraisal of the development-assistance programmes in developing countries. Within that context, the term has come to mean different things to different people. In 1997, a World Bank progress report on Africa defined it as: "…an investment in people, institutions and practices that will, together, enable countries in the region to achieve their development objectives" (World Bank 1997). Capacity building is a four-step process involving a needs assessment, strategic planning to change the situation, training of personnel to implement the changes, and an evaluation of the results.

A United Nations Development Programme (UNDP) report describes capacity building as a continuous process that ought to take place at various levels: individual, institutional and societal (Fukuda-Parr et al. 2002). The first two levels involve expanding local knowledge and skills. At the societal level, it is about creating opportunities to engage the trained individuals to their fullest potential. All three levels are interdependent and need to be pursued concurrently in order to achieve the maximum benefit.

In a report published in 2000, UNDP acknowledged that due to the different levels of development among countries, some countries may never be in a position to deploy cutting-edge technologies. Nevertheless, these countries need local expertise to understand and adapt technologies for national use, consistent with their development goals.

4.2 Background

It is widely accepted that the application of modern biotechnology could be important to economic development, but may also involve inherent risks (UNECA 2002; CBD 2005d). Thus, all countries, be they developers or net importers of products derived from modern biotechnology, should introduce measures that safeguard human health and environmental safety. In fact, many governments are in the process of developing legal instruments/regulatory systems that address human health and environmental safety. The effectiveness of such measures will be determined by a country's capacity (both in terms of human resources and infrastructure) to expeditiously handle the evaluation, management and risk communication of each new product of modern biotechnology. While evaluation and risk management may be done on a case-by-case basis, risk communication activities undertaken by governments should address the process according to which decisions are taken.

Starting in the 1970s, R&D in biotechnology has been important to development collaboration (Jenny 1999). This trend was supported by the adoption in 1992 of Agenda 21 (UNDESA 1992) and, more recently, the Convention on Biological Diversity (see CBD 2005a). These two agreements include specific sections on the application and use of biotechnology in major economic sectors such as agriculture, industry and energy. To complement this, many donor agencies, NGOs, the private sector and governments in industrialized countries have focused their capacity-building policies and objectives on maximizing the benefits of biotechnology in developing countries through technology transfer/extension. The database of capacity-building initiatives of the CBD Biosafety Clearing House (CBD 2005b) demonstrates the strategies intended to target progress towards the Millennium Development Goals (World Bank 2000b).

Agenda 21 (UNDESA 1992) is a comprehensive plan of action to be taken globally, nationally and locally by organizations of the United Nations system, governments and major groups in every area in which humans place a burden on the environment. It was adopted in June 1992 by over 178 governments at the United Nations Conference on Environment and Development (UNCED 1992).

This approach has addressed one specific area (technology development), but has failed to impart the skills and knowledge necessary to undertake associated activities, such as development and implementation of regulatory and food-safety frameworks.

Safety issues with regard to protecting the environment and human health are different and require different expertise. Biosafety tends to be the responsibility of the department of environment or agriculture, whereas the authority for food safety often lies with the department of health. Hence, the legal instruments for regulation may differ.

At the international level, 15 legally binding instruments and non-binding codes of practice address some aspect of GMOs, but none of these on its own integrates the regulation of biotechnology across all sectors (Glowka 2003). Such sector-based regulations and powers increase the already overstretched capacity needs of developing countries, and present challenges to developing a fully coherent policy and regulatory framework for modern biotechnology (FAO 2002). The challenge for developing countries is to achieve coherence in national legislation for crops, livestock, fish, forest trees and microorganisms, while meeting international obligations and ensuring harmonization (Glowka 2003).

The shortcomings of most capacity-building programmes lie in the simplistic notion that assumes a 'one size fits all' development path (Fukuda-Parr et al. 2002). Donors often prescribe programmes that are largely based on the experiences of developed countries, on the assumption that these will work equally well for developing countries. Unfortunately, this is rarely the case and can result in limited or disappointing outcomes.

A sound capacity-building programme is determined by its ability to focus on human development, in order to foster the skills and resources needed to sustain its own progress. In other words, a capacity-building initiative must act as a support and catalyst to self-reliance and tap into a country's ability to master its own development, in harmony with its natural environment and any other national imperatives such as economic sustainability (ECDPM 2003).

Capacity-building initiatives must be sustained beyond the life of the activity as an integral part of a development programme and not be a once-off activity (Anon. 1999). In turn, developing countries must participate in and take ownership of an activity and be encouraged to take charge of their own development. Demand-driven knowledge development is more likely to be absorbed if it reflects local circumstances, and more likely to be applied by society.

4.3 Capacity needs

Food safety is attracting increased attention because of its implications for public health (World Bank 2000a). In general, food control systems in developing countries are poorly developed, and less organized than in most developed countries. Their overall capacity needs in terms of food safety can be summarized as follows (FAO 1999a): (1) basic infrastructure; (2) national food control strategy; (3) food legislation and regulatory framework; (4) food inspection services; (5) food control laboratories and equipment; and (6) implementation of food quality and safety assurance systems.

The work in food safety is multidimensional, and there are frequently several food laws under the authority of different agencies (WHO 2002b). In many countries, effective food control is undermined by the existence of fragmented legislation, multiple jurisdictions and weaknesses in surveillance, monitoring and enforcement mechanisms. Food-safety legislation developed specifically for the safety of GM foods should be integrated within the existing food laws, taking into account the special risk-management requirements.

In order to make informed decisions on the safety of GMOs and GM foods, governments need substantial human and institutional resources in the disciplines required for assessing the risks for the

environment and for human food presented by GMOs. Developing countries have limited expertise in the required fields of science, as biotechnologists in these countries are generally engaged in research and therefore mostly unavailable to the regulatory bodies and as policy-makers (Mugabe 2000). In most developing countries, those same scientists sit on national biosafety committees, and are involved in both risk assessment and policy-making. There are three vulnerabilities in this scenario: (a) when developers are also risk assessors, the potential for conflict of interest is magnified; (b) because most members of the national biosafety committee are recruited on a voluntary basis, they do not devote too much time to this responsibility; and (c) because membership of the national biosafety committee generally rotates, there is no continuity in the capacity gained through experience.

While many developed countries have adopted mechanisms to govern modern biotechnology, most developing countries are either in the process of developing national biosafety frameworks or are yet to start the process. To date, no more than 10 developing countries have implemented national biosafety laws (CBD 2005c). A further 20–30 are in a state of transition whereby some or all elements are at different stages of development. A few developing countries that permit the commercial planting of crops derived from modern biotechnology have modest capacities to implement a regulatory framework (Paarlberg 2001b).

Where national biosafety frameworks are in place, they vary between countries according to national priorities and statutory structures. In addition, the different social conditions that prevail in different countries make it difficult to determine the appropriate regulatory systems that should be enforced by developing countries (Nuffield Council on Bioethics 2003). Notwithstanding the diversity, a number of elements are essential and form the core of many national frameworks:

- national policy and strategy;
- regulatory framework consisting of regulations and guidelines;
- mechanism for handling applications and issuing permits;
- system for enforcement; and
- system for information dissemination.

The impetus to establish regulatory frameworks for biosafety seems to be a significant factor in determining the process whereby they are developed. In some cases, scientists have raised interest in regulating local research, while in others the trigger may have come from multinational companies seeking to continue seed production in the Southern Hemisphere during the northern winter months. Recently, the importation of food aid has triggered some form of regulation in those countries that have been faced with food shortages.

Many countries with regulatory systems have developed and implemented these systems in a stepwise fashion, usually in response to an immediate demand (Cohen 2001). The first step has involved the establishment of voluntary guidelines to set in process a structured progression of the regulatory framework. The guidelines initially set the principles for safety in laboratory practices, which are later adapted to ensure environmental safety for enabling field trials.

The advantage of guidelines is that revising and incorporating new information requirements in line with an evolving technology can be done very swiftly. However, guidelines are voluntary and compliance cannot be enforced unless supported by regulations (McLean et al. 2002).

4.3.1 Institutional and human-resource constraints

Many countries face major constraints with respect to enhancing their regulatory capacity needs. These constraints fall into three categories: institutional, human resources, and cost (Juma and Konde 2002). The first two are interdependent in many respects.

The Codex *Principles for the risk analysis of foods derived from modern biotechnology*, adopted in 2003 (CAC 2003b), recognize the need for improving the capabilities of regulatory authorities in handling risk analysis. Capacity-building programmes for developing countries are also being discussed within the Codex system.

Capacity building is one of the essential elements of the Cartagena Protocol on Biosafety (CBD 2000). Its *Article 22* is devoted entirely to this issue, while paragraph *3* of *Article 28* deals with the financial support that developing countries may require in meeting their capacity needs if they are to be effective in implementing the Protocol.

Countries with a weak knowledge- and skills-base tend to develop highly protective regulations at the expense of innovation. In contrast, flexibility in regulatory structures tends to be encouraged by a broad knowledge and capacity base (McLean et al. 2002).

The capacity-building needs of developing countries can be grouped according to (among other aspects): the level of biotechnology research; the capabilities to develop marketable products; the level of development that would determine whether a country becomes an importer or exporter of products derived from modern biotechnology. This last issue is of crucial importance in the needs assessment. It enables a country with limited resources to plan and invest realistically in the capacities that will be used.

4.3.2 Financial constraints

Recognizing the need to regulate modern biotechnology, and appreciating that developing countries may need to re-evaluate their spending priorities, the cost implications of establishing national biosafety regulatory frameworks, including GM food-safety regulations, should be assessed.

A country's financial situation has an overriding influence on the development and implementation of national frameworks for the regulation of modern biotechnology. For a framework to be effective, an identification of existing resources, gaps and training should be made in order to build on the expertise and experience available in a given country. However, the national priorities of developing countries may differ from those of developed countries, so that these governments may elect to use their limited resources in other ways.

Cost in itself raises important questions with respect to finding the right balance between meeting obligations under international agreements and addressing national priorities. The cost of establishing a national biosafety framework, including a food-safety framework, will vary dramatically among countries according to their judicial systems, their individual capacities, and their regulatory objectives.

In 2002, the World Bank and the World Trade Organization (WTO) announced the launch of a fund, the Standards and Trade Development Facility (STDF) (see WTO 2005), in collaboration with FAO, the World Organisation for Animal Health (Office International des Epizooties; OIE) and WHO. The main objective of the Facility is to coordinate the activities of the international organizations in order to maximize the financial and technical support given to developing countries for implementing international standards for food safety, plant and animal health.

In 2000, the Council of the Global Environment Facility (GEF) agreed to support the *Initial strategy for assisting countries to prepare for the entry into force of the Cartagena Protocol on Biosafety*, a three-year project implemented by the United Nations Environment Programme (UNEP), for the establishment of country-driven national biosafety frameworks. This project, initiated in June 2001, had enlisted 123 countries globally as of September 2004 to set up frameworks for the management of products derived from modern biotechnology at the national level, and it is hoped to establish cooperation at subregional, regional and international levels.

According to UNEP and GEF, 139 countries meet the criteria set and therefore qualify to participate in the *Development of national biosafety frameworks project* estimated at US$38.4 million. Assuming the enlisted 123 countries get assistance from the project, an estimated US$400,000 per country is required to establish a national framework. One-third of this total is to be contributed by the country in cash or in kind.

The MATRA project of the Netherlands Ministry of Foreign Affairs invested US$60,000 per country in the pre-accession countries of Central and Eastern Europe (CEE). These funds were used over a three-year period to establish national biosafety frameworks that conform to the relevant European Community directives and the CPB.

When the project was initiated, the CEE countries were at different stages of developing national frameworks as some (e.g. Hungary and Poland) had benefited from the UNEP/GEF *Pilot biosafety enabling activity project*. At its conclusion, the countries were not only ready to join the EU, but had a regional web site hosting information on their frameworks and regional activities, and established centres of excellence that will sustain capacity development in the region.

Other costs that need to be taken into consideration include systems for monitoring compliance, and costs associated with review of the scope and effectiveness of the legal requirements in keeping pace with new scientific developments and public opinion.

4.3.3 Food safety capacity development

In order to support countries wishing to fulfil the mandate set by the CPB (CBD 2000), the secretariat of the CBD maintains a global database of capacity-building initiatives as a component of the Biosafety Clearing House (CBD 2005b). The purpose of this database is to give an overview of past, present and prospective capacity-building initiatives. The secretariat intends to use the information to develop a method for coordinating capacity-building initiatives, thus ensuring that they complement one another, use funding efficiently and strengthen resources in the recipient countries. Although the secretariat's interest is in initiatives that would support the effective implementation of the CPB, the database covers a wider range of initiatives, such as technology transfer and those directed towards biotechnology research.

To date, 89 initiatives have been listed in the database, illustrating a broad range of implementing agencies. According to the secretariat, more than half of the registered initiatives have been negotiated bilaterally and through industry interest groups. United Nations agencies, intergovernmental organizations, or individual governments, industry or NGOs supported most of these countries through bilateral agreements. While the capacity-building initiatives collectively cover all the aspects associated with the application of modern biotechnology, no single one covers the entire range — each is limited to its own specific focus. For example, the FAO/WHO expert consultations and capacity-building programmes supported by both organizations train individuals in food-safety-related issues only.

WHO has advised Member States and assisted in building their capacity for food-safety-related issues for many years. The food-safety activities of WHO have increased significantly over the years, with the establishment of international expert scientific bodies such as the Joint FAO/WHO Expert Committee on Food Additives (JECFA) in 1956, to evaluate the safety of food additives, contaminants, naturally occurring toxicants and residues of veterinary drugs in food; the Joint FAO/WHO Meeting on Pesticide Residues (JMPR) (1963) to evaluate the safety of pesticide residues in food; the Joint FAO/WHO Expert Meeting on Microbiological Risk Assessment (JEMRA) (2000) to provide risk-assessment guidelines for selected pathogens and for microbiological hazards in food and water. Also in 1963, the Codex Alimentarius Commission was created to implement the joint FAO/WHO Food Standards Programme.

To strengthen its in-house activities, WHO created the Food Safety Programme in 1978, operating at national, regional and international levels. The recognition of food safety as a major public-health concern by the World Health Assembly in 2000 has also increased the profile of food-safety-related issues, not only within the Organization but also at the national level (WHO 2000b). These activities were further supported by the endorsement of the WHO Global Strategy for Food Safety by the WHO Executive Board in 2002.

In this strategy, WHO proposes to "formulate regional food safety strategies on the basis of the WHO global food safety strategy and of specific regional needs such as technical support, educational tools and training".

Considerable technical assistance has been provided to developing countries to create and/or enhance food-safety control systems, but these activities have not been effectively coordinated and therefore not been adequate in meeting the public-health needs of recipient countries.

The SPS Agreement of WTO (WTO 1995, Article 9) calls for assistance to developing-country Members to enable them to strengthen their food safety and animal and plant health protection. The Agreement encourages Members to enter into bilateral arrangements for technical assistance, or to seek training through other international organizations. Such assistance can be in the area of processing technology, research or infrastructure development, and may take the form of technical advice, expertise, financial assistance or procurement of adequate equipment.

As previously mentioned, food-safety activities within WHO take place at the international, regional and country levels. The regional and country offices provide assistance in developing and strengthening national food-safety programmes, whereas WHO headquarters develops guidelines for such work, including the framework for risk analyses and setting international standards (Mahoney 2001). The division of these activities is arbitrary as headquarters also participates in activities at the national and regional levels, with technical know-how and capacity-building guidance. These activities include (FAO/WHO 2003b):

- developing regional and national food-safety policy and strategies;
- preparing food legislation, regulations, standards and codes of hygienic practice;
- implementing food inspection programmes;
- promoting methods and technologies designed to prevent foodborne diseases, including the hazard analysis and critical control point (HACCP) system;
- developing or enhancing food analysis capability;
- developing methods for assessing the safety of the products of new technologies;
- establishing healthy markets and enhancing the safety of street food; and
- promoting the establishment of foodborne disease surveillance systems.

Many WHO activities to build food-safety capacity are developed in collaboration with FAO. However, FAO also administers a major, separate technical cooperation programme building capacity in this and other agriculture-related areas in many developing countries.

Although most developing countries have national food-control systems, these are often not based on modern scientific concepts. Moreover, they cannot be adapted to cope with developments in food science and technology (Gupta 2002). The specifications for an effective food-control system include: regulations, capacity for assessing the risks associated with the food, and ongoing monitoring and evaluation of the risks. A capacity-building programme for the risk assessment of products of modern biotechnology (see *Section 3.2*) would involve:

- use of the concept of a comparative safety assessment (see *Section 3*);

- hazard identification and characterization;
- assessment of food intake, including consumption profile and effects;
- use of integrated toxicological evaluation;
- use of integrated nutritional evaluation;
- risk characterization; and
- application of risk-management strategies, such as labelling and monitoring.

4.3.4 Other considerations

Apart from the human resources and physical facilities in which to perform biosafety-related research, competent authorities need information relating to trends in biotechnology and biosafety to keep abreast with biotechnology developers. Information exchange systems as provided by a number of organizations fulfil this need by facilitating international cooperation, but can only be used by developing countries where the appropriate expertise exists. Even more limiting, several of these information networks are difficult to search, while others are limited in scope (Louwaars et al. 2002). The Intergovernmental Committee for the CPB, realizing the capacity constraints of developing countries, has established a coordination mechanism to maximize synergies, complementarity and collaboration between the numerous international initiatives.

The evaluation of food is not only about science. It should also take into account the social, ethical and religious concerns of the local populations (see *Section 6*).

4.4 Harmonization

At the international level, protocols have been agreed upon that implicitly promote the harmonization of regulatory systems. While the Codex *Principles for the risk analysis of foods derived from modern biotechnology* (CAC 2003b) are available to guide the safety assessment of GM food, they have no binding effect on national legislation, but do form the basis for harmonization under the SPS Agreement (WTO 1995, Article 3.4). On the other hand, the CPB has established legally binding rules for environmental risk assessments (CBD 2000). In addition, OECD has experience in promoting international harmonization in the regulation of biotechnology by ensuring efficiency in the evaluation of environmental and human-health safety, through its working group for harmonization in biotechnology and its task force for the safety of novel foods and feeds (OECD 1995, 1996).

Developing countries therefore have sets of agreed principles (regulatory and risk assessment of foods) for guidance, and the advantage of learning from the experiences of their forerunners by investigating best practices and adapting them to suit their individual situations.

Although agreement has been reached on the scientific principles of food-safety assessment, consensus has not been achieved on the extent of data required to comply with these principles or on the role of the data in decision-making.

Harmonization of components of the scientific review process has a potential benefit where a lack of resources threatens effectiveness, and the affected countries in the region have determined and agreed on the regulatory objectives. The advantages of regional/subregional cooperation are to facilitate regulation, promote the sharing of resources, synchronize the assessment of foods derived from modern biotechnology, and expedite information exchange (McLean et al. 2002). The Nuffield Council of Bioethics (2003) recommends the implementation of international standards and the sharing of risk-assessment methodologies and results, particularly between developing countries with similar ecological environments.

Moreover, integrating some activities could reduce the overall requirement for new financial resources. Harmonization can be achieved at several levels, i.e. some elements of the framework can be implemented at the regional level. The countries of the Association of South-East Asian Nations (ASEAN) have come together to cooperate on various levels, including: (i) harmonization of legislation for products derived from modern biotechnology and intellectual property rights; (ii) R&D in biotechnology; and (iii) environmental protection. ASEAN is also looking at a regional approach to biosafety, although it is not clear what is intended, i.e. whether regional assessment and national decision-making would be considered. Those countries in the region that have made some progress have gone as far as developing labelling regulations, although they acknowledge that implementation may not be possible in the near future due to a lack of human resources.

After the 2002 humanitarian crisis in southern Africa, where a number of countries experiencing severe drought and food shortages questioned the use and safety of GM food aid, a Council of Ministers of the Southern African Development Community (SADC) established an Advisory Committee on Biosafety and Biotechnology (SADC 2003) to develop a common position on biotechnology and harmonize biosafety legislation in the region. The objective is to facilitate the movement of food products that may contain GM material across the region in future.

Although harmonization may absorb some of the costs that could be incurred in establishing regulatory frameworks, the flexibility allowed by international agreements creates room for divergence from the basic principles. Also, none of the regimes give guidance on regulations. Therefore, achieving harmonization in this context may be debatable as countries grapple with criteria for the precautionary approach and socioeconomics. Nevertheless, particular attention should be paid to supporting and creating new strategic partnerships. Countries need to find effective ways of working together, and analyze the benefits and costs of harmonization.

4.5 Conclusions

Many capacity-building initiatives to date have tended to address a specific need: to develop competency for implementing an international treaty. Nonetheless, several are independent and not linked to any international treaty.

The broad information base required for decision-making with regard to the adoption of modern biotechnology indicates that developing countries need a clear understanding of all the issues. To develop this awareness, the development of human resources needs to extend beyond biosafety training and include food safety, intellectual property rights management, and trade issues. The relevant intergovernmental organizations (CBD, FAO, UNEP, WHO and WTO) should consider coordinating their capacity-building efforts to achieve this holistic approach to imparting knowledge and supporting national capacity building.

Many developing countries cannot afford the seemingly considerable capacities required for the adoption of modern biotechnology. Measures must be taken to ensure that developing countries are not impeded in effective regulation by development problems, and that they derive benefit from their participation in international regulatory instruments.

One way of safeguarding developing-country interests would be to establish a global roster of experts, ideally with a regional balance. However, experience in biosafety is largely gained on the job. Therefore, scientists that may have had exposure to international discussions or even had training may not necessarily know which questions to ask in a safety assessment, because their training may have been theoretical and not given them experience of a real-life situation.

Alongside the above-mentioned activities, a potential normative role exists for WHO to coordinate the scientific food-safety assessments of products of global importance.

5. GM FOOD AND FOOD SECURITY[3]

5.1 What is food security?

The official definition of food security, adopted at the World Food Summit of 1996 (FAO 1996), states:

> "Food security exists when all people, at all times, have physical and economic access to sufficient, safe and nutritious food to meet their dietary needs and food preferences for an active and healthy life."

This definition is understood within the framework of sustainability and was drawn from chapter 14.6 of Agenda 21 (UNDESA 1992), adopted at the 1992 United Nations Conference on Environment and Development (UNCED), which states: "The major thrust of food security...is to bring about a significant increase in agricultural production in a sustainable way and to achieve a substantial improvement in people's entitlement to adequate food and culturally appropriate food supplies."

The underlying assumption is that the means of increasing food availability in many countries exist, but are not being realized because of a range of constraints. In identifying and resolving these constraints, it is necessary to find sustainable ways of improving and reducing year-to-year variability in food production and open the way for broader food access.

The causes of food insecurity involve a complex interplay of economic, social, political and technical issues. An analysis of this interplay should determine the potential solution and best approach for a given population group (FAO 1996). The issue for some communities is being able to produce sufficient food. For others, lack of money to purchase a wider selection of foods is the problem.

Food insecurity and poverty are strongly correlated. The Swedish International Cooperation Agency (SIDA) defines poverty as a three-fold deficiency: a lack of security, ability and opportunity. Poverty is the main cause of food insecurity, and hunger is also a significant cause of poverty. Hunger is not only about quantity — it goes hand-in-hand with malnutrition. Food insecurity and malnutrition impair people's ability to develop skills and reduce their productivity. A lag in farm productivity is closely associated with rural poverty and hunger (FAO 1999b). Food insecurity nevertheless is a reality experienced by the vulnerable in all societies and in all countries, developed and developing.

In developed countries, the problem of food security is often a reflection of affordability and accessibility through conventional channels. Food security for the rural poor in developing countries is about producing or securing enough to feed one's household and being able to maintain that level of production year after year. Hunger and malnutrition increase susceptibility to disease and reduce people's ability to earn a livelihood. In instances where hunger is related to household income, improving food security by ensuring access to food or increasing the purchasing power of a family is essential. Providing poor communities with the skills to improve conditions in an economically and ecologically sustainable manner creates a window of opportunity to alleviate poverty at the subsistence-farming level and, on a larger scale, by having an impact on the economic development of the country.

5.2 The challenges to food security

In developing countries, 800 million people are undernourished, of which a significant proportion live on less than US$1 per day, despite a more than 50% decline in world food prices over the past 20

[3] Throughout this study, the term 'food security' refers to the definition given in *Section 5.1* and should not be construed in the narrower meaning that relates to protection of the food supply from the deliberate use of chemical, biological and radionuclear agents.

years (Pinstrup-Andersen 2000). Global food production has soared, making a variety of foods available to all consumers.

Although the decline in food prices in developed countries has benefited the poor who spend a considerable share of their income on food, this trend has not had much impact on the majority in the developing world, with sub-Saharan Africa painting the gloomiest picture (FAO 2003). Due to the substantial price reduction in this commodity sector, cereals have become the staple foods in the diet of poor people (WHO 2000c). While yield increases in the major cereal crops (rice, wheat and maize) has meant more calorific intake of food, micronutrient malnutrition remains a serious problem (FAO 2003).

Regional analyses depict sub-Saharan Africa as the only region where both the number and proportion of malnourished children have consistently risen in the past three decades (FAO 2003). However, malnutrition in South Asia is also very high.

The world population is projected to reach 8 billion by 2025, and it is estimated that most of this growth will occur in developing countries (FAO 2002a). Feeding and housing an additional 2 billion people will cause considerable pressure on land, water, energy and other natural resources.

Looking at projections to 2020, the worldwide per capita availability of food is expected to increase by approximately 7%, i.e. 2900 calories per person per day (World Bank 2003). Nonetheless, an average availability of 2300 calories is projected for individuals in sub-Saharan Africa, a figure that is just above the recommended minimum calorie intake for an active and productive life.

In terms of agricultural output, preliminary world estimates for 2001 suggested that growth was as low as 0.6% (Pinstrup-Andersen et al. 1999). Annual rates also demonstrate a trend of decreased productivity, particularly in developing-country regions. Output growth in Asia has systematically declined over the past five years the rates experienced in sub-Saharan Africa are lower than average.

Agricultural productivity is important for food security in that it has an impact on food supplies, prices, and the incomes and purchasing power of farmers (FAO 2002b). Improving food security at the national level requires an increase in the availability of food through increased agricultural production, or by increasing imports. To augment domestic production and maintain an adequate supply of food, food-insecure countries often rely on imports and food aid. Export earnings are frequently low and do not suffice to provide foreign exchange to finance imports. Thus, in the long term, importing food is unsustainable.

Historically, increased food production in the developing countries can be attributed to the cultivation of more land rather than to the deployment of improved farming practices or to the application of new technologies (FAO 2002b). By its very nature, agriculture threatens other ecosystems, a situation that can be exacerbated by over-cultivation, overgrazing, deforestation and bad irrigation practices. However, increased demands for food in Asia, Europe and North Africa have to be met by increasing yields because most land in these areas is already used for agriculture. The potential to expand agricultural land exists in Latin America and sub-Saharan Africa only, where much of the remaining land is marginal for agricultural expansion. The implication, therefore, is that the increase in food production needed to feed the world's growing population can only be met by increasing the amount of food produced per hectare (Shapouri 2000; USDA 2000).

Recognizing the extent of environmental degradation caused mainly by human activities, the multilateral agreements that arose from the UNCED meeting of 1992 were intended to address the compromised food-security situation on a global scale. One such agreement is the United Nations Convention to Combat Desertification (see UNCCD 2005). This agreement promotes the implementation of practices intended to reverse desertification for sustainable land use and food security.

As the more affluent developed countries tend to produce more food, some argue that redistribution of these surpluses could feed the escalating populations of developing countries. Redistribution, however, requires policy changes that may be impossible to implement on a global scale (Conway and Toenniessen 1999). Therefore, a substantial proportion of the food demands of developing countries will have to be met by the agricultural systems in these countries. Enabling a consistent and sustainable supply of food will require an overhaul in the production processes and the supporting infrastructure.

Finding solutions to declining crop yields requires an effort that will improve the assets on which agriculture relies; namely, soils, water and biodiversity. Transforming the agricultural systems of rural farmers by introducing technologies that integrate agro-ecological processes in food production, while minimizing adverse effects to the environment, is key to sustainable agriculture (Foster and Leathers 1999; Kwa 2001). In addition, increases in crop yield must be met with the use of locally available low-cost technologies and minimum inputs without causing damage to the environment (Feenstra et al. 1991).

5.3 Attaining food security

Within the context of the definition, three distinct components appear central to attaining food security: availability, accessibility and adequacy (Busch and Lacy 1984; Pretty 2001; Agriculture and Agri-food Canada 2005). Within each component, questions are raised which may need to be addressed to improve the food security situation at a national, regional or international level. The questions raised here are intended to demonstrate the complexity of the issue and are by no means exhaustive:

- Availability: is there enough food available through domestic production or imports to meet the immediate needs? Is production environmentally sustainable to meet long-term demands? Are the distribution systems effective in reaching low-income and rural communities?
- Accessibility: do the vulnerable in society have the purchasing power to attain food security? Can they afford the minimum basic diet of 2100 calories per day required for an active and productive life?
- Adequacy: does the food supply provide for the differing nutritional needs, i.e. a balanced diet, offering the necessary variety of foods at all times? Is the food properly processed, stored and prepared?

Global food productivity is undergoing a process of rapid transformation as a result of technological progress in the fields of communication, information, transport and modern biotechnology. A general observation is that technologies tend to be developed in response to market pressures, and not to the needs of the poor who have no purchasing power. As agriculture is the main economic activity of rural communities, optimizing the levels of production will generate employment and income, and thus uplift the wealth and well-being of the community. Improving agricultural production in developing countries is fundamental to reducing poverty and increasing food security.

Investment to raise agricultural productivity can be achieved through the introduction of superior technologies such as better-quality seeds, crop rotation systems etc. (USAID 1992). It is argued, however, that the adoption of earlier agricultural technologies has led to the emergence of more virulent strains of pests, pathogens and weeds, soil deterioration and a loss of biodiversity (UNDP 2003). The Green Revolution, in particular, focused on wheat and rice — not much attention was paid to staple crops such as sorghum, cassava or millet. Also, the seeds and fertilizers required to grow the higher-yielding varieties were expensive and therefore not accessible to all.

Reaffirming support for the principles agreed upon at the UNCED, the United Nations Millennium Development Goals (World Bank 2000b) have set a road map for protecting the environment.

Embraced in these time-bound goals is a new development ethic that demands sustainability in a framework where progress is measured in terms of actions reconciling the economic and ecological factors of food production for the benefit of present and future generations? Extending this understanding to agriculture, sustainable agriculture is defined as (World Bank 2000b):

- environmentally sound, preserving resources and maintaining production potential;
- profitable for farmers and workable on a long-term basis;
- providing food quality and sufficiency for all people;
- socially acceptable; and
- socially equitable, between different countries and within each country.

A secure food system is one in which the ecological resources on which food production depends allow for their continued use, with minimum damage for present and future generations. In other words, food security and sustainable agriculture are interlinked and both are central to the concept of sustainable development (Bonny 1994).

The FAO Anti-hunger Programme (Baraclough 2000) reported that increasing investment in agriculture and rural development can reduce hunger. To reduce the number of hungry people by half by 2015, it estimated that funding of US$24 billion would be required for agricultural research, emergency food assistance, and improving rural infrastructure. By contrast, at the current rate of progress, the number of food-insecure would fall by only 24%.

For people to be food-secure, they must have access to the resources needed to buy or produce their own food. Breaking the poverty cycle of rural communities, whose livelihoods depend on agriculture, will require investment in different technologies to address the different constraints experienced in different world regions (WHO 2002b).

The production problems experienced by farmers vary between countries and communities, and technological solutions need to be relevant to those circumstances, i.e. one solution will not be suitable everywhere. The potential of some of these technologies has been demonstrated in various world regions *(*Kwa 2001; FAO 2002d) — for instance, agro-ecological improvement programmes involving (Kwa 2001):

- better harvesting and conservation of water, even in rain-fed environments;
- a reduction of soil erosion by adopting zero tillage combined with the use of green manure and herbicides as in Argentina and Brazil; and
- pest and weed control without pesticide or herbicide use, e.g. Bangladesh and Kenya, has been well tested and established.

Indeed, such programmes are now widely accepted as being at the core of sustainable agriculture. The communities that participated in these projects were able to transform food production through the use of resource-management strategies that focused on improving the soil by growing leguminous crops and applying agro-forestry, zero tillage and green manure. These and other projects (Sanchez 2002) have proved that the sustainability of any farming practice and the conditions under which production can be maintained at reasonable levels cannot be predicted with absolute certainty. Some regions may be better able to transfer high-yielding technologies with varying degrees of success (Dommenlen 2000). The uptake of new production systems has proved successful where the programmes have included the participation of entire communities and have not been introduced to isolated groups of farmers (World Information Transfer 1996).

Producing nutritionally enhanced properties in staple crops eaten by the poor could reduce the burden of disease in many developing countries. Scientists at the International Crops Research Institute for

the Semi-Arid Tropics (ICRISAT, India) have developed a pearl millet variety enhanced with beta-carotene (Prasad and Reddy 1999). The trait naturally occurs in two Burkina Faso millet lines from which it was transferred by conventional breeding methods. Genetic modification of japonica rice with a ferritin gene has not given superior results compared to rice with an 80% increase in iron density produced by conventional plant breeding at the International Rice Research Institute (Jayaraman 2002).

Research and technology alone will not drive agricultural growth (Gregorio 2002). Inadequate infrastructure and poorly functioning markets tend to exacerbate the problem of food insecurity. The cost of marketing farm produce can be prohibitive for small-scale farmers, as their isolation prevents the link between agricultural and non-agricultural activities among adjacent villages and between rural and urban areas. Building roads in rural areas is vital to facilitating growth, trade and exchange of farm and non-farm products in rural communities, even those that can adequately feed themselves (IFAD 2001). For instance, government investment in irrigation projects, storage and transport facilities, roads connecting villages to larger markets in the rural areas of China and India, has made an impressive impact on employment and productivity and ultimately provided opportunities for poverty alleviation in the affected areas (USAID 1992). According to UNDP, basic thresholds in roads, power, ports and communications must be reached in order to sustain growth.

5.4 A potential role for modern biotechnology

The Convention on Biological Diversity dictates the use and application of relevant technologies as a means of achieving the objectives of conservation and sustainable use with specific reference to biotechnology.

Modern biotechnology is purported, from a technical perspective, to have a number of products for addressing certain food-security problems of developing countries. It offers the possibility of an agricultural system that is more reliant on biological processes rather than chemical applications (Rosegrant and Cline 2003). The potential uses of modern biotechnology in agriculture include: increasing yields while reducing inputs of fertilizers, herbicides and insecticides; conferring drought or salt tolerance on crop plants; increasing shelf-life; reducing postharvest losses; increasing the nutrient content of produce; and delivering vaccines (Bonny 1999). The availability of such products could not only have an important role in reducing hunger and increasing food security, but also have the potential to address some of the health problems of the developing world.

Achieving the improvements in crop yields expected in developing countries can help to alleviate poverty: directly by increasing the household incomes of small farmers who adopt these technologies; and indirectly, through spill-overs, as evidenced in the price slumps of herbicides and insecticides. Indirect benefits as a whole tend to have an impact on both technology adopters and non-adopters, the rural and urban poor.

Indeed, some developing countries have identified priority areas such as tolerances to alkaline earth metals, drought and soil salinity, disease resistance, crop yields and nutritionally enhanced crops. The adoption of technologies designed to prolong shelf-life could be valuable in helping to reduce postharvest losses in regionally important crops. Prime candidates in terms of crops of choice for development are the so-called ‘orphan crops’, such as cassava, sweet potato, millet, sorghum and yam. Multinationals have found no incentive to develop these crops and have instead invested in marketable crops with high profit returns. This strategy is intended to target wealthier farmers in temperate-zone countries with the financial capacity and tradition of supporting new seed products. However, here is a potential for multinational companies to develop crops grown largely in developing countries. The investment costs are low and the potential markets considerably large (Conway 1999).

While some public-sector research institutes in developing countries are forging ahead with the application of modern biotechnology, a small number are supported by government policy and

therefore follow a defined agenda (Skerritt 2000). Still other governments believe that the risks (safety, environmental and/or economic) associated with modern biotechnology outweigh the benefits.

Currently, the many promises of modern biotechnology that could have an impact on food security have not been realized in most developing countries (Luijben and Cohen 2000). In fact, the uptake of modern biotechnology has been remarkably low owing to the number of factors that underpin food security issues. In part, this could be because the first generation of commercially available crops using modern biotechnology were modified with single genes to impart agronomic properties with traits for pest and weed control, and not complex characteristics that would modify the growth of crops in harsh conditions. Secondly, the technologies are developed by companies in industrialized countries with little or no direct investment in, and which derive little economic benefit from, developing countries. Thirdly, many developing countries do not have the necessary biosafety frameworks to regulate the products of modern biotechnology. For example, it took over two years for the Kenyan authorities to approve the field-testing of a virus-resistant sweet-potato variety because the scientific capacity for evaluating the product was unavailable (Juma 2001). It should be noted, however, that such delays in the approval process have also been seen in developed countries, especially during the initiation of national regulatory evaluation.

However, this trend is quickly changing as a number of developing countries either adopt or develop appropriate biotechnologies or regulatory infrastructures. A report by the International Service for National Agricultural Research states that more than 40 crops are the focus of public-sector research programmes of 15 developing countries involving disease-resistant traits in rice, potato, maize, soybean, tomato, banana, papaya, sugarcane, alfalfa and plantain (Paarlberg 2001a). *Table 2* lists some of the local crops in the priority research list of research institutions in developing countries. For example, the Brazilian Agricultural Research Corporation has concentrated research into genetically modified crops on disease resistance in beans, papaya and potatoes. The research programme at the University of Cape Town (South Africa) focuses on the development of crops resistant to viruses and to desiccation. The university has recently had a breakthrough with maize streak-virus resistance. In Thailand, the National Centre for Genetic Engineering and Biotechnology has supported research into disease resistance of rice, pepper and yard-long beans.

Table 2 Regional distribution of the application of modern biotechnology to food crops under development by public institutions in developing countries. (Numbers represent studies being undertaken for each crop in each region**)**

Food crops	***Africa***	***Asia***	***Latin America***
Alfalfa	–	–	3
Banana and plantain	2	3	3
Barley	1	1	1
Beans	2	3	5
Cabbage	–	4	–
Cassava	1	2	2
Maize	7	8	5
Nuts	1	3	–
Papaya	–	13	4
Peppers	–	7	–
Potato/sweet potato	5	6	8
Rice	1	35	2
Squash/zucchini	1	–	2
Sugar-cane	2	2	4
Tomato	3	3	-
Wheat	1	3	2
Other fruit	3	4	6
Other vegetables	1	4	2

Source: adapted from Skerritt (2000).

Although current commercial GM crops are not designed to address the specific issues of developing countries, their adoption has shown that they can be relevant in some developing countries — for example, the planting of herbicide-tolerant soybeans in Argentina and *Bt* cotton as a cash crop by resource-poor farmers in China and South Africa (Paarlberg 2001a).

There is little information on the economic costs associated with R&D of products of modern biotechnology, or on the impact of their introduction on production costs. An in-depth analysis of the short- and long-term economic and social costs and benefits is necessary (Taylor and Fauquet 2000).

Qaim and Zilberman (2003) report that farmers in Argentina that adopted herbicide-tolerant soybeans reduced per hectare production costs through the reduced number of herbicide applications, and thereby increased total factor productivity by 10%.

On average, the *Bt* cotton farmers in China reduced pesticide spraying for the Asian bollworm by 70%, producing a kilogram of cotton at 28% less cost than the non-*Bt* farmers (Huang et al. 2002b). These benefits have had a significant impact on the agronomic, environmental, health and economic situations of approximately 5 million resource-poor farmers over eight provinces. Similarly, farm-scale trials in China of GM rice containing genes which make them resistant to insect larvae that devastate rice crops showed 80% less pesticide use and yields increased by 6–9% (Coghlan 2005). In addition, farmers who grew the GM varieties suffered less pesticide-induced illness than those growing the old varieties (Coghlan 2005).

A two-year study of the economic impact of *Bt* cotton adoption by the farmers in the Makhathini Flats of Kwa-Zulu Natal Province of South Africa showed that farmers not only experienced yield increases, but that the savings from reduced chemical applications outweighed the higher seed cost (Ismael et al. 2001). Between 1997 and 2001, the number of South African cotton farmers who adopted the planting of *Bt* cotton increased 16-fold (Bennett et al. 2003).

Several agro-economic studies have been commissioned since the introduction of seed derived from modern biotechnology in the USA. One report illustrates that the greatest yield increases were achieved with insect-resistant maize, while the greatest reduction of input costs was seen in herbicide-tolerant soybean (Gianessi et al. 2002). The economic benefits associated with the cultivation of *Bt* maize by farmers in the USA in 2001 were primarily the result of the decreased need for pesticides. The financial gain takes into account the seed-price premium paid by farmers for *Bt* maize seed. Benbrook (2002) argues that farmers in the maize belt forfeit a significant proportion of their farm income to biotechnology companies because of the seed-price premium.

While evidence shows that GM crops can lead to significant productivity and health gains, they are nevertheless not a 'magic bullet' that will solve all problems in agriculture. Modern biotechnology must be applied to complement and expand the reach of conventional methods (Pingali 2001). It has been alleged that focusing on modern biotechnology may narrow the research agenda of many countries and deny them the opportunity to explore solutions that can be freely adopted, adapted and exchanged (UNECA 2002). For instance, where the cause of declining farm productivity can be attributed to poor soil fertility, the current technologies do not provide any remedies. On the other hand, almost half of the world's potentially cultivable tropical land has acidic soil, caused by excessive soil aluminium (Herren 1999). The production of GM aluminium-tolerant crops would allow the productive cultivation of millions of hectares of acidic soil lands in tropical Asia and Latin America (Herrera-Estrella 1999). It should also be borne in mind that conventional breeding is still the technique most often used for achieving yield increases and for developing crops with resistance to diseases, insects and abiotic stresses (de la Fuente et al. 1997). Moreover, conventional breeding still contributes the bulk of new crop varieties used in general. It is, however, alleged that with the anticipated increase in the world population over the next 25 years, grain production will need to increase by 26 million tonnes per year. In addition to traditional breeding methods, it may be necessary to apply other techniques to achieve the required yield increases and yield stability of rice and other grains (Huang et al. 2002a).

Developing countries with limited financial and human resources need to find the right balance for investing in conventional and modern biotechnology research programmes. While alliances with the private sector may contribute to the search for new technologies, the public sector needs to focus on crops and traits in which the former may be unwilling or unable to invest (Khush 2003). The extent to which priority is given to modern biotechnology over other research methods should be linked to a country's agricultural priorities and objectives as well as to its environmental concerns.

Ultimately, investment in interventions that support good governance, the development of rural infrastructure and market access is required before any of the promises of modern biotechnology can be realized. In general, policies that stimulate economic growth and target poverty reduction may have significant bearing on the health and well-being of the population (Luijben and Cohen 2000**)**.

5.5 Research ownership

Research is a critical part of any effort aimed at improving food production and reducing poverty. Globally, much of agricultural R&D is carried out in the public sector, thereby serving the interests of developing countries (Conway 1999). Public research in developed countries and Latin America is mostly conducted by government institutions and universities, whereas almost all agricultural research in Africa is carried out in public institutions, including R&D, technology transfer and dissemination of improved plant varieties (Cohen and Pinstrup-Andersen 2002). In general, international agricultural research institutions form a second level of research development and technology providers in developing countries. Public research institutes have, in the past, researched and improved orphan crops, mainly for donation to poor farmers or at cost.

Generally, academic institutions are perceived as producers of knowledge that benefit and protect the public. Also, national and international research institutes aim to address the agricultural problems of resource-poor farmers in developing countries, e.g. increasing productivity through the use of a variety of techniques, including modern biotechnology (Pardey et al. 2001a). In reality, public institutions are now exposed to the forces of globalization and compelled to compete for their survival.

In the current climate, government intervention in R&D worldwide has dwindled; hampering the level of innovation generated for public good. In fact, research facilities in many developing countries are poorly equipped, often limiting experiments to traditional and outdated research. The diminishing role of public research institutes is perceived to have a major impact on the adoption of modern biotechnology in terms of introducing relevant products to those that need them most (Barton and Berger 2001; Pinstrup-Andersen and Cohen 2003).

Most of the field trials in the EU and the USA are conducted by private companies (Fresco 2003). An analysis of field-trial data from the USA shows that three crops (maize, potato and soybean) account for 64% of all trials, of which 69% express herbicide- and pest-resistance traits. Of the trials conducted in the EU, 67% involve maize, sugar beet and rapeseed, and 71% of the novel gene categories presented herbicide- or pest-resistance traits. Less than 1% of all the trials in the EU and the USA are of plant varieties grown in tropical and subtropical climates, half of which have been conducted by the public sector.

Most of the public-sector research involving modern biotechnology in developing countries (except China) is still in the laboratory phase — none of the crops have progressed to marketable products (Arundel 2002; Fresco 2003). China, on the other hand, has approved the field-testing of over 500 GMOs to date and the commercial release of 50, including a prolonged shelf-life tomato, virus-resistant sweet pepper and vaccines for animal use.

The experiences limiting the progression to commercializing research efforts range from: a lack of resources for meeting the high costs of regulatory requirements (see *Section 4.4.1*); lack of foresight, planning and business acumen for enabling the transition from research to a commercial product; and

lack of capacity to negotiate patent licenses. Also, developments in modern biotechnology have occurred independently of the sustainable agricultural goals and priorities of the developing countries concerned. Furthermore, a needs assessment for a particular technology has often not been carried out before a research project is begun (Taylor and Fauquet 2000). Nevertheless, it is often argued that the commercialization of some products would encourage monocropping as national agricultural research has focused on a few crops (Juma and Konde 2002; Falck-Zepeda et al. 2002), whereas rural communities tend to grow a wide range of crop species and plant varieties.

The focus of international agricultural research centres is on plant production and protection (78%), livestock production and health (21%) and food processing (1%). With respect to food crops, research emphasis appears to be spread equally between cereals, root crops and legumes. However, within the cereals, research devoted to rice far outweighs research on maize and sorghum (Taylor and Fauquet 2000).

A large proportion of the total agricultural research activities of many developing countries are donor-funded. International research institutes, such as the Consultative Group on International Agricultural Research, depend on government grants and donations from philanthropic organizations for their survival, and yet investment in this sector has fallen in real terms (Pardey et al. 2001a). A significant fraction of the funding spent on international agricultural research institutes is used on activities covering a relatively large number of crops. The beneficiaries of such initiatives are a small number of countries with relatively advanced scientific capabilities (Pardey et al. 2001a).

During the 1990s, developing countries as a group invested more in agricultural research than developed countries, even though the spending was unevenly distributed. In industrialized countries, private-sector investment in R&D far exceeds government spending on technology development, so that much of the public good previously entrusted to public research institutes is now privately owned (Cohen and Pinstrup-Andersen 2002). In comparison, private-sector investment in developing countries is around 1% of total global spending in this sector (Taylor and Fauquet 2000) and developing countries invest less than 5% of the total private sector spending in biotechnology. Although the agricultural sector in developing countries is large and of significant importance to the domestic economy, spending in agricultural research does not match this level of activity. For instance, 80% of the food consumed in sub-Saharan Africa is obtained from domestic production (FAO 2002b).

5.5.1 Impact of intellectual property rights on research

Intellectual property rights (IPRs) have been relevant to agriculture since their inception but have gained importance with regard to research in developed countries in the past 20–30 years. In particular, IPRs have been used to protect and preserve the value of products produced by conventional methods, e.g. the trademark registration of food products (Dutfield 2001). The rationale for IPRs is that they encourage the inventor to advertise the invention and disclose the new knowledge, while simultaneously holding the rights to protect the invention from competitors (Taubman 2004). Accordingly, disseminating this information is thought to stimulate new ideas and further rounds of innovation and technological advancement. IPRs afford time-limited protection to artistic, scientific, technological or economic products, and can be protected by way of copyrights, trademarks, design patents, utility patents, plant patents, plant breeders' rights and trade-secret law. Of these mechanisms, patents are considered the most powerful tool of the IPR system (Wendt and Izquierdo 2001).

Patents play different roles in different technologies and sectors. Patent protection of biotechnology makes it a tool for technology transfer and securing new markets in a global economy (Barton and Berger 2001) (see also *Section 6.5.1* on TRIPS). Without protection, new ideas and information are entirely in the public domain. This can, in certain systems, lead to underinvestment in R&D or the withholding of knowledge (Wendt and Izquierdo 2001).

Plant variety protection (PVP) provides less protection than patents in that generally it makes provision for farmers' rights, allowing them to use harvested seed, and includes an exemption for research use. Despite the increase in availability, new plant varieties continue to be inaccessible or inappropriate for poor farmers, and the rate of innovation remains largely unchanged in countries with a PVP system (Pardey et al. 2001b). Studies have indeed shown that in middle-income countries, the principal beneficiaries of PVPs are commercial farmers and the seed industry.

PVP is seen as a system that protects small advances in plant breeding, while a patent regime is thought to lead to the protection of big leaps in technological achievements (Helfer 2002). Patent protection for products of modern biotechnology is important because they are expensive to develop and easy to copy. Even so, developing countries have limited capabilities to innovate in industrial fields such as modern biotechnology, and to effectively enforce IPRs. A significant number of developing countries have not established intellectual property regimes that cover plants. This situation may thus discourage private-sector investment (Chaturvedi 2001). With no assurance that they can recoup some profit on GM products, multinationals are unlikely to devote much attention to the challenges of developing countries unless seen in a development aid context or through public–private partnership. Although this situation impedes private-sector investment in developing countries, it also implies that the freedom to operate on products designated for local markets is not hindered (Wendt and Izquierdo 2001).

Exercising this freedom to operate is not a well-understood concept. For example, in the case of 'golden rice', where permission was required for the use of about 70 patents, the impression was that the patents were being relinquished in favour of the poor. In fact, most of the patents involved are not valid in the major rice-consuming countries. The technology donated for the development of virus-resistance in non-commercial potato varieties is free of patents relevant to Mexico, and the same holds true in the case of virus-resistant sweet potatoes in Kenya. Researchers are usually unaware of the proprietary status of the technologies they are using in their work (Salazar et al. 2000; also see WIPO 2005).

Nevertheless, the proliferation of broad patents is thought to impede the research capabilities of other interested parties (Salazar et al. 2000). Some countries grant very broad patents conferring monopoly rights over large areas of research, thereby potentially threatening the other goal of intellectual property, namely the right to build upon the original invention. The prevailing patent rules have the potential to limit the accessibility of these technologies to public institutions and ultimately poor farmers (Krattiger 2002). Furthermore, the strengthening of IPRs is thought to restrict the flow of germplasm and inhibit the development of new plant varieties (Barton 1999). This is because if and when researchers in public institutions do get permission to develop the technologies further, access is granted under licence agreements with restrictions on commercializing innovations. It is also argued that a stringent, multilateral IPR system will not benefit all countries equally. Indeed, the benefits will largely be influenced by the economic and technological levels of development in each country (Barton and Berger 2001).

According to the United Kingdom Commission on Intellectual Property Rights, "the critical issue in respect of IPRs is perhaps not whether it promotes trade or foreign investment, but how it helps or hinders developing countries to gain access to technologies that are required for their development."

During the 1990s, obtaining a patent application (excluding the cost of filing, which varied in different countries from US$355–4771) in the USA cost US$20,000 and twice as much in the EU (Barton and Berger 2001). In general, PVP is cheaper; valued at one-tenth of the patent price. Moreover, the preparation of a food-safety dossier for a product derived from modern biotechnology, for example, is estimated to be around US$1 million (Tansey 1999). These estimates cannot be compared with the regulatory costs in developing countries. Although significantly lower than figures quoted above, the cost of regulation in developing countries does not encourage the commercialization of products of modern biotechnology developed by public-sector research institutes (Lesser 1997). In most cases, the regulatory costs far exceed the research costs.

Many developing countries do not have the resources to match private-sector investment in modern biotechnology. In this new playing field, public institutions also need resources to deal with intellectual property rights to help compensate and increase the public benefit. Otherwise their involvement in R&D could be deterred by lack of funding. If public institutions are to use the techniques of modern biotechnology, then the use of IPRs as a framework for facilitating technology transfer must be emphasized more than its handling as a revenue-generating system. IPRs can, however, play a major role in clarifying the mechanisms for access to technology, and determine the downstream aspects of use and exploitation of genetic resources.

There are several ways in which public institutions and small companies in developing countries can gain access to patented genes and enabling technologies to overcome the current barriers to research. The first of these includes a measure of goodwill by multinationals to relinquish their rights to technologies for use by researchers in developing countries by adopting programmes of social responsibility as in the case of 'golden rice', a variety containing beta-carotene (a precursor of vitamin A), virus-resistant sweet potatoes (in Kenya) and a virus-resistant non-commercial potato variety in Mexico (Falck-Zepeda et al. 2002).

A different type of programme initiated in the USA has established an intellectual property clearing house to make information on the intellectual property owned by public research institutes, including universities, available to researchers around the world (Toenniessen 2000).

There are also suggestions that redesigning patent laws to narrow the type and scope of patent coverage ought to make more technologies accessible to public institutions. The thinking behind these suggestions is that applying a stronger standard for rejecting patent applications for inventions that are 'obvious' should deter the patenting of minor inventions. In addition, a law that requires an invention to be genuinely useful in theory should reduce the number of patent applications being submitted. At present, it is possible in some countries to submit patent applications for abstract concepts that potentially protect large areas of research and thereby exclude innovation by others.

Another option that may be attractive to developing countries is the creation of collaborations that involve research institutes, universities and the private sector (Khush 2003; Pray and Naseem 2003). The nature of these collaborations is likely to be influenced by the level of expertise and resources within the national public research institutes (Toenniessen 2000). Where a solid knowledge base exists, the public partners may be in a position to develop or acquire a technology that could be transferred into locally adapted varieties. Smaller institutes are more likely to provide the genetic resources and a positive public image. It is believed that such alliances would benefit public institutions and private companies; offering them an opportunity to license and distribute the technology (Barry and Horsch 1999).

The most well-known public–private sector partnerships include organizations such as the International Service for the Acquisition of Agri-biotech Applications (ISAAA) that negotiate access to private-sector technologies for the improvement of subsistence crops and/or the transfer of technology and know-how.

Although several types of public–private sector alliances already exist (James 1999;Salazar et al. 2000), the two newly established initiatives worth mentioning are the Global Cassava Partnership and the African Agricultural Technology Foundation (AATF), launched in November 2002 by FAO and in March 2003 by the Rockefeller Foundation, respectively. The former is a partnership involving some of the world's leading experts in cassava research, working mainly in public institutions. The AATF intends to function as a clearing house of available technologies with the primary aim of improving food security and reducing the poverty situation of small farmers, by facilitating transfer and use of appropriate technologies (Pray and Naseem 2003).

Such licensing arrangements have been put to the test in other fields (AATF 2005). However, as in the case of the AATF, a clearing house is required to acquire the necessary technologies and permit

their further use for developing-country needs. The drawback may be a requirement to divide the commercial sector into subsistence, middle-income and commercial markets. This market division may not be easy to achieve as some large developing countries have both commercially important markets and subsistence farmers.

A briefing paper commissioned by the United Nations Industrial Development Organization (UNIDO) (Salazar et al. 2000) proposes six activities that build upon private-sector investment and enable biotechnology transfer:

1. enabling government policies;
2. access to up-to-date authoritative information;
3. regional brokering service to strengthen public–private partnerships;
4. a regional biotechnology investment service;
5. an international intellectual property escrow service; and
6. initiatives for risk-shifting.

Each of the above proposals can be implemented as a stand-alone project or in combination, as best suits the national and/or regional situation.

5.5.2 Access to genetic resources

Historically, plant genetic resources were freely provided by developing countries to gene banks worldwide. The resources in question did not belong to a particular individual, and are often considered a common heritage of mankind. The application of modern biotechnology to genes that could be incorporated in genetic resources of importance in rural populations raises concerns in that the small-scale farmers may have originally supplied the genetic resources for improvement. Once privately owned, these resources may be unavailable to the people who have ensured their conservation for centuries. Equally important is the aspect of access by researchers to genetic resources for further development on terms that recognize the contributions made by farmers to the conservation and sustainable utilization of these resources.

At the international level, the importance of national ownership of such resources is duly recognized. The International Treaty on Plant Genetic Resources adopted at an FAO conference in 2001 (FAO 2001c) provides the legal framework for dealing with the resources on which food security and sustainable agriculture depend. The Treaty gives a directive on the conservation and sustainable use of plant genetic resources for food and agriculture, making provision for the fair and equitable sharing of the benefits arising out of their use, in harmony with the principles of the Convention on Biological Diversity (CBD 2005a), but introducing the concept of farmers' rights.

In the discussions on farmers' rights, the main issues of concern revolve around benefit-sharing and prior informed consent (see *Section 6*), and the protection of traditional knowledge from 'biopiracy'. This means access to genetic resources must be on mutually agreed terms to promote their use and emphasize their importance to development. A number of organizations are discussing the protection of traditional knowledge and folklore (World Intellectual Property Organization, WIPO; CBD; FAO; WHO; United Nations Educational, Scientific and Cultural Organization, UNESCO; United Nations Conference on Trade and Development, UNCTAD).

The Treaty establishes a multilateral system of facilitated access and benefit-sharing (MLS) for key crops, emphasizing the interdependency of countries in terms of plant genetic resources for food and agriculture. Developing countries rich in genetic resources are encouraged to place germplasm in the MLS. The users of the material will sign a material transfer agreement, incorporating the conditions for access and benefit-sharing through a fund established under the Treaty. In return, the owners of the genetic resources will get a share of the benefits arising from their use and development in the way

of information, technology transfer and capacity building. *Ex situ* material, collected before the entry into force of the CBD, does not come under the purview of the Convention, and would thus be dealt with under the Treaty. So far, 35 food and 29 feed crops have been entered into the system.

In principle, the genetic resources stored under this system are available for improvement to all interested researchers. Such wide-scale availability of germplasm has a potentially positive influence on access to improved technologies and nutritionally enhanced staple crops for the food-insecure. Genetic resources obtained from the MLS cannot be patented, even though it is not clear whether a gene isolated from such material may be protected or not.

5.6 Globalization

Globalization is a complex set of developments including trade liberalization, opening up of economies and integration of international markets (Diaz-Bonilla and Thomas 2001). It involves policy reforms in trade and reducing barriers to the international flow of goods, capital, labour, technology and ideas (UNDP 2003). Technological advancement is the driving force of improvements in world food production and the integration of the world economy. Knowledge in agricultural science depends on building onto experiences already gained. In this respect, the introduction of biotechnology ought to be perceived as nothing but a phase in the modernization of agriculture which started centuries ago. In its evolution, a global trend is emerging where fewer farmers produce more food. The global commercialization of agriculture has increased competition in domestic and international markets. Globalization has accelerated substantially since the 1980s, as the economies of developing countries have become subject to international market forces.

New technologies appear to drive the transformation of world food systems towards industrialized food processing, long-distance marketing and retail-business dominance. The benefits of globalization, however, seem to have bypassed low-income countries and, in particular, rural regions.

Even though the profit potentials were different, the merging of agrochemical and pharmaceutical divisions to form life sciences companies in the mid-1980s was a strategic synergy of R&D that allowed the production of new drugs, pesticides, GM crops and genetic treatments for disease (Chataway et al. 2002). This has led to new patterns of alliances with companies that develop routes to create and capture value.

The integration of economies cuts across all sectors and likewise is central to the emergence of new patterns of R&D. The phenomenon of globalization has raised concerns about the global acquisition of seed companies and mergers with chemical interests that have strategically strengthened their ability to market new products, and placed a substantial number of agricultural patents in the control of five major companies, namely Bayer, Dow Chemicals, Du Pont, Monsanto and Syngenta (Ching 2001; Graff and Newcomb 2003). The top 10 seed companies control one-third of the global seed market (RAFI 2000). This kind of consolidation has also placed much of the know-how under the control of these multinationals. To overcome problems of overlapping patent rights and reciprocal infringement lawsuits, companies make strategic alliances, mergers or acquisitions to obtain technologies in specified fields of research. Similar consolidation trends have been observed in developing countries, where PVP legislation is the only means of protecting improved seed — resulting in a proportionately small number of companies dominating global markets related to food and agriculture.

Overall, the seed industry can be divided into three segments: commercial seed, farm-saved seed, and public-supplied seed (James 1997). Farmers' sources of seeds tend to be flexible in that they respond to local needs and circumstances and therefore can greatly vary for the same crop according to location (Musa 1998). Farmers in most developing countries depend on farm-saved and public-supplied seeds. The latter provide seeds for the most important crops, while farm-saved seeds account for over 90% of the planted crops (see Musa 1998). Global consolidation of seed companies is likely

to homogenize seed quality and limit choice (McGuire 1997). By the same token, the same genetic traits can be introduced into locally adapted varieties in different world regions. It is important, then, that when considering the effects of consolidation in the commercial seed market, it should be kept in mind that the commercial seed market is just one segment of the total seed market and, since it tends to concentrate on high-value seeds, provides less than 20% of the planted seed material in both developed and developing countries (Cromwell 1996). Furthermore, it should be recognized that GM seed represents only a minority of the commercial seed market, i.e. approximately 13% (James 2002b).

5.7 Market access

More than 50% of the workforce in developing countries makes a living from agriculture, and so it follows that economic development in these countries relies on agricultural performance. The most important indicators of agricultural performance are an increase in domestic production and accelerated access to markets. Trade liberalization, as negotiated in the Uruguay Round, was intended to create opportunities that improve market access for the commodities of developing countries by eliminating agricultural subsidies, high import duties and other trade-distorting measures adopted by developed countries. At present, agriculture is subsidized at US$1 billion per day in the OECD countries, making it impossible for poor countries to compete on an equitable basis.

Limited market access represents the greatest hurdle to international trade, and consequently to technology access and acceptance (Juma and Konde 2002). If developing countries are to be integrated into the global economy, they must have something to offer that in turn translates into beneficial implications for food security. Policy options for those developing countries whose exports largely rely on agricultural trade will be influenced by the regulatory climate and consumer preferences in trading-partner countries, including agricultural-subsidy schemes that make the products of developing countries less competitive (Juma and Konde 2002; Paarlberg 2002). The continued support by developed countries of high agricultural subsidies creates inequitable trading conditions for developing countries. In addition to the two major barriers to trade (tariffs and standards) for developing countries, a third hurdle in relation to the products of modern biotechnology may be the implementation of the CPB (CBD 2000). The CPB adopted in 2000, entered into force in September 2003. A legally binding instrument to its parties, it aims to regulate trade in products of modern biotechnology by protecting biodiversity and taking also into account effects on human health.

The backbone of the CPB is an advanced informed agreement that requires the party of export to seek consent from the party of import before the first shipment of living modified organisms intended for release into the environment. A simplified procedure is mandated for commodity trading. This is based on the proactive information exchange between the party of export and its potential trading partners via an Internet-based Biosafety Clearing House (CBD 2005c). The process is intended to facilitate trade by providing easy access to data and thereby enabling early assessments in prospective recipient countries. This, in effect, makes available information on the regulatory status of a new trait in any country before the initiation of trade or the delivery of food aid. Timely handling of this information by developing countries will be put to the test now that the CPB has entered into force.

The SPS Agreement of WTO (WTO 1995) ensures that internationally traded food meets minimum standards based on the scientific principles set by the Codex Alimentarius Commission. It is expected that when dealing with commodities containing products of modern biotechnology, the SPS Agreement will make reference to the Codex *Principles for the risk analysis of foods derived from modern biotechnology* (CAC 2003b) and the guidelines for risk/safety assessment of such foods (CAC 2003c,d). The Codex Alimentarius Commission approved the principles and guidelines in 2003.

The SPS Agreement both offers opportunities for improving food safety in developing countries and poses potential problems (Unnevehr 2001). The science and research-based requirements of the SPS Agreement can be substantial. Yet for countries that can implement the Codex standards for their

export products, the opportunity to expand trade and acquire much-needed foreign currency is guaranteed. Those developing countries that cannot find resources to improve their food safety systems may find themselves excluded from international trade. More importantly, the limited capacity to do scientific risk assessment can compromise their ability to assess whether or not to import the products of modern biotechnology.

The increased international trade in food has created greater dietary diversity, year-round availability and often low prices in many countries. Non-traditional foods are becoming increasingly available worldwide. Producers in developing countries can benefit from expanded food exports which earn foreign exchange and increase rural incomes. These benefits, however, may not be realized if food safety and quality standards required in high-income markets cannot be met.

Capturing these new opportunities places the onus on developing countries to manage safety from farm to table (Wilson 2001). Testing of hazards at several points in the production process is expensive, and therefore prevention and control through documented production practices is often the only way to verify food safety. The concept of process control and hazard prevention is generally well understood in developed countries.

When a product is consumed domestically, and investments to meet export market standards for that product affect a large portion of production, those investments will have positive spill-over for domestic consumers. However, some products may be produced almost entirely for export, in which case investment to meet high standards of safety and quality in export will have little or no direct spill-over for domestic safety.

Nielsen and Anderson (2000) looked into the policy ramifications resulting from the economic effects of adopting GMOs. The study highlights the implications for the global economy when selected regions adopt modern biotechnology, in terms of agricultural production, trade and economic welfare. Analysis is made of the trade in cereal grains (excluding rice and wheat) and oilseeds. The authors suggest that similar analyses of crops unlikely to cause food-safety concerns in other areas and that are of potential economic importance to developing countries should be conducted. They believe prejudices in the more affluent countries may hinder the adoption and production of all products of modern biotechnology in all regions, unless more informed debates are held to discuss the potential opportunities for developing countries.

The United Kingdom Government's (2003) Strategy Unit also concluded (245) that trade, policies and consumer behaviour in the EU and United Kingdom would influence the decisions of developing countries related to the use of GM crops.

While export markets may be important for the rural poor, meeting higher standards may require additional management, capital investment, purchased inputs, monitoring and certification. Government focus on public-health issues will not necessarily address the export barriers.

5.8 Conclusions

Technologies in agricultural R&D have always been considered a major contributor to improving food security. Nonetheless, their successful application will depend on their relevance to poor people, the resolution of IPR disputes, and national and international, regulatory, trade, political and economic frameworks. The application of modern biotechnology in food and agriculture has the potential to reduce some problems associated with food insecurity. Many developing countries will need to overcome a number of obstacles before they can take full advantage of what modern biotechnology has to offer.

The development of products of modern biotechnology is capital-intensive as proprietary research tools must be licensed from the private sector in many systems. This situation has caused restrictions

on innovations and is a barrier to the availability of the tools of research in both developed and developing countries. If developing countries are to rely on importation of new varieties, especially those developed with biotechnology, then allowing more flexible IPR standards makes good economic sense.

Research agendas in developing countries should focus on widening the crop base, and on enhancing the yield and nutritional value of the crops that are important to rural communities. Taking stock of national capabilities and prioritizing research objectives in line with the goals of sustainable agriculture will help put realistic opportunities into perspective for both conventional breeding and modern biotechnology techniques. A needs-driven technology is a tool for growth and development which the private sector is unlikely to undertake, because such crops are of low commercial value. Governments should take the responsibility of investing in public research that is crucial to reducing food gaps between rich and poor.

Depending on their goals and objectives, developing countries have choices with regard to the application of modern biotechnology:

(1) leave its development to the private sector;

(2) strengthen national public R&D capacity; and/or

(3) create an enabling environment to build upon private-sector investment in public–private alliances.

The continued marginalization of developing countries from international trade will have a negative impact on the adoption and application of emerging technologies, including modern biotechnology. Therefore, a thorough consideration of all the issues pertinent to the application of a specific technology is critical to informed decision-making for the governments of developing countries. The use of new technologies in food and agriculture has become so politicized that regulatory institutions are obliged to provide assurance that deployment of such technologies will lead to improved nutrition and food security. Such policy and legislation cannot be developed in isolation and independently of international obligations and public opinion.

6. SOCIAL AND ETHICAL CONCERNS ABOUT GM FOODS

6.1 Cultural variability and public perception

Across the world, food is a part of cultural identity and societal life, and has religious significance to people. Therefore, any technological modification, including changes to the genetic basis of crops or animals used for food, may be met with social resistance. In many countries, people's interaction with nature, often correlated with religious perspectives, causes social and ethical resistance to modifications that interfere with genes. Whereas the objectives of food safety in its limited sense are more clearly realized and harmonized internationally, the objectives of nature protection, environmental safety and sustainable agriculture are much more complex, unclear and variable in different regions of the world.

Investigations of public perception in areas of the world with relatively high resistance to GM foods indicate that lack of information is not the primary reason (Lewenstein 2002; Birner and Alcaraz 2004). The public is not for or against GMOs *per se* — people discuss arguments both for and against GMOs, and are aware of contradictions within these arguments. Also, people do not demand zero risk. They are quite aware that their lives are full of risks that need to be balanced against each other and against the potential benefits. People may also discriminate in their perception of different technologies where a general positive perception can be observed for applications with a clear benefit for society, e.g. for modern medicines. A key finding is that people do not react so much to genetic modification as a specific technology, but rather to the context in which GMOs are developed and the purported benefits they are to produce.

Nevertheless, the techniques of genetic engineering are often described as 'pushing nature beyond its limits'. Many of the concerns expressed about GMOs, including those about 'unnaturalness', have also been expressed in relation to other agricultural innovations, such as the use of pesticides, animal-derived animal feed and antibiotics in animal feed. Organic agriculture is perceived as reversing or opposing these developments, whereas GMOs are perceived as the ultimate manifestation of this trend (Marris et al. 2001). GM-free areas are, therefore, seen as a way of preserving nature (Haslberger 2001).

The opposition to GM crops and foods has as much to do with social and political values as with concerns about health and safety. Consumers' growing awareness of their rights and farmers' increasing fear of dependence on multinational companies are symptoms of a deeper concern about values and priorities, the type of environment people want, the role of biodiversity, tolerance of risk and the price that people are prepared to pay for regulation. Some people are concerned about the level of control exercised by a few chemical companies on seed markets. GMOs are emblematic of the powerful economic fears that globalization inspires. In certain regions, hostility to GMOs is symbolic of a broader opposition to the encroachment of market forces. These are perceived to be creating a world in which money rules with little consideration for historical traditions, cultural identities and social needs (Gaskell et al. 1999, 2000).

6.2 Labelling of GM foods and consumer choice

In establishing GM food labelling policies to ensure that consumers receive meaningful information, regulatory authorities have had to grapple with a complex array of issues related to GMOs. These have included scientific, health, environmental, political, cultural and economic issues, as well as the appropriate compliance and enforcement requirements.

At the core of international debate in this area are two inherently different uses of labelling: (a) a requirement to relay information of health relevance (e.g. presence of an allergen or altered composition); and (b) a mechanism to convey information on the method of production. While (a) is basically accepted in all regions, labelling as described under (b) is only used in some countries.

Although authorities in most, if not all, countries agree that GM foods allowed on the market after adequate assessment is as safe as traditional foods, different national systems reflect different attitudes towards the use of labelling to convey information on the method of production, i.e. in this case, genetic modification. It is noteworthy that the (b) type labelling seems to have been developed primarily relative to GM foods, although some parallels could be said to exist in the systems of labelling of food produced under organic production systems.

National authorities have developed several approaches to labelling foods containing or derived from GMOs. In some of the countries with mandatory GM food labelling regimes, conventional foods may contain traces of GM material within set threshold levels, e.g. soya from sources containing GM soya, without labelling. Foods specifically declared as GM-free mostly need careful analytical proof that no GM material or processes have been involved.

Two broad regulatory approaches for labelling of GM food exist:

- voluntary labelling — which is driven largely by market forces, with no legislative requirements to declare the use of GMOs in food production; and
- mandatory labelling — which requires declaration of characteristics imparted to a food by the use of gene technology (be they health-and-safety and/or process-related), or use of gene technology itself in food production.

As of 2004, some form of mandatory labelling standards for foods produced using gene technology had been adopted or planned by over 30 countries worldwide (*Table 3*). These standards generally require a declaration of health and safety characteristics brought by the GM commodity, and identification of the use of gene technology in the food production. The most frequently legislated requirement is for the words 'genetically modified' to be used in association with the name of the food or the relevant ingredient.

Table 3 Examples of national labelling regimes for GM foods, as of 2004

Major elements of labelling regimes	*Countries*
Fully regulated mandatory labelling regime	
Method of production labelling. Mandatory labelling of all foods derived from or containing ingredients derived from organisms produced using gene technology.	European Union*
Composition of food labelling. Mandatory labelling of all GM foods and ingredients where novel DNA and/or protein are present in the final food.	Australia, New Zealand, Russian Federation
Composition of food labelling. Mandatory labelling of designated food items that contain GM foods or ingredients as major components of food only where novel DNA and/or protein are present in the final food.	China, Province of Taiwan, Japan, Republic of Korea, Thailand, Malaysia (proposed)
Mix of regulatory and voluntary labelling regime	
Equivalence labelling. Mandatory labelling of GM food only where it is significantly different from its conventional counterpart.	Canada, United States of America, China, Hong Kong, South Africa (proposed)
Voluntary labelling. Voluntary regime (where GM is similar to conventional counterpart) reliant on general provisions in food or fair trading law relating to false, misleading and deceptive labelling or advertising, and an industry code of practice developed to assist with compliance.	Canada, United States of America
No regulation	
Other. No regulation in place. May allow for voluntary labelling but no evidence of guidelines or code of practice.	Many developing countries

Source: adapted from FSANZ (2003).

* As of 18 April 2004, GM food and feed are regulated in the European Community under Regulation EC 1830/2003 concerning the traceability and labelling of genetically modified food etc (European Commission 2003a).

The range of actual (or proposed) GM food-labelling regulations includes:

- voluntary labelling that indicates that a product may contain GMOs or products derived from GMOs (under development in Canada and South Africa);
- compulsory labelling of products that are derived from modern methods of biotechnology or contain products from GMOs (currently in the EU, Australia, Japan and New Zealand);
- regulations which enforce labelling when a product is likely to contain ingredients derived from genetic modification (EU); and
- labelling of products where consumers are informed that production methods are likely not to involve any steps which involve genetic modification (so called 'negative claims').

For some countries, the reason for labelling GM foods (and foods in general) is to provide consumers with information on the safety of relevant ingredients. In the USA, food labelling is usually not considered mandatory for non-safety reasons. However, consumer groups in other countries have

pointed to the consumer's right to know, suggesting that GM food labelling allows consumers to choose products according to their preference (Consumers International 1998; Haslberger 2000). Different ways and proposals for labelling reflect the cultural and social background of countries; hence, international harmonization is likely to be hard to achieve. Some groups also stress that labelling must not take away the responsibility of authorities for risk assessment and decision-making.

Some labelling regulations require the use of analytical methods for the detection of recombinant proteins or DNA as a criterion for labelling. Such analytical methods, especially polymerase chain reaction (PCR), have become so sensitive that marginal contamination with recombinant DNA can be detected, thus threshold limits for unintended contamination have been introduced.

The lack of international consistency in regulations for GM food commodities, both with respect to safety evaluation and labelling, has brought increasing uncertainty to their development, ongoing use and international trade. The Codex Alimentarius Commission has worked since the mid-1990s to achieve consensus on international standards for safety assessment and labelling of foods produced through modern biotechnology. Codex standards, guidelines and recommendations are increasingly used as benchmarks under international trade agreements (e.g. the SPS Agreement). Thus, strong incentives exist to establish and conform to such standards.

Codex has initiated two streams of work with respect to food produced from GM commodities. The first, established in 1999, is the Ad Hoc Intergovernmental Task Force for Foods Derived from Biotechnology to develop standards, guidelines and recommendations regarding safety and nutritional evaluation for these foods. The Task Force completed the development of risk-assessment principles in 2003 (CAC 2003a), aided by a number of expert consultations run jointly by FAO and WHO (see *Section 3.2.1*). The work on food derived from biotechnology is being continued by a new Task Force.

The second Codex initiative is being addressed by the Codex Committee on Food Labelling (CCFL) which since 1991 has intensively debated the nature and extent of labelling for foods produced through biotechnology, at meetings and through working groups. While there is general agreement on the need for food labelling standards addressing health and safety issues arising from the use of gene technology (such as altered allergenicity, composition, nutritional value or intended use), divergent views exist among Member States on appropriate guidelines for process-based labelling of such foods. As positions on process-based labelling are as divergent as national regulatory approaches, progress in achieving consensus is likely to be slow. In 2001, the Codex Alimentarius Commission agreed to a proposal by the CCFL to adopt mandatory labelling of allergens in foods derived from biotechnology in the general food-labelling standard for prepackaged foods. However, there has been little progress by CCFL in addressing other labelling issues.

While consumers in many parts of the world are demanding to be informed of the health and safety issues that arise in relation to GM food commodities, divergent regulatory approaches have been applied for identifying through labelling the use of gene-technology processes in food production. Voluntary labelling systems established in the major GM commodity-exporting countries are being re-evaluated as increasing numbers of mainly importing countries establish mandatory process-based labelling regulations, and as internal consumer demands and market needs develop. Significant inconsistencies exist between several countries that have adopted mandatory process-based GM labelling standards. These include: differences in the type and range of foods to be labelled (all or selected GM commodities; main ingredients and/or processing aids/additives); the triggers for labelling (recombinant DNA and/or expressed protein versus any derivative of a GM food commodity); and tolerances and thresholds (no GM label required below 1%, 3% or 5% of total or unintended ingredients; or for top 3 or top 5 ingredients).

6.3 Coexistence of different agricultural practices

The potential risk of outcrossing and contamination by dispersed material from GM plants can pose problems for organic farming, as defined in Codex *Guidelines* (CAC 2001b). Dispersal of materials from GM crops (e.g. seeds) can occur over wide distances, depending on the plant characteristics and climatic conditions. Outcrossing and dispersal are natural phenomena that can affect the production of conventional seeds. The future prospects of providing GM-free seeds and crops have been debated as a solution for addressing consumer choice. Coexistence of agricultural practices must respect the threshold limits set for contamination of organic products and realize the difficulty of adhering to this goal for certain plants (European Commission 2003a,b; Messéan et al. 2003). Contamination of honey with GM constructs as a result of insect vectors has also been identified.

Agricultural practices that include GMOs may need to develop improved agricultural or molecular systems which enable a benign coexistence of GM and GM-free agriculture, in which a limited level of outcrossing is accepted. Otherwise, separation of GM plants with a significant potential for outcrossing from conventional or organic farming may be necessary.

At present, views on the problems of coexistence as well as management solutions vary from country to country. In various countries, representatives of specific areas are developing strategies for segregation of GM crops and crops of conventional or organic farming. Also the question of liability, especially the compensation for economic loss in the event of adventitious presence, needs to be considered according to the report of the European Commission (2003b), and regulatory approaches need to be discussed.

The possibility of implementing GM-free zones in regions with specific interests or risk issues (e.g. centres of origin or regions with specific natural importance) has been suggested, e.g. in comments to EU communications, through voluntary local arrangements between farmers and industry and/or through legislative and enforcement means (Tappeser et al. 2003). It should, however, be borne in mind that a political decision to enforce regional zoning will also raise issues of individual justice towards those producers that have a strong motivation contrary to the zoning policy. In that respect, the coexistence of such zoning solutions remains to be seen.

6.4 Economic cost of adopting GM crops

Numerous reports from organizations either in favour or critical of GM foods have been published, and numerous claims for increased or decreased profitability of agricultural practices including GMOs can be found (Carpenter and Gianessi 2001; Brookes 2002; James 2004b).

A review of the United States National Centre for Food and Agricultural Policy (Carpenter and Gianessi 2001) concludes that biotechnology is having, and will continue to have, a significant impact on improved yields, reduced grower costs and reduced pesticide use. GM *Bt* cotton seems to have relevant benefits for smallholder farmers in many areas around the world (James 2002a). On the other hand, some report lower yields, continuing dependency on chemical sprays (Soil Association 2004), loss of exports and critically reduced profits for farmers as a consequence of using biotechnology.

A United States Department of Agriculture report on the economic consequences of GM crops summarized a positive impact of the adoption of *Bt* cotton on net farm returns, but a negative impact in the case of *Bt* maize. An improvement of returns has also been seen with herbicide-tolerant maize, whereas no significant impacts were observed with herbicide-resistant soybean (Fernandez-Cornejo and McBride 2000).

A very detailed study by the European Commission on the economic impact of GM crops on agriculture found that a quick adoption by farmers in the USA was the result of strong profitability expectations. However, there was no conclusive evidence on the farm-level profitability of GM crops.

The most immediate and tangible ground for farmer utility of GM crops appears to be the combined effect of performance and convenience of GM crops — in particular, herbicide-tolerant varieties. These crops allow for greater flexibility in growing practices and, in given cases, for reduced or more-flexible labour requirements. For insect-resistant crops like *Bt* maize, yield losses are more limited than for conventional maize. However, the cost-efficiency of *Bt* maize depends on a number of factors, especially growing conditions (European Commission 2002a).

Profitability of GM crops should be analyzed within a long-term time frame. Firstly, there are important yearly fluctuations in yields and prices and it is difficult to isolate the possible effects of biotechnology. Secondly, developments on the supply and on the demand sides of the food chain have to be jointly considered (European Commission 2002a).

A recent study analyzing international diffusion of gains in the use of GMOs shows the need for differentiation between crops and regions (van Meijl and van Tongeren 2002).

In China, a region with a typically high baseline of pesticide use and cases of pesticide poisoning in farmers, a report (James 2002a) showed that the use of *Bt* cotton substantially reduced the use of pesticides without reducing the output per hectare or the quality of cotton. This resulted in substantial economic and health benefits for small farmers.

There seems to be evidence of profitability of certain GM crops under specific situations, especially growth conditions which are significantly dependent on regional agro-ecological factors, especially the baseline of pest pressure and pesticide use. On the other hand, there seem to be situations where these factors would not provide for profitability of growing GM crops, or where other practices for planting may be more valuable because of various regional or market-related reasons.

In some countries, there is a perception in parts of the population that measures prohibiting the planting of GM crops would give the region a marketing edge by guaranteeing that none of its food exports contain GM crops (Nuffield Council on Bioethics 1999b; Gilfillan 2001; Novis 2003;). Also, the question of liability is debated in this respect but needs to be seen in the context of regulations not only specifically for GM food.

In various countries, representatives of specific areas are developing strategies for segregation of GM crops and crops of conventional or organic farming. Improved molecular methods for containment of the transgenes as well as farm-management measures have been used. These include specific isolation distances, buffer zones, pollen barriers, control of volunteer plants, crop rotation and planting arrangements for different flowering periods as well as monitoring during cultivation, harvest, storage, transport and processing. The question of compensation for economic loss in the event of adventitious presence should also be considered (European Commission 2003a).

6.5 Socioeconomic aspects in the use of GMOs

Socioeconomic consequences arising from the adoption of GMOs in agriculture require an analysis of consequences for specific groups and interests in society. It has been claimed that there are benefits for large-scale farming, as opposed to small-scale farming, as a result of better adoption of practices associated with GMOs by large-scale farmers, as well as an ability to deal with IPRs (Johnston 2001). There has been polarization between agribusiness and commodity farming with agrochemicals supported by agricultural subsidies, and small-scale peasant farming. Microenterprises and microcredit schemes are considered by some to be the way to achieve the Millennium Goal of eradicating poverty (IFAD 2002). Some groups analyzing trade and agriculture feel that the impact of large-scale production and marketing of GMOs would overshadow potential success stories from a few GM products in developing countries.

Social scientists often discuss the importance of a shift from rural areas with labour-intensive workplaces to areas with 'high-tech' industry. Such shifts could also potentially take place as a result of the introduction of GMOs. An example here could be whether the economies of tropical oil-producing countries could be affected if GM alternatives to palm and coconut oils are engineered and production then moved to other countries (IFAD 2002).

6.5.1 Diversity, monopolies and IPRs

Another complex societal issue is the problem of different approaches to exploring and supporting new technologies and their integration into society. In general, IPRs (as explained in *Section 5.5.1*) are thought to promote innovation, recovery of R&D costs, and dissemination of knowledge. The detrimental effects can result from a lack of public involvement, acceptance or control of technological progress. IPRs may delay scientific progress, especially if no provision is made for a one-year grace period during which published results can be patented. IPRs also support monopolistic tendencies with unfavourable socioeconomic consequences, such as lack of access to technologies and the absence of effective licensing requirements.

Current developments in the preservation of crop diversity and crop breeding are under discussion with regard to their effects on farmers, society and diversity. The possible problem of losing genetic diversity, especially the loss of many locally adapted land races, has been attributed to the consequences of IPRs, in combination with the tendency to improve and propagate only a few selected lines of the main crops using marker-selected breeding and modern biotechnology. The same regulations are also discussed in connection with restrictions on farmers' privileges to use their produced material as seeds, with potentially more detrimental consequences for small-scale farmers.

Another widely discussed concern is the problem of patenting life forms. Narrow interpretation of the exclusion of life forms as worded in the Agreement on trade-related aspects of intellectual property rights (TRIPS) has, in fact, led to their patenting, as illustrated by the expanded categories of living organisms considered eligible for patent protection. The WHO report *Genomics and world health* (WHO 2002a) asserts that currently the patenting of discoveries arising from genomics is somewhat chaotic. The monopolies awarded by patents on genes is retarding rather than stimulating scientific and economic progress, and is therefore not in the public interest. Attempts to reform the patent system have not led to shifts in policy frameworks. To facilitate progress in this area, the report urges that the following key questions be answered:

- Can patents on DNA sequences continue to be justified in the context of current technology?
- Are such patents really necessary for successful innovation in health care?
- What are the real thresholds for novelty, inventiveness and utility?
- What are the duties of patent-holders in licensing their inventions?

The report concludes by recommending that these issues be addressed by an international policy forum.

6.5.2 Socioeconomic concerns and trade

The question of whether socioeconomic concerns, such as animal welfare, the environment and biodiversity should be addressed within or separate from food-safety regulatory systems is controversial. Many countries emphasize the importance of taking account of such factors in their food-safety regulations. In these countries, socioeconomic factors are included in the basis for selecting risk-management measures, but not in the assessment of health risks. In the field of environmental safety or biodiversity, the importance for the consideration of socioeconomic factors under the SPS and Technical Barriers to Trade (TBT) Agreements could arise from often very different local biosafety conditions and regulations, which need to be taken into account. Other

countries express concern that the introduction of socioeconomic factors in decision-making may undermine the integrity and credibility of food regulatory systems, and could be used to unjustifiably impede trade in agricultural and food products.

Codex principles on food safety do not have a binding effect relative to national legislation, but are referred to specifically in the SPS Agreement and can be used as a reference in case of trade disputes (WTO/WHO 2002). Similar principles are demanded by some NGOs in the field of environmental or social safety.

6.6 Ethics in the development and use of GMOs, equity and shaping of markets

The risks of biotechnology, the problems of interfering with nature, evolution and creation, and ethical considerations are of increasing importance in the civil-society debate on the development and introduction of GMOs. Ethical committees are more frequently established and consulted to provide answers to issues beyond the scope of scientific committees. Such committees are often selected to include a diverse range of representatives, so that generally agreed compromises are more likely to be reached. International agreements related to nature and food production are summarized in a report by FAO on ethical issues in food and agriculture (FAO 2001a,b). They include the value of food, the value of enhanced well-being, the value of human health, the value of natural resources and the value of nature, whereas the Convention on Biological Diversity recognizes that nature itself is to be valued for what it is. The summary of these objectives shows that all the main arguments usually discussed in a risk–benefit evaluation of food biotechnology interfere with each other, thus requiring a high level of ethical consideration. This relates especially to arguments about enhanced productivity for increasing food production, improving health and nature protection.

The FAO report points out that current trends such as human population growth and demographic shifts, pressure on natural resources, industrialization of agriculture, concentration of economic power, globalization, human-induced environmental changes, new biotechnologies and information technology are the main issues which need to be taken into account in an analysis of problems and means of improving. An emerging global economy — but in contrast, not a global society — may divide people between those who participate in the market and those who lack the means to do so, and it is essential to resolve conflicts and deal with the gaps between the poor and the affluent, between the food-insecure, between the winners and losers of globalization, and between cultures and generations. In recent years, food and agriculture have undergone major changes, including rapid technological advances, a restructuring of the resource base, the creation of new and expanded international markets and closer ties with environmental management. For the first time, the development of the food and agriculture sector is being conceptualized globally. As a result of these developments, all societies have some point of convergence with one another (Nuffield Council on Bioethics 1999a; Groth 2001; Wagner et al. 2001).

As the international food-safety system comes to terms with the need and responsibilities for risk communication, several considerations should be kept in mind. Firstly, communication should be structured to ensure that ethical components of food-safety decisions are clearly identified as early in the process as possible. Secondly, the system should function so that value-laden choices made by risk managers are made in an open, participatory process that respects the rights and roles of all stakeholders. Following such a strategy will not necessarily make food-safety risk analysis more efficient, as dealing with any difficult questions may be time-consuming. But a strategy that is more sensitive to ethical issues should make food-safety risk analysis more effective, by making decisions sounder, more transparent, more democratic and better understood. This, in turn, should make risk-analysis decisions more acceptable to and useful for the governments and citizens of all nations (FAO 2001a). Transparency through the deliberation of the purpose, benefits and risks of modern biotechnology ought to be a part of responsible management (FAO 2001b). For ethics to be an integral part of the safety assessment of food derived from modern biotechnology, a framework with the appropriate extension of the principles used in the biomedical field could be developed. Such a

framework would make ethical assessments more transparent, methodical and amenable to quality assurance.

6.6.1 Ethical values underlying food safety policy

There is broad international agreement that food-safety standards and related guidelines must have an objective basis in science. Many risk assessors now agree that risk analysis, and especially risk management, requires consideration of numerous, more subjective and value-laden factors to determine the appropriate level of protection and to choose the preferred risk-management option(s). The scientific community has developed ways to resolve disagreements over scientific facts, but disagreements over the value and ethical components of food-safety decisions are often much harder to sort out. Internationally, food-safety agencies also agree on the value of science as a significant tool in food-safety policy-making and the development of food standards. The general policy guidelines of the Codex Alimentarius Commission contain statements of principle concerning the role of science in the Codex decision-making process and the extent to which other factors are to be taken into account.

The first two of these statements are as follows (CAC 2004):

> "1. The food standards, guidelines and other recommendations of Codex Alimentarius shall be based on the principle of sound scientific analysis and evidence, involving a thorough review of all relevant information, in order that the standards assure the quality and safety of the food supply.
>
> 2. When elaborating and deciding upon food standards, Codex Alimentarius will have regard, where appropriate, to other legitimate factors relevant for the health protection of consumers and for the promotion of fair practices in food trade."

While risk assessment is based on science, scientific evidence and analysis cannot always provide immediate answers to questions posed. Much scientific evidence is tentative, as the established processes of science include checking and rechecking outcomes in order to obtain the required level of confidence. Decisions usually are defended as based on 'science' and sometimes on economic costs and benefits as well, which offer seemingly objective, verifiable evidence that the policy choice is 'correct'. Decisions explicitly based on ethical principles and value preferences can be just as defensible, if the society agrees broadly on the ethical assumptions used to make policy. The emphasis on science and the exclusion of ethical argument as the basis for decisions may polarize the scientific debate. Stakeholders who find that risk managers will not entertain a serious discussion of, for example, their right to avoid consuming a food they believe is not safe enough, may argue instead that the food is not safe, exacerbating technical disagreements about inherently ambiguous evidence of risks. To assist with understanding the values implicit in decisions about food safety, a FAO Expert Consultation on food safety science and ethics identified five groupings of values: the right to adequate food, trust, optimization, informed consent and equity (FAO 2002).

An important aspect of science-based food-safety assessments is that they involve a measure of uncertainty. These uncertainties should be presented by risk assessors and addressed in a transparent manner by risk managers (FAO 2001a,b) if the assessments are intended to be a useful and responsible basis for societal decision-making. Currently, this need is not sufficiently realized within the scientific community.

6.6.2 Social inequity and development

The Chairman of the WHO conference *Biotechnology and genomics for improvement of health in developing countries* (Chen 2002) highlighted that a recurring theme underlying social worries is social inequity. Concern about inequity is escalating, in part because of the globalization of private markets. Rapid transnational flows of money, goods, services, technology, culture and people are

introducing new vulnerabilities, uncertain risks and heightened public consciousness about distant people in a shrinking world. Lack of a profitable market provides little incentive for industry to pursue R&D to develop technologies for the poor, and problems of a genomic divide have been addressed in public debates. The questions remain of how to ensure production of essential global public goods, and how to shape markets to generate more equitable outcomes.

Certain goods wanted and needed by everyone cannot be produced by private markets and need to be appropriately generated by public action and public financing, where the problem of the cost of R&D needs to be solved. Public–private partnerships are believed to be an approach to produce public goods in health. Problems of IPRs are another issue where advances such as the management of intellectual property in health R&D (MIHR), recently established by the Rockefeller Foundation to assist non-profit organizations in negotiating IPRs, licensing, etc., could serve as an example for improvements.

6.7 Research and development, societal objectives and a role for WHO

Until now, the development of most societies has been driven by scientific findings that have been translated into the use of new technologies, mainly through market forces. Certain social consequences have been dealt with by public regulatory measures which aim to minimize hazards (sometimes fatal) for individuals, groups or societies in different regions and periods. Some societies have implemented scientific systems to predict the consequences of new technologies with a view to developing appropriate social measures for minimizing negative consequences over time. These attempts have been summarized as methods for the assessment of technologies, and various systems are still under investigation for improved predictability. However, the prediction of social consequences resulting from the adoption of new technologies is difficult in view of the quantity and specificity of factors which need to be taken into consideration, as well as their interdependence and uncertainty.

In considering needs for improved ways of integrating new technologies into society, especially in the field of biotechnology, innovative ways of interacting between technologies, science and society have been proposed. Aiming for specific developments or even concrete products may be better directed by public policy based on agreed societal needs. In the field of modern biotechnology in food production, some experts strongly recommend that present developmental and risk-assessment procedures be reconsidered, and that an interactive dialogue between researchers, industry, consumers and competent authorities involved in risk assessment and risk management be implemented at the very beginning of product development (‘safety first’) (Kapuschinski et al. 2003). For instance, new participatory techniques such as consensus conferences have been designed within the framework of modern technology assessment to meet this challenge.

Technology is neither inevitable nor immutable. Social and cultural controls can be exercised. How the global community exercises such controls on modern biotechnology is a central question facing the world today. The revolution in genomics and biotechnology has generated and will continue to generate many vexing ethical and social dilemmas that cannot be addressed entirely within nations. A globalizing ethic will need to address the question of which technology for whom, why and how.

As most of the exercises in this field are related to the mandate of WHO, the Organization has been challenged to take up many of these issues and to carry on from previous efforts. An example of the way WHO has responded to the challenge is the launch of the Genomics for Health Initiative following the release of the report *Genomics and world health* (WHO 2002a). The draft terms of reference for the Initiative offer nine possible activities: annual forums, capacity building, innovation in developing countries, mobilization of financial resources, building of bioethics capacity, establishing codes of conduct, advocacy, public engagement and global governance. Many of these activities would harmonize and synergize with activities to shape conditions where biotechnology can contribute to the secure generation of nutritious foods according to regional needs, where sustainable

food production preserves biodiversity and respects the values of nature, and accepts ethical objectives and social equity in respect to regional specificities (WHO 2002a).

6.8 Conclusions

Modern methods of biotechnology enable the accelerated development of food products with recombined or improved traits with an increased specificity compared with conventional techniques. However, risk assessment and procedures for adoption or rejection of GM foods by society need to address ever-innovative methodological possibilities.

For an analysis of the costs and benefits of GM food, the costs to be taken into account and the intended scope of beneficiaries should be defined. Cost–benefit ratios can relatively easily be estimated for manufacturers and farmers (who may benefit from certain GM products in the short term). But of more interest are the costs and benefits for society as a whole and in the long term. This includes aspects such as sustainability of agricultural production systems, and the cost of mitigating potential effects on health and the environment. Such estimates require a complex form of analysis.

New ways for improving communication between scientists in the development of products and society on the subject of the desired outcomes of public goods should be found. Financial tools to ensure the development of public goods also need to be created.

There is a need to investigate opportunities to shape social and market conditions where biotechnology can contribute to the secure generation of nutritious foods according to regional needs. Such opportunities should be based on sustainable food production preserving biodiversity and respecting the values of nature, while taking into consideration ethical objectives and social equity in respect to regional conditions, needs and wants.

Annex 1

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Annex 2

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