FOOD SAFETY AUTHORITY OF IRELAND

Food Safety and Genetically Modified Foods

Genetically Modified Organisms and Novel Foods

Food Safety
and
Genetically Modified Foods

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CONTENTS

FOREWORD i

1. BACKGROUND 1

2. THE TECHNIQUES OF GENETIC MODIFICATION 2

2.1 Genetic Modification of Plants

2.1.1 How are Plants Modified?

2.2 Genetic Modification of Microorganisms

2.2.1 How are Microorganisms Modified?

2.3 What Kind of Genes are used in Genetically Modified Organsims?

3. HOW ARE GENETICALLY MODIFIED ORGANISMS REGULATED IN THE EU? 5

3.1 Council Directive 90/220/EEC

3.1.1 Information Required under Directive 90/220/EEC

3.2 EU Regulation 258/97

3.3 EU Regulation 1139/98

3.4 Interplay between Regulation 258/97 and Directive 90/220/EEC

3.5 Role of the Environmental Protection Agency (EPA) and the Department of Health and Children in relation to Genetically Modified Food and Feed Products

4. PROCEDURE FOR PLACING GENETICALLY MODIFIED FOODS ON THE MARKET UNDER EU REGULATION 258/97 10

5. PRODUCTS REVIEWED BY THE GMO AND NOVEL FOODS SUB-COMMITTEE 11

5.1 Products Reviewed under EU Regulation 258/97

5.2 Products Approved under Directive 90/220/EEC

5.2.1 Part C of Directive 90/220/EEC

5.2.2 Part B of Directive 90/220/EEC

6. WHAT FOOD SAFETY CONCERNS HAVE BEEN EXPRESSED ABOUT GENETICALLY MODIFIED FOODS? 13
6.1 Labelling
6.2 Use of Antibiotic Resistant Marker Genes in Genetically Modified Foods
6.3 Allergenicity and Toxicity
7. WHAT ARE THE ADVANTAGES OF GENETICALLY MODIFIED FOODS? 17
8. ISSUES ADDRESSED BY THE GMO AND NOVEL FOODS SUB-COMMITTEE 18
9. CONCLUSIONS 19
10. APPENDIX 20
Table A.1 European Union Legislation Regulating Genetically Modified Organisms
Table A.2 European Union Legislation in Preparation
GLOSSARY 22
REFERENCES 23
MEMBERS OF THE GMO AND NOVEL FOODS SUB-COMMITTEE 24

FOREWORD

For generations, plant and livestock breeders have been breeding crops and animals to improve yields, for disease resistance and for composition. The crops and livestock we consume today bear little resemblance to those our forefathers consumed, in that plants and animals have been selectively bred to produce certain desirable traits. For example, we now have high-yield cereals, fruit and vegetables; faster maturing poultry; hens that lay more eggs; cows that give more milk; pigs with leaner meat and a range of varieties of cattle selectively bred for beef production.

Scientists are now capable of identifying the genes that are responsible for some of these desired traits and are able to manipulate them. This technique is known as genetic engineering or genetic modification and we can expect an increasing number of foods arriving on the market that have been produced using this method. A wide variety of such foods are already on the market in the U.S.A., but in Europe there are only a small number of genetically engineered food ingredients on the shelves. However, consumers have expressed concerns about these food products.

These concerns cover a wide range of issues such as food safety, potential damage to the environment, disruption of ecosystems and ethical or moral objections. The GMO and Novel Foods Sub-committee of the Food Safety Authority of Ireland (FSAI), formerly of the Food Safety Advisory Board, was formed in November 1996. This Sub-Committee was established in response to a request from the Environmental Protection Agency (EPA) for advice on food and feed safety issues concerning 'live' Genetically Modified Organisms (GMOs) such as unprocessed GM soyabean seed. In accordance with its remit, the Sub-Committee has considered the GMO issue only in terms of potential risks to consumer and animal health and not in terms of environmental, economic or ethical considerations.

This report sets out to address a number of issues; the nature of GMOs, the mechanism by which GMOs are regulated in the EU, the issues considered by the Sub-committee to date, concerns expressed about this new technology and potential benefits from the technology.

Genetic engineering is a powerful tool that must be treated with respect. Like any tool, if it is used unwisely, it could have unfortunate consequences, but if used cautiously, it could prove to be extremely beneficial. The GMO and Novel Food Sub-committee of the FSAI will continue to play a role in reviewing each product for safety before it can be launched on the market.

I would like to take this opportunity to thank the members of the GMO and Novel Foods Sub-committee and the staff of the Food Safety Authority of Ireland for their assistance in producing this report.

Colin Hill, Chair, GMO and Novel Foods Sub-committee

CHAPTER 1: BACKGROUND

Biotechnology is the application of biological systems in industrial processes. This can be achieved through the use of a living organism or a biological agent derived from an organism such as an enzyme. One of the principal techniques employed by biotechnologists to improve biological processes has been to take advantage of the natural tendency of living organisms to undergo genetic variation. Modification of the genetic material of plants, animals and microorganisms can be exploited in order to achieve certain desired products or results. Biotechnology in this form has been practised for millennia. Examples of this method of genetic manipulation include:

- plant breeders selecting seed from their best plants for subsequent planting
- livestock farmers selectively breeding faster maturing poultry, poultry laying more eggs, pigs producing leaner meat, cows yielding greater quantities of milk and cattle for beef production
- growers cross breeding to produce valuable new hybrids
- food processors selecting the best microbial strains for food fermentations e.g. cheese, yoghurts and fermented meats.

While these examples all involve heritable changes in the genetic material of living organisms, none of the products derived in this manner is subject to regulatory control since they are deemed to be natural processes.

All living organisms use the same basic genetic systems and strategies for expression. This genetic system comprises genes, which are found in every cell of every living organism. Genes consist of strands of a chemical known as deoxyribonucleic acid or DNA. In recent years, it has become possible to introduce changes to the DNA of living organisms in a precise manner using recombinant DNA technology (often referred to as genetic modification or genetic engineering). Essentially, DNA (encoding a specific property) is isolated from one organism, purified and introduced to the same or a second organism. When the proper signals have been provided, the newly introduced DNA is functional and the new property is conferred on the host. This 'new' organism is referred to as a GMO and in EU legislation it is defined as:

"any cellular entity capable of replication or of transferring genetic material in which the genetic material has been altered in a way that does not occur naturally by mating or by natural recombination."[1]

Over the past 25 years, these 'new' techniques have brought about many useful advances in medicine, agriculture, food processing, bioremediation and other areas. In contrast to foods derived from what are deemed natural processes, foods derived from genetic modification are subjected to stringent regulatory control.

This report primarily concerns itself with the use of GMOs or products derived in the food chain from GMOs.

CHAPTER 2: THE TECHNIQUES OF GENETIC MODIFICATION

Genetic modification has been applied on an experimental basis to animals, plants and microorganisms but only those plants and microorganisms that have undergone extensive safety tests are available on the market.

2.1 Genetic Modification of Plants

It is now possible, using the techniques of genetic modification, to produce plants that have the following properties:

- disease and pest resistance
- greater yields
- herbicide tolerance
- modified protein and oil content
- improved nutritional properties
- improved flavour due to delayed ripening
- resistance to environmental stress e.g. drought, salinity, or cold
- production of pharmaceuticals and other chemical substances

2.1.1 How are Plants Modified?

A transgenic plant is one that has received a segment of DNA or gene(s) from another organism. The DNA that has been transferred using recombinant DNA techniques is known as heterologous or foreign DNA. The foreign segment of DNA is incorporated (i.e. integrated) through natural systems present in plant cells into the plant's genome. The newly introduced gene(s) are subsequently inherited in a normal Mendelian manner through pollen and egg cells.

The process of introducing DNA into plants is called transformation and it can be achieved both in monocotyledonous plants, such as wheat, barley, and rice, and in dicotyledonous plants, such as soyabean, potato, and tomato, mainly using the following two methods:

a. *Agrobacterium tumefaciens* is a soil bacterium that causes 'crown gall' disease on some plants. Many dicotyledonous species are susceptible to infection by this species. In causing 'crown gall' disease *A. tumefaciens* transfers DNA (the transferred DNA or T-DNA) from the bacterium to the plant. In nature the transferred bacterial DNA cause the symptoms associated with 'crown gall' disease. In the early 1980s scientists removed the disease causing genes from this bacterium and the T-DNA is now routinely used to transport foreign genes into plants. *Agrobacterium* cells, carrying the foreign gene(s) of interest, are incubated with cultured cells of the recipient crop plant and transgenic plants are regenerated from them. Not all cells subjected to this process are successfully modified so it may be necessary to identify the modified cells using marker genes which are closely linked to the genetic material that is transferred. These selectable marker genes usually confer resistance to an antibiotic such as kanamycin or resistance to a herbicide.

b. Particle bombardment is used to transform the monocotyledons such as cereal crops. This involves coating metal particles (usually gold particles - 1nm in diameter) with DNA and shooting them into plant cells (using a particle gun) capable of subsequent plant regeneration. A small proportion of the plant cells become transformed and transgenic plants can be regenerated from these cells.As with *Agrobacterium*, it is common practice when using particle bombardment to use an antibiotic marker gene for selection purposes.

To date, selectable marker genes based on antibiotic resistance have been used in the generation of transgenic plants. These selectable markers are closely linked to the genes being transferred and are only required for the initial plant transformation. Ultimately they are not necessary in the GMO, particularly at the commercial stages of seed production. Alternative selectable markers such as herbicide resistance could replace antibiotic resistance based markers and in limited circumstances it may be possible to replace these markers with fluorescent markers. Alternative strategies are being developed to segregate the antibiotic resistance markers from the desired transgene(s).

In order for genetic engineering to contribute to the development of new crop varieties it must be used in conjunction with the plant breeding techniques that have been tried and tested for the best part of a century. The array of novel genotypes produced using this genetic modification must also be subjected to a multi-location, multi-season, field testing and evaluation process.

2.2 Genetic Modification of Microorganisms

Genetically modified or recombinant microorganisms contain genetic material that is artificially introduced and rearranged in an intentional and predetermined manner which is unlikely to occur in nature. Examples of genetically modified microorganisms include:

- bacteria that produce or enhance the amounts of novel and/or modified enzymes e.g. rennet for cheesemaking
- bacteria that produce substances (peptides or proteins) with medical applications e.g. interferon for cancer treatment and insulin for diabetics
- viruses with medical applications e.g. disabled vaccinia virus which is used in gene therapy
- bacteria that can be used as live-vaccines
- bacteria that can clean up toxic compounds or protect plants from pests and frost.

2.2.1 How are Microorganisms Modified?

Genetically modified microorganisms are created through the introduction of genetic material by recombinant DNA technologies. This genetic material may be integrated into the resident chromosome or may reside on autonomously

replicating units called plasmids, which are extra-chromosomal structures that carry genes which encode for a variety of functions. In either case the genetic information is inherited through a process of replication, cell division and plasmid / chromosome segregation. The introduction of genetic material changes the genotype of the microorganism and this process is called transformation. Transformation of microorganisms is usually achieved using one of the following procedures:

a) **Electroporation** - This method is used to transform a wide variety of microorganisms and requires a brief exposure to a high-voltage electric field to introduce genetic material into a microorganism. Electroporation is the most popular technique for introducing genetic material in microorganisms because of its simplicity, efficacy and versatility.

b) **"Natural" transformation** - Some bacteria such as *Bacillus subtilis*, *Streptococcus pneumoniae and Haemophilus influenzae* have a natural capacity to take up DNA and incorporate it as part of the host genome. This property is sometimes used to introduce recombinant DNA into these hosts.

c) **Transformation through artificial competence** - Incubation of certain bacteria in certain salt solutions results in pore formation thus allowing the introduction of recombinant DNA.

2.3 What Kinds of Genes are Used in Genetically Modified Organisms?

In theory, almost any gene can be transferred from one organism to another and carry out its function, provided that the proper signals are present to enable the host recognise the gene. Thus, it has been possible to construct microorganisms capable of producing human insulin or bovine rennet. Many of the genes used in transgenic plants provide resistance against herbicides or against certain insect pests. Other examples include the use of genetic manipulation to switch off plant genes, such as those which cause tomatoes to soften and rot after ripening.

CHAPTER 3: HOW ARE GENETICALLY MODIFIED ORGANISMS REGULATED IN THE EUROPEAN UNION?

Guidelines designed to ensure the safety of biotechnology in food production have been developed by independent international bodies such as the Organisation for Economic Co-operation and Development (OECD), and the United Nations World Health Organization (WHO) and Food and Agriculture Organization (FAO).

In the EU three separate pieces of legislation govern the use of GMOs in foods; Directive 90/220/EEC, the Novel Foods Regulation (258/97) and Regulation 1139/98 (labelling of certain foodstuffs). For a complete list of EU legislation governing GMO use see Appendix 1; Tables 1 and 2.

3.1. Council Directive 90/220/EEC (Deliberate Release of Genetically Modified Organisms into the Environment)

EU Directive 90/220/EEC regulates the deliberate release of GMOs (plants, micro-organisms and animals) into the environment. The main focus of the Directive is the protection of human health and the environment. It covers the environmental risk assessment and release approval of all GMOs through both the research and development stage as well as the placing of products containing or consisting of GMOs on the market. As defined in this Directive, a GMO includes any organism that has been modified by the manipulation of its DNA such as using procedures typically described as genetic engineering. It excludes any plant, animal or microbial species that is the product of techniques such as cell fusion, in vitro fertilisation or conjugation. There are two different types of release covered by this Directive:

- research and development purposes i.e. field trials (Part B of the Directive)
- placing of products on the market (Part C of the Directive).

Directive 90/220/EEC was transposed by Regulations in December 1994 and is known as the Genetically Modified Organisms Regulations, 1994 (S.I. No. 345 of 1994). The Environmental Protection Agency (EPA) was nominated as the Competent Authority for these Regulations in January 1995. These Regulations have since been amended:

- Genetically Modified Organisms (Amendment) Regulations, 1996 - concerning criteria for the classification of GMOs (S.I. No. 348 of 1996),
- Genetically Modified Organisms (Amendment) Regulations, 1997 - concerning labelling (S.I. No. 332 of 1997).

3.1.1 Information required under Directive 90/220/EEC

Before a GMO can be placed on the market under 90/220/EEC the notifier (company or individual requesting to launch the product on the market) is obliged to submit an application to the EPA in Ireland (or to the equivalent Competent Authority in the Member State where the GMO is to be launched), providing information that includes:

- general information - name and address of notifier, including the name, qualifications and experience of the responsible scientists
- information relating to the GMO - complete name, reproduction, survivability, dissemination
- information relating to the genetic modification - methods used for transformation, type and source of the vector
- information relating to the genetically modified plant - description of the trait(s), information about the gene sequence used, stability of the insert, information on any toxic or harmful effects on human health and the environment arising from the genetic modification
- information obtained from the research and development stage (field trials) on the impact of the release on human health and the environment
- information on the potential environmental impact from the release of the genetically modified plants
- information on data or results from previous releases
- an assessment of any risks for human health or the environment related to the GMO
- name and address of the manufacturer or distributor
- type of expected use
- where the product will be used
- environmental and human health assessment for example toxicity and allergenicity aspects linked to the cultivation
- information relating to the introduced genetic material e.g. the nucleotide sequence that could be included in a register of modifications
- measures to take in case of unintended release or misuse
- storage and handling instructions
- labelling requirements - until July 1997, there were no specific requirements under EU Directive 90/220/EEC, to label products indicating that they contained GMOs or were derived from GMOs, unless the products were substantially different to non-modified products. However, in July 1997 Directive 90/220/EEC was amended and the Regulations S.I. No. 332 of 1997 came into operation to cover proposed labelling as follows:

"This must include in a label or an accompanying document an indication that the product contains, or consists of genetically modified organisms. In the case of products to be placed on the market in mixtures with non-genetically

modified organisms, information on the possibility that the GMOs may be present, is sufficient."[2]

3.2 EU Regulation 258/97 (Concerning Novel Foods and Novel Food Ingredients)

Regulation 258/97 concerns the placing on the market of novel foods and novel food ingredients where novel foods are:

"foods and food ingredients which have not hitherto been used for human consumption to a significant degree within the Community"[3]

The categories of novel foods food and food ingredients are:

a) containing or consisting of GMOs within the meaning of Directive 90/220
b) produced from but not containing GMOs
c) with a new or intentionally modified primary molecular structure
d) consisting of or isolated from micro-organisms, fungi or algae
e) consisting of or isolated from plants and food ingredients isolated from animals, except for foods and food ingredients obtained by traditional propagating or breeding practices and having a history of safe use
f) to which has been applied a production process not currently used where that process gives rise to significant changes in the composition or structure of the foods or food ingredients which affect their nutritional value, metabolism or level of undesirable substances.

To launch a novel food or novel food ingredient onto the market for human consumption, the notifier must receive approval under this Regulation. The approval procedure is set out in Chapter 4. The Competent Authority in Ireland for this legislation is the Department of Health and Children which acts on advice from the GMO and Novel Foods Sub-committee of the Food Safety Authority of Ireland. To date, no application has been received to launch a novel food product on the Irish market.

3.3 EU Regulation 1139/98 (Concerning the Compulsory Labelling of Certain Foodstuffs Produced from Genetically Modified Organisms)

Two different genetically modified crops, soya (developed by Monsanto) and maize (developed by Novartis), were launched on the EU market prior to the introduction of Regulation 258/97. While this Regulation provides for compulsory labelling, the legislation cannot be applied retrospectively and so did not apply to these two products. In order to bring the labelling of these two products in line with future GM products, EU Regulation 1139/98 was introduced in July 1998. The Department of Health and Children is responsible for this Regulation.

The Regulation applies to all foods and food ingredients produced in whole or in part from GM soya or maize, which are to be placed on the market for human consumption. It specifies that where DNA and/or protein resulting from the process of genetic modification are detectable in these foodstuffs, the product must be labelled. The Regulation expands further to give rules on precisely what the label must say i.e. "produced from genetically modified soya" or "produced from genetically modified maize" as appropriate.

A national laboratory facility capable of carrying out the relevant tests to identify whether or not a particular food is derived from genetic modification is vital for this Regulation to be properly enforced. The State Laboratory is developing such a facility.

3.4 Interplay Between Regulation 258/97 and Directive 90/220/EEC

In response to a request from EU Member States the European Commission prepared an interpretative document. The main features of this document are summarised as follows:

- Article 9 (1) of Regulation 258/97 states that Articles 11-18 of Directive 90/220/EEC shall no longer apply to foods and foods ingredients that contain or consist of GMOs. This means that to place a GMO on the EU market for food use, the manufacturer (notifier) must obtain consent under Regulation 258/97.
- Regulation 258/97 does not cover animal feed uses. This means that a product containing or consisting of GMOs that is to be placed on the market for both food and feed uses has to be assessed under both Regulation 258/97 and 90/220/EEC.
- Article 9 (2) Regulation 258/97 states that in the case of foods or food ingredients containing or consisting of GMOs, an environmental risk assessment must be carried out as laid down in 90/220/EEC. This risk assessment is designed to ensure that all appropriate measures are taken to prevent adverse effects on human health and on the environment that might arise from the deliberate release of GMOs into the environment.
- Human health aspects linked to the placing on the market of a GMO as food or food ingredient is exclusively assessed under Regulation 258/97. Directive 90/220/EEC is only concerned with human health aspects of feed and seed.
- Regulation 258/97 does not cover the placing on the market of seeds destined for cultivation. Therefore, in the absence of the necessary seed-specific legislation incorporating a similar risk assessment to that in 90/220/EEC, the environmental and human health assessment for the cultivation of seed falls under 90/220/EEC, while the placing on the market of foods and food ingredients resulting from those seeds, falls under Regulation 258/97.

3.5 Role of the Environmental Protection Agency (EPA) and the Department of Health and Children in relation to Genetically Modified Food and Feed Products

The following modus operandi is in operation:

- food products containing or consisting of GMOs or products derived from GMOs being placed on the market after May 1997 are regulated under Regulation 258/97 by the Department of Health and Children which acts on advice from the Food Safety Authority of Ireland
- feed products containing or consisting of 'live' GMOs are regulated by Directive 90/220 by the EPA in Ireland. Until there is specific EU feed legislation, environmental and human health assessment (toxicity and allergenicity linked to the cultivation of GM crops) will be assessed under 90/220 by the EPA.

CHAPTER 4: PROCEDURE FOR PLACING GENETICALLY MODIFIED FOOD PRODUCTS ON THE MARKET UNDER EU REGULATION 258/97

The notifier of a GM food product destined for the market for human consumption must follow a strict procedure in order to obtain approval to launch the product.

Procedure for Placing Genetically Modified Food Products on the Market under EU Regulation 258/97
1. The application, containing a complete dossier of the required information, must be submitted by the company to the Competent Authority in the Member State where the product will be launched. At the same time, the notifier must forward a copy of the request to the European Commission.
2. Upon receipt of the request, the Member State must ensure that an initial assessment is carried out within a period of three months.
3. The initial assessment, accompanied by the opinion formed by the Member State (either favourable or unfavourable), must then be forwarded to the Commission. If the report is unfavourable, then an additional safety assessment must be carried out (see 6).
4. The Commission then forwards the initial assessment to the other Member States and any comments or objections must be presented to the Commission within a period of sixty days.
5. Where no objection is raised the initial Competent Authority must inform the notifier who may then freely launch the product.
6. Where an additional assessment is carried out or an objection is raised the Commission is assisted by the Standing Committee for Foodstuffs. If this Committee approves the application with a qualified majority* the initial Competent Authority must inform the notifier who can freely launch the product.
7. If no qualified majority is reached the Commission forwards the application to the Council of Ministers. The Council has three months to make a qualified majority decision.
8. If no qualified majority is reached, or if the Council has not acted, the proposal must be adopted by the Commission.

*To reach a qualified majority 62 votes are required out of a possible 87. These votes are weighted by country where the weighting broadly reflects the country's population. When using qualified majority voting Ireland has 3 votes, medium sized countries such as Greece and Belgium have 5 and larger countries such as the UK and Germany have 10.

Based on the scientific evidence available or on the basis of an opinion delivered by one of the Competent Authorities, a notifier can claim their food product to be substantially equivalent** to existing foods or food ingredients. In making this claim, the notifier notifies the European Commission when they first market the product. The Commission then forwards a copy of this notification to other Member States. The labelling requirements of Regulation 258/97 still apply to these products even though they are deemed substantially equivalent.

**"*Substantial equivalence embodies the concept that if a new food or food component is found to be substantially equivalent to an existing food or food component (already on the market), it can be treated in the same manner with respect to safety (i.e. the food or food component can be concluded to be as safe as the conventional food or food component)…When substantial equivalence is established for an organism or food product, the food is regarded to be as safe as its conventional counterpart. When substantial equivalence cannot be established, it does not necessarily mean that the food product is unsafe.*" Joint FAO/WHO Consultation September 1996.[4]

CHAPTER 5: PRODUCTS THAT HAVE BEEN REVIEWED BY THE GMO AND NOVEL FOODS SUB-COMMITTEE

5.1 Products Reviewed under EU Regulation 258/97

The GMO and Novel Foods Sub-committee of the Food Safety Authority of Ireland has reviewed a small number of applications to launch products on the market in other Member States at the request of the Department of Health and Children (Table 5.1). However, no application has been received to launch a novel food on the Irish market and to date no food product has received full approval at EU level under Regulation 258/97.

Table 5.1
Food Products Reviewed by the GMO and Novel Foods Sub-committee under Regulation 258/97 (April 1999)

• Tomato with reduced levels of pectin degrading enzyme
• Stevia rebaudriana Bertoni plants and other dried leaves
• Phospholipids from egg yolk
• Green hearted chicory with male sterility
• Raddichio rosso with male sterility
• Yellow fat spreads with added phytosterol esters

5.2 Products Approved under Directive 90/220/EEC

5.2.1 Part C of Directive 90/220/EEC (placing on the market)

As of February 1999, eighteen GMO products received full consent at EU level under Part C of Directive 90/220 and these products can be marketed in any EU Member State. They are:

- three animal vaccines: two against aujeszky's disease; one against rabies*
- herbicide tolerant tobacco
- four herbicide tolerant oilseed rapes-hybrids
- herbicide tolerant soyabean
- herbicide tolerant male sterile chicory
- four genetically modified maize insect protected and herbicide tolerant
- genetically modified microorganisms kit to detect antibiotics in milk
- three genetically modified carnations - traits include colour changes and increased vase life.

*Since 1993, Regulation 93/2309/EEC regulates products containing or consisting of GMOs for medicinal or veterinary use.

5.2.2 Part B of Directive 90/220/EEC (Field Trials)

Between October 1991 and the end of September 1998, 1,266 genetically modified (crop) releases Summary Notification Information Formats (SNIFs) relating to genetically modified plants (>70 different plant species) have been circulated in the EU under part B of Directive 90/220/EEC for field trials. In Ireland to date, one field trial was carried out on two GM sugar beets during the 1997 growing season. Five field trials on one GM sugar beet in 5 locations were carried out during the 1998 growing season. Four field trials with a GM sugar beet were planted at three locations in Ireland in April 1999.

CHAPTER 6: WHAT FOOD SAFETY CONCERNS HAVE BEEN EXPRESSED ABOUT GENETICALLY MODIFIED FOODS?

In the past foods were not required to undergo a formal pre-marketing safety evaluation and the responsibility to ensure that they were safe rested with those who were introducing the new foods. New strains and varieties of food organisms that were developed using classical selection and breeding techniques came on to the market without a formal safety evaluation.

However, strategies for assessing the safety of foods produced by genetic engineering were devised by the FAO/WHO in 1991 and by the OECD in 1992. The opinion of these international agencies was that food safety considerations regarding organisms produced by techniques that change the heritable traits of an organism are basically of the same nature as those that might arise from other ways of altering the genome of an organism, such as conventional breeding.

In the EU, genetically modified foods or food components are subjected to an extensive range of analytical tests for food safety evaluation. The approach to assessing the safety of genetically engineered food products is to focus on the gene product and its function, including the product produced as a result of its function. This includes chemical analysis and evaluation of nutritional composition for proteins, amino acid profiles, fat, carbohydrates, fibre, vitamins and minerals, digestibility tests, toxicity studies, animal feeding studies, phenotypic characteristics, molecular characterisation, immunotoxicity, genotoxicity and allergenicity testing. The assessment of the safety of GM organisms addresses both intentional and unintentional effects that may result as a consequence of genetic engineering of the food source.

6.1 Labelling

Consumers object to GM foods for a variety of reasons including a fear of potential damage to the environment, ethical or moral concerns and perceived food safety risks. Irrespective of the reason they have the right to know the origins of the food they are buying. Each consumer is entitled to clear, unambiguous labelling in order to make informed purchasing choices.

The current labelling position has been outlined in Section 3.3, however there are limitations to the legislation. Additives are exempt from labelling requirements under Regulation 1139/98. Many soya derivatives such as lecithin are used as additives in food production and there is significant consumer demand for the labelling of all GM products even if they are legally exempt. However for the purposes of this labelling regulation, all GMOs are treated identically in relation to the information provided, and thus labelling relates to the process used and not the specific modification that may be present in the particular product. The European Commission is currently developing proposals for the labelling of food additives and flavouring produced from a genetically modified source.

The inadvertent contamination of non-GM crops may occur during production, distribution or processing of these crops. There is debate surrounding a threshold level that should be set for an acceptable quantity of GM DNA or protein in non-GM products that would occur as a result of this contamination. Any non-GM product containing quantities of GM DNA or protein above this threshold level would have to be labelled as 'containing GMOs'. The establishment of this threshold is under discussion at EU level and the Food Safety Authority of Ireland is actively participating in this process.

Producers and retailers who voluntarily claim their products are "GM-free" would have to provide audit trails to their original source to prove their claim. Alternatively, this claim would have to be supported with the use of analytical laboratory techniques. The validation of such a label would have to be carried out by a regulatory authority or an independent organisation. The concept of "GM-free" is easily understood by the consumer and is supported by the regulatory agencies in most EU countries, however the term "GM-free" is still open to misinterpretation if the threshold level is taken into account.

6.2 Use of Antibiotic Resistant Genes in Genetically Modified Foods

Antibiotic resistant genes are used routinely in both plant and microbial genetic engineering as selectable markers. When the gene of interest is closely linked to an antibiotic resistant gene, it is relatively easy to detect those cells which have been successfully transformed. Thus, a number of GMOs possess antibiotic resistance genes. This has caused some concern, in that it is possible in theory at least, that these genes might be transferred to other organisms after release. The two antibiotic genes used most commonly in plant biotechnology are the *npt11* gene which codes for resistance to kanamycin and the *bla* gene which encodes ß-lactamase, an enzyme that rapidly degrades ampicillin. It is important to note that these genes encode resistance to, and do not produce the relevant antibiotic and also, that bacteria resistant to these antibiotics are widespread in the environment, particularly in slurries and farm yard manures.

The Joint FAO/WHO Consultation in 1996 concluded that in the case of GM crops,
"as the possibility of horizontal gene transfer is considered to be vanishingly small, data on such gene transfer will only be needed when the nature of the marker gene is such that, if transfer were to occur, it would give rise to a health concern. In assessing any potential health concerns, the human or animal use of the antibiotic and the presence and prevalence of resistance to the same antibiotic in gastrointestinal microflora should be considered".[4]
Despite extensive research, there has been no recorded case of antibiotic resistance being transferred from antibiotic resistant marker genes to animals or humans.

With respect to GM microorganisms, the 1996 Consultation

"affirmed the recommendations from the 1990 FAO/WHO Joint Consultation regarding GMOs, including:

1) *that vectors should be modified so as to minimise the likelihood of transfer to other microbes; and,*
2) *selectable marker genes that encode resistance to clinically useful antibiotics should not be used in microbes intended to be present as living organisms in food.*

Food components obtained from microbes that encode such antibiotic resistance marker genes should be demonstrated to be free of viable cells and genetic material that could encode resistance to antibiotics".[4]

Due to consumer demand and despite the fact that the risk of horizontal gene transfer is extremely low, the GMO and Novel Foods Sub-committee of the FSAI recommend that selectable markers based on antibiotic resistant genes should be avoided. Alternative markers such as those based on herbicide resistance or where applicable by flourescent marker genes or other techniques such as strategies to segregate antibiotic resistant marker genes from the desired transgene should be employed.

In a vote under Article 21 of Directive 90/220/EEC the UK Competent Authority on the advice of the UK Committee on Novel Foods and Processes (ACNFP), voted against a genetically modified maize variety due to food and feed safety considerations as the product contained the ß-lactamase gene. The UK ACNFP was concerned that the *bla* gene in the unprocessed product for animal feed could be transferred to gut microflora which could have veterinary and clinical implications. However, as this gene would be destroyed during processing, the UK Committee pointed out that it would have no objection to the marketing of this product for seed production and processing for human food or animal feed.

6.3 Allergenicity and Toxicity

Concerns have also been expressed that:

- the introduced gene product may itself be toxic
- the introduced gene may lead to production of toxins in the GMO
- the introduced gene may modify the allergenic properties of the crop for food or feed use or products in the environment, such as pollen.

The issue of allergenicity has been considered in some detail. It is acknowledged that GM foods share with products of conventional breeding, the difficulty of predicting allergenicity of any new or novel protein incorporated into any food product. In attempting to predict the potential allergenicity of foods derived from genetically modified plants, animals and microorganisms the examination of a number of parameters that are common to many potential food allergens is required. The Joint Consultation of FAO/WHO

in 1996 identified a number of relevant criteria and careful consideration should be given to them when assessing novel foods for safety:

- **Source of transferred genetic material** - Particular caution must be exercised if the source of this material contains known allergens.
- **Sequence homology** - The amino acid sequence of many allergens is readily available.
- **Heat and processing stability** - Labile allergens are those that can be easily destroyed by heating or other processes - These labile allergens that are eaten cooked or undergo other processing before consumption are of less concern.
- **Effect of pH and/or gastric juices** - Most allergens are resistant to gastric acidity and to digestive proteases.
- **Prevalence in foods** - For example new proteins expressed in non-edible portions of plants that are not of a concern in terms of food allergy.

The Consultation also states that foods found to contain an allergen that was transferred from the organism providing the DNA, should not be considered for marketing approval unless they can be clearly identified in the marketplace and this identity would not be lost during distribution or processing.

CHAPTER 7: WHAT ARE THE ADVANTAGES OF GENETICALLY MODIFIED FOODS?

The GMOs approved in the EU to date have, like many crops previously developed using more conventional plant breeding techniques, been introduced with improved agronomic or disease resistant traits. The technology does have the potential to produce foods that could be of direct consumer benefit, such as

- fruit and vegetables with increased vitamin content
- non-allergenic peanuts
- potatoes with higher starch content thus resulting in healthier chips
- corn with increased essential fatty acid content
- wheat with increased levels of folic acid
- tomatoes that can ripen on the vine for better taste but yet have a longer shelf life

The GMO and Novel Foods Sub-committee welcomes any new food product that provides a healthier option or increases consumer choice and this Sub-committee will continue to assess each new GM crop as well as foods derived from those crops. This assessment will be carried out on a case by case basis and each individual application will be examined and assessed on its merits.

CHAPTER 8: ISSUES ADDRESSED BY THE GMO AND NOVEL FOODS SUB-COMMITTEE

The Sub-committee has assessed many applications on GMOs to date. A number of concerns have been repeatedly expressed by the Sub-committee in response to these applications and can be summarised as follows:

a) The issue of GMOs containing antibiotic resistant genes has been of particular concern to the GMO and Novel Food Sub-committee. The Sub-committee takes the view that such genes should not be present where possible in GMOs destined for human consumption in the absence of suitable processing and encourages the use of alternative selection strategies during the construction of GMOs.

b) The Sub-committee agreed that while protein sequence database homology data is useful for assessing allergenicity and toxicity potential, there is still a need for notifiers to carry out toxicological and allergenicity testing on animals.

c) The Sub-committee welcomed the July 1997 amended labelling requirements under 90/220/EEC and the fact that all 'live' GMOs must now be labelled under both 90/220/EEC and Regulation 258/97. The Sub-committee also welcomed the new labelling Regulations (1139/98) which provides detailed rules for the labelling of foods derived from genetically modified soya and maize that are destined for human consumption.

CHAPTER 9: CONCLUSIONS

It is likely that increasing numbers of GM foods will emerge in the near future with a variety of modifications and associated benefits. The **minimum** requirement should be that the GM food should be as safe as the original product and should present no threat to human health. While most products are essentially equivalent to conventional foods there may be justifiable claims of associated benefits to human health in the reduced use of pesticides or herbicides, or economic benefits such as reduced loss of food due to spoilage.

It is also possible to envisage other types of GMOs with direct benefits to human health. For example, it should be possible to modify organisms to produce the following:

- drought resistant crops - such crops would enable farmers, particularly those in developing countries, to extend both the growing season and the number of places where crops could grow
- transgenic animals producing therapeutic compounds in milk
- crops with improved nutritional value, such as vegetables with enhanced vitamin content
- foods with reduced allergenicity, such as non-allergenic peanuts.

Genetic modification and modern biotechnology will touch the lives of most people in the areas of food, medicine and environmental protection. This technology requires careful regulation to ensure that there is no threat to human or animal health as a consequence of introducing a GM foodstuff. Adequate labelling, and the provision of accurate product information, are some of the measures that are strongly recommended as a means of ensuring public confidence in the safety of GM foods and also as a means of providing those with objections to the technology with a means of avoiding these foods.

APPENDIX

Table A. 1
European Union Legislation Regulating Genetically Modified Organisms

Directive/ Regulation	Purpose	Competent Authority	Aspects Regulated
Directive 90/219	• Regulates the contained use of Genetically Modified Microorganisms (GMMs)	• Environmental Protection Agency (EPA)	• Contained use of GMMs and GM animals and plants
Directive 90/220	• Regulates the deliberate release of GMOs into the environment for: - R&D purposes (field trials) - Placing GMO products on the market	• Environmental Protection Agency (EPA) • Dept of Environment and Local Government are responsible for certain functions e.g. decisions to place GMOs on the market under Article 21 of 90/220	• Environmental assessment for the cultivation and importation of GMOs in the EU • Animal feed aspects – feeding of 'live' GMOs to animals • Human health aspects (including allergenicity and toxicity) relating to the cultivation of GM crops in the EU
Directive 90/679	• Regulates biological agents in the workplace	• Health and Safety Authority (HSA)	• Workplace contact
Directive 94/55	• Regulates the transportation of certain GMOs	• Department of Enterprise, Trade and Employment	• Transportation
Regulation 258/97	• Regulates novel food and novel food ingredients including GMOs	• Department of Health and Children	• Food and food ingredients containing or consisting of GMOs • Food and food ingredients produced from but not containing GMOs e.g. oil from GM soyabeans
Regulation 1139/98	• Regulates the labelling of certain foodstuffs produced from GMOs	• Department of Health and Children	• Labelling of foods from GM soyabean and GM maize
Regulation 2309/93	• Regulates GMOs for medicinal and veterinary uses	• Irish Medicines Board	• Regulates medicinal and veterinary products including those products which contain or consist of GMOs
Directive 91/414	• Regulates the use of plant protection products	• Department of Agriculture and Food, Pesticide Control Service	• Regulates the use of herbicides, insecticides and fungicides on crops including GM crops

Table A. 2
European Union Legislation in Preparation

Directive	Purpose	Proposed Competent Authority	Aspects Regulated
Seed for cultivation	• Proposed directive will amend current directives relating to seed	• Department of Agriculture and Food	• Expected to regulate GM seed to be placed on catalogues for use in agriculture
Animal feed	• Proposed directive will amend current directives relating to animal feed	• Department of Agriculture and Food	• Expected to regulate animal feedingstuffs containing or consisting or GMOs and feed derived from GMOs

GLOSSARY

Allergen:
Any substance, usually a protein, capable of inducing an allergy.

Antibiotic:
A chemical substance produced by microorganisms, which has the capacity to destroy or inhibit the growth of other microorganisms.

Autonomously:
Functions independently, without extraneous influence.

Chromosomes:
A long thread of DNA that transmits genetic information.

Competent Authority:
The authority to which the legal capacity to make changes in the particular field is given.

Cultured cells:
Animal cells grown or maintained within an artificial environment.

Dicotyledonous:
Pertaining to a flowering plant with two seed leaves in its embryos.

DNA:
Deoxyribonucleic acid, the primary genetic material of all cellular organisms.

Enzyme:
A protein molecule that catalyses chemical reactions of other substances without itself being destroyed or altered upon completion of the reactions.

Field trials:
Tests to display performance, efficacy, or durability of an 'invention'.

Genome:
The complete gene complement of an organism.

Genotype:
The entire genetic constitution of an individual.

Heterologous:
Made up of tissue not normal to the part.

Host:
The recipient of genes transplanted from another organism.

In vitro:
Within an artificial environment.

Mendelian:
Pertaining to the laws of inheritance of single-gene traits that form the basis of the science of genetics.

Microbial:
Of or pertaining to or caused by microbes where microbes are minute living organisms.

Microflora:
The entire population of microorganisms present in, or characteristic of, a special location.

Microorganisms:
Microscopic organisms, such as bacteria, viruses and fungi.

Monocotyledonous:
Pertaining to a flowering plant with one seed leaf in its embryos.

Nucleotide:
A compound consisting of a nucleoside, which is linked to ribose or deoxyribose, linked to phosphoric acid.

Organism:
Any individual living thing whether animal or plant.

pH:
A measure of the acidity or alkalinity of a solution.

Plasmid:
A structure found in bacterial cells that carries genes for a variety of functions not essential for cell growth.

Vector:
A plasmid used to introduce foreign DNA into a host cell.

REFERENCES

1. Council Directive 90/220/EEC of 23 April 1990 on the deliberate release into the environment of genetically modified organisms Official Journal L117, 08.05.1990, p15-27
2. Genetically Modified Organisms (Amendment) Regulations, 1997; S.I. No. 332 of 1997
3. Regulation 258/97/EC of the European Parliament and of the Council of 27 January 1997 Official Journal L043, 14. 02.1997, p. 1
4. Joint FAO/WHO Expert Consultation on Biotechnology and Food Safety - Report of a Joint FAO/WHO Consultation, Rome, Italy, 30 September - 4 October 1996, p. 4

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