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# GENETICALLY MODIFIED PLANTS FOR FOOD USE

## Contents



## Summary

1. *Just as the food requirements of today's population of nearly 6 billion people could not have been met by the technologies of the 1940s, we cannot assume that current practices will feed the population of 8 billion expected by 2020. New approaches are needed in addition to the continued improvement of existing methods of crop and animal husbandry and food processing.*

2. *The advent of genetic modification over the last two decades has enabled plant breeders to develop new varieties of crops at a faster rate than was possible using traditional methods, with huge potential for further beneficial developments. Tobacco was the first plant to be genetically transformed, in 1983, with cereals beginning in 1990, but it is only recently that products such as GM soya have reached the market place in Europe and, for a variety of reasons, given rise to concern and controversy. The concern must be addressed seriously if society is to exploit the new technologies appropriately.*

3. *The Royal Society's Council appointed a group of experts to examine various aspects of the controversy, including the scientific evidence concerning the risk of transfer of genes from GM crop plants to wild species and non-GM crops, the uptake of genes from GM food by the digestive system and the current state of the regulatory system. The experts concluded that the chances of gene transfer happening are slight provided the regulatory processes are followed, but that this must be kept under consideration. These conclusions, and others, are discussed in detail in the main body of the report which is also available, free of charge, from the Science Advice Section at the Royal Society (Telephone 0171 451 2585 email: angela.halpin@royalsoc.ac.uk).*

4. *The uptake of genes via the food chain is not a new issue because genes (ie DNA) are normal constituents of the human diet. Many products from GM plants, such as sugar prepared from GM sugar beet, are absolutely identical to conventional products. Others such as GM tomato paste are so similar that they are regarded as 'substantially equivalent'. Others, for example flour from GM soya, may contain a new gene or its product, although many of the purification processes involved in food production will destroy any DNA present in the raw material.*

5. *Some GM foods have been produced using an antibiotic resistance 'marker' gene, which is a laboratory device designed to identify genetically transformed plants. The Society is concerned about the use of such genes in food products and we support the Government's advisory committees which concluded that any further increase in the use of such markers in the human or animal food chain would be undesirable.*

6. *The Society also has some concerns about the regulatory processes governing the development and use of GM crops and the lack of mechanisms for considering GM policy as a whole. The life history of a GMO crop plant starts with many years work in the laboratory. Once a potentially useful crop plant has been developed, a programme of field trials is essential to evaluate its performance. If the results of such trials are satisfactory, the next stage will be to market the product. European Union Directives tightly regulate the development, production, release and marketing of GM plants. In the UK these Directives are enforced by regulations which require that potential GM crop plants must be registered and assessed by several Government departments and independent advisory committees at each stage of the development process. A consent is required from the appropriate Secretary of State before crops may be released or marketed. Applications for a consent must include a*

*thorough risk assessment and the consent will only be granted on the advice of all the assessors.*

7. *GM crop plants have been produced to improve insect tolerance and virus resistance, and to include herbicide tolerance, so that other plants such as weeds may be eradicated without harming the crop species. To ensure that unwanted side-effects are not transferred to non-target species of plants and that the development of resistance by target pests is minimised, the regulatory authorities must be assured that (i) any negative effects would be no greater than those resulting from conventional procedures; (ii) any long-term effects on the environment and ecology would be closely monitored, with statutory restrictions in place to control marketing; and (iii) best practice advice was adopted by growers.*

8. *Although mechanisms are already in place to regulate many individual aspects of GM technology, there is no means for looking at GM technology as a whole. The Royal Society therefore urges Government to establish an independent overarching regulatory body to span departmental responsibilities, monitor the enforcement of existing or future regulations and strengthen the guidelines to growers of such crops, such as those specifying the isolation distances between GM and non-GM crops. The body should also review and monitor the membership of advisory committees and regulatory bodies.*

9. *The use of Genetically Modified Organisms (GMOs) has the potential to offer real benefits in agricultural practice, food quality, nutrition and health. There are, however, uncertainties about several aspects of GMOs. Continued research, funded in part from public sources with the results made openly available, is essential if these uncertainties are to be properly addressed, the risks understood and the full potential of the new technology made clear. All parties must appreciate the public's legitimate concerns: consumer confidence, based on an appreciation of the scientific evidence and the regulatory checks and balances, is central to whether GMOs will contribute to feeding the world's rapidly expanding population.*

# Genetically Modified Plants For Food Use

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## Introduction

The use of Genetically Modified Organisms (GMOs) in food may offer benefits in agricultural practices, food quality, nutrition and health, and we support ongoing research in this field. However, we recognise that it has aroused concern amongst some consumers, coming at the same time as other, unrelated, concerns about food safety, notably BSE and *E.coli* O157 food poisoning. It is important that such concerns are respected and information made available which will help consumers to make informed choices. The Royal Society therefore appointed a working group to review the use of GM plants in food. This document aims to explain what a GMO is, discuss the use of GM plants and their products in food and agriculture, identify some of the issues which have been of greatest concern, take a position on these issues and provide policy advice to regulators on how such problems may best be approached. The statement is not intended to cover ethical issues since these will be covered by the current consultation exercise being carried out by the Nuffield Foundation.

This summary document is intended for consideration by policy advisors as well as for a general readership and is also available from the Science Advice Section of the Royal Society (Telephone 0171 451 2585 email: angela.halpin@royalsoc.ac.uk).

## Outline

The advent of genetic modification has enabled plant breeders to develop new varieties of crops with a wide range of characteristics, at a faster rate than would be possible with traditional methods, and brings with it a huge potential for further beneficial developments (Section 1). However, the development of such new techniques raises several concerns which need to be addressed. The release and marketing of GM plants is strictly regulated in the UK at present (Section 2). However, each application to release or market a GMO is considered on a case by case basis and there is a case for having a mechanism for viewing the development of the technology, and any wide-ranging effects, as a whole.

Section 3 covers specific issues relating to transfer of genes from GM plants to other organisms and provides recommendations on areas in which further research is required and ways in which the current regulations may be amended. Issues regarding possible impacts on the ecosystem when GM crop plants are grown on a large scale in the environment are discussed in Section 4. We have specifically considered insect tolerant

crops (Section 4.1), herbicide tolerant crops (Section 4.2) and virus resistant crops (Section 4.3) since these are areas in which a majority of current research is underway.

Section 5 considers issues related to the use of GM plants in human and animal foodstuffs, which has been the focus of consumer concern. The current situation regarding labelling of food containing GMOs or their products is summarised in Section 5.1 and much greater detail provided in Annex VI. Annexes I-V provide details of the membership of the Government advisory committees and a short history of plant breeding.

## 1.What is genetic modification?

Plants have been cultivated by humans for thousands of years, during which time crop plants have been continually selected for improved yield, growth or food characteristics. The improvement of a plant species by conventional techniques involves the selection for breeding purposes of certain plants that express important characteristics. As a result of human intervention in selecting which plants to use for production of offspring, it is possible to produce new varieties at a much faster rate than would occur in the wild situation. Crop species have therefore been selected for a large number of different characteristics, resulting in a great number of varieties being produced to help feed the expanding World population[1]. In their search for new characteristics, particularly for genes conferring pest and disease resistance, plant breeders continue to seek novel sources of breeding materials to bypass the normal barriers to sexual crosses. For example, in their search for fungal resistance genes, sunflower breeders use a technique called embryo rescue[2]. Modern genetics offers an important additional source of such genes.

The characteristics of an organism are determined by its DNA (deoxyribonucleic acid) which is the information-containing component of the chromosome[3]. DNA provides the genetic code which determines how the individual cells, and consequently the whole organism, will be constructed. This code is divided up into functional units, or genes, in the same way that a paragraph can be divided into individual words. The total characteristics of a plant will depend on which genes it has received from the parent plants, whether or not those genes are 'switched on'(expressed) and also the interactions between the genes and environmental factors.

The advent of modern techniques of genetic modification has enabled researchers to remove individual genes from one species and insert them into another, without the need for sexual compatibility. Once the new gene has been inserted into a plant, offspring that will contain copies of the new gene can be produced in the traditional manner. For example, this has enabled researchers to insert a bacterial gene into a maize plant, to give it resistance to certain insect pests (specifically the European Corn Borer). Genetic modification has also made it possible to remove or switch off an undesirable gene already present in a particular variety, or modify the metabolism of the plant to improve the quality of the food product (for example, GM tomatoes which remain fresh for longer periods).

[1] Annex I gives a brief chronology of plant breeding.

[2] If crosses are performed between sunflowers that have greatly differing genetic makeups, the pollen will fertilise the receiving plant but the resulting embryo will abort before a seed is produced. In embryo rescue, the embryo is removed before abortion occurs and grown outside the parent plant to produce a new plant. to enable crosses to be made between sunflower species which would not normally be sexually compatible.

[3] Chromosome - rod-like structure within the cell which plays an important role in passing on genetic information to the offspring.

## 2. Is genetic modification regulated?

In the EU the production, release and marketing of genetically modified plants is very tightly regulated by two Directives (Directives 90/220/EEC (covering release and marketing) and 90/219/EEC (covering use in containment). Each Member State has to implement these Directives by individual regulations.

Initial work to develop a new GM crop plant starts in the laboratory with transfer of individual genes. In the UK, each laboratory involved in genetic modification must be registered under the Genetically Modified Organisms (Contained Use) Regulations 1992 (as amended 1996 and 1998). Registration involves submitting a notification to the Health and Safety Executive describing the work to be carried out. Under the regulations, each centre carrying out genetic modification must have a Genetic Modification Safety Committee to advise on and review notifications. Once submitted, each notification is reviewed by the Health and Safety Executive and other Government departments (including the Department of the Environment, Transport and the Regions (DETR), the Ministry of Agriculture, Fisheries and Food (MAFF), the Department of Health (DH), the Scottish Office (SO) and the Welsh Office (WO) as appropriate). An independent advisory committee, the Advisory Committee on Genetic Modification (ACGM), may also be consulted[4]. Laboratories carrying out genetic modification work are regularly inspected by HSE specialist Inspectors to ensure compliance with the regulations.

Once a potentially useful variety of GM crop plant has been produced in the laboratory, the next stage is to move to small-scale field trials to monitor how the crop performs in an agricultural situation and address any questions regarding potential risks. In the UK, GMOs may not be released into the environment unless they have received a consent under the Genetically Modified Organisms (Deliberate Release) Regulations 1992 (as amended 1995 and 1997). Applications for consent must describe the GMO, and give details of the proposed release, and must contain a full risk assessment. Applications are submitted to the Department of the Environment, Transport and the Regions (DETR), and reviewed by DETR and other Government departments (including HSE, MAFF, DH, SO, WO, etc). Each application is also reviewed by another independent committee of experts, the Advisory Committee on Releases to the Environment (ACRE)[5]. Applications to release GMOs are reviewed within a statutory 90 day period. However, certain GM plants of designated low risk or applications that are a repeat of previous field trials, are eligible for a 30 day 'fast-track' review procedure. Trial sites of GM crops are regularly inspected by HSE Specialist Inspectors who are responsible for enforcement of the legislation.

Once field testing has been completed, the next stage is to submit an application to market the GM plant variety. Applications to market GM plants for growth by farmers in the EU are first submitted to a single Member State which reviews the application under its own legislation. For example, if a company submits an application to market a GM crop plant to the UK authorities, it is reviewed under the Genetically Modified Organisms (Deliberate Release) Regulations by government departments and ACRE. If the Member State concludes that a consent to market the product should be granted, the application is sent to all other Member States (via the European Commission), who will also review it and give their opinion on whether a consent should be granted. If there is a majority opinion recommending that the product be marketed, a consent is granted by the Member State to which the original application was submitted, to allow marketing in the EU as a whole.

[4] See Annex II for membership of ACGM.
[5] See Annex III for membership of ACRE.

Once a marketing consent has been granted there may also be additional regulatory procedures in individual Member States governing, for example, use of pesticides or plant variety registration.

Applications to market GM plants, or their products, for use as foodstuffs are governed by The Novel Food Regulations 1997. In the UK, applications are submitted to the Ministry of Agriculture, Fisheries and Food and are reviewed by other Government departments in conjunction with a third independent advisory committee, the Advisory Committee on Novel Foods and Processes (ACNFP). Advice on food labelling is provided by the Food Advisory Committee (FAC) and advice on toxicology from the Committee on Toxicology (COT)[6]. Again, if a Member State is satisfied that a marketing consent should be issued, the application is circulated to all Member States of the EU for review. If a consent to market a GM food is issued it will therefore be valid across the EU. It is interesting to note that several countries in the EU have unilaterally banned the import of specific GM products already granted EU-wide approval. This highlights the importance of harmonising the approach to this technology across Europe.

Although genetic modification and the release of GMOs are tightly regulated in the UK, concerns have been expressed that there is no over-arching body to monitor the impact of GM crops on agronomic practices or to look at the cumulative effects of such crops, since applications are reviewed on a case by case basis. In 1994 the BBSRC held a Consensus Conference on plant biotechnology at which a cross-section of lay persons considered the implications of these technologies. We agree with the recommendation of the panel that the regulatory authorities should address the wider issues surrounding the introduction of GM commodity crops by putting in place a monitoring mechanism or over-arching organisation, and urge the Government not to delay further in taking action in this direction. A majority of the issues we raise in this document would lend themselves to consideration by such a body, which would benefit from a wider perspective than is currently available to regulators dealing with individual cases. We acknowledge that many of the concerns raised cannot be addressed without the information gained from long-term small-scale field trials and laboratory work. In particular, the over-arching body should consider the enforcement of the regulations and review the membership of the associated Governmental advisory committees on a regular basis.

## 3. Will genes transfer from GM plants?

*3.1 Transfer of genes from GM crop plants to wild plant species*

Crop systems can be divided into three groups with respect to the possibility of natural transfer of genes from genetically modified (GM) crop plants to wild relatives:

- No sexually compatible wild relatives in the region where the crop is grown, therefore no gene transfer to other species can occur (e.g. GM maize or potatoes grown in the UK)
- Gene transfer unlikely due to the nature of the crop species (eg. Rice and Soya which are inbreeding species)[7]
- Gene transfer likely (e.g. Oilseed rape which is an outbreeding[8] species and has many wild relatives in the UK)

[6] See Annexes IV and V for membership of ACNFP and FAC.
[7] Inbreeding - crosses only occur between closely related parent plants.
[8] Outbreeding - crosses occur between distantly related parent plants.

The likelihood of gene transfer to wild relatives therefore depends on the species of crop and the location in which the crop will be grown. For example, relatives of oilseed rape can be found growing near crops in the UK, whereas cereal relatives are rare. It may therefore be necessary to take special measures with the former.

However, there are several steps involved in gene transfer: the pollen must contain a copy of the inserted gene(s); it must then move away from the area in which the crop plant is grown and come into contact with the part of a compatible plant that receives pollen; if fertilisation occurs successfully, it may not always result in a plant able to grow successfully, or if a plant is produced then it may not compete well with other species in the environment. In addition, if the resulting plant produces pollen that goes on to fertilise other plants, then the inserted gene(s) will become increasingly diluted in the overall population if there is no selective advantage for the plants that contain it. It is inevitable that some gene transfer will occur from certain crops, but the level of gene transfer to wild relatives from GM crops is likely to be exactly the same as from non-GM crops.

If gene transfer is judged to be likely, then it is important to assess what the consequences will be. This will depend on whether the inserted genes are likely to have a deleterious or advantageous effect as a result of expression in the plant to which they are transferred, if expressed in the wild species. The fate of crosses between crop species and wild relatives will be largely crop dependent. In general cultivated crop species or 'escapees' will not be competitive in the wild. Indeed, most crosses between different species will produce sterile hybrids. Hybrids[9] produced from crosses between most crops and wild relatives are unlikely to survive many generations, with the exception of oilseed rape which exists as wild populations in the UK. It is also notable that disease and pest resistant crops have been available for many years as a result of conventional breeding techniques, and we are not aware of any reported problems as a result of transfer of such traits.

Nevertheless, we recommend that the over-arching body referred to above should address the question of transfer of genes between crops (whether GM or non-GM) and sexually compatible species, in particular genes which may be associated with a strong selective pressure in some environments. We recognise the difficulties associated with monitoring such transfer, but we suggest that methods of doing so be evaluated by the relevant body or a working group set up for the purpose. Experiments to monitor such transfer could be carried out using molecular markers that are unique to a particular species rather than using GM crops, if necessary.

*3.2 Transfer of genes from GM crops to non-GM crops*

As with the transfer of genes to wild plant species, the likelihood of transfer to non-GM crops will depend on the biology of the crop species and the location in which it is grown. The chance of transfer from a GM crop species to a non-GM member of the same species is increased if the crops are adjacent. Transfer may also be possible between crops: for example, wheat can occasionally be pollinated by rye[10]. However, cross-pollination of a

[9] Hybrids are the result of crosses from two genetically distinct parents. Hybrids are often more vigorous and higher yielding than either of the parents. A hybrid contains one copy of each of the parents' chromosomes. Hybrid seed is not usually replanted because in the next generation the chromosomes will be inherited unevenly and the effects in the resulting crop may be difficult to predict. Overall, second generation seed from a hybrid will be non-uniform and much lower yielding.

[10] Rye is very unlikely to hybridise with European wheats, but can hybridise with more primitive wheat species. Hybrids are almost always sexually sterile, but a very small proportion can sometimes be female fertile.

hybrid crop is unlikely to be a problem for seed production since such crops are not used to produce seed for the next crop (see Footnote 9), so any acquired genes will not be deliberately propagated, although some movement of seed from the release site via birds or animals is inevitable. However, if two herbicide tolerant varieties crossed, the resulting seeds may be tolerant to both herbicides. This could have an impact on the control of volunteer plants[11] in the next crop or in set aside land. There will therefore be a need to assess the consequences of any potential transfer.

Inserted genes may have potentially harmful effects if transferred to other crop plants. For example, genes for production of vaccines or pharmaceutical products in food plants should be prevented from entering the general food chain, by molecular methods (such as prevention of pollen formation) or by growing the crop at an isolation distance that minimises pollen transfer. This is normal practice for plant breeders and farmers who must enforce strict isolation distances when producing certified seed for sale. Also, for example, oilseed rape is grown for human consumption with low levels of erucic acid. Industrial oilseed rape produces high levels of erucic acid, which is toxic to humans. High erucic acid oilseed rape is therefore grown at suitable isolation distances from edible rape varieties[12].

Transfer of genes from GM crops to non-GM crops may also have an unwanted effect if the latter are grown organically. If the award of organic certification depends on the grower being able to guarantee that no inserted genes are present, then problems will arise if the crop has been grown in fields adjacent to a GM crop. Crops able to outbreed, such as maize or oilseed rape, will be affected to the greatest extent. It may be that the only way of resolving this problem is to introduce guidelines for minimum isolation distances between crops and an agreement on the level of acceptable gene transfer below which products can be labelled as not containing GM material. For example, guidelines issued recently by Austrian organic farmers and retailers state that if greater than 0.1% of the total weight of the product consists of protein encoded by "foreign" genes it may not be labelled as 'GM free'. However, such guidelines rely on the availability of suitably accurate and officially recognised methods of analysis.

We recommend that, as part of their investigation into gene transfer from GM crops to non-GM crops, any over-arching body or organisation should consider strengthening any existing guidelines on isolation distance in an analogous way to the guidelines issued for purity of seed stocks or isolation of oilseed rape.

*3.3 Ways to minimise or prevent gene transfer*

In addition to isolation of the crop from other crops, there are currently three alternative approaches to minimisation of gene transfer. We recommend that any over-arching body or organisation investigates the need for further work to be carried out on methods to minimise gene transfer from crops with inserted genes which may be problematic if transferred.

[11] Volunteer plant - plants that grow in a field in the year after the original crop was grown as a result of seed being shed from the crop and remaining dormant in the soil for some time. Some volunteer plants may germinate several years after the original seed was shed.

[12] The Essex Seed Zoning Committee, representing growers and seed traders, produces guidelines for the isolation of high erucic acid oilseed rape from conventional rape (amongst other isolation guidelines). A distance of 600 metres must be maintained between the two crops and the Committee is empowered to request the Minister to enforce this isolation distance (Protection of Seed Crops (North Essex) Order 1968).

As mentioned earlier, gene transfer from crops that are hybrids may not be a problem because such seed is not propagated in the next generation and the farmer buys new hybrid seed each year. More and more crops are now grown from hybrid seed so this provides an in-built protection against crop to crop gene transfer, which is relevant to purity of seed stocks. Currently maize, sorghum, sugar beet, and sunflower are hybrid crops. Oilseed rape hybrids are under development and breeders are still evaluating the potential of wheat, rice and cotton hybrids.

Inserted genes, or 'transgenes', can be introduced into the chromosomes of the plant cells or, with greater difficulty, into the additional genetic material that is contained in other parts of the plant cell such as the chloroplasts[13]. The advantage of insertion into the chloroplasts is that the genes may not be transferred by the pollen, as the chloroplasts may be excluded during fertilisation. This approach may consequently be preferable if there is a desire to prevent gene transfer by pollen, for example when inserting genes for tolerance to certain herbicides or production of pharmaceutical compounds. However, this technology is still in its infancy and is unlikely to be effective for all genes. It is not effective in certain species in which chloroplasts are transferred between generations by pollen (biparental chloroplast transformation). In addition, herbicide tolerant crops may produce hybrids by pollination by weed species. Hybrid seeds may then be disseminated by birds or animals.

A second approach that may minimise gene transfer would be to link the inserted genes to genes conferring sterility by switching off pollen production. Alternatively another molecular method called, 'terminator technology' may be used. Terminator technology refers to a genetic manipulation technology described in a recent US patent by which the seeds of GM crop varieties can be prevented from germinating. In agriculture, this would mean that farmers would have to buy new seed each year. It is possible that, in time, this type of technology could be adopted by all the major seed breeding companies. Concerns have been raised that this would severely disadvantage farmers wishing to store seed for future use. However, in developed countries, saved seed may soon be liable to royalties. In addition, farmers are free to choose which variety to grow depending on relative advantages and disadvantages.

Farmers in developing countries have expressed concern regarding terminator technology for the same reason, although Breeding Centres, such as the International Rice Research Centre in the Phillipines, could continue to produce conventionally bred varieties which could compete directly with GM varieties incorporating terminator technology. Although there may be obvious advantages to developing countries in GM crops in general, (such as drought tolerance, increased yields, or ability to exploit poor soils), there are also general concerns regarding intellectual property rights, financing and the necessity for adequate regulatory mechanisms.

### *3.4 Uptake of genes via the food chain*

One of the concerns associated with the introduction into the diet of foods and ingredients derived from, or produced with the aid of, genetically modified plants is the possibility that the genes from such plants may be taken up by consumers when eaten, and become part of their own genetic makeup. It is worth remembering that the medical profession have been trying to develop ways to insert genes into the body cells of humans for some time, with so far rather limited success. We are not aware of any evidence for transfer of intact genes to

[13] Chloroplast - photosynthetic compartment within the cell which contains its own DNA and in which energy is produced.

humans, either from bacteria in the gut, or from foodstuffs such as potatoes, wheat or chickens, despite daily consumption of DNA in the diet. We are aware that MAFF are attempting to address this issue with further research, although we recognise the inherent difficulties with such studies.

Experiments have shown that DNA remaining after digestion consists of very small fragments and have failed to show survival of intact DNA in stools or blood of animals fed with large quantities of DNA. There is no reason to suppose that DNA in GM plants would behave differently. For DNA to have any effect, any fragments would need to be of sufficient size to contain a whole gene and these experiments showed that such fragments are too small to contain intact animal or plant genes. In addition to the necessity for fragments of a sufficient size, a body cell would have to take up the DNA in question and integrate it into its own genetic material. Also, the acquired gene must have the ability to be switched on in the animal cell (genes from bacteria are not switched on if transferred to an animal cell).

It is also important to distinguish between foodstuffs that actually contain the genetically modified material (e.g. fresh GM tomatoes), foodstuffs in which the DNA has been degraded by processing (e.g. tomato paste from GM tomatoes), and foodstuffs that contain the products of genetically modified organisms but not the original gene (e.g. cheese made with enzymes manufactured by GM micro-organisms). Foods that contain ingredients derived from GM plants, such as oils and sugars, will not contain genetic material from those organisms as the product is highly purified and processed before addition to the food. It should be noted, however, that foods produced from GM micro-organisms such as vitamins or supplements should be subject to the same quality control measures as those produced by traditional methods. This was highlighted in the production of the amino acid tryptophan (used as a dietary supplement) by GM bacteria. Owing to relaxation of quality assurance measures the resulting product contained impurities which were toxic to humans.

*3.5 Antibiotic Resistance Genes in GM food*

When researchers wish to insert a new gene into a plant, for example to express a protein that will make the plant resistant to a specific insect pest, it is often linked to another gene known as a 'marker gene'. During the late 1980s, genes for resistance to a range of antibiotics were introduced as markers for selection. The marker genes are used to make it easier to select in the laboratory the cells, and subsequently the plants, in which the genes have been successfully inserted. Plants that contain a gene for resistance to an antibiotic will grow on material that contains that antibiotic, whereas if the genes have not been successfully inserted the plants will not grow. Because the 'marker gene' is linked to the other gene, those plants that have grown on the antibiotic will also contain the gene for resistance to the insect pest. The most commonly used antibiotic resistance marker genes in GM plants confer resistance for such purposes to kanamycin or hygromycin. In GM bacteria, ampicillin resistance marker genes are more often used.

The use of antibiotic resistance as a marker for selection in GM plants for human or animal consumption has resulted in the fear that these genes may be transferred into the bacteria present in the stomach of the consumer. If this were to happen then the genes might be transferred from these bacteria into bacteria that cause disease in humans, making them resistant to the antibiotics that are usually prescribed. It is likely that if transfer occurs, it would only occur following consumption of the unprocessed GM plant, since processing of food causes DNA present in the food to be degraded. Further research is necessary to determine whether such gene transfer could occur, and to what extent. However, it should be noted that the widespread use of antibiotics as feed additives for animals, and as over-

the-counter and prescribed medicines for humans, carries a greater risk of creating antibiotic resistant bacteria than transfer of marker genes from GM plants and alternative strategies should be sought. Indeed, a large number of bacteria present in the gut already carry resistance to several antibiotics, including kanamycin and ampicillin. Nevertheless, we support the Government's advisory committee, the ACNFP, which has concluded that any further increase, however small, in the number of resistant micro-organisms through the transfer of markers from GM food would be undesirable.

Although the insertion of 'marker genes' is a necessary part of the selection process, it should be emphasised that it is possible (although time consuming) to remove such genes later. In addition, recent developments have made it possible to use alternative marker systems that do not utilise antibiotic resistance. We believe that it is important to encourage further research into alternatives to antibiotic resistance marker genes and that it is no longer acceptable to have antibiotic resistance genes present in a new GM crop under development for potential use in foodstuffs. In particular, researchers in both academia and industry, should not produce GM plants containing genes that confer resistance to those antibiotics that are used to treat infections in animals or humans. The Government's advisory committees on GM crops (ACRE and ACNFP) have both made recommendations to this effect.

## 4. Will GM crops harm the environment?

### *4.1 Insect tolerant crops*

To date, all commercially-released insect-tolerant GM crops express toxins derived from the bacterium *Bacillus thuringiensis* (Bt), which are toxic to insects but not humans and provide a very high level of protection against specific insect pests. In addition, an increasing number of other genes are being transferred experimentally into crop varieties, in particular ones encoding plant proteins (e.g. lectins and inhibitors of insect digestive enzymes). At present, most insect tolerance genes incorporated into GM plants are continuously switched on and expressed in most parts of the plant.

Aside from its commercial prospects, the development of insect-tolerant plants offers numerous potential benefits to agriculture. Such crops could dramatically reduce the use of conventional, wide-acting, insecticides in some cropping systems, as well as overcome the dependence of pest control on factors such as weather and the efficiency of traditional application methods. However, this area of biotechnology does also introduce risks, especially those of unwanted side-effects to non-target species, and of pests adapting rapidly to become resistant to engineered insecticidal toxins.

#### 4.1.1 Effects on non-target species

Many crops are home to a range of insect parasitoids[14] and predatory arthropods[15] that often play an important role in the regulation of pest insects. The most obvious way that GM crops can affect these natural enemies is by severely depleting the supply of prey or hosts. Such effects will be most profound for natural enemies that live exclusively on insects which the GM crop is designed to kill (e.g. European Corn Borer on GM maize). However, this also applies to all pest control measures and is by no means unique to insect-tolerant GM plants.

[14] Insect parasitoid - species whose larvae develop on, or inside, individuals of other insect species, leading to the death of the host.

[15] Predatory arthropod -free-living insect or mite that feeds on other species, including pest insects.

More subtle effects on the survival, reproduction and/or behaviour of beneficial species are possible, and may require sophisticated experimentation to detect and interpret. The majority of field and laboratory studies conducted to date have not disclosed any significant, adverse impact of Gm crops on the abundance or performance of a range of parasitoids and predators including lacewings, ladybirds and damsel bugs. However, one report of reduced survival of lacewings (*Chrysopa carnea*) fed on prey reared on GM maize (containing a toxin gene from *Bacillus thuringiensis*), and one of reduced fertility of ladybirds fed on aphids reared on potatoes expressing a lectin gene, highlight the importance of continued work on this topic. Indeed, the evaluation of side-effects on non-target organisms such as these is now a mandatory part of most approval schemes for insect-tolerant GM crops. To retain a balanced perspective, it is essential that any negative effects identified are judged in relation to those of the conventional insecticides that these crops are intended partly to replace.

Another concern is the effect of GM crops on insect pollinators such as bumblebees and honeybees. Since proteins are very unlikely to occur in nectar, the main risk of exposure is through expression of toxins in pollen, which depends on the promoter[16] used and varies between GM varieties. Toxins from *Bacillus thuringiensis* have so far shown no adverse effects against bees, but further studies are underway. Proteinase inhibitors have been shown to affect bee behaviour, but only at far higher concentrations than are likely to be encountered in practice.

### *4.1.2 Pest resistance to insect-tolerant GM crops*

The ability of pests to evolve resistance to crop protection agents has been a long-standing problem with conventional insecticides, and without proper management there is no reason to assume that this problem will not be repeated for GM crops. At present, most attention is focused on pests that have historically developed resistance most readily, including heliothine bollworms on cotton and Colorado beetle on potatoes. However, even species that have so far appeared less prone to resistance (e.g. cornborers on maize) could constitute a threat under extended exposure to GM plants.

The simplest and probably most effective way to reduce the selection pressure for resistance of target insects to GM plants is to provide refuges in which susceptible individuals survive and reproduce. This would also be one way of maintaining biodiversity by allowing survival of a greater variety of species. Such refuges can be created deliberately (e.g. by providing areas of non-GM crops) or may arise through the availability of alternative hosts. Management of refuges is also an important consideration; those treated with conventional insecticides need to be considerably larger than ones left entirely unmanaged, in order to have the required dilution effect.

The level at which toxins are produced in plant tissues could, in principle at least, be adjusted to combat resistance development. Lowering expression to allow even a relatively small proportion (10-20%) of target insects to survive exposure could assist with delaying resistance, although the resulting loss of efficacy may necessitate other control measures, and could reinstate a need for insecticide sprays. There is also a threat of environmental influences on gene expression being more pronounced when aiming for moderate rather than complete kill of pests. Indeed, there is stronger theoretical support for raising expression levels as far as toxicological and environmental considerations permit, in the

[16] Promoter - DNA sequence which receives specialised proteins which bind and switch on a gene.

hope of killing heterozygous resistant insects[17] as well as fully susceptible ones. The effectiveness of this tactic depends on genes for resistance still being rare in the pest population, and on the provision of refuges generating susceptible insects to mate with any resistant ones that do survive on the GM plant.

Other possible approaches to contending with resistance to GM crops entail moderating exposure through time- or tissue-specific expression of toxin genes, alternating between varieties expressing different toxins, or the stacking (or pyramiding) of more than one toxin gene in the same plant (ensuring that pest insects are exposed to several mechanisms of toxicity simultaneously). All are limited at present by technical difficulties and/or lack of alternative toxins as effective as those derived from *Bacillus thuringiensis*.

In summary, large-scale use of insect-tolerant GM plants can pose a significant risk of resistance development by target pests and unforeseen effects on non-target organisms. Anticipating this risk and developing effective countermeasures (e.g. the use of refuges) requires a sound knowledge of the biology of target pests, and we recommend that the regulatory authorities consider making this a compulsory consideration prior to commercial release. In addition, regular monitoring of the responses of pests to GM crops is vital to detect incipient resistance problems as quickly as possible. To minimise such effects, it may also be necessary to introduce statutory restrictions on the marketing of such crops as has already been done in other countries.

### *4.2 Herbicide Tolerant Crops*

Advances in genetics have enabled plant breeders to develop crop varieties that are tolerant to a specific herbicide or group of herbicides which cannot normally be used on those crops. This can be achieved by the utilisation of traditional breeding and selection techniques, or by the use of genetic modification. Although these new GM crops are not yet commercially grown in the UK, the majority of applications for field releases and marketing of GM crops have been for herbicide tolerant crops, specifically those with tolerance to herbicides containing the chemicals glyphosate or glufosinate ammonium (for example Roundup® and Basta®). Insertion of such genes allows the crops in question to be sprayed with a broad-acting herbicide so that weeds can be destroyed without harming the crop species (such herbicides would normally kill the crop as well as the weeds). The companies marketing such GM crops claim that they result in use of less herbicide and altered agronomic practices, producing increased yields for the growers and environmental benefits.

#### *4.2.1 Transfer of genes to wild relatives*

One concern which has been raised with regard to such crops is that the genes will transfer to wild relatives of the crop species and produce weed species resistant to herbicides and therefore more difficult to control. The more extreme possibility is that transgenes from several herbicide tolerant varieties could be concentrated in one weed species and create a 'superweed' that is resistant to several herbicides. This concern is not specifically related to GM crops, as agriculture has been developing herbicide tolerant crops for several years by traditional breeding.

[17] Heterozygous insects contain only one copy of a resistance gene and are generally more susceptible than resistant homozygous individuals which contain two copies. When resistance is rare, resistant homozygous individuals are rare owing to crossing of resistant and non-resistant insects producing heterozygous individuals. Killing heterozygotes can therefore slow down the build-up of resistance in pest populations.

As already mentioned, extensive field trials in the UK and elsewhere have indicated that the likelihood of genes from GM crops spreading into the non-farm environment is no different from that of the conventional crops from which they are derived. While cross-pollination and outcrossing is to some extent inevitable, the significance of it depends on the crop species being used, and the types of wild plants which surround the growing area.

The development of herbicide tolerant crops by traditional methods does not appear to have been accompanied by an increase in problems due to herbicide tolerant weed species. In addition, if weed species were to become more resistant to glyphosate or glufosinate ammonium herbicides it should be remembered that there are alternative, more selective herbicides available. Control of weeds resistant to herbicides is therefore an issue for effective agricultural management and crop rotation, and it is important that sufficient guidelines are available to provide advice to growers on best practise for growth of GM crops. Nevertheless, such guidelines may not always be observed and this should be taken into consideration by policy makers.

*4.2.2 Transfer of genes to non-GM crops*

There is also concern that herbicide tolerance genes will be transferred to non-GM crops, or to other GM crops. This could result in the formation of herbicide tolerant 'volunteer' plants (see footnote 11) in follow-on crops. Alternatively GM crops that are resistant to several herbicides may be created that may also cause a 'volunteer' problem. However, studies have shown that volunteers of GM oilseed rape are no greater problem than non-modified crops, since alternative herbicides are available for use.

Again, this is an issue that should be dealt with by appropriate agricultural management and it is important that guidelines for use of herbicide tolerant crops are provided to growers. Such guidelines should specify crop separation distances for each GM crop to reduce the likelihood of cross-pollination occurring. The likelihood of multiple herbicide tolerance arising from transfer of several genes is considered to be small. However, crop rotation proposals in growers' guidelines should define appropriate crop rotation strategies. We recommend that any over-arching body or organisation analyse such guidelines and consider whether it would be beneficial to make the provision of guidelines to growers an obligatory feature of sale.

*4.2.3 Will the use of the herbicide affect other plants and animals?*

The field environment is not a 'natural' system as the habitat is already highly controlled irrespective of the use of herbicide tolerant crops. The use of land for crop production whether non-GM or GM crops, will lead to what is essentially a monoculture, with many plant and animal species existing at much lower levels than would be the case without cultivation. Wildlife biodiversity is partly influenced by improved control of pests, diseases and weeds in the agricultural environment. If there has been a decrease in biodiversity in recent years, as indicated by recent studies, this is likely to be a feature of current agricultural practices. It is therefore important to ask how GM crops will influence such practices.

GM crops may result in reduced use of agrochemicals which may be beneficial to the environment. However, the major suggested adverse environmental effects of the use of herbicide tolerant crops derive from more effective destruction of weeds. This is likely to reduce the availability of habitats for various insects and other invertebrates. It would also

have effects on the organisms that are associated with the root systems of weed species. In turn, this may have an effect on the availability of food for predators that feed on them. It may be possible to incorporate features to minimise such environmental effects in guidelines issued to growers of herbicide tolerant crops. For example, herbicide spraying of headlands, hedgerow bottoms, and field margins could be precluded. Advisory bodies should consider whether such guidelines should be obligatory. However, it should be noted that licensing of herbicides in the UK includes a review of their potential environmental impact. In addition, there is a monitoring programme in place to assess overall use of herbicides. We recommend that this organisation liaises closely with any over-arching body investigating wider issues associated with GM crops.

As GM herbicide tolerant crops have only been grown commercially since 1995 (in the US and Canada but not at all in the UK to date) there are insufficient research data relating to possible effects on the field environment. A detailed programme of post-release monitoring of environmental impact should be a requirement of all releases of GM herbicide tolerant crops. It may be necessary for such monitoring to be carried out by an independent body or organisation on behalf of the company or companies marketing the crop. It will also be highly desirable to have separate scientific studies of specific topics, such as the effect of herbicide tolerant crops on numbers and variety of species of nematodes or bacteria; population structures of insects; and numbers of birds and animals. It should also be noted, however, that there have been herbicide tolerant non-GM crops on the market for several years which were produced by traditional breeding methods. So far as we are aware, there has been no systematic monitoring of the ecological effects of such crops, therefore any further research should consider the effects of both GM and non-GM herbicide tolerant crops. It may be necessary to set up a working group to draw up protocols for post-release monitoring so that adequate monitoring is ensured. It is also important that any monitoring compares results with those obtained from current agricultural practice to give a realistic baseline.

*4.3 Virus resistant crops*

Virus resistance was one of the first targets for genetic modification of crops as plant viruses have a relatively simple genetic makeup, the function of which is reasonably well understood. There have now been several releases of GM virus resistant crops. Three basic types of genes are used in such plants. The most common method is to use viral DNA sequences themselves which, when inserted into plants and expressed, interfere with the infecting virus to give what is called 'pathogen-derived protection'[18].The second type of anti-viral GM plant utilises genes from various sources that express anti-viral proteins which usually operate against a stage in the viral replication cycle. A third method is to use virus-resistance genes isolated and transferred by genetic modification to species which are sexually incompatible with the donor source.

Most of the risk assessment considerations regarding GM virus resistant plants have focused on genes derived from viral sequences. Three possible risks have been identified, all environmental, as there is no increased risk to human health since we all eat virus infected

[18] There are two basic mechanisms by which pathogen-derived protection is thought to operate with such viruses: The transgene can be expressed as protein, such as viral coat protein which is thought to interfere with the disassembly of the incoming virus, or as other proteins which have been used as dominant negative mutants. More recently, the importance of RNA transcribed from the transgene giving resistance has been recognised. It is thought that this resistance operates through a mechanism of co-suppression of gene expression, a phenomenon which is currently being extensively studied.

plant material every day. Firstly, in plants containing coat protein[19] genes there is a possibility that such genes will be taken up by unrelated viruses infecting the plant. In this situation, the foreign gene changes the coat structure of the virus and may confer properties such as changed method of transmission between plants. We support the initiative for Government-funded research currently underway on the phenomenon. The second potential risk is that there is recombination between the inserted gene and unrelated viruses infecting the GM plants creating a new virus. This too is currently being studied in the UK and in other countries. Third, there is the possibility that switching on the inserted gene at the same time as the plant is infected with an unrelated virus will aggravate the symptoms. All these potential risks have to be viewed in relation to the natural situation of joint infections by two or more viruses, a common occurrence in plants. There is relatively little information on how viruses interact in natural simultaneous infections, but it is well known that transgenes are expressed to much lower levels than those reached in normal virus infections.

There has been relatively little assessment of potential risks resulting from the other two basic type of transgenes as these are at early stages of research and development. Antiviral proteins will have to be assessed on a case by case basis, especially as they may have implications in human health or food safety. The possible risks associated with transferring natural plant virus resistance genes across the species barrier will be similar to those for other plant genes.

## 5. Specific issues related to GM plants for food use

There are concerns amongst some consumers about the addition of GM crop plants to food, because ingredients derived from GM crops are beginning to be used in food manufacture. However, the difficulty in guaranteeing segregation of GM and non-GM commodity crops, such as soya and maize, due to long distribution lines between growers and consumers and differing regulations between producer countries, is causing severe problems with attempts to offer consumer choice through clear labelling. It is important for companies to recognise the widespread desire on the part of the consumers to have appropriate labelling of foods. In the following paragraphs we have considered specific concerns relating to GM plants and their products in food.

### *5.1 Labelling and segregation*

Directive 90/220/EEC (as amended), governing release and marketing of GMOs, requires a company making an application to market a GMO (see Section 2) to provide information on the proposed labelling, including an indication that the product contains, or consists of, GMOs. In practice, the UK has followed the Food Advisory Committee guidelines which required labelling only in specific cases such as to meet ethical, religious, or health concerns. For example, if a gene from a pig had been inserted into a soya bean, the resulting product would have to be labelled on ethical and religious grounds. Directive 90/220/EEC does not cover non-viable products derived from GMOs and it was amended in 1997 to require labelling of all living GMOs.

Regulation EC/258/97 was introduced to complement Directive 90/220/EEC and introduce labelling requirements for all Novel Foods. This regulation requires labelling of any food, or food ingredient, which is 'no longer equivalent'[20] to its conventional counterpart. Since two

[19] Coat proteins - most plant viruses consist of RNA surrounded by a protein capsule or coat.

[20] 'no longer equivalent' - a novel food or food ingredient is deemed to be 'no longer equivalent' if scientific assessment, based on an appropriate analysis of exiting data, can demonstrate that the characteristics assessed are

crops, varieties of soya and maize, were given marketing approval prior to the entry into force of this regulation, there is an additional regulation, Regulation EC/1139/98, which comes into force on 1 September 1998, covering foods and food ingredients derived from the two crops which are 'to be delivered as such to the final consumer'. However, there are a number of aspects which still require technical clarification and agreement at European level. A more extensive discussion of problems related to labelling of foods containing GMOs and their derivatives may be found in Annex VI.

We strongly support the labelling of foods containing GM material, where the new foodstuff is substantially changed (according to specified criteria) from that of its conventional counterpart, to allow customer choice. We also recognise that segregation of commodity crops and derivatives through long supply chains on a global scale will cause difficulties of traceability for those manufacturers and retailers who wish to source products which do not contain GMOs or their derivatives.

For enforcement purposes, it will be essential to recognise a minimum level for adventitious presence of GM material, below which a product can be considered to be free of GM derivatives. Scientifically validated testing methods would have to be developed and agreed in order for such enforcement to be carried out in a reliable, readily repeatable and practical basis. We recommend that the regulatory authorities, the European Commission and relevant bodies work together to resolve this issue.

Any over-arching body set up to monitor the regulations should also investigate methods by which information can be disseminated to all members of the supply chain in order for such labelling to be effective. In view of the imprecise nature of the regulations governing labelling, there is also a pressing need for the regulatory authorities to re-evaluate the requirements relating to the labelling of GM foods and ingredients, derived from each of the three current statutory requirements and to distil from these general principles which can be applied equitably and uniformly to all current GM crops and to those likely to be approved during the foreseeable future.

*5.2 Toxic or allergenic effects as a result of the inserted gene*

It is important to stress that highly purified materials derived from a GM crop, for example sucrose derived from a sugar beet genetically modified to be resistant to insects, will be identical to material derived from the non-GM variety. Such material is therefore no more likely to be toxic or allergenic than material from non-GM sources.

A number of plants produce toxins as a protection against insect and fungal pests. These are part of their innate defence systems and as such are important to maintain. They are generally present at low levels that humans and animals are able to tolerate. Genetic modification may be used beneficially to remove allergens or toxins in existing food crops. It is possible however, that such toxin levels could be increased by genetic modification (by switching on genes to a greater level); this would be taken into consideration during assessment of applications for release or marketing.

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different in comparison with a conventional food or food ingredient, having regard to the accepted limits of natural variations for such characteristics (Article 8 of regulation 258/97).

There are many databases of known allergens[21]. that could help to identify proteins that may be problematic if inserted into food products. When submitting an application to market a GM plant for growth in the EU, information on likely toxic or allergenic effects must be included in the application. However, the current system of relying on identification of known allergens in the GM plant, coupled with the reliance on 'substantial equivalence' may result in potential allergenicity problems being impossible to predict if there are no data available on the substances in question, particularly since mechanisms of allergenicity are often poorly understood.

Article 8 of the EU Novel Food Regulation requires any ingredient which is no longer equivalent (as defined in footnote 20) to be labelled. Specifically, the regulations require that products are clearly labelled if they contain genes that may result in toxicity or allergenicity, particularly if such genes would not normally be expected to occur in the food. For example, if an allergen gene from a nut were to be inserted into a potato to be used for food purposes, such products would not be approved for marketing under the current regulatory system without such labelling being a condition of approval. GM plants which contained expressed toxins which are harmful to humans would not receive regulatory approval. We recommend that any over-arching body analyses the current regulations giving particular attention to consideration of whether long-term animal feeding studies are necessary to provide greater information on allergenicity or toxicity.

*5.3 GM crops containing non-food genes*

Several commodity crops that would normally be used for food, for example oilseed rape, are currently being developed as 'bioreactors' to express genes for production of pharmaceutical compounds or ingredients for biodegradable plastics. Such plants are intended to act as 'factories' for the safe and economic production of such compounds. In addition, food plants, such as bananas, are being specifically targeted for insertion of genes for the production of vaccines. It is important that such plants are well segregated from food crops to prevent genes inadvertently entering the food chain by cross-pollination, or mixing of crops during harvesting. Alternative methods of minimising gene transfer may also be necessary. In practice it is envisaged that production plots will be grown mostly in glasshouses.

In another technology being developed, vaccines for humans will be produced in virus particles that can be grown in plants without causing disease. Here, production is contemplated by harvesting the heavily inoculated crops. This work will be carried out only in containment owing to the value of the product and necessity for frequent monitoring.

*5.4 Phenotypic[22]/ genotypic stability of GM crops*

Concerns have been raised that expression of genes that have been inserted by genetic modification may be easily lost, returning the crop to its non-GM state. Any set of genetic modification experiments yields a variety of plants, some genetically unstable, others stable. Selection is made on the basis of stability and efficacy, first in the greenhouse and then in the field. Ultimately, the chosen GM plants are crossed by the plant breeder into elite lines of the crop in question so that the gene(s) of choice can be put into the best possible

[21] Allergen - substance that provokes an allergic reaction when an individual is exposed to it by consumption or contact

[22] Phenotypic - related to the observable characteristics of an organism produced by the interaction of genes and the environment; genotypic - related to the genetic information contained within an organism.

commercial background. This is tested extensively, usually in multi-locational trials over three years to check for overall performance. In Europe, the authorities approve new varieties on the basis of D.U.S. criteria. Distinctiveness - is it genetically different from anything already on sale? Uniformity - are all the seeds in the bag what they should be? Stability - is the product stable over several generations? Aside from this, it is not in a company's interest to produce an unstable product. To do so could involve them in lawsuits, compensation costs and would severely prejudice their market share in future years.

*5.5 Pleiotropic[23] effects of genes*

Pleiotropic effects are indirect effects arising from the insertion of the genes into the GM plant. For example, the insertion of a gene attached to a strong promoter into the plant's chromosome might cause a problem if it was inserted next to a toxin gene that had previously been present but not expressed in the plant. The insertion might trigger the expression of the toxin in addition to the novel gene product.

Pleiotropic effects are not confined to plants created as a result of modern methods of genetic modification. Indeed, plant breeders often rely on such unexpected effects to produce useful varieties. However, if deleterious effects are produced from traditional breeding then the line would no longer be grown as it would not be useful from an agronomic point of view. In GM plants, information is available about the gene which has been inserted, such as where it is in the plant's DNA and what effects it has. In this respect, it may be easier to predict pleiotropic effects arising from genetic modification. Whilst we recognise that such effects are unlikely, and therefore it is difficult to design experiments to investigate them, we recommend that Governmental advisory committees maintain vigilance for them and that the over-arching body considers possible research into the likelihood of their occurrence.

## Summary of Recommendations

- We recognise the impact of plant biotechnology on the quality of food and its importance in the development of crops for non-agricultural purposes. For these reasons, we support the continuation of research in biotechnology and recognise the importance of potential developments in the field. However, we also recognise the concerns expressed with regard to the technology and believe that these should continue to be addressed through collaboration between industrialists, the public sector scientists, regulatory authorities and environmental organisations.
- We believe that any further increase in the number of antibiotic resistant micro-organisms resulting from transfer of antibiotic resistance markers from GM food should be avoided. We recognise that in the early stages of the technology, alternative marker genes may not have been available. However, such genes, if used in future, should be removed at an early stage in development of the GM plant, and where possible, alternative marker systems should be used.
- We strongly support mechanisms by which consumers can be informed about developments in biotechnology, including the labelling of foods containing GM material where the equivalence of a food is substantially changed, according to established criteria and provided such labelling is appropriately monitored. Nevertheless, we recognise the associated practical problems, whether related to the complexity of international trade, detection limits, complexity of product formulations or processing techniques. We recommend that the Government departments continue to work with

[23] Pleiotropic - (of a gene) having an effect simultaneously on more than one characteristic of the offspring.

the European Commission and all interested parties towards increased clarity in the labelling regulations. To ensure labelling is possible, the regulatory authorities will also need to analyse information exchange throughout the supply chain for GM food products.

The reliance on a case by case approach to the legislation may result in a lack of analysis of the overall impact of the technology on agriculture and the environment, and of the long-term effects of GMOs We therefore recommend that the remit of the appropriate advisory committees should be extended to include, where relevant, the following points. In addition, an over-arching body or 'super-regulator' should be commissioned by the Government to span departmental responsibilities and have an ongoing role to monitor the wider issues associated with the development of GM plants. Such a body should consider those of the following points which cannot be considered by individual advisory committees for practical reasons. In addition, the proposed Food Standards agency might have a role to play.

- review enforcement of regulations
- review mechanisms by which GM crops plants could be monitored in the environment and make recommendations for long-term monitoring of impact on ecosystems
- review current guidelines for isolation of certified seed crops and high erucic acid oilseed rape and provide recommendations regarding isolation of GM crops and possible statutory provisions
- review available methods for minimising gene transfer and recommendations regarding further research
- consider possible effects of insect tolerant crops on the ecosystem and provide guidelines for growth of such crops and recommendations for further research, as applicable
- consider current guidelines for growth of herbicide tolerant crops and the potential for statutory measures
- review advisory committee membership regularly
- analyse the current regulations, with particular attention to whether allergenicity and toxicity of GMOs receive adequate consideration.
- consider applications for herbicide use on a GM crop in conjunction with applications for release of the GM herbicide tolerant crop. Implement a mechanism by which the long-term impact of such crops on agricultural practises could be monitored
- consider the effects of GM crops in comparison with the effects of current agricultural practices in general on ecosystems and the environment as a whole.

- We recommend continued research on the following topics:
  - alternative markers to antibiotic resistance genes and methods of removal of marker genes when they are no longer needed
  - the possible impact of virus resistant plants on the ecosystem
  - pleiotropic effects and transgene instability in GM plants
  - optimisation of pest control using insect tolerant plants in conjunction with minimisation of resistance development and study of likely impacts of insect tolerant plants on the ecosystem

# Annex I
## Historical Development of Plant Breeding

1694 Discovery of sexual reproduction in plants
1719 First recorded plant hybrid (intraspecific hybridisation)
1799 First report of cereal hybrid
1866 Mendel publishes his work with pea crosses
1876 Interspecific and intergeneric crossing (leading to Triticale Wheat x Rye cross)
(Triticale now grown on 2 million hectares)
1900 Start of hybrid maize breeding in USA
1909 Protoplast fusion reported
1927 Mutation via x rays
1937 Polyploidisation
1940s Single seed descent technique developed (SSD)
1960s Embryo rescue refined
1970 recombinant DNA technology (start of modern biotechnology)
1970s Double haploid techniques
1983 First genetically modified transformed plants (tobacco)
1990 First genetically modified cereals

# Annex II

## Membership of the Advisory Committee on Genetic Modification (ACGM) (at August 1998)

**Chair -** Professor Kay Davies - Oxford University

**Employer Nominees -**
Dr Richard Skinner - Wellcome Medical Research Centres
Professor Steven Hughes - Unilever Research
Dr Kenneth Edwards - Vice-Chancellor, University of Leicester
Dr Mike Gale - John Innes Centre

**Employee Nominees -**
Mrs Dot Carey - Institute of Virology and Environmental Microbiology, Oxford
Dr Julian Kinderlerer - University of Sheffield
Dr Ron Owen - Medical -Advisor, TUC
Mr Roger Spillar - Manufacturing, Science and Finance Union

**Independent Members -**
Professor Michael Roberts - Institute of Terrestrial Ecology
Professor John Beringer - University of Bristol
Mr Steven Vranch - Jacobs Engineering
Mr Colin Franks - Brighton Borough Council

### Membership of ACGM Technical Sub-Committee (at August 1998)

**Chairman -** Mr Steve Vranch - Jacobs Engineering

**Employer Nominee -** Mr John Thorley - Consultant

**Employee Nominee -** Dr Julian Kinderlerer - Sheffield University

**Independent Members -**
Dr Penny Hirsch - Institute of Arable Crops Research
Professor Tony Atkinson - Macranal Ltd and Consultant
Professor Douglas Young - Imperial College
Dr Joanna Marshall - Oxford University
Mr Stephen Eley - Defence Evaluation Research Agency
Professor Tony Minson - University of Cambridge
Dr Mike Mackett - Patterson Institute for Cancer Research
Professor Don Jeffries - St Bartholomew's Hospital Medical College
Professor David Onions - University of Glasgow
Dr Philip Minor - National Institute for Biological Standards and Control

# Annex III

## Membership of the Advisory Committee on Releases to the Environment (ACRE) at August 1998

**Chairman -** Professor John Beringer - University of Bristol

**Members -**

Dr Phil Dale - John Innes Centre (ACNFP)
Dr Ian Garner - PPL Therapeutics Ltd
Professor Alan Gray - Institute of Terrestrial Ecology
Ms Julie Hill - Green Alliance
Dr Julian Kinderlerer - University of Sheffield
Mr John Macleod - National Institute of Agricultural Botany
Professor Bevan Moseley - Independent
Professor David Onions - University of Glasgow
Professor Nigel Poole - Zeneca Limited
Dr David Robinson - Scottish Crop Research Institute
Dr Kate Venables - Imperial College School of Medicine
Dr Ingrid Williams - IACR Rothamsted

# Annex IV

## Membership of the Advisory Committee on Novel Foods and Processes (ACNFP) (at August 1998)

**Chairman -** Professor Janet Bainbridge - Director of Science and Technology, University of Teesside

**Members -**

Professor Peter Aggett - Head of Lancashire Postgraduate School of Medicine and Health
Professor Charlie Brown - Vice-Principal Heriot-Watt University
Dr Phil Dale - John Innes Centre
Dr Micael Gasson - Institute of Food Research, Norwich
Dr John Heritage - University of Leeds
Professor David Ledward - University of Reading
Reverend Dr Michael Reiss - University of Cambridge
Mrs Elizabeth Russell - Consumer Representative
Professor Ian Rowland - Head of Northern Ireland Centre for Diet and Health
Professor Tom Saunders - King's College, London
Professor Herbert Sewell - University Hospital Medical School, Nottingham
Dr Norman Simmons - Guy's and St Thomas' Hospital Trust
Dr Kate Venables - Imperial College of Medicine, London
Professor Ron Walker - University of Surrey
Professor Frank Woods - University of Sheffield

# Annex V

## Membership of the Food Advisory Committee (FAC) (at August 1998)

**Chairman -** Professor Sir Colin Campbell - Vice-Chancellor, University of Nottingham

**Members -**

Mr Roger Manley - Cheshire County Council
Mrs Matti Alderson - Director General, Advertising Standards Agency
Mr Malvern Barnett - Director Central Scientific Laboratories
Mr Neville Craddock - Nestlé Uk
Mrs Dorothy Craig - National Federation of Consumer Groups
Dr Maureen Edmondson - Mars Inc
Professor Catherine Geissler - King's College, University of London
Dr Catherine Humphries - Cooperative Wholesale Society
Professor Alan Malcolm - Chief Executive, Institute of Biology
Mr Tom Miller - Whitbread plc
Professor Christopher Ritson - University of Newcastle upon Tyne
Ms Barbara Saunders - Freelance Consultant on Consumer Policy
Professor Susan Shaw - University of Strathclyde
Mr Phillip Strachan - Food Industry consultant
Professor Frank Woods - Dean of the Faculty of Medicine, University of Sheffield

# Annex VI
## Segregation and labelling

The first commercially available GM food ingredient in the UK was a canned tomato pureé derived from GM tomatoes. This was clearly, voluntarily labelled and accompanied by explanatory leaflets in the retail stores concerned. Furthermore, conventional tomato pureé continued to be sold alongside the new product; consumers were therefore able to choose freely between them. Segregation of the GM tomato pureé was technically very easy to achieve. The GM tomatoes were grown in relatively small quantities and processed in a single factory close to the growing area (California). The tomato pureé was canned on site, labelled and transported in its finished state to the respective UK retailers. Other tomato derivatives from the same canning plant have not been labelled and are freely available throughout the USA.

More recently, the EU has given approval for the marketing of one variety of GM soya and one variety of GM maize. The specific variety of GM soya is approved for growing in the USA and Argentina; however, soya is also imported to the EU from Canada and Brazil, with trade between all four major soya producers occurring in large quantities. Currently, there is no requirement - commercial or legal - to segregate GM from conventional varieties in any producing country. Furthermore, the US Government has made it clear that, since safety is not an issue, any moves by the EU to ban imports of soya or maize would be considered a breach of World Trade Organisation rules. It is reasonable to assume, therefore, that any commodity soya imported from the USA, Canada, Brazil or Argentina will contain a proportion of GM soya.

In 1998, GM soya will account for 8 million hectares (30%) of US soya production; in 1999, it is likely to increase to 19 million hectares (approximately 65%). Total US soya crop is some 65-70 million tonnes, of which only a small percentage is exported to Europe.

The EU is relatively self-sufficient in maize and virtually no US maize is imported for direct human consumption. The GM variety approved for growth in the EU is a fodder maize, only a proportion of which will be processed into starch and other derivatives. During 1998, it is expected that only 2,000 hectares will be grown in France, with perhaps 40,000 hectares grown in Spain; in addition a further quantity of US maize (some of which could be GM) will also be imported into Spain and Portugal.

It is therefore apparent that the segregation of GM tomatoes for pureé production and suggestions for segregation of commodity crops represent very different challenges. Estimates of the cost of segregation have suggested a premium of between 10-100%; the premium in practice would be charged only to the derivative of the crop for which segregation was deemed necessary - e.g. not all soya or maize derivatives are used in food or feed; some are used industrially.

Soya beans are only very rarely consumed as such. Soya is processed primarily for its oil, with other valuable ingredients such as lecithin and the protein fraction also being used for food purposes. Press-cake from the oil extraction is processed, together with other protein sources, into hydrolysed vegetable protein and other flavouring materials; the protein fraction is refined to produce ingredients with between 50-90% protein, which may be textured or used for their functional properties in a wide variety of foodstuffs. Most of these ingredients are traded internationally, and are used at relatively low levels (a few percent) in

the final food. Full segregation of all ingredients, throughout the food chain, into guaranteed GM-free or other streams, may therefore be virtually impossible to achieve.

Segregation has therefore been largely superseded as a concept by Traceability. However, for the reasons indicated above, full traceability of every consignment of all or any ingredient, still less the finished foodstuff, would be an inordinately expensive, bureaucratic exercise. A parallel and independent processing chain would be required.

The National Farmers Union (NFU) and other Industry Groups such as the British Society of Plant Breeders (BSPB) have recently taken initiatives on segregation of crops grown in the UK by launching guidelines, which may ultimately enable foods containing materials derived from UK-grown Gm crops to be identified. However, for derivatives of imported commodity crops, the situation is far more complex.

The issue of labelling of foods containing ingredients derived from genetically modified plants or micro-organisms has attracted a great deal of debate. Although the EU has recently adopted a Regulation (1139/98/EC), specifically covering only the soya and maize above, these new rules are uncertain in their scope. The Regulation applies, from 1 September 1998, to all foods and food ingredients 'to be delivered as such to the final consumer'. It does not define the 'final consumer'; it could, therefore, be held to require labelling in catering outlets and restaurants.

Specified forms of 'GM declaration' are given, their use on foods or food ingredients to be triggered by analytical detectability of the novel (GM) DNA or, where this may have been destroyed by processing, novel (GM) protein. However, no officially validated methods for the determination of GM materials present in the product exist; these, and an agreed limit of detection, are yet to be decided at EU level (research is currently being carried out on behalf of the European Commission into standard detection methods). Furthermore, it is suggested that consideration should be given to the agreement of a minimum presence of GM material, below which threshold labelling would not be required.

Finally, and fundamentally, there is a requirement for the authorities to develop a list of those derivatives in which identifiable DNA or protein is not likely to be present and which, therefore, will be legally exempt from labelling (the so-called 'negative list'). Likely materials would include refined oils, starch hydrolysates, glucose syrups etc. The status of ingredients such as corn starches and hydrolysed proteins or soy sauce is uncertain, but could be determined on the basis of a minimum presence of GM material.

Technically, the above Regulation (1139/98) applies only to the two specified GM crops; any other GM crops and their derivatives will fall under the general provisions of the Novel Food Regulation (Regulation 258/97). This requires labelling of any food or food ingredient which is no longer equivalent to its conventional counterpart. A food is considered to be no longer equivalent if scientific assessment, based on an appropriate analysis of existing data, can show that the characteristics assessed are different in comparison to a conventional food, taking into account the accepted limits of natural variations for such characteristics. In this case, the labelling must indicate the properties modified and the method by which the new characteristic was obtained.

Where the inserted genetic material may be the subject of ethical, religious or health concerns, (for example, an animal gene inserted into a plant) the specific origin of the new genetic material should also be given.

Again, these requirements are imprecise for practical purposes. There is now a pressing need for the regulatory authorities, possibly in the form of the proposed new Food Standards Agency, to re-evaluate the requirements relating to the labelling of GM foods and ingredients, derived from each of the three statutory requirements and to distil from these some general principles which can be applied equitably and uniformly to all current GM crops and to those likely to be approved during the foreseeable future.