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Executive summary

Genetically modified foods for human health and nutrition: the scientific basis for benefit/risk assessment

The purpose of this monograph is to provide an independent analysis of the scientific basis for assessing the benefits and risks of genetically modified (GM) crops and food, specifically in relation to their current and future impacts on human health and nutrition worldwide.

One of the objectives of the International Council for Science (ICSU) is –

> 'to encourage and promote international scientific and technological activity for the benefit and well-being of humanity'

In 2000, two of ICSU's member unions, the International Union of Nutritional Sciences (IUNS) and the International Union for Toxicology (IUTOX) initiated this present project on GM food (GMF) and GM crops for human health and nutrition, in order to contribute to the development of ICSU's views on the applications of gene technology, and the relative risks and benefits involved. Four other ICSU member unions and two ISCU scientific committees, representing a breadth of scientific interests, joined in the project.[1]

It is hoped that the findings of this project, combined with the outputs of other ICSU entities concerned with various aspects of gene technology, will enable ICSU to speak with authority on the scientific basis for understanding the risks and benefits of the uses of gene technology.

Structure of the monograph

The monograph reflects the discussions at the final of three ICSU workshops organised to evaluate the scientific basis for the assessment of potential risks and benefits to human health and nutrition of the use of GMF crops. International experts in nutrition, medicine, toxicology, molecular biology, microbiology, genetics, economics and social science, including representatives of the science unions, participated in the workshop, which was held in Manchester, UK in May 2002. Prior to the meeting invited experts in relevant fields prepared working papers, which form the basis of Chapters 1 to 10 of the monograph. Each chapter was modified and finalised at the workshop in the light of discussions at the workshop. Only publicly available information and research results have been included in the monograph.

Chapter 1 considers the role of science in the development and application of transgenic (genetic modification) technologies, in relation to the needs and concerns of society in general. Chapters 2 to 4 review topics pertaining to GM crops and food quality and human nutrition, improving agricultural practices, and industrial products and processes; Chapters 5 to 7 review GM fish, livestock, poultry, and microorganisms. Each of chapters 2 to 7 reviews, where appropriate, current knowledge on the expected or potential contribution of genetic modification technology, outcomes and impacts of the use of GM organisms (GMOs), standards of use, methods for the evaluation of outcomes and impacts, and knowledge gaps. Chapter 8 reviews the scientific basis for risk assessment of GMOs. Economic and social issues pertaining to the use and control of GMOs are reviewed in Chapter 9, and public attitudes towards GMFs are discussed in Chapter 10. Overall conclusions are outlined in Chapter 11. The monograph is intended to serve the increasing dialogue between society and science and thus contribute to ongoing discussions about the application of the technological innovations that make GMFs possible.

[1] International Union of Biochemistry and Molecular Biology (IUBMB), International Union of Food Science and Technology (IUFoST), International Union of Pure and Applied Chemistry (IUPAC), International Union of Soil Science (IUSS), Advisory Committee on Genetic Experimentation and Biotechnology (ACOGEB; formerly Steering Committee on Genetics and Biotechnology (SCGB)) and Committee on Sciences for Food Security (CSFS).

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Addressing public concerns

Public discussions about the ethical and socioeconomic issues surrounding the development and use of applications of modern biotechnology for agriculture are widespread, particularly discussions about the development of GMFs and GMOs and the safety and efficacy of the new products.

Public concerns about gene technology lie in four major areas, namely ethical concerns, socioeconomic issues, effects on the environment and food safety and human health.

Although acknowledging the importance and the interconnectivity of all these areas, the special issue's principal focus is the scientific basis for assessing the risks and benefits to human health of GMFs and GM crops. It also seeks to identify ways in which knowledge gained from the health and nutrition sciences can contribute to the broad public debate, help clarify choices for individuals, communities and countries and inform policy development, while recognizing that the context in which choices are made varies significantly with differences in societies, environments and economies across the world. In support of these aims the special issue also identifies gaps in knowledge where additional scientific research may help resolve uncertainties about safety, benefits, utility, acceptability and other aspects pertinent to the development and use of GMFs.

Context

The ideal relationship between scientists and society is one of dialogue amongst those who are mutually concerned with improving the human condition and minimizing inequalities. Such dialogues must consider the values of diverse groups and identify the desirable balance between science directed at applied missions and science conducted for the sake of generating new knowledge.

The present biological revolution is based on a series of key discoveries in genetics, molecular biology and related fields. These include Mendel's description in the late 19th century of the principles of genetic inheritance, Watson and Crick's discovery in the 1950s of the double helix structure of DNA and the recent elucidation of the human genome. Developments associated with this continuum of discoveries have sometimes been responsive to dialogue between society and science. Successful exchanges are reflected in the early implementation of recombinant DNA technology in medicine. For example, many new pharmaceuticals, including new forms of insulin widely used by diabetics, are presently produced using new biotechnology. The present lack of consensus on appropriate uses of gene technology for the modifications of food and fibre crops is an example of a failure in exchange.

The special issue focuses on risks and benefits to human health, including the possible improvement of human nutrition, by transgenic modifications of plant and animal food sources. Its principal focus is the technological dimension of transgenic modifications. Other important issues are discussed where they illustrate the impact of setting technical priorities. Many of these other complex issues, such as any direct and indirect impacts of GMOs on the environment, bioethical considerations, and other social and economic concerns, are addressed more comprehensively elsewhere.

The special issue takes no position on appropriate policies that societies should adopt as a consequence of the scientific knowledge that is reviewed. It strives to assess scientific reliability, while recognizing that quantifiable boundaries of (un)certainty are a defining characteristic of scientifically derived data. It is motivated by two global forces, mounting population pressures and rising quality-of-life expectations worldwide, and one principal assumption, namely that solutions and responses to the problems and challenges those forces present have technological dimensions.

Human health is not achievable unless adequate amounts of wholesome and safe foods are available and accessible during all life stages. The aim of 'food-for-all' is driven not only by humanitarian concerns but also by the biologic imperatives for achieving nutrient and food security that are linked to health and economic development.

Assumptions

The special issue's focus on the transgenic modification of plants and animals explicitly assumes that gene technology has the potential to achieve positive, dramatic, and useful results. The robustness of this assumption is tested throughout the special issue. Generally, arguments promoting the utility of transgenic technologies are based on the increased versatility and speed by which such modifications can be produced relative to traditional breeding techniques. This focus is not intended to imply that solutions and responses to the problems and challenges the future holds should be solely or even partially technological in nature. The only assertion made by this focus is that the technological dimension merits consideration along with others, for example economic policies such as those that govern global trade and agricultural subsidies. Most importantly, full accessibility to diverse, affordable, nutritionally adequate, wholesome diets remains the goal for all.

Two further assumptions are that the capabilities for exploiting technological possibilities enabled by current scientific advances must be available in the developing world and that transgenic modifications of plants and animals hold known and unknown risks, as do all technologies, old or new. Implicit in the latter assumption is

that absolute safety is not an achievable standard.

In the light of the above assumptions, it is essential to identify the following: the type and 'magnitude' of benefits and risks; who is likeliest to benefit from the application of specific technologies; to whom risks are likeliest to accrue; and the time frame for anticipated benefits and risks. The special issue explores how scientific knowledge can help answer these questions.

Benefits and risks associated with the products and process of transgenic modification

Traditional breeding techniques have led to documented contributions to human nutrition of technologies based on genetic modification of plants and animals. Such successes include, in particular, applications that result in increased and more efficient production (i.e. improvements in productivity). Increases in food availability enabled by these advances have had significant health benefits.

There are no known examples whereby the intentional modification of the composition of specific plant and animal foods through genetic techniques (traditional or modern) has resulted in documented improvements in human nutritional status at a population level. Transgenically modified plant foods currently in the food system were designed, for the most part, to achieve herbicide tolerance or resistance to pests. Other than fish, the development of transgenic animals intended for human consumption remains in the research and development phase.

There is evidence that modification of plants by any process may result in increased risks to human health, owing to unexpected changes in the chemical composition of the plants. For example, in some cases, conventional plant breeding in celery and potato has increased levels of plant toxins. These changes are usually detected in the screening process, prior to the release of new plant varieties.

The current lack of clearly demonstrated benefits to consumers from the first generation of GM foods and conflicting opinions about the likelihood and potential significance of unintended adverse effects of transgenic modifications may have influenced views on their safety for human health and the environment.

Thus, the current debate about the 'safety' of transgenic foods needs reliable information on the safety of the results of genetic modifications, the safety of the inserted DNA itself, the potential risk of expressing gene products in another organism and the safety of the process itself. The special issue gives greatest attention to the predictability of effects of genetic modification on the composition of the product and to the risks and benefits to human health associated with compositional alterations in GMFs and GM crops.

Anticipated benefits and risks

Transgenically modified plants and animals are projected to give rise to benefits and risks in two broad areas: health and the environment. Four categories of health benefits are recognised: enhancement of food security; enhancement of nutrient security; more targeted health benefits, such as immunization; and reduction of diet related, adult-onset chronic diseases (through the manipulation of specific food components, e.g. manipulation of fat composition). Health risks associated with the approaches that are reviewed generally also fall into four categories—allergies, toxicities, nutrient imbalances, and decreasing diet diversity.

Environmental effects focus on the direct and indirect impact of GMOs and associated agricultural practices on the environment. These effects include potential negative and positive impacts on biodiversity, at the gene, species and ecosystem levels. For example, decreases in biodiversity may result from GM crops showing enhanced competitiveness in the field or from agricultural policies and economic pressures favouring the production of GM crops at the expense of other more genetically diverse alternatives. Changing agricultural practices may have beneficial, environmental effects. For example, environmental (and also health) benefits are likely when genetic modification of crops enables reduced insecticide use.

Determining what and how much information is needed

Guidelines are useful to help determine the magnitude of effort that is appropriate to assure 'reasonable certainty of no harm,' and to trace foods through the production, processing, marketing, and distribution system. Several groups that have examined various facets of GMFs have included such guidelines, implemented with suitable flexibility, in their recommendations. Some proposed guidelines are as follows.

- Actions should be proportionate to the nature of the potential risk
- Consistent precautionary limits should be applied in assessing all food products, irrespective of their production processes
- More stringent limits should be applied to risks that are not easily reversible
- The extent to which precaution advances or detracts from relevant societal goals should be examined
- The costs that caution imposes should be considered

Guidelines such as these are useful only if they are developed sufficiently so that the information needed for their effective application can be identified. Understanding what information is required, determining the limits of uncertainty that are appropriate to its derivation, and developing objective processes for the dis-

covery of knowledge are all key areas that need the participation of science. However, it is equally clear that good science will not be enough, as each guideline incorporates dimensions that are broader than those normally encompassed by the scientific process.

Food quality and human nutrition

Consumers in Europe and North America spend perhaps 10% of their income on food. The situation is very different in developing countries where poor consumers typically spend 70% of their income on food. The diets of the latter consist primarily of staple foods, which lack the vitamins and minerals necessary to sustain good health, whereas a range of foods (animal and fish products, fruits, pulses, and vegetables), rich in bioavailable vitamins and minerals or micronutrients, is necessary for good health and a productive life. Micronutrient malnutrition is widespread in poor countries, affecting more than one-half of the population in the developing world; women and children are particularly at risk. Except for pockets of extreme poverty and dislocations arising from natural disasters and situations of conflict, staple foods, such as cereals, roots and tubers, are generally available in sufficient supply. Although non-staple foods are also generally available, combinations of high prices and low purchasing power make them too expensive for many potential consumers. Low incomes also preclude poor people from access to competent health care.

There are three broad ways that biotechnology may benefit consumers in developing countries. First, biotechnology offers a powerful, new tool to improve crop productivity, both by making conventional breeding faster and more efficient and by introducing new traits, by the insertion of novel genes in a crop species using transgenic methods. Second, pesticide applications may be reduced through adoption of pest and disease resistant crops; this can benefit the health of farmers, reduce input costs and benefit the environment. Third, biotechnology may improve the nutrition and health of consumers in developing countries through increasing the vitamin and mineral content of staples and other foods and/or by reducing allergens. Several such products are under development but none have been introduced commercially.

Possible biotechnology-based strategies should be considered in the context of alternative interventions that might help solve malnutrition and health problems in other ways. As one example, consideration of the relative costs of supplementation and commercial fortification programmes indicates that biofortification may be implemented for a fraction of the recurrent estimated costs of around US $165m per year for vitamin A supplements in developing countries. Consideration of the recent history of attempts to improve the micronutrient content of staple food crops using both biotechnology and conventional plant breeding is also informative; the example of rice serves to illustrate several key generic issues associated with using biotechnology to breed for new characteristics that may have benefits for consumers.

The optimal solution to micronutrient malnutrition in developing countries is a substantial improvement in dietary quality by higher consumption of pulses, fruits, vegetables, fish, and animal products. Realisation of this goal will require several inputs:

(i) substantial investments by farmers, private businesses, and public agencies to build the infrastructure to produce and bring to market the requisite supply of non-staple foods;
(ii) sound government policies to stimulate agricultural and economic growth; and
(iii) considerable increases in the incomes of the poor during the course of economic development over many decades.

In the meantime, breeding staple foods that are dense in minerals and vitamins could provide a low-cost, sustainable strategy for reducing existing levels of micronutrient malnutrition.

However, such an approach requires that there should be no serious, negative agronomic consequences associated with the characteristic being added, that consumers' quality preferences should be taken into account, and that the characteristic being added will result in a measurable improvement in the nutritional status of the malnourished, target population. The hazards associated with the various possible strategies should also be addressed.

Agricultural practice

New scientific developments in agricultural biotechnology are being used to increase the productivity of crops, primarily by reducing the costs of production by decreasing the needs for inputs of pesticides and herbicides, mostly in crops grown in temperate zones. New varieties of plants are being developed that should give higher yields with fewer inputs, can be grown in a wider range of environments, and provide both more nutritious harvested products and low-cost food supplies to consumers.

The traits these new plant varieties contain include insect resistance (cotton, maize), herbicide resistance (maize, soybean), and delayed fruit ripening (tomato). The benefits of these new crops are better weed and insect control, higher productivity, and more flexible crop management. These benefits accrue primarily to farmers and agribusinesses, although, by facilitating low-cost food production, there are also potential economic benefits for consumers.

Potential health benefits for consumers are also emerging from new

varieties of corn and rapeseed with modified oil content, the benefits of which are especially relevant in developed countries. Other broader benefits to the environment and the community, in both developed and developing countries, come through reduced use of pesticides. Further crop/input trait combinations presently being field-tested, and of particular benefit to developing countries, include virus-resistant melon, papaya, potato, squash, tomato, and sweet pepper, insect-resistant rice, soybean, and tomato, disease-resistant potato, and delayed-ripening chilli pepper.

The development of crops resistant to biotic and abiotic stresses is critical for sustainable food production in the developing world. The use of GMF crops should go hand-in-hand with other technologies such as plant tissue culture, marker assisted breeding and conventional plant breeding. GMF crops could decrease the cost of production and have positive effects on the environment in both developed and developing countries. It is, however, prudent that the outcomes and impacts of the use of GMF crops are scientifically monitored with respect to farming efficiency, food production and environmental impacts.

The estimated global area of transgenic crops for 2001 is 52.6 million ha grown by 5.5 million farmers in 13 countries. More than one quarter of the transgenic crop area in 2001 was grown in six developing countries. The number of farmers that planted GM crops increased from 3.5 million in 2000 to 5.5 million in 2001. More than three-quarters of all farmers planting GM crops were resource poor farmers, mainly in China but also in South Africa, who planted cotton carrying an introduced *Bacillus thurigiensis* gene (*Bt* cotton), which confers insect resistance. The primary benefit of the introduction of *Bt* crops has been an increase in yield; however, a secondary benefit has been a decrease in the use of toxic chemical insecticides, for example by 60–80% in China. Such reduced insecticide use can be a major health benefit, especially in developing countries where spraying is usually by hand.

Industrial products and processes

Industrial crops are those grown as sources of chemicals or components that serve non-food uses. Products derived from plants for industrial applications include oils, fibres, fuels and pharmaceuticals. Genetic modification of crops to improve industrial applications is relevant to human health because there are very few crops that are grown solely for industrial use and some parts of such crops could be consumed. For example, soybean is grown for both food and industrial oils, cotton is grown as a fibre crop but also produces seed oil for human and animal consumption, and maize is grown as a starch crop.

Although there are many GM crops for industrial applications under development, there are a limited number that have been introduced commercially. Soybean, cotton and maize are the major crops for which there are commercial GM varieties; currently Laurate Canola and High-Oleate Soybean are the only commercially available GM crops that have changes in composition that make them more useful for industry.

A principal concern is how to use genetic modification technology in a way that gains the advantage of using renewable resources to replace products from petroleum and other non-renewable resources while maintaining a safe and adequate human food supply. It is also crucial to ensure that GM crops designed to produce industrial products do not inadvertently enter the human food chain or contaminate food crops with their transgenes, if these traits may pose a risk to the environment or to human health. Risk assessment of the ecological impact of crops grown to produce pharmaceuticals needs to be undertaken prior to their widespread cultivation.

Fish

Many species of fin fish have been subjected to genetic modification. Although some of these are being considered for the food market, and for some regulatory approval is pending, no GM fish is known to be produced commercially for food at present. The main species that have been genetically modified are Atlantic salmon, coho salmon, common carp, tilapia, and channel catfish. Although the principal parameter modified to date is growth rate, other traits of interest include cold tolerance, disease resistance, and sterility.

A number of factors should be considered in the risk assessment of the environmental impact of GM fish: the possibility that GM fish could escape from the physical containment under conditions of storm, flood, theft or human interference; survival of the fish in cold or warm water, and in salt, brackish or fresh water; whether the transgenic fish are sterile or partially sterile; the presence of wild fish of the same species in the surrounding waters; and whether the GM fish could become established as a novel pest species if they were to escape or be released.

Risk assessment for GM fish as consumer products also needs to consider several factors: the copy number of the transgene and the arrangement of the multiple copies; any evidence for insertional mutagenesis in any of the fish carrying the transgene; how many generations of fish have been produced; whether the food intake of the GM fish is different from the wild type; whether the physiology or anatomy of the fish is altered; any alteration in the texture and flavour of the fish; and whether the GM fish is more or less prone to known diseases of such fish species.

GM fish may become important in the developing and industrial world as sources of protein, and may help meet the growing demand for fish cost-effectively. Nonetheless, consumer concerns related to food and environmental safety

and ethical issues need to be incorporated into regulatory processes and commercialisation practices.

Livestock and poultry

No food product derived from GM livestock and poultry is currently under market production. Applications of transgenic technologies, with the main species of livestock and poultry, are now possible in two fields, namely agriculture and human healthcare. Agricultural applications focus on developing alternatives to current methods for animal breeding, with the potential added value of the ability to introduce genetic changes that cannot be achieved by other methods. Genetic modification technology could offer alternative production systems to fulfil demands for livestock that differ across geographical and socioeconomic regions of the world. Applications for human health are primarily targeted at healthcare products.

The risks associated with specific modifications will require analysis on a case-by-case basis, depending on the use of the GM product. New food products from livestock and poultry will require assessment in much the same way as GM plant products. The risks to the environment of GM livestock and poultry are considerably less than those potentially associated with GM plants or fish. There is a substantially lower likelihood of escape and dissemination of GM livestock and poultry, owing to the lack of competition with wild and related animals and bird species.

Methods involved in genetic modification of livestock and poultry are inefficient and expensive. Much research is still required to identify useful targets for genetic modification and to increase the overall efficiency of genetic modification methods, from frequency of production of transgenic animals to effective transgene expression. High costs mean there is little support from research funding agencies or from the relevant industries for development of the technology in relation to food production. In addition, economic factors and public acceptability may inhibit the introduction of GM animals into the breeding stock of the animal breeding industries and dissemination to producers.

Potential hazards to humans, involved in production or when the products become part of the food chain, will require assessment through a regulatory process with appropriate licensing powers. These regulatory processes are already established in many countries, for example within the European Union. There are serious public concerns about the ethics of manipulating domesticated animals and about the animal welfare effects of genetic modifications. These should be considered and evaluated in a system that can be applied equally to animals and birds produced by genetic modification and to animals and birds produced by conventional breeding methods.

Microorganisms

No genetically modified microorganism is currently used in foods although some are used to produce food ingredients. Microorganisms (bacteria, yeasts and filamentous fungi) can be used in food production as integral parts in preparation of various fermented foodstuffs or to produce food additives and processing aids (organic acids, flavouring agents, food enzymes, etc.). In fermented foods the GM microorganisms (GMMs) can either be dead, inactivated or viable, leading to different safety implications. Owing to the plasticity of microbial genomes and the existing gene exchange mechanisms, genetic containment for GMMs represents a fundamentally different situation to that for other GMOs.

Food fermentation is an ancient practise and still valuable today. The successful application of GMMs in food fermentation is hampered by the lack of knowledge of the impact of specific genes on the fermentation process. This is particularly true with complex properties like aroma ripening and texture, which are often influenced by environmental factors. It might even be questionable whether genetic modification technology is the optimal methodology to improve many of the traditional processes; in many cases conventional strain selection and adjustment of the process will also be future methods of choice. Introduction of new, nutritionally valuable or health promoting properties into fermented foods by designed GMMs would be an attractive line of future research and product development. However, there are numerous areas of uncertainty, not least in the safety and regulatory aspects.

Interactions of GMMs with host microflora and associated host-functions are critical for many of the eventual benefits and potential hazards. However, conventional microorganisms associated with fermented foods can also influence host microflora. The role and function of human microflora in health and disease are still poorly understood.

The safety assessment of any future GMM applications should be rigorous, as with other novel foods, while accepting that no food can be completely risk free. The identified hazards should be weighed against the expected benefits.

The safety evaluation of processing aids or food additives produced by GMMs should follow the same guidelines and practices applied to conventional products. However, special emphasis should be directed to the elimination of unintended effects each time a production organism or process has been modified, either by recombinant DNA techniques or conventional methods.

Regulation and risk assessment

The safety assessment of GM food crops has attracted widespread attention. Regulatory principles and practices are in place in most developed and in several developing countries, and the Organisation for Economic Co-operation and Development (OECD) and the World Health Organisation (WHO) in col-

laboration with the UN Food and Agriculture Organisation (FAO) have published regulatory guidelines for GM foods.

Safety assessment of GM foods is carried out on a case-by-case basis, taking the specific modifications into account, and comparing the properties of the new food with those of the traditional counterpart. This comparative approach, applying the so-called principle of *substantial equivalence,* is based on the assumption that conventional foods are generally considered as safe for consumption, based on a history of use. Identified differences between the GM food and its counterpart are assessed with respect to their safety and nutritional implications for the consumer. The concept of substantial equivalence, as developed by the OECD and endorsed by the FAO/WHO, is a starting point for a safety evaluation and contributes to an adequate food safety assessment strategy.

Safety testing of whole foods is difficult. Generally assessment of 'safety/toxicity' relies on the description of dose–response relationships. It is not possible to produce similar information on whole foods using the conventional techniques used for chemicals. However, conventional tests reflect past technological possibilities and limitations, and new approaches for safety assessment of whole foods, taking advantage of modern molecular-biological, toxicological and analytical methods, are possible.

There are concerns about the possibility of unintended consequences and the risks these represent, and present knowledge does support the likelihood of unanticipated compositional effects arising from the use of gene technology. However, it is emphasized that unintended effects do also occur in traditional plant breeding.

Present approaches to detecting expected and unexpected changes in the composition of GM food crops are primarily based on measurements of a limited selection of single compounds (targeted approach). In order to increase the possibility of detecting unintended effects, new profiling methods using gene expression technologies, proteomics and metabolomics, should be further developed and validated (non-targeted approach). Growing capabilities in proteomics and metabolomics permit increasingly comprehensive assessments of compositional changes. New approaches to safety testing are of particular interest for the safety and nutritional assessment of future GM crops with improved nutritional or health beneficial properties. However, the principal problems associated with advanced technologies for the determination of compositional changes lie not in the compositional analyses themselves, but in assessing the significance of the results of those analyses.

The comparative safety assessment approach should also be followed for the new generation of GMF crops in order to establish the degree of equivalence with presently available foods. The unmodified host organism may function as the relevant comparator for testing the degree of equivalence, but a possible outcome may be that a safety assessment of the new food *per se* is necessary. This may be the case for GM crops with extensive modification of existing metabolic pathways or addition of new ones, or for GM plants with decreased levels of naturally occurring toxins, which previously could not be used as food sources. Strategies should be designed on a case-by-case basis.

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

Socioeconomic aspects relevant to sustainability

The rapid adoption of GM crops has raised several ethical, ecological, economic and social concerns. Currently available GMOs may have both positive and negative effects on three indicators of sustainable agriculture and rural development, namely stocks of natural resources and environmental capital, efficiency and equity. The effects depend on the socioeconomic conditions underlying the development, use and control of GMOs, including new crop varieties.

Three policy options are key to the sustainable development, use and control of GM foods, namely intellectual property protection, trade liberalisation and biosafety implementation. The effects of policy options that shape socioeconomic conditions are intricate; a policy option that directs socioeconomic conditions in one way may affect another policy option that leads in a different direction (i.e. policy options in intellectual property, trade liberalisation and biosafety are sometimes mutually contradictory). Ensuring policy coherence is particularly challenging.

Societal issues and public attitudes

Public perceptions and attitudes about emerging biosciences and other new technologies are critical determinants of how likely it is that the implementation and development of such technologies will succeed.

As well as considering the psychological determinants of people's perceptions and attitudes, it is necessary to consider public trust in institutions, both those concerned with regulatory matters and

those concerned with the strategic development of science. While it is important to develop best practice in science communication pertinent to the risks and benefits of GMFs, this alone will not increase public confidence in gene technology. Rather, it is also important to consider new ways to involve members of the public explicitly in the debate about technology innovation and commercialization and to improve the relationship and dialogue between science and society. Improved dialogue needs to be a two-way process that makes a difference to policy development and regulatory practice.

Overall conclusions

Considering the reviews of current knowledge in the special issue as a basis for expert opinions and projections about the development, use and risk assessment of GMFs for human health and nutrition, workshop participants reached a number of overall conclusions, as outlined below.

Categories of risk

- The process of the development of transgenic organisms presents no new categories of risk compared with conventional methods for improving plants, animals or microorganisms. However, specific traits introduced by either approach might pose unique risks, which need to be identified.

Food quality and human nutrition

- The potential benefits of improving the nutritional quality of foods are higher for low-income countries, where food budgets account for two-thirds or more of total expenditures and where poor dietary quality and micronutrient malnutrition are widespread. Most consumers in rich countries have access to a relatively inexpensive supply of safe and healthy food.
- Nutritional and quality traits of foods can be altered through transgenic methods. A large number of products are under development and testing.
- The nutritional efficacy of these products and risks of unintended harmful effects have yet to be tested and demonstrated.
- The commercial viability of these products has yet to be demonstrated.
- The sustainable solution to malnutrition in developing countries is provision of a sufficient quantity of high quality diet, which the poor desire but presently cannot afford. During the long-term process of achieving this goal, biofortification is a low-cost strategy, which complements other technological and social interventions—assuming that the nutritional efficacy and commercial viability can be established.

Agricultural practice

- The development of crops resistant to biotic and abiotic stresses is critical for sustainable food production in the developing world. The use of GMF crops should go hand-in-hand with other technologies such as plant tissue culture, marker assisted breeding and conventional plant breeding.
- GMF crops could decrease the cost of production and have positive effects on the environment in both developed and developing countries.
- It is, however, prudent that the outcomes and impacts of the use of GMF crops are scientifically monitored with respect to farming efficiency, food production and environmental impacts.
- Gaps in knowledge about GMF crops include their efficacy compared with conventionally bred varieties with similar traits and potential direct and indirect effects on the environment, such as their risks of invasiveness, their impact on non-target organisms and possible unintended effects. Some of these gaps may be filled by new technologies under development and by continuing ecological research.

Industrial products and processes

- Crops can be genetically modified to produce oils, starch, fibre, protein or other chemicals useful for industrial processes. For example, soybean oil, with high oleate content, and canola oil, rich in laurate, are both being produced commercially using these methods.
- A principal concern is how to use genetic modification technology in a way that gains the advantage of using renewable resources to replace products from petroleum and other non-renewable resources while maintaining a safe and adequate human food supply.
- It is also crucial to ensure that GM crops designed to produce industrial products but not registered for human use do not inadvertently enter the human food chain or contaminate food or other crops with their transgenes.

Fish

- GM fin fish of a variety of species have been produced, many involving the use of model fish for fundamental research, although some of the modifications are applicable to species important in aquaculture.
- The present and projected increasing demand for fish suggests that GM fish may become important in future in both the developed and

developing worlds. However this will only be possible if consumer acceptance is achieved.

Livestock and poultry

- Food products derived from GM livestock and poultry are far from commercial use.
- The methods involved are presently inefficient and expensive. There are significant issues for the introduction of GM animals into breeding stock and dissemination to producers.
- Potential hazards to humans, involved in production or when products become part of the food chain, will require assessment through a regulatory process with appropriate licensing powers.
- There are serious public concerns about the ethics of manipulating domesticated animals and the possible welfare effects.

Microorganisms

- At present no GMMs are used commercially in food fermentations; however, many enzymes produced by GMMs are routinely used in the food industry.
- The safety evaluation of GMM-derived food additives and processing aids should follow the same guidelines and practices as the conventional products; however, special emphasis should be placed on the detection of possible unintended effects.

Regulation and risk assessment

- Safety assessment of GM foods is carried out on a case-by-case basis, taking the specific modification features into account, and comparing the properties of the new food with those of the traditional counterpart. This comparative approach, applying the so-called principle of substantial equivalence, is based on the assumption that conventional foods are generally considered as safe for consumption, based on a history of use. Identified differences between the GM food and its counterpart are assessed with respect to their safety and nutritional implications for the consumer. The concept of substantial equivalence is a starting point for a safety evaluation and contributes to an adequate food safety assessment strategy.
- Safety testing of whole GM foods needs improvement. The use of specific *in vitro* models and new methods such as DNA microarray technologies may elucidate mechanisms of action and interactions of biologically active compounds in food.
- Present approaches to detecting expected and unexpected changes in the composition of GM food crops are primarily based on a targeted approach (measuring a limited selection of single compounds). In order to increase the possibility of detecting unintended effects a non-targeted approach (using new technologies such as the gene expression technologies – proteomics and metabolomics) can be used.
- The usefulness of post-market surveillance to obtain information on long-term effects of foods or food ingredients, either GMO-derived or traditional, should not be overestimated, given the multifactorial origin of many food-related diseases and the variability in genetic predisposition of the human population. It may be useful in cases with specific biological outcomes, for example allergenicity or food intolerance, or when the exposure assessment provides insufficient insight into the diets of specific consumer groups.

Socioeconomic considerations

- The currently available GMOs are suggested to have both positive and negative effects on three indicators of sustainable agriculture and rural development. These are stocks (of natural resources and environmental capital), efficiency and equity. These bilateral effects depend on the socioeconomic conditions underlying the development, use and control of GMOs.
- The three key policy options that shape socioeconomic conditions are intellectual property protection, trade liberalisation and biosafety implementation. The effects of applying these options on the socioeconomic conditions are very intricate, as optimising one option may have contrary effects on the other options and thus on the socioeconomic conditions.

Societal issues and public attitudes

- Communication activities need to take account of the factors driving public concern, which may be different in different countries. This should include taking account of cross-cultural differences in information needs, if appropriate. In particular, discussion of ethical issues and effective communication about known and potential uncertainties and unintended effects must be addressed.
- Failure to consult the public about policy development leads to a loss of public confidence in science and technology. The purpose of such consultations is to make a difference to policy development.