Genetically Modified Food

Research Paper 94/74
June 1994

This paper discusses some issues related to the genetic modification of food and the question of whether such food should require special labelling.

Christopher Barclay
Science and Environment Section

House of Commons Library

CONTENTS

[1]Author: Jeff Vernon, Science and Environment Section

I Background

(a) What scientists can do

Genetically modified (GM) food is a product of "the biochemistry revolution" following on from the discovery of the structure of DNA in 1953 by Crick and Watson. Although it took some decades for the possibilities to develop into commercial techniques, since the 1970s many new applications have appeared.

Food has been the product of science for millennia. Processes such as winemaking, brewing or the preserving of foods have always been scientific. Selective breeding of animals has been undertaken for centuries - particularly for horses and hunting dogs - and systematic selective breeding of farm animals to develop better stock has been operating in the UK for about two hundred years. Modern food, of course, is partly the result of the application of modern science. Crops are grown with the help of fertilisers and pesticides. Additives are used to help preserve the food and to control its taste. Otherwise it would simply not be possible to obtain such a wide range of foods, of uniformly good quality, on the supermarket shelves.

The techniques of biotechnology go well beyond that. It is becoming increasingly possible to identify, within an organism, exactly which gene confers each particular quality and to either alter that gene, or even transfer that gene to an organism of a different type. Of course, the complexity of life is such that a particular quality is not always determined by a single gene, but there are cases where the transfer or alteration of a single gene can change particular qualities, either in a plant or occasionally in an animal. **However, it is very important to note that only copies of the information contained within genes are inserted in all cases; the original genes themselves are not transferred.**

The term "genetic modification" when applied to food refers to any artificial alteration in the genetic makeup of a food animal or plant, or to the use of genetic engineering techniques in the production and manufacturing of food. It therefore covers a whole range of techniques.

Some changes may be quite subtle. For instance, an animal may be dosed with a hormone which is essentially identical to one that is produced naturally, but which has been manufactured artificially in large amounts in the laboratory using genetic engineering techniques. This is only altering that animal's physiology, not its genes. However, the food from that animal (its meat or milk for instance) has been genetically modified.

Alternatively, the genetic makeup of an animal or plant may be changed. A gene can be removed and isolated, amplified or copied many times over, altered, and finally reinserted into animals or plants. Various techniques for achieving this have been developed.

Genetic modification techniques are explained in detail in section VI. To give just a few examples here, molecules called "restriction enzymes" can be used to precisely chop up DNA and isolate the stretch of DNA or gene of interest. A technique known as the polymerase chain reaction (PCR) might then be used. PCR has revolutionised genetic engineering. Typically, the amount of DNA isolated from an organism (or recovered from a scene of crime by forensic scientists, or extracted from an insect fossilised in amber) is minute and thus very difficult to work with. PCR provides a way of amplifying fragments of DNA by copying them over and over again millions of times in the test tube.

The information contained in the genes, the DNA itself, may be altered through a technique such as "site specific mutagenesis". (Scientists can use agents such as radiation or chemicals to change DNA, but these cause random mutations of little use. Site specific mutagenesis provides a means of targeting precise changes at chosen sites.) Finally, the natural properties of very simple viruses might be used to deliver modified DNA into a host's cells. Alternatively, modified genetic material might simply be injected into an animal's just-fertilised eggs under a microscope; changes inserted at such very early stages of embryo development will be present in every cell of the adult animal.

Copy genes do not have to be put back into the same type of animal or plant from which they were extracted. They might originate from one organism and be inserted into another species altogether. Bizarrely enough, this transfer can take place from an animal to a plant, so that an animal gene is copied into a plant, or *vice versa*. Any animal or plant which carries genes from another species is known as a "transgenic" organism[1].

Important applications have already been developed. Plants can be genetically modified to confer resistance against pests or so as to remain edible longer before becoming mouldy. Such genetic modification might reduce the need for pesticides or it might merely benefit the retailer. Animals can be genetically modified so as to gain qualities that are advantageous to the farmer or consumer. Pigs could be genetically modified so that they go on and on eating because their body no longer gives the signal that they are full up. Already in 1993 salmon that were artificially modified to make them sterile were going on sale in UK supermarkets. According to the *Sunday Times* (16 September 1993) "In contrast to the salmon's natural image, the genetically altered variety is deprived of its instinct to migrate upriver from the sea to spawn. Such fish would stay put and grow to twice the normal size of farmed fish". However, since such sterile salmon also occur naturally this technique does not raise so many questsions as the introduction of genes from other species to produce a result that could not occur in nature. Only two sets of introductions of transgenic fish into confined outdoor facilities have so far taken place[2].

---

[1] For further details, see Library Research Paper 93/55, *Genetically Modified Organisms, Transgenic Animals and Animal Patenting*

[2] *Genetic Modification of Fish - A UK perspective,* DoE 1994

Pigs can be treated with genetically produced porcine somatotropin (a naturally occurring pig hormone) so that their meat is leaner and healthier for human consumers. Similarly, cows can be treated with genetically produced bovine somatotropin (a cow hormone) so that they produce more milk. In such cases, the genetic makeup of the animals themselves has *not* been altered but their body physiologies have been altered through the application of genetic engineering techniques; genetic engineering has played a part in the food manufacturing process.

A recent article described a protest by German chefs[3]:

> This contained a menu of genetically altered foods : for starters, smoked trout fillets with the gene for human growth hormone and tomato salad with flounder-fish gene; grilled chicken with bovine growth hormone gene and baked potato with scorpion gene for the main course; melon with virus gene for dessert. This menu was not drawn up from a fevered imagination : all these foods have already been developed by genetic engineers in laboratories and tested in the field.

The scope offered to scientists by these techniques is enormous. Some people feel that genetic modification of food should require special labelling. On the one hand, consumers have the right to know what goes into their food and to choose whether to eat food made in a particular way. On the other hand, labelling might mislead consumers and persuade them not to buy the result of harmless scientific advances. This paper discusses the reasons for a polarisation of views on the issue, and how regulation is operating in the USA.

(b) The current system of controls

There is strict control over novel foods. First of all, there are considerable environmental implications in the release of GM organisms and these are regulated under an EC Directive[4]. A consent, only granted after stringent checks, is required at national level before deliberate release. At the moment, there is concern about a licence issued for the experimental release of a particular pesticide onto caterpillar-infested cabbages. The pesticide is a genetically-modified virus, to which a scorpion toxin gene has been added. Some scientists complain that the testing was undertaken on a new "fast track" system because similar substances were tested in the past. They fear that the scientists who undertook the tests do not appear to know

---

[3] *Independent*, 16 October 1993

[4] 90/220/EEC

what the engineered virus would do, once released[5]. However, an alternative view is that such controls are too strict in the UK, since they are more lax in some countries and once the plants are planted somewhere in the world, they will eventually spread widely. China, in particular, is less concerned about stringent checks and is more anxious to get potentially useful products developed.

If a marketing consent is required, then there has to be agreement with the other EC states, although the final consent will be actually issued by the member state concerned. If the result is to be used as a food, the (UK) Advisory Committee on Releases to the Environment would require that consent be given by the Advisory Committee on Novel Foods and Processes. This latter requirement is not laid down in statute and it is sometimes said that the British system of control is a voluntary one, but that is not true in practice since that requirement could not be evaded by an unscrupulous operator.

Few of the theoretical, or even laboratory, developments have appeared as practical foods. The first item to be approved in the UK was genetically modified bakers yeast in 1990. The Advisory Committee on Novel Foods and Processes was satisfied that there was no food safety reason why the use in food of the GM yeast should not be permitted. The Committee recommended that the manufacturers "should carry out regular checks to ensure that there is no genetic drift in the yeast genome in use and that the product offered for sale complies with the specification of the yeast evaluated by the Committee". In addition, the Health and Safety Executive were advised by its Advisory Committee on Genetic Manipulation that the proposal posed no unacceptable risks to wider aspects of human health and safety. The yeast has been used, but is apparently not in commercial use at the moment.

The second product to be approved in this way was chymosin, which is the product of a GM organism, but not a GM organism itself. It is an enzyme which can replace the rennet normally used in cheese-making. There are different versions on the market. Most recently, approval has been given for another GM yeast for use in brewing, although this has not yet come into use.

(c) Who Benefits?

In one sense, it is clear that scientific developments will be adapted commercially if they benefit the producers and retailers. According to the *Independent* (16 October 1993) : "It is estimated that of the food products being engineered, about 98% are being altered to facilitate food production and processing; only the residual 2% offer a direct benefit to the consumer in the form of improved nutrition or taste". Yet it would be unrealistic as well as

---

[5] *Independent*, 17 May 1994

cynical to suggest that such benefits would not spread to consumers. It is worth remembering that intensive chicken farming brought the price of chicken down from that of a luxury to a cheap food, while fish farming has done the same for salmon.

There is a slight paradox in that most consumers are extremely conservative about food, and they do not really want novel tastes. Attempts to market different types of fish make little impact and in the West (but not in China) there is a strong taboo against eating more than a very small range of animals. Probably what consumers really want is quality, reliability and a good taste of the type that they already know. Therefore GM foods are likely to concentrate on ways of providing this, rather as an extension of the scientific effort already directed towards this objective by the food industry.

There has been interest in the development of fruit which stays fresh longer without rotting, or which can be more conveniently picked. While that obviously helps the retailer who does not waste his unsold stock at the end of the day, it also helps the consumer by reducing costs and therefore providing lower prices. It is also clear that such techniques can be used to improve taste, partly because the fruit is in prime condition for longer and partly because the genes coding for undesirable taste features can be removed. It may also be possible to reduce the number of additives in processed food, since many of them are inserted to improve the keeping quality of the food. Enzymes are extensively used in food production and genetic engineering will allow the production of purer enzymes.

There are potential environmental benefits because genetic resistance to pests might reduce the need for pesticides. This is no trivial matter, since it is estimated that some 13% of world crop production is lost to insect pests and well over $6 billion is spent on insecticides worldwide[6]. Genetic modification may also confer on plants resistances to viruses, which are increasingly difficult to control with chemicals. Higher yields should reduce costs and offer another benefit to consumers.

Many issues arise. There are problems of animal welfare and of food safety. There are mechanisms in place for dealing with those issues. The range of specific objections might go wider - to include ethical issues or worries about possible environmental consequences. More generally, people might find the whole approach to food production so distasteful that they want no part of it. The official view - in the UK, the EC and in the USA - is that labelling is only required in certain special circumstances. Indeed, in some circumstances labelling may not be allowed.

---

[6] *Genetically modified crops and their wild relatives - a UK perspective*, DoE 1994, p.11

II The UK Position

(a) Will the GM food be labelled?

The EC in particular is concerned about the ways in which health claims (eg. lower in fat) are used that may be good advertising but are misleading for health purposes. The EC Directive on Nutrition Labelling restricts the nature of the health claims that can be made. Nutrition labelling is not compulsory, but where it exists it has to be in a standard form, with terms clearly defined. Food products also have to be labelled to show all the ingredients. Sometimes labelling has a perverse effect. One EC idea was to classify all food additives that were judged safe and give them an E number, so that people throughout the Community could judge their food on the same basis. However, many people who resent additives, and sometimes attribute allergies to them, concentrated upon E numbers. Many people came to think that E numbers showed particularly harmful additives and avoided the products which included them.

The requirement to list ingredients on food labels does not cover the nature of the manufacturing process. It is possible that the public might be put off by knowing more about some very long-established food processes like the contents of sausages or meat pies. Scientists in the food industry, trying to develop new products and processes, may consider this discrepancy unfair.

There has been some discussion about irradiated food, a technique by which the shelf life of food can be increased without impairing its flavour. It has been passed as completely safe and is allowed in the UK and elsewhere. However, the then agriculture minister (Mr Gummer) was clear on labelling[7]: "I am fully committed to providing consumers with information on food labels to enable them to choose between foods which have been irradiated and those which have not."

In the UK, retail chains are of great importance in the supply of food, and the future of GM food in this country is likely to depend in part on the decisions that they take as to whether to stock such foods and, if so, whether they would be labelled. The Co-op has already announced that it would require special labelling for any GM foods on sale in its stores. However, other major retailers say that they will strictly follow Government guidelines rather than going beyond them.

If the products of genetic modification became common and labelling of products as "free from genetic modification" was widespread, it is likely that some labels would be challenged

---

[7] HC Deb 17 December 1991 c143W

on the grounds of representing a misleading health claim.

(b) The Polkinghorne Report and Government policy

The Government set up a committee on the ethical problems involved, under the chairmanship of J. C. Polkinghorne, a distinguished scientist and clergyman. The report appeared in October 1993[8]. The committee did not cover issues of animal welfare or food safety but examined techniques and discussed whether labelling should be required. Their conclusion was a compromise between the strong desire of consumer and religious groups for labelling to allow informed choice, and the reluctance of the industry to accept this. The report argues that copy genes of animal or human origin do not merit a special ethical status, and therefore do not need to be identified in food. However, the report continues[9]

> Nevertheless, it is quite clear that our perception is not shared by many of the groups from whom we received evidence. We believe, therefore that the **first and most important requirement is for a system of labelling which permits informed choice in relation to the presence of ethically sensitive transgenes in food.** We believe this implies that labelling should apply to copy genes of human origin, copy genes originating from cattle and pigs introduced into other farm animals, and copy genes of animal origin introduced into plants or micro-organisms. This list should be kept under review and consideration given to its extension...

This conclusion was accepted by the Food Advisory Committee who were looking into the more general issues of labelling genetically modified food. The Government recently announced its decision in a reply by Mr Soames[10]:

> The Food Advisory Committee takes the view that it would be unrealistic to label every food whose product has involved genetic modification. It has however accepted that there should be provision for choice in relation to those foods which raise real concerns for a significant proportion of the population. It has therefore proposed that a GM food should be labelled if it:
>
> (a) contains a copy gene originally derived from a human;
>
> (b) contains a copy gene originally derived from an animal which is the subject of religious or dietary restrictions; or
>
> (c) is a plant or microbial material and containing a copy gene originally derived from an animal.

---

8 *Report of the Committee on the Ethics of Genetic Modification and Food Use*, HMSO 1993

9 para 5.4

10 HC Deb 4 November 1993 cc313-314W

> These rules would not apply if the inserted copy gene had been destroyed by processing and was not, therefore, present in the food. I am grateful to the committee for its careful and thorough handling of the issues. It is continuing its work, in particular in the form of labelling that might be used. Meanwhile, its advice coincides very closely with that of the Polkinghorne committee and I propose to accept it. The Government will therefore seek provisions on these lines in the proposed novel foods regulation which is currently under discussion in Brussels. Since very few GM foods have yet come on the market and public understanding of the technique is still limited, we shall also seek a provision for a review in a few years' time.

The Food Advisory Committee considered the matter a little further[11]

> 11. The Committee then went on to consider the appropriate *forms* of labelling which might be required to indicate the presence of copy genes in a foodstuff. The Committee felt strongly that, if the criteria for labelling were met, the requirement for a labelling declaration should be a statutory one. It did not consider that labelling could be satisfactorily achieved by other means, such as non-statutory guidelines.

> 12. Based on the evidence which the consultation exercise produced, the Committee considered that the primary concern of consumers was to be able to identify when a copy gene likely to be a cause of concern to a significant proportion of the population was present in a foodstuff. This was reflected in the criteria which it recommended should trigger a labelling declaration. As far as the form of labelling was concerned, it concluded that what was required was a simple declaration - "contains copies of x genes" (where x is human, pig etc). For single-ingredient foods and foods sold loose, it considered that the declaration should form part of, or accompany, the name under which the food was offered for sale. For prepacked foods with ingredients that contained copy genes, it recommended that the statement should be required to accompany the name of the ingredient in the list of ingredients. However, the Committee considered that if the copy gene was present in an ingredient which under current rules did not need to be listed, the declaration about its presence should nevertheless be made, either in the ingredients list or next to the name of the food.

---

[11] Food Advisory Committee Annual Report 1993

(c) The Attitude of the Public

It is normally assumed that if the public knows that a particular food is the product is the product of the biotechnology industry, then it will be avoided. For example, an article in the *Independent* (16 October 1993) commented : "This industry quite correctly assumes that if genetically engineered foods were labelled as such, most shoppers would avoid them like the plague". A study in Holland, which surveyed 870 people, concluded that most people were unwilling to accept food that is produced by biotechnology or genetic engineering. On a scale of acceptability ranging from 1 (totally unacceptable) to 38 (totally acceptable), people gave genetically engineered foods an average rating of just 5.6. The report found that people were most likely to accept genetically engineered food if they could see obvious benefits either to the consumer or to the environment. People questioned in the survey gave their highest score (7.8) to foods from crops that had been manipulated to reduce the amount of pesticides applied to the fields[12].

Another survey was recently undertaken in the UK by the Consumers Association, although only with a sample of 176 shoppers across the country[13]. They were asked what they thought the wording used on the Co-op label (produced using gene technology) meant, and whether they would buy foods that were labelled in this way.

> Half had no idea what "produced using gene technology" meant. The other half had a stab, but only about one in seven came close, saying that it has something to do with genes or breeding plants and animals. In fact, only about one in five had heard of gene technology. 43% said they wouldn't be likely to buy foods genetically engineered : 20% would (a third weren't sure). The main reasons for reluctance were : feeling they knew little about it, being cautious and wanting to know more, preferring "natural foods", and ethical concerns.

The Consumers Association concluded that the proposed labelling requirements in the UK do not go far enough. "All foods where production has involved genetic engineering should be labelled, so we can make up our own minds. As our survey shows, a public information campaign is needed, too, to raise awareness of the whole subject."

However, such studies are heavily dependent upon the way in which the question is posed. It is not clear exactly how processes could be labelled in a way that would, succinctly, describe how the food was produced. It is likely that some descriptions would alienate

---

[12] *New Scientist* 17 August 1991

[13] *Which?* May 1994

consumers while others would not. It is not realistic to expect the public to take a deep interest in what transgenic technology means or to interpret a label in the way that scientists do.

On the other hand, even if people are not entirely happy at the thought of what is going on, that does not necessarily mean that they will refuse to buy the food. Both organic vegetables and free range chickens are generally approved of, but they only have a tiny share of the market. In practice, most people shop for food on the basis of cost and taste.

III The EC Position

The whole issue of GM food is bound to be one for the EC, mainly because the whole principle of the single market would be undermined if GM food were allowed in some parts, but not allowed to be exported to other parts of the Community. If one member state were to insist upon labelling for all GM food but others did not, it would not be in a position to prevent imports of unlabelled GM foods from other parts of the EC. The Commission has put forward a proposal for a Regulation on novel foods and novel food ingredients.

The original proposal appeared in 1992[14]. The Regulation would establish common rules for the marketing of novel foods and foods produced by novel processes, including those involving GM. It proposes a positive approval system to operate at two levels. As a general rule, novel foods would be considered by national experts, who would be nominated by Member States. The decision of the national experts would be transmitted to the Commission and other Member States, who would have three months in which to object to the marketing of the novel food and/or to request a referral to the EC's Scientific Committee for Food for a further safety review. For foods which are or which contain viable GM organisms, the proposal would bring together the environmental impact assessment required under **Directive 90/220/EEC** (on the deliberate release of GM organisms into the environment) with the food safety assessment to ensure a "one step" approval arrangement.

This proposal was considered by the European Parliament under Article 189a (2) of the **Treaty of Rome**. Various amendments were proposed, on the whole rather hostile to the use of GM organisms in food. The Commission produced an **Amended Proposal for a European Parliament and Council Regulation (EC) on novel foods and novel food ingredients (11294/93).** The Explanatory Memorandum explained their thinking, stressing the importance of making the placing on the market of novel foods subject to a single

---

[14] 8050/92

procedure, leading to a single decision valid throughout the Community:

> In this context, the Commission is unable to accept the amendment calling for a separate authorization procedure under Part C of **Directive 90/220/EEC** for foods or food ingredients containing or consisting of genetically modified organisms. Such a double procedure would run counter to the Community's policy of trying to ensure a single integrated safety assessment for new products from biotechnology covering all aspects of safety. Moreover, **Directive 90/220/EEC** itself provides for the establishment in vertical product legislation of a single integrated assessment of the type proposed by the Commission. However, in order to meet Parliament's concerns, the Commission has attempted to clarify certain aspects of the procedure.
>
> **Labelling** : the Commission accepts that in addition to the application of the general rules on food labelling laid down in **Directive 79/112/EEC**, additional specific labelling requirements may need to be laid down in the authorization to ensure that the consumer is informed of significant differences in the characteristics of the novel food or food ingredient concerned, when compared with conventional foodstuffs, and it has amended its proposal accordingly. However, as already indicated to Parliament, the Commission is unable to accept the amendments calling for the introduction of systematic technology specific labelling of foods containing or consisting of genetically modified organisms or produced with their aid because it considers that such provisions tend to stigmatise biotechnology while providing little useful information for the consumer.

IV US Experience

(a) BST in milk

The issue of Bovine Somatotropin (also called Bovine Growth Hormone in the USA) is discussed in another Library Paper (93/101). This is a naturally-occurring hormone which can be synthesised in large quantities using the techniques of biotechnology and which increases milk yield. Its use remains banned in Europe by the EC at least until the end of the year because of the possible effect on the viability of small farmers. No evidence of damage to animal welfare of risk to human health has been found. In the USA the use of the hormone has been allowed by the Food and Drug Administration (FDA) an independent agency of the US Government.

In February 1994, the FDA issued guidelines which had the effect of forbidding the labelling

of products as not containing BST, on the grounds that there is no practical way of detecting whether synthetic BST has been used, while naturally occurring BST is always present in dairy products. Therefore the claim that a product was BST-free was classified as a "misleading health claim". This approach attracted some criticism. The *New Scientist* (26 February 1994) argued that concern about BST related to animal welfare (concerns that cows are producing more milk than their bodies are designed to do) and economics, rather than the fact that it was derived from biotechnology, so it was unfair not to allow labelling. Indeed, although synthetic BST is undetectable, milk from small producers whose milk is not pooled with other producers' could in theory be labelled, much as eggs from free-range or from small farms are labelled, so that consumers could make a choice on the basis of animal welfare criteria.

In practice, there has apparently been extensive labelling of dairy products as BST-free. Monsanto, the biotechnology corporation whose product has been licensed, has filed lawsuits against Swiss Valley Farms and Pure Milk & Ice Cream Company. Monsanto also wrote to other producers and retailers saying the company considered their advertising campaigns to be misleading[15]. It is unclear whether this legal action will succeed. Some people believe that such tactics could have the reverse effect, by encouraging consumers to be suspicious of the biotechnology industry, and to resent its intrusion into the production of food. One of the reasons why the EC has prevented the use of synthetic BST is the fear that consumers would be less prone to think of milk as a pure, healthy drink and simply drink less of it. There is a more vociferous anti-biotechnology campaign in the USA, with the Pure Food Campaign and the approach of the FDA is bound to be tested in the Courts.

(b) The Flavr Savr Tomato

The **flavr savr** tomato has been developed by Calgene with the use of biotechnology, to have an increased shelf life, of two to seven days more, while retaining premium quality and competitive price. This is the first food to have new genes that could not be gained by conventional plant breeding. There are two genes, very close together. One is an antisense or "reverse" copy of a gene that codes for polygalacturonase, an enzyme that breaks down cell walls. This blocks the action of the polygalacturonase gene and so stalls the softening of tomatoes, allowing them to ripen at a more leisurely pace on the vine, enhancing their flavour. The second gene is there purely to provide a marker to show whether the antisense gene has been taken up successfully. It is a gene that confers resistance to the antibiotic kanamycin. By exposing the tomatoes to kanamycin at an early age, those without the resistence gene, and so without the antisense Flavr Savr gene, are killed off[16].

---

[15] *New Scientist* 30 April 1994

[16] *Science,* 22 April 1994 p.513

The product is ready to be launched, although there has been opposition from the Pure Foods Campaign and some, but not all, groups of chefs. According to *Science*[17]

> It was the resistance gene that provoked controversy among critics of genetic engineering, as some thought it might be passed on to humans, jeopardising kanamycin's use as an antibacterial. But studies done by Calgene and others confirmed that "there was no reasonable probability of this happening" because the gene's products get destroyed in digestion, says Tom Churchwell, President of Calgene Fresh...

After several months of delay, the product gained approval from the FDA on 18 May 1994. Apparently that approval was not strictly required, but the company wanted to have stringent safety checks before going ahead. One striking aspect is that Calgene plans to flaunt the product's origins so as to boost its claim of freshness. Every tomato will carry a brand name and a statement that it was grown from Flavr Savr seeds. Information at the point of sale will describe the benefits of genetic engineering. In other words, Calgene is challenging the conventional wisdom that the public will dislike the idea of eating the product of genetic engineering and that the origins should therefore be concealed. The company is obviously aiming at producing a high-quality product which will sell at a premium price.

V Opponents of GM Food

GM food has not yet become a large issue in this country, partly because very few of the new techniques have yet been tried in practice. It is difficult to know whether in practice consumers would be disgusted by the idea of genetic modification or whether they would welcome high quality food at reasonable prices, if that was what was on offer. In the USA, there is a definite lobby against GM foods, led by the Pure Food Campaign, based at the Foundation on Economic Trends at Washington. An article by two leaders of this campaign[18] noted evidence from polls that the public overwhelmingly rejects the placing of animal genes in plants and, by an even larger majority, the placing of human genes in animals. It criticised the FDA authorisation of such foods, without a requirement that they be specially labelled, and argued that consumer fears were well-founded, for several reasons.

Their first set of objections related to the agricultural consequences of growing GM crops. There was a serious risk of "biological pollution" if foreign genes from engineered plants were carried via pollen into other crops. For example, resistance to pests or herbicide could be transferred into weeds, with disastrous consequences. Herbicide tolerance might encourage

---

[17] op cit

[18] J Rifkin & T Howard, Consumers reject "frankenfoods", *Chemistry & Industry*, 18 January 1993

increased use of herbicides. Crops engineered to produce their own toxins might result in the evolution of pests resistant to that toxin.

The second objection related to health, and particularly to the Flavr Savr tomato.

> As part of the genetic engineering technique, an antibiotic-resistant gene has been introduced into the tomato; this gene is expressed in every cell of the plant. Some scientists are concerned about the significant health hazard of consuming genetic material that confers resistance to common antibiotics. These same kinds of genes are being placed in dozens of varieties of produce, including squash, melons and berries. Other potential health problems include engineering plants that have increased levels of toxicants and allergens.

The article returns to agriculture for its conclusion.

> Perhaps the most important consideration of all is the impact this technology will have on our farming system. Researchers are already predicting that within our lifetime, genetically engineered food production will eliminate farming as we've known it. Agriculture will move off the soil and into biotechnology companies and corporate giants like ICI, Monsanto, Upjohn and others.

In other words, a whole range of objections is produced against GM foods. Opponents of GM foods fear that biotechnology companies will come to dominate agriculture, and that by the time problems associated with GM foods become apparent, traditional varieties and methods may have been lost. In some sense the objections to GM are inconsistent- part of the objection is that they will inadvertently damage agriculture, while another objection is that they will be so successful as to replace agriculture. The controls over the release of GM organisms have been mentioned in the first section. Proponents of GM would point out that it would be difficult for cross-fertilisation with unrelated wild plants to take place and to transfer qualities such as herbicide resistance to the wild. Plants of different species have mechanisms to prevent them from cross-breeding to create hybrid species, and have evolved not to do so.

The overall collection of objections cannot really be satisfied by any particular points made in defence, because they range so widely. Yet that does not necessarily make them invalid. When new scientific processes come into operation there is often opposition based on a

general idea that what is being undertaken is potentially harmful, not so much because of a specific danger that can be highlighted as because there are bound to be unpredictable consequences which might be dangerous. Arguments of this type have often proved their worth in environmental questions, although they would, of course, exclude major advances and raise the issue of how far the "precautionary principle" should be extended.

There is also a paradox of support for the biotechnology industry as a great modern industry to create wealth and jobs in Europe and the USA, but a strong reluctance to use its products. However, critics of GM food may be willing to use genetically modified products as medicine, on the grounds that medicine is only occasionally used, and often there is no substitute for a particular function. That raises less objection than the example of food, where there are plenty of alternatives and consumption is large, on a regular basis.

Appendix How GM Food is Made

Note: Basic information on genetics may be found in two Library Research Papers 93/55 *Genetically Modified Organisms, Transgenic Animals and Animal Patenting* and 93/66 *Gene Therapy.*

For this discussion, it is essential to know that double-stranded DNA is the usual genetic material in bacteria, plants, animals and some viruses. It is made up of four 'bases' which can be called A,C,G,T. The DNA is generally found as one or more thread-like chromosomes inside cells. Every cell of an organism contains the same DNA. The total DNA present in any cell is called the genome. The genome of higher vertebrates and plants is typically about 5,000,000,000 bases long. The genetic code is written as sequences of the four 'bases'. A triplet of bases in DNA codes for a single amino acid. Amino acids are the building block of proteins, which are the complicated and versatile molecules that make up over half the dry weight of cells. The two strands which make up DNA are paired with each other, but only in a certain way; A with T and C with G. It is said that A is *complementary* to T, for example.

One of the DNA strands is the `sense' strand which is copied when a protein is made. The `copy' is actually made up of the *complementary* sequence to that in DNA. It is known as messenger RNA, and its presence in a cell is the signal that a gene is active. The fact of base-pairing makes it possible to `detect' a sequence of DNA - a gene - by making a probe with the complementary sequence. It also makes the **flavr savr** tomato possible, because messenger RNA from the polygalacturonase gene will base-pair to the messenger RNA from the `antisense' gene that was introduced experimentally. This stops the polygalacturonase enzyme from being synthesised by the cell. Next to genes are `promoter' regions which are stretches of DNA controlling the way genes are copied. In higher plants and animals, much

of the DNA in a chromosome has no known function.

Only stable and well-characterised modifications are incorporated into GM foods. How are animals and plants modified in the first instance? DNA is isolated, modified and put back into the same or another organism. Geneticists can create both random and targeted mutations in the genome of an organism. The mutations can be made by inserting, replacing or deleting segments of DNA. Inserted DNA may come from the same species or from another species, and may itself have been modified. However the genetic modification is brought about, it can be as small as one base pair (the smallest possible insertion, replacement or deletion) or as large as several complete genes - that is, sequences coding for complete proteins, together with regulatory sequences which control the way the gene is copied. A single base change can lead to complete loss of function of the gene, or the protein it codes for. Other genes tolerate the removal of whole stretches of DNA. The point of genetic modification may be to get a plant or animal

1. to make more of a certain gene product (for example a crop resistance protein) or

2. to use a gene that it did not previously possess, from another species, or

3. to use a gene that no organism previously possessed, because a native gene has been altered. The effect of this might be (for example) that a protein folds up in a different way and works better under conditions of stress.

To manipulate genes in this way, geneticists need to isolate the gene which may be a tiny fraction of the total genome of an organism, and then obtain enough copies of it so that it can be worked with and eventually transferred to another organism. Gene transfer is difficult in itself, and is discussed near the end of this section. The problem of isolating and copying genes is addressed by *gene cloning*. Geneticists can exploit the fact that one-celled yeasts and bacteria cells can harbour independently-replicating pieces of DNA separate from their main genome. This separate DNA occurs naturally in many bacteria, as *plasmids*. These small circles of satellite DNA carry relatively few genes, and can be derivatised to make cloning vectors. In yeast, geneticists have introduced YACs, or Yeast Artificial Chromosomes.

Cloning techniques were first perfected in the bacterium *E. coli*. The essential features of a cloning vector are 1) the ability to reproduce in a bacterial (or other) cell and yield multiple copies of itself and 2) the capacity to carry pieces of DNA, such as genes, which have been introduced into it artificially. This feature is made possible by the presence of *restriction sites*. These are short sequences of DNA - typically 6 bases long - that are 'recognised' by a special class of enzymes. A restriction enzyme will cut through the vector at this point, leaving `sticky ends' which can be sealed up after a gene has been inserted. The same enzyme will

cut the same sequence every time it occurs in any other piece of DNA, leaving fragments having `sticky ends' which complement those in a vector. 1000 restriction enzymes are now known, leaving the experimenter the choice of short or long recognition sequences. If the total genome from a cell is to be fragmented, a restriction enzyme recognising a four-base sequence has a higher probability of cutting than another recognising an eight-base sequence, and will generate more and shorter fragments.

Cloning vectors are usually made with multiple restriction sites into which several fragments can be inserted and retrieved later. Advanced cloning vectors can now be bought from biotechnology firms. The vectors have their own 'promoter' DNA sequences which switch genes on, and all the sequences needed for plasmid replication. They also have genes making cells carrying plasmids resistant or sensitive to chemicals, or give a colour test (sensitivity to kanamycin was mentioned in the section on the flavr savr tomato). If it is important to the experiment that the gene makes its protein, then a binding site for RNA polymerase can be inserted. If a gene is only required to be active in a certain tissue, then a tissue-specific promoter DNA can be incorporated.

The principle of cloning is simple. DNA fragments are obtained by digesting a chromosome, or even the total genome, with a restriction enzyme. One of these fragments will be a gene, or part of a gene, which is interesting to the experimenter. These fragments are mixed with cloning vectors 'restricted' with the same enzyme. Ideally, every vector will seal up with a DNA fragment (this does not happen in practice). The vectors are then introduced into cells of *E. coli*, another bacterium, or a yeast. (In fact, not every cell will take up a plasmid). Each cell divides and makes a colony on a dish. The vectors and their DNA inserts are copied every time the cell divides. This gives colonies of hundreds of cells containing DNA inserts. The genes, originally present in one copy in the restriction digest, have been copied hundreds of times. The genes are said to have been cloned. The single gene that is wanted has to be detected, but this is made easier now that there is more than one copy of it.

When a genome is fragmented and inserted into vectors, it is said that a genomic *library* has been prepared. For 99% confidence that every 20,000 base fragment from a DNA digest the size of the human genome is present at least once, then sampling statistics says that about 650,000 different cloning vectors are needed. This gives an idea of the size of the library. A library of the complete genome is not always needed. Every cell in an organism has the same genome, but no cell *expresses* (uses) all the genes it has. This is why nervous tissue (say) is different from skin. The geneticist may be interested only in genes which are expressed in skin cells. A library can be prepared of genes which are only expressed in these cells. Genes which are being actively expressed are copied into messenger RNA. If all the RNAs from two tissues are mixed together, the ones that are common to both tissues can be made to stick together. These can be detected. The other RNAs are unique to each tissue. In practice, some way of telling which of the two tissues the non-sticking RNAs came from is needed. A library can be made of the RNAs from the chosen tissue, instead of DNA from the whole

genome.

E. coli reproduces very rapidly and is excellent for cloning bacterial genes but the genes of yeasts, plants and animals are different from bacteria. These higher organisms are known an eukaryotes. Their genes have long stretches of 'silent' DNA called introns which bacterial cells cannot cope with easily. For cloning eucaryote genes, an abbreviated version of the genome called complementary DNA (or cDNA) is used, rather than fragmented whole genome. cDNA is a copy of messenger RNA, and the enzyme which makes this copy removes all the introns from the RNA so that none are present cDNA. This does not completely solve the problem of cloning eukaryotes genes in a bacterial cell. *E. coli*-derived cloning vectors cannot accept very large DNA inserts. This particular problem is overcome by using cosmid vectors; these are derived from *E. coli* plasmids but also contain a viral gene called *cos*. During cell infection by a virus called phage lambda, the entire viral DNA is first copied, and then packaged into the virus 'head.' The head assembles with a tail to make a mature virus particle which can be released from the cell to infect another cell. The *cos* gene is required for packaging the DNA into the head. It can package any other DNA fragment (up to a certain size) into a virus head. If a bacterial plasmid is cut and then sealed with inserts of the *cos* gene and a long eucaryote cDNA, the whole plasmid will package into virus heads, and the heads will assemble with tails, in a test tube (heads and tails can be bought off the shelf). These virus particles can be used to infect *E. coli* cells where they will make multiple copies of the foreign DNA insert.

Some geneticists prefer to clone eukaryote genes in eukaryote cells, such as those of the yeasts *Saccharomyces cerevisiae* or *Schizosaccharomyces pombe.* Yeast Artificial Chromosomes and the whole genome from an organism can be cut with the same restriction enzyme, and a library prepared. The YACs are then introduced into yeast cells, where they replicate themselves and any genes that have slotted into them. YACs replicate rapidly and tolerate the presence of genes from higher organisms. Restriction enzymes can be used to cut the replicated YACs to retrieve the cloned genes, or to make further insertions or deletions.

Whether bacteria or yeast is used, not all of the cells will take up a vector (ie YAC or plasmid vector). In bacteria, the ones that do can be detected by a colour test. Some vectors have a gene called lac which turns bacterial colonies blue. If a foreign gene is inserted at a restriction site in the lac gene, colonies carrying it will fail to go blue and can be picked out. Of these colonies, a subset will have plasmid with a copy of a DNA fragment which is genetically interesting. These can be picked out by using an synthetic *oligo*, a piece of DNA about 17 bases long which is predicted to match a part of the gene (see introductory paragraph on complementary sequences). The prediction can be made from knowledge of the protein the gene makes. Any particular 17-base sequence is likely to occur only once or twice in a library of the total genome of a higher organism, and cells detected by the oligo probably contain the desired gene. These cells can be selected and grown up to produce thousands of copies of the gene. However, in 1985 a cell-free technique was developed

which rapidly produces large amounts of any interesting gene that has hybridised to an oligo. The polymerase chain reaction (PCR) is a rapid method of *amplifying* a small piece of DNA present in a library against the background of the total genome. DNA containing the gene to be amplified is mixed with an enzyme which copies DNA. Two short DNA *primers* which are needed to start the reaction off are added. The mixture is repeatedly heated and cooled. After one cycle, there are two DNA copies, which can each be copied in their turn. After 40 cycles there are (in theory) about a million million copies.

Hit-and-run vectors have been developed from plasmid vectors to produce targeted changes to genomes, ie mutations at chosen sites. The whole vector inserts itself and its foreign DNA into the host genome. Most insert randomly, but a proportion will come to sit next to the target gene. The foreign DNA which will introduce a small mutation is not quite the same as the target gene. In these circumstances, pairing can occur spontaneously between the two sequences of DNA, and one of them will be excised, together with the rest of the hit-and -run vector which had inserted itself into the genome. The non-random mutations can be selected more reliably if the introduced gene needs a *promoter* which is present in the host cell genome. Only an introduced gene which inserts next to the promoter and displaces the native gene will be `switched on.'

For the production of a transgenic plant, cloned DNA with the desired modifications must be inserted into the host plant genome. No plant plasmids are known, but transformation of plants can be achieved using *Agrobacterium*, the only bacterium known to fuse any part of its DNA with that of higher plants, thereby crossing the conceptual barrier between bacteria and higher organisms. A vector can be prepared which incorporates *Agrobacterium's* virulence gene and the foreign DNA which is to be introduced, and any of the other features which have been discussed above. Many crop plants - among them tobacco, wheat, tomato -have been modified since 1983.

For the production of a transgenic animal, different protocols are necessary. Cloned and modified DNA may be microinjected one of the two nuclei of a fertilised egg cell, but *electroporation* is currently commoner. A suspension containing vectors is mixed with cells derived from later embryos (eight to thirty-two cell stage). A high voltage pulse causes some of the cells to take up vectors. About 12 of these cells may then be injected into the fluid filled cavity of a 32 cell embryo which is put back into a pregnant female. These cells proliferate in the embryo and contribute to many structures in the live young. If their progeny are interbred, pure-breeding transgenic animals can be obtained. These techniques are more advanced in the mouse than in farm animals. Cows, pigs and sheep produce fewer eggs, their nuclei are difficult to discern, their embryos are more resistant to manipulation, and sheep and cattle rarely give birth to more than two offspring.

Further Reading

1) Report of the Committee on the ethics of genetic modification and food use. Chairman John Polkinghorne (HMSO 1993)

2) House of Lords Select Committee on Science and Technology, Regulation of the United Kingdom Biotechnology Industry and Global Competitiveness (1992/93 HL 80)

3) Genetically Modified Organisms, Transgenic Animals and Animal Patenting, (Library Paper 93/55)

4) Genetic Modification of Fish - A UK Perspective (DOE 1994)

5) Genetically Modified Crops and their Wild Relatives - A UK Perspective (DOE 1994)

6) A New Technological Era for American Agriculture (US Office of Technology Assessment 1992)

7) Christopher Wills, Exons, Introns and Talking Genes, 1992 (OUP). This book on the human genome project gently introduces the lay reader to the jargon of modern genetics. It is not a book about GMOs or GM food.

8) R W Old and S B Primrose, Principles of Gene Manipulation, 4th edition, 1992 reprint (Blackwells). This is a standard undergraduate text.

9) A L Joyner, Gene Targeting, 1993 (IXL Press). This is a lab manual on the creation of rational gene mutations. It updates Old and Primrose in some respects. There is a discussion on introducing changes into higher organisms.

Please cut

Research Paper 94/ **Section Code: SES**

Title: Genetically Modified Food

It would greatly help to ensure that Research Papers fulfil their purpose if Members (or their staff) would fill in and return this brief pre-addressed questionnaire. Negative responses can be as useful as positive.

For your purposes, did you find this paper:

	Very useful	**Quite useful**	**Not much use**
1.	☐	☐	☐
	Too long	**The right length**	**Too short**
2.	☐	☐	☐
	Clear	**Not always clear**	**Rather unclear**
3.	☐	☐	☐

Any comments? _____

_____

_____

_____

_____

_____

_____

_____

_____

Name ..... **MP/Assistant to** .....

(Please print)

Please fold

INTERNAL

Miss Nicola Harland
House of Commons
Department of the Library
1 Derby Gate
London SW1A 2DG

Please fold

SCIENCE AND TECHNOLOGY

Other papers in this subject area include

93/55 Genetically Modified Organisms, Transgenic Animals and Animal Patenting

93/66 Gene Therapy

FOOD