July 6, 2001

Scientific Issues in Relation to the Safety of Genetically Modified Food and Crops

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Public concerns about the use of genetically modified organisms (GMOs) lie in four major areas: 1) food safety and human health; 2) impact on the environment; 3) socio-economic issues and 4) ethical concerns. All these issues need to be openly debated, and choices made by individuals, communities and nations. This paper reviews the scientific basis of the first two issues: namely food safety and environmental impact.

Firstly, in relation to food safety, there are concerns as to assessing the risks of genetically modified foods to human health; and understanding the potential benefits of new genetically modified foods to consumers. Secondly, in relation to environmental effects, the concerns relate primarily to assessing the risks and benefits of releasing genetically modified organisms (GMOs), into the environment, and the effects such releases may have on the environment. These effects may be through direct effects, such as impact on biodiversity, or indirect effects through changing agricultural practices that affect the environment. Each of these issues is discussed in more detail in the following sections.

The safety concerns about genetically modified food and crops are concentrated on the human health and environmental risks associated with the applications of biotechnology in the development of transgenic strains. Transgenic strains are those that contain a gene from another species. These strains are also termed living modified organisms (LMOs) or genetically modified organisms (GMOs).

The international conference on the safety of GM foods, sponsored by the OECD in Edinburgh in February 2000 (OECD 2000) noted the need for progress on the following points, in relation to the applications of biotechnology in food and crops:

- Factual points of departure as to where there is agreement and disagreement on human health risks from genetically modified foods;
- Benefits versus risks, for specific applications, in particular countries and environments
- Management of genetic modification technologies
- The role of stakeholders and consultative processes
- An international program of activities to inform the public debate and policymaking.

The International Council of Scientific Unions (ICSU) has recently initiated a study on the scientific basis of assessing risks and benefits of genetically modified foods, including a review of the scientific assessments of the safety of genetically modified foods, as a contribution to the ongoing debates, nationally and internationally. This paper draws on these ICSU studies, which are in progress and will be completed later in 2001.

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Food Safety and Human Health

Risks to human health

There are several areas of public concern with regard to potential human health risks of GM foods. These relate to understanding the potential of proteins and/or other molecules in GM foods to cause allergic reactions, to act as toxins or carcinogens, and/or to cause food intolerance reactions amongst the population. Presently available methods of testing and evaluating these types of risks are being applied to genetically modified foods so as to detect any increased risks associated with particular foods (Leher 2000; Metcalfe and others 1996).

A recent consultation between the Food and Agricultural Organization (FAO) and the World Health Organisation (WHO) reported that “the Consultation was satisfied with the approach used to assess the safety of the genetically modified foods that have been approved for commercial use” (FAO/WHO 2000). The US Food and Drug Administration (FDA) has also stated that “we have seen no evidence that the bioengineered foods now on the market pose any human health concerns or that they are in any way less safe than crops produced through traditional breeding” (FDA 2000). Recent comprehensive studies in Belgium and Canada have drawn similar conclusions (VIB Belgium 2001; Royal Society of Canada 2001).

As noted in the Edinburgh 2000 conference, there have been no documented instances of harmful effects on human health caused by genetically modified foods (OECD, 2000). However, that does not mean that risks do not exist as new foods are developed with novel characteristics. 

Genetically modified foods should be assessed on a case by case basis, using scientifically robust techniques, so as to ensure that the foods brought to market are safe for human consumption.

Allergenicity

Any protein that has been added to a food should be assessed for its potential allergenicity, whether it is added by genetic engineering or by manufacturing processes (Leher 2000). 

Allergenicity can be raised in foods either by raising the level of a naturally occurring allergen (eg in peanuts) or by introducing a new allergen. More than 90 percent of the food allergens that occur in 2 percent of adults and 4-6 percent of children are associated with eight food groups. These include crustacea, eggs, fish, peanuts, soybean, nuts and wheat. These foods merit close attention when examining GM foods for the potential for increased risk of allergenicity (Lehrer 2000). There is also a need to assess the allergenic potential of unknown proteins introduced into crops for their allergenic potential.

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

For example, these risk assessment techniques were used to test the safety of increasing the protein content in soybean by introducing a protein from Brazil nut. However food allergy tests showed that this transferred a potential allergen to soybean. Hence further commercial development of this genetically modified, high protein soybean ceased.

There is also a need to assess the allergenic potential of unknown proteins, such as those produced by genes from Bacillus thuringiensis (Bt) in plants for their allergenic potential. It was the
presence of a heat tolerant Bt protein in Starlink corn that caused the FDA to withhold approval for its use for human consumption as the FDA scientific advisory panel considered that this protein posed a moderate allergy risk.

**Antibiotic resistance**

There are also concerns that antibiotic-resistance genes used as selectable markers in genetically modified crops will be transferred to microorganisms that are human pathogens, adding to the increasing problem of antibiotic resistance in human pathogens. WHO, OECD and FAO have assessed the risk of transfer of an antibiotic marker from a GM crop to a human pathogen as been remote. Nevertheless, the use of these antibiotic markers is being phased out. Other selectable markers that can be removed from the plant in the development phase are replacing them (Escalar, 2001).

**Benefits to human health**

The risks in genetically modified foods need to be weighed against the benefits. The next generation of genetically modified foods is likely to include a number of *functional foods* that may offer some nutritional benefits to consumers. Human health benefits of genetically modified foods lie in the potential for introducing traits that may convey factors such as:

- Improved nutritional quality of foods (eg higher vitamin content, lower fat content);
- Reduced toxic compounds in food (eg cassava with lower levels of cyanide; maize with reduced levels of mycotoxins); and
- Crops grown with lower levels of chemical pesticides, thus reducing pesticide and residues in food.

**Labeling of genetically modified foods**

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

Informative labelling of GM foods requires that the nutrient content of the food is disclosed, in relation to similar foods produced by traditional techniques of crop improvement and cultivation, as well as any additional protein (or other) content resulting from the specific transgene modification. Labelling of food as *GM* or *non GM* may indicate the use of particular plant breeding techniques but it conveys no useful information as to the nutritional content or safety of particular foods.

**Food safety standard and regulations**

One result of public concerns about the safety of GM foods is that GM foods are now required to meet higher standards of safety than foods produced either by conventional agriculture or by organic agriculture.
Given increasing global concerns about food safety, all countries will need to have in place food safety regulations and human and institutional capacity to be able to set and apply food safety standard, so as to ensure the safety of their food supply.

Environmental Risks and Benefits of Genetically Modified Crops

In regard to the risks and benefits of genetically modified organisms (GMOs) in the environment, public concerns are based on the premise that when such organisms contain genes introduced from outside their normal range of sexual compatibility, these organisms may present new risks to the environment. Present recombinant DNA technology enables such genetic modifications to be made to introduce new and potentially useful traits into plants, trees, microorganisms, livestock and fish. This review considers the risks and benefits associated with the release of genetically modified crops into the environment. These are the only genetically modified organisms in widescale commercial use, albeit in a small number of countries.

In year 2000, there were some 44 million ha (100 m acres) of transgenic crops being cultivated commercially, in 15 countries. The majority of this area (68%) is planted in North America. The new crop varieties being grown commercially are mainly genetically modified corn, cotton, potato, rapeseed and soybean, modified with new genes for insect resistance, herbicide tolerance and/or virus resistance (James 2000). Amongst emerging economies, China (PRC) has at least 0.5 million ha being cultivated with transgenic crops. This is mainly transgenic cotton with insect resistance, which is being grown by some 3 million farmers across China. Other countries where transgenic crops are being cultivated commercially include Australia, Canada, France, Spain and some countries in Eastern Europe, as well as Argentina, Mexico and South Africa (James 2000).

The concerns about the impact of transgenic crops on the environment are about the risks of direct ecological effects, such as adverse impacts on biodiversity and indirect environmental effects. The latter may be caused by changing agricultural management practices brought about by the use of transgenic crops, in intensive crop management systems. There are also potentially beneficial effects of genetically modified crops in the environment, when compared to present agricultural practices. These also need to be taken into account in risk/benefit analysis of specific applications in particular environments.

Some of the concerns for the potentially harmful effects of genetically modified crops on the environment include:
- the use of genes from *Bacillus thuringiensis* (Bt) as a source of resistance to insect pests may lead to “super” pests;
- the use of crops with resistance to glyphosate (Round-up herbicide) may lead to greater use of broad spectrum herbicides;
- virus-derived genes used as a source of virus resistance in crop plants may lead to new viruses with potential to kill native plants.

Governments, research organizations and companies must respond to these concerns, and have in place the means to scientifically assess and report on the risks and the benefits to the environment of genetically modified crops, so that environmentally favorable decisions can be taken by regulatory authorities, farmers and consumers (Cook 2000).
Direct ecological effects of genetically modified plants in the environment

Cook (2000) reported on an approach to science-based risk assessment for plants intended for use in agricultural or other managed environments. In addressing the risks posed by the cultivation of plants in the environment, five environmentally related safety issues need to be considered (OECD 1993). These issues are the potential for:

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

Gene flow and transfer of traits to other species

Gene transfer is an issue when crops are being grown in areas close to their wild relatives with whom they are able to cross to form inter-specific hybrids. Natural hybridization occurs with 12 of the world’s 13 most important food crops and their wild relatives (the exception being banana (*Musa* spp.) since cultivated banana is infertile). Thus, the world’s major cereal crops (corn, wheat, barley, sorghum), oilseeds (rapeseed, soybean and peanut) and root and tuber crops (cassava and potato) can cross with their compatible wild relatives. Such wild relatives occur in the centers of origin of these crops (see map of the centers of origin of the world’s major food crops (Serageldin and Persley 2000)). Natural hybridization may occur at low frequency when pollen blows or is otherwise transported from crops to wild relatives in the vicinity (e.g. Rapeseed-*Brassica napus* - in Europe). Such gene flow and inter-specific crosses cannot occur in crops where their center of origin and closest wild relatives are on other continents. (e.g maize in Europe, since its center of origin is in Mexico).

Recent research confirms that genes introduced into some genetically modified crops will spread into related native species (Chevre et al 1997). This is not unexpected since genes have long been known to move from conventionally bred crops to wild relatives, at low frequency. For example, in the UK, such hybrids occasionally occur between oilseed rape (*Brassica napus*) and native species like wild turnip (*B. rapa*) (Raybould and Gray 1993).

The difference with gene movement from genetically modified crops is that genes inserted into GM crops are often derived from other phyla, conveying traits that have not been present in wild plant populations. The concern is that these genes may change the fitness and population dynamics of hybrids formed between native plants and related GM crops, eventually backcrossing new genes into the native species. The importance of pollen transfer from GM crops to wild relatives is not that it occurs but whether the resulting hybrids survive and reproduce and introgress genes back into the native population. Published studies on the gene transfer issue are dominated by rapeseed (Wolfenberger and Phifer 2000).
The issue is not so much the rate of gene flow (on which there has been much research), rather the impact that this might have on agriculture and the environment (on which there has been very little research). Conventional plant breeding, using techniques such as mutagenesis and embryo rescue, also produces new genes in crops, about which we also know very little of their behavior in the wild (Johnson 2000).

Genetic modification of native species: There is some experimentation on genetic modification of native species (e.g., Eucalyptus in Australia). These developments greatly increase the risks of gene transfer because the genetically modified native organisms will be completely cross-fertile with native species. There is also a risk that genetically modified varieties of native plants would be ecologically fitter than native species and able to colonize natural ecosystems with unpredictable results (Johnson 2000).

Weediness

There are risks that GM plants could have negative impacts on natural ecosystems by increasing weedy possibilities by two routes. Firstly, the GM plants could establish self-sustaining populations outside cultivation themselves. The concern is these plants may become invasive weeds that outcompete wild populations and thus lead to further decreases in biodiversity in native plant habitats. Weeds having tolerance to a range of herbicides could also emerge (Johnson 2000).

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

Transfer of certain genes, such as resistance to insects, fungi and viruses may increase fitness (ability to reproduce) of any resulting hybrids. For example, if hybrids acquired insect resistance from GM crops, they could damage food chains dependent on insects feeding on previously nontoxic wild plants. Not only would there be a direct effect, for many insects are entirely dependent on single plant species, but acquisition of resistance in wild plants would probably change their population dynamics, increasing the risks of them invading agricultural land and natural ecosystems (Johnson 2000).

Some geneticists would argue that most "foreign" genes introduced accidentally from GM crops to crop/native plant hybrids would decrease their fitness in the wild, leading to rapid selection of these genes out of the population. A recently published, ten year study by Imperial College, London on the fitness of genetically modified plant to survive in the wild supports this hypothesis. Genetically modified maize, rapeseed and sugar beet (all with herbicide tolerance) and potato with insect resistance were compared with conventionally bred crops. All four GM crops were out-competed by their conventionally bred relatives (Crawley et al 2001). Thus the genetic modifications in these species for herbicide tolerance and insect resistance made them less competitive and less fit to survive in the wild, in this experiment. In general, plant breeding tends to reduce rather than increase the weediness characteristics of crop plants (Cook 2000).

Trait effects

Trait effects are the effects of traits that may be harmful to non-target organisms. For example, plants modified to produce pesticidal proteins such as Bt toxins may have both direct and indirect effects on populations of non-target species. One group of Bt toxins primarily targets Lepidoptera (butterflies and moths, particularly the European corn borer) and the other affects Coleoptera
(beetles). The effects of Bt toxin-producing plants on non-pest species amongst these insect groups may vary widely, depending on the sensitivity of different insect species, the concentration of Bt toxin in the transgenic plants and environmental conditions.

Laboratory experiments demonstrated that the larvae of Monarch butterflies (a relative of the European corn borer) were susceptible to pollen from Bt corn when ingested in large amounts (Losey et al 1999). The actual ecological significance of this laboratory experiment is not clear. Subsequent field experiments in several locations in North America, found that there were no significant differences between Monarch butterfly survival in areas planted with Bt corn and those planted with conventional crops (Henderson 2000).

In assessing trait effects, and their impact on non-target species, it is important to compare the potential risks of genetically modified crops with the effects of present agricultural practices, including chemical pesticide use, on non-target species.

**Genetic and phenotypic variability**

This is the tendency of a plant to exhibit unexpected (pleotropic) characteristics in addition to the expected characteristics. This trait is well known from conventional breeding, but becomes an identifiable hazard if the variability leads to one of the other safety issues, such as greater weediness or greater tendency for outcrossing.

**Expression of genetic material from pathogens**

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

**Indirect environmental effects of genetically modified plants**

**Genetically modified crops and agricultural intensification**

The management of some genetically modified crops is likely to be very different from conventional intensive agriculture or organic farming. For example, in the United States, genetically modified, herbicide tolerant crops are grown under a regime of broad-spectrum herbicides applied during the growing season. Farmers report almost total weed elimination from such crops, which include cotton, soybean, maize, sugar beet, and oilseed rape. Recent research in the United Kingdom confirms that weed control in genetically modified sugar beet is likely to become much more efficient (Read and Bush 1998).

This weed control system, based on introducing genes for herbicide tolerance into crops, will soon be available, at least experimentally, for many agricultural crops, including vegetables. Broad-spectrum herbicides used on commercial scale genetically modified crops during the growing season may be far more damaging to farmland ecosystems than the selective herbicides they might replace. Using these herbicides in the growing season may also increase the impact of spray drift onto marginal habitats and watercourses. It is not the volume of herbicides that is the issue but their efficiency and impact on wildlife. When insect resistance and herbicide tolerance are combined in the same crop variety, there may be few insects capable of feeding on the crops and few invertebrates and birds would be able to exploit the weed-free fields (Johnson 2000).
The use of more effective pesticides (including herbicides) over the past 20 years has been a major cause of the decline in farmland birds, arable wild plants, and insects in several European countries (Johnson 2000). The more widespread use of broad-spectrum herbicides may accelerate this trend. This may be of more concern in Europe where farming, wild landscape and wildlife habitats are in closer proximity than in other areas such as North America and Australia.

Besides the aesthetic and scientific reasons for conserving biodiversity within and around agricultural crops, there is another important utilitarian reason for wanting to do so. There is a danger of losing the food chain links between native species and crop systems. This link is vital to preserve the function of biodiversity to deliver early warning of dangers in crops or the chemicals used to manage them.

On the other hand, there is evidence that the use of GM crops with insect resistance is reducing the volume and frequency of pesticide use on cotton, corn and soybean in North America (Wolfenbarger and Phifer 2000) and China (Prey 2000).

The future development of new crops with improved tolerance to abiotic factors (such as drought, salinity, frost) and the advent of ‘pharmed’ crops that may be used to produce vaccines and industrial products, may also change crop management practices. They may either increase or decrease demand for arable land in the long term. They may also put further pressure on natural biodiversity on marginal land.

The problem with assessing the environmental impact of these changes in crop management is that the regulatory system and the public have little scientific data on which to assess the risks, and potential benefits, from adopting new crop systems. In the United Kingdom, 27 field-scale experiments are in place to try to answer some of these important questions. Further research is required to help understand the ecological consequences of using GM crops. Data from such research can then be used by regulators to make more informed and publicly defensible decisions about whether GM crops should be commercialized, and under what conditions (Johnson 2000).

**New scientific developments**

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

- Securing fungal resistance in adult plants by switching on resistance genes that are active in the seed, but not currently in adult plants. This seems to be an elegant and safe use of biotechnology that could lead to significant reductions in fungicide use.
- Achieving insect resistance by altering physical characteristics of plants, perhaps by increasing hairiness or thickening the plant cuticle. This could reduce insecticide use, without using in-plant toxins.
- Altering the growing characteristics of crops, for example by shortening the growing season or changing the timing of harvests, offers the prospect of allowing more fallow land and less autumn planting. The recent discovery of dwarving genes could be a significant step towards the production of higher yielding and more reliable spring-sown cereals.
- Developing crops and trees that can tolerate high levels of natural herbivory yet remain viable.
- Preventing outcrossing by engineering pollen incompatibility and other mechanisms into crops. This could significantly reduce the risk of spread of novel traits into native species.
It is possible that some of these traits may be transferred from one crop variety to another or be accomplished by switching on or off genes already present in the plant. Such changes are likely to be more acceptable to the public than moving genes between phyla (Johnson 2000).

The new regulations governing genetically modified crops in Australia state that if a new crop variety is produced by moving one or more genes within a plant genus, it is not a transgenic crop, irrespective of the gene transfer techniques used, as such exchanges could occur in nature. If such new crop varieties do not contain any DNA from foreign species (e.g., as markers), they will not need to be regulated as genetically modified plants (Millis 2001).

The new developments in genomics, which is giving new insights into how genes function, offer a new range of options for how to use land. For the first time, it may be possible to design crops to suit the land and the purpose rather than having to adapt land and purpose to suit the crop. These could become important components of sustainable farming systems that combine yield increases with environmental sustainability. This is also important for developing countries where biotechnology may be able to offer new solutions to old problems of crop pests and disease in locally adapted crops, rather than trying to export conventional, chemically-based agriculture with its damaging effects on biodiversity and the wider environment.

There may also be scientific options that could be used in future generations of GM crops that would mitigate some of the ecological risks. For example, it may be possible to include in GM crop plants in-built mechanisms, such as pollen incompatibility, to prevent gene flow. Another means to ensure genetic isolation is to make sure that wherever possible plants used for genetic transformations are unrelated to native species and edible crops within the intended market territory. This principle would influence the choice of which crops to choose as platforms for biomedical and industrial product transformations, (e.g., higher starch production, vaccine production in plants). If gene technology is to become a standard technique for plant breeding, genetic isolation of crops from the rest of the living environment may become normal practice, as will the removal of marker genes for antibiotic resistance (Johnson 2000).

Environmental risk assessments

The US National Academy of Sciences (NAS 1987) released one of the earliest studies on the safety of GMOs in the environment. Its four conclusions were:

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

Subsequent studies by the US National Academy of Sciences, based on several thousand field trials conducted with GM crops in North America over the past decade, have led the NAS to reiterate these conclusions in more recent reports (NRC 1988, NRC 2000). They also stress the
continuing need for science-based risk assessments for plants that are intended for use in agricultural and other managed environments.

**Future ecological research**

There is an urgent need for ecological research and developing agreed standards and protocols to enable the continuing monitoring of the behavior of genetically modified crops after their experimental (small-scale) and commercial (large-scale) releases into the environment. Such data would then feed back into risk assessments, so as to inform future decisions on the development and management of genetically modified crops being developed for agricultural purposes.

There are concerns that the science needed to be able to assess these ecological risks is not being undertaken (Johnson 2000). There is clearly a need to set up effective monitoring systems to detect gene transfer and research to assess its ecological impacts. Research in this area would be in the interests of both the industry and the environment as it would yield data that would form a scientific basis for regulatory decisions.

A recent review of the scientific literature reveals that key experiments on both the environmental risks and benefits of genetically engineered plants are lacking (Wolfenbarger and Phifer 2000). The complexity of ecologically systems presents considerable challenges to designing experiments to assess such risk and benefits.

**Conclusion: Plurality of Views**

In assessing the potential impact of biotechnology, the interpretation of data is subject to the interests and value judgements of a variety of stakeholders. Identical information can lead some to consider agricultural biotechnolgies to be amongst the most powerful and promising means of ensuring future food security and generating additional wealth for presently disadvantaged nations, communities and individuals. Others perceive biotechnology as a threat to the wellbeing and livelihoods of people, countries and the environment in both industrial and developing countries. Differing realities and plurality of opinions coexist. The use of new biotechnology, particularly GMOs, offers a number of economic, social and environmental risks. Not all are a consequence of the technology per se. They arise from the particular social settings, transcending the nature of the technology employed within those settings.

There are also ethical issues involved in not pursuing the use of new technologies or in restricting access to new technologies that may contribute to improving the productivity and sustainability of agriculture, especially in emerging economies. The Nuffield Council on Bioethics (1999) concluded that there was a compelling moral imperative to enable emerging economies to evaluate the use of new biotechnologies as tools to combat hunger and poverty.

Creative dialogue amongst governments, the scientific community, the private sector and civil society could provide new ways for sharing and evaluating new technologies where they offer prospects for greater efficiency or precision, for solving specific problems that have not able to be addressed by traditional practices or by other technology options.
Selected Bibliography


