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Genetically Modified (GM) Crops And The EU:
What Are The Prospects?

TABLE OF CONTENTS

TITLE - **PAGE**

METHODOLOGY

Research undertaken for this report came almost exclusively from sourced material such as scientific journals, books, articles, television programmes and the internet, although individuals were spoken to both in person and via email to ascertain public opinion on the subject of genetically modified (GM) crops.

A considerable amount of time was spent by the author of this report seeking relevant information on the assigned topic and then analysing material obtained. It was soon found that a wealth of information and opinion was available which required serious consideration as to how it should be presented.

The inclusion of an appendix serves to inform the reader of some basic techniques used in genetic engineering.

Overall the author aimed to present a very diverse subject in a balanced way that was both easy to read and understand, highlighting issues of importance regarding GM crops and Europe.

SUMMARY

Genetic manipulation, regardless of the target organism, raises political, social and environmental issues which have caused many individuals to ask what are the prospects of genetically modified organisms (GMO)? This report aimed to address this question and issues associated with it concentrating on the European perspective and perception of genetically modified (GM) crops.

Plants are historically one of the oldest organisms modified by humans, however within the past decade there has been a major shift in the way this modification occurs. The advent of genetic engineering allowed plant breeders to overcome one of the main limitations of conventional breeding techniques, the species barrier, which prevents the cross breeding of unrelated species. By overcoming this barrier scientists were able to access genes from any species and insert them into a completely unrelated organism creating a hybrid or genetically modified organism (GMO) which would otherwise not naturally exist.

The Case For GM Crops -

A commonly held view of those in favour of GM crops is that it will revolutionise agriculture allowing us to create the 'perfect organism' with the ability to become more resistant to adverse environmental conditions such as drought or frost, thereby expanding the range of habitats in which that crop may be cultivated. Many argue that with an increasing global population expected to reach 8.9 billion by 2050 we have no choice but to utilise the potential power of GM crops to solve the problem of global food security.

Monsanto, the world's largest GM seed company foresees three waves of beneficial GM products; crops resistant to insects, disease and tolerance of herbicides, crops with increased nutritional value such as an increased vitamin or fibre content and finally crops containing edible vaccines or other substances which will help individuals to prevent/fight disease.

Public Opinion -

The development of GM crops has been an extremely controversial subject since its conception in the early 1990s most notably in Europe, where public opinion has been largely anti-GM.

Throughout Europe public opinion seems to be rather negative towards GMOs, this is best shown by the adoption of GM-free policies by various supermarkets in the UK. Four out of five Italians said they would be willing to spend more for healthier food, a view supported by findings of the Nordic Industrial Fund which found that '*being non-GM was a major benefit in itself*'.

The Case Against GM Crops –

Genetic engineering is not a subject of isolation but one of integration whereby species barriers are broken down allowing for the creation of hybrid organisms which would otherwise not naturally exist. Moving genes encoding proteins between species may result in allergic reactions, If these proteins have never before been found in our food supply how can we guarantee safety when a proteins allergenic characteristics are unknown?

In the US, analysis of four years of data from the US Department Of Agriculture found that contrary to Monsanto's claims herbicide use in the US has increased largely due to two factors. The first arises due to the nature of Glyphosate which allows it to be applied all year round, whereby previously herbicides were generally applied before the crop was grown. In addition were weed resistance is beginning to develop and the effectiveness of Glyphosate is decreasing other more toxic and persistent herbicides are being used as well.

Antibiotic resistance genes have been used as markers in GM crops to identify which plant cells have successfully incorporated the desired foreign genes during modification. However in 2000 the British Medical Association warned that '*the risk* *to human health from antibiotic resistance developing in micro-organisms is one of the major public health threats that will be faced in the 21st century*'.

The UK governments official advisor on GM foods, the 'Agriculture and Environment Biotechnology Commission' (AEBC) has said it would '*be difficult and in some cases impossible to guarantee*' that any British food was 'GM free' if commercial growing of GM crops went ahead. This concern is also widely held by members of the public throughout Europe who felt that contamination was a major threat to biodiversity.

Commercial GM Crops In Europe -

In Spain the introduction of Bt maize has resulted in a 5-7% increase in yield over conventional maize, equivalent to an additional €10.82-€15.22 million increase in terms of value. This example highlights how under certain circumstances GM crops can provide great benefits, whereby crops previously susceptible to high pest pressures can be engineered to maximise yields under these conditions.

RR soybeans have been a massive success in Romania increasing yields by up to 51% with an average increase of 31%, a larger increase than experienced with Bt maize in Spain. One reason for this success has been due to better weed management and the ability to kill Johnson Grass using Glyphosate. In other regions of the world where RR soybeans have been adopted such as Canada and the US yield increases have been largely neutral as weeds are less of a problem and therefore cause less reduction in yield.

Future Prospects -

Much of the objection to GM crops stems from the view that they are of little benefit to the average individual, whilst at the same time are also regarded to be harmful and potentially dangerous to the environment. Perhaps the next generation of GM crops will experience less resistance as 'quality traits' become commonplace, this is especially relevant to today's society as more individuals are becoming health and environmentally conscious. Ultimately the aim of biotechnology will remain the same

- to produce a plant that is considered better in some way than its wild type relative, one possibility involves the production of edible vaccines.

The European Union –

GM foods were first allowed into Europe in 1990, however in 1998 the EU agreed to improve laws governing the release of GMOs into the environment, whilst this was happening a number of European countries decided not to approve any new GMOs until the public and environment were better protects; this was called the 'de facto' moratorium and lasted for six years before it was broken by the approval Bt11 Maize in May of 2004.

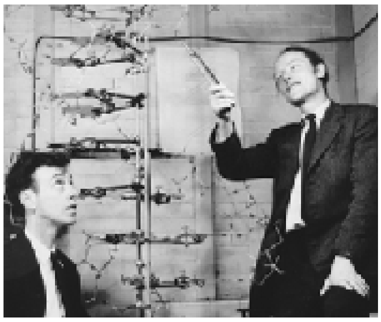
In May of 2003 the US, Argentina and Canada acting through the World Trade Organisation (WTO) launched a trade dispute against the EU complaining that the EU moratorium and national bans were a barrier to trade. On November 29th of 2004 European members states were asked to vote on whether or not these bans should be lifted.

The future prospects of GM crops in Europe could be decided this year.

GENETICALLY MODIFIED (GM) CROPS AND THE EU: WHAT ARE THE PROSPECTS?

INTRODUCTION –

FIGURE 1 – DISCOVERING DNA[1]

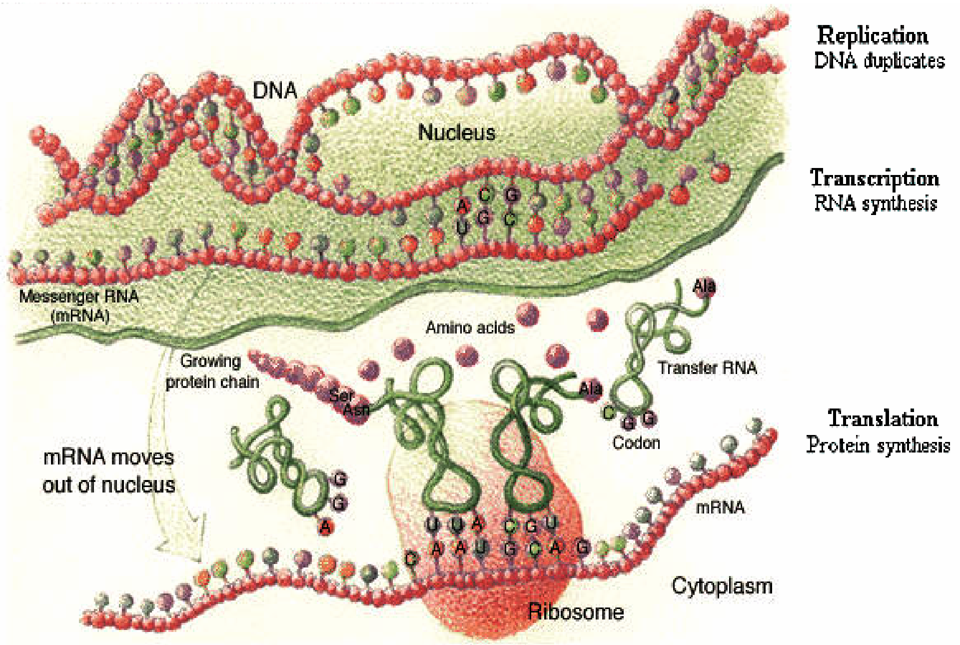


In 1953 Watson and Crick (*figure 1*) discovered the '*Mona Lisa of modern science*'[2], deoxyribonucleic acid (DNA) soon prompting the statement that they '*had found the secret of life*'[3]. Half a century later the human genome was sequenced and humankind were on the '*verge of gaining immense new power to heal*'[4].

DISCOVERING GENES –

Early observations of the cell's nucleus revealed '*threadlike structures*' which scientists called chromosomes, leading Walter Sutton to speculate they contained units of heredity called genes[5]. Mendel previously demonstrated that these genes or '*factors*' led to height or colour variation in pea plants[6] and by doing so created a foundation for future genetic studies.

FIGURE 2 – FROM GENES TO PROTEINS[7]



Today we know that these genes exist in multiple forms called alleles whose ultimate expression as a protein product (*figure 2)* determines an organism's characteristics, leading to possible predisposition or inheritance of disease.

Therefore by sequencing the entire genetic complement, the genome, it is in theory possible to design the perfect organism through the selection of desirable and elimination of undesirable traits encoded by these genes.

However the act of genetic manipulation, regardless of the target organism, raises political, social and environmental issues causing many individuals to ask, what are the prospects of genetically modified organisms (GMOs)? This report aims to address this question and issues associated with it, concentrating on the European perspective and perception of genetically modified (GM) crops.

THE 'GREEN REVOLUTION'

FIGURE 3 – THE GREEN REVOLUTION[9]

During the 1960s high-yielding varieties of wheat and rice were created by conventional breeding techniques, allowing many third world countries such as India to move away from a position of food scarcity and become net exporters of these cereals.

This was achieved by crossing desirable traits from crop varieties found throughout the world into semi-dwarf lines, ultimately leading to new varieties that matured quickly and were insensitive to photoperiod, thereby allowing crops to be grown more than once per year[8].

The 'green revolution' (*figure 3)* required that farmers not only adopted the new seeds but also signed up to a high-input method of agriculture which included the use of fertilisers, herbicides and pesticides in order to obtain the maximum yield. However as the revolution progressed so did the opposition, many groups and individuals claimed that despite the global increase in food production millions still remained hungry and that the high-input nature needed to sustain these increases was damaging the environment; a new revolution was called for.

THE 'GENE REVOLUTION'

Plants are historically one of the oldest organisms modified by humans, however within the past decade there has been a major shift in the way this modification occurs. The advent of genetic engineering allowed plant breeders to overcome one of the main limitations of conventional breeding techniques, the species barrier, which prevents the cross breeding of unrelated species. By overcoming this barrier scientists were able to access genes from any species and insert them into a completely unrelated organism, creating a hybrid or GMO which would otherwise not naturally exist.

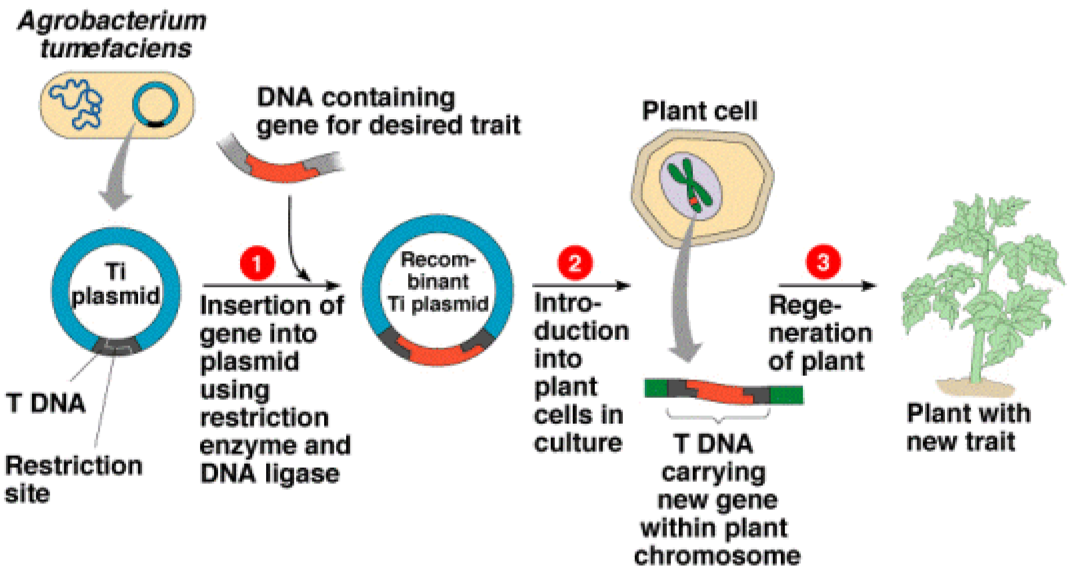
THE GENERATION OF GM CROPS –

FIGURE 4 – CROWN GALL DISEASE[10]

Although many techniques exist which allow for the genetic modification of plants, one of the most commonly employed procedures is the use of a Gram-negative soil bacterium entitled *Agrobacterium tumefaciens.* Infection of plant wound sites at the soil-air interface ultimately results in the formation of a tumorous tissue growth called crown gall disease (*figure 4*).

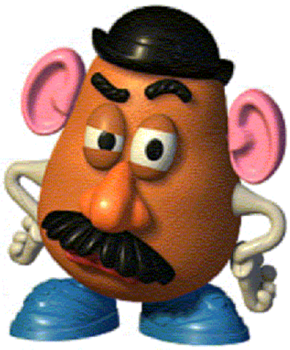
Crown gall formation depends on the presence of a Ti plasmid, by inserting DNA sequences between the left and right border of the T-DNA region of the Ti plasmid, genes of interest may be incorporated within the plant genome during the infection process, as summarised in figure 5.

FIGURE 5 – AGROBACTERIUM MEDIATED PLANT TRANSFORMATION[11]



Under natural conditions, characteristics of a plant such as fruit size are controlled by groups of functionally related genes which provide co-ordinated control of the trait. Novel genes inserted into a plant also need regulatory sequences to function correctly, one commonly used sequence is the viral 35s promoter sequence taken from the plant pathogen Cauliflower Mosaic Virus (CaMV) resulting in the constitutive expression of the gene[12].

FIGURE 6 – A GM POTATO?[13]



However the insertion of novel genes from one organism to another is not without its problems and most attempts to create GM crops fail. This is largely due to the random nature of the insertion process which can result in variable levels of gene expression or the silencing of native genes (*figure 6*).

Since genes do not function in isolation but rather as interacting partnerships with neighbouring and distant genes, it is not uncommon for introduced genes to behave unexpectedly as a result of these interactions. For example researchers at the University of Oxford modified potatoes in order to better understand cell respiration, but unexpectedly created high starch potatoes. They commented '*We were as surprised as anyone. Nothing in our understanding of the metabolic pathways of plants would have suggested that our enzyme would have such a profound influence on starch production*'[14].

Therefore whilst it is important to recognise the many potential benefits of genetic modification it is also important to recognise the many potential complications and uncertainty associated with the technology. These two points have largely contributed to a division of opinion regarding GMOs, with those in favour of the technology promoting it as a solution to problems such as world hunger and those against, urging caution warning that we do not know enough about the long term consequences.

THE CASE FOR GM CROPS –

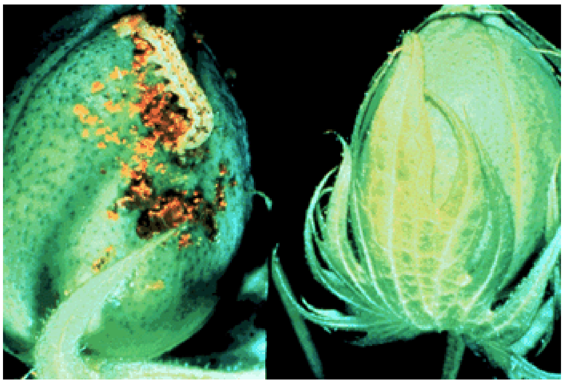
A commonly held view by those in favour of GM crops is that it will 'revolutionise agriculture' allowing us to create the 'perfect organism' with the ability to become more resistant to adverse environmental conditions such as drought or frost, thereby expanding the range of habitats in which that crop may be cultivated. Many argue that with an increasing global population expected to reach 8.9 billion by 2050[15] we have no choice but to utilise the potential power of GM crops in order to solve the problem of global food security.

Monsanto, the world's largest GM seed company foresees three waves of beneficial GM products; crops resistant to insects, disease and tolerance of herbicides, crops with increased nutritional value such as an increased vitamin or fibre content and finally crops containing edible vaccines or other substances which will help individuals to prevent/fight disease[16].

FIGURE 7 – ROUNDUP COMPARISON[17]

They also claim that GM crops will displace resource and energy intensive inputs such as fuel, fertilisers and pesticides thereby reducing negative impacts on the environment. For example the first wave of GM crops were designed to be tolerant of the herbicide glyphosate (Roundup) increasing yield through better weed management whilst at the same time reducing the number of sprays needed to control the weeds (figure 7).

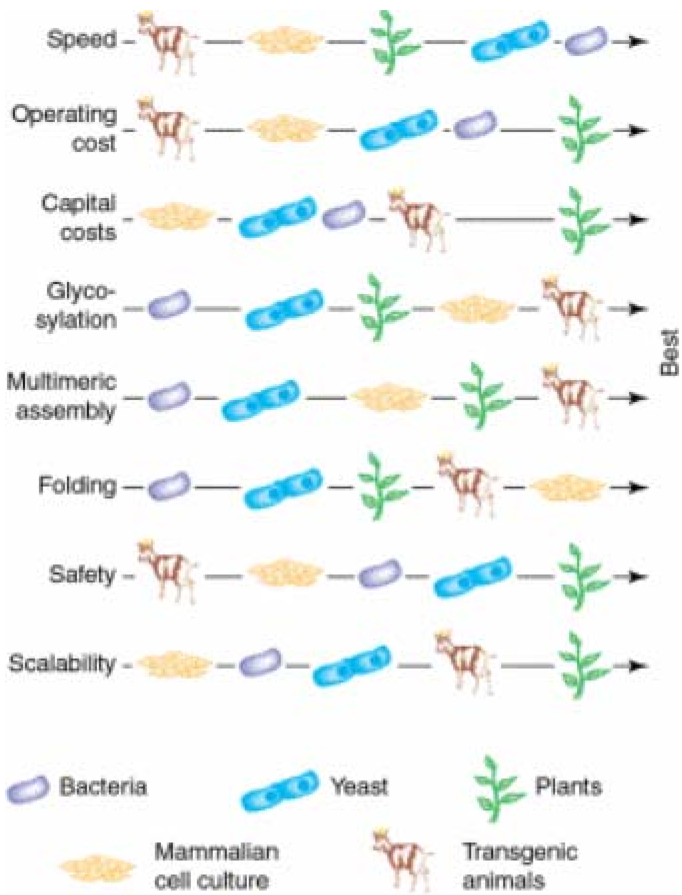
FIGURE 8 – CONVENTIONAL VS BT COTTON[18]



Plants have also been engineered to produce pesticide which can kill agricultural pests responsible for loss of yield, such as the European Corn Borer. Several companies have developed strains of maize, cotton and potatoes containing a gene from the naturally occurring soil bacterium *Bacillus thuringiensis* (Bt) who protein product (*Cry)* the Bt toxin, causes death by starvation of feeding insects (*figure 8*).

Ultimately replacing chemical sprays with genetically based resistance could lower the use of pesticides having the advantage of targeting only pest organisms, and a lower cost since equipment associated with spraying (such as planes) will no longer be needed. Figure 9 depicts possible reasons and advantages of using plants rather than other organisms for genetic manipulation.

FIGURE 9 – BENEFITS OF USING PLANTS[19]



Some individuals may often find themselves amazed by the technology available to today's society and how far science and technology have come within a relatively short time period, the 'GM industry' should be complemented for contributing to this progress. But progress is a double edged sword for we as a species have reached a pivotal moment in human history whereby we possess technology which has the potential to destroy us. New technologies produce greater risk and greater opportunities, we must see that we harness the opportunities and avoid the risks of misuse (*figure 10*).

FIGURE 10 – PROGRESS…BUT AT WHAT COST?[20]

The development of GM crops has been an extremely controversial subject, most notably in Europe, where public opinion has been largely anti-GM. The following sections shall examine possible reasons for this objection starting with the Europeans perception of GMOs.

WHAT DO THE PUBLIC THINK?

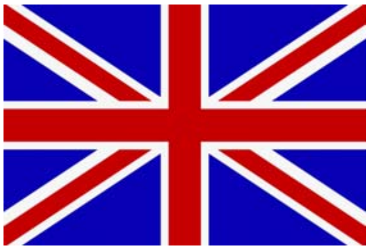
European Union –

FIGURE 11 – EU[21]

The resistance to GM foods in Europe is gaining momentum, there are currently 162 European regions and provinces now declaring themselves 'GM free zones' or publicly wishing to restrict GM crops, over 4500 local governments are calling for restrictions to commercial growing[22]. These actions are reflected by an opinion poll published by the European Commission, a branch of the European Union, which found that 94.6% of European Union (EU) citizens want the right to choose, 85.9% want to know more before eating GMOs and 70.9% do not want GM food at all[23].

United Kingdom –

FIGURE 12 – UNITED KINGDOM[24]



In November of 2003 the 'British National Trust' voted for the Trust to go GM free and ban GM crops from being grown on Trust land. The Trust is the largest private owner of agricultural land in England, Wales and Northern Ireland owning more than 600,000 acres of land over 80% of which is farmed or depends upon farming for its management[25].

On September 2nd of 2004 a survey by the 'Consumers Association' found more people stated they were against GM crops than in a similar study conducted two years previously. 6 out of 10 Britons said they were concerned about the use of genetic modification in food production and wanted to avoid GM foods[26]. Like many other regions in Europe public perception of GM crops is largely negative, and some individuals have taken to vandalising GM field test sites. Prince Charles, a publicly voiced opponent of GM foods stated '*this kind of genetic modification takes mankind into the realms that belong to God and God alone*'[27].

Wales –

FIGURE 13 – WALES[28]

In February of 2004, the Welsh and Scottish Executive blocked the go-ahead for the first commercial GM crop in Britain, GM maize T25, patented by Bayer. The Welsh executive pointed out that '*UK regulations stipulate that a particular crop can be grown in one country only if the other two agree*'[29].

Wales appears to be the most anti-GM country in the UK with the Welsh Assembly declaring itself as a 'GMO free region' having 35 councils who approved GMO free resolutions[30].

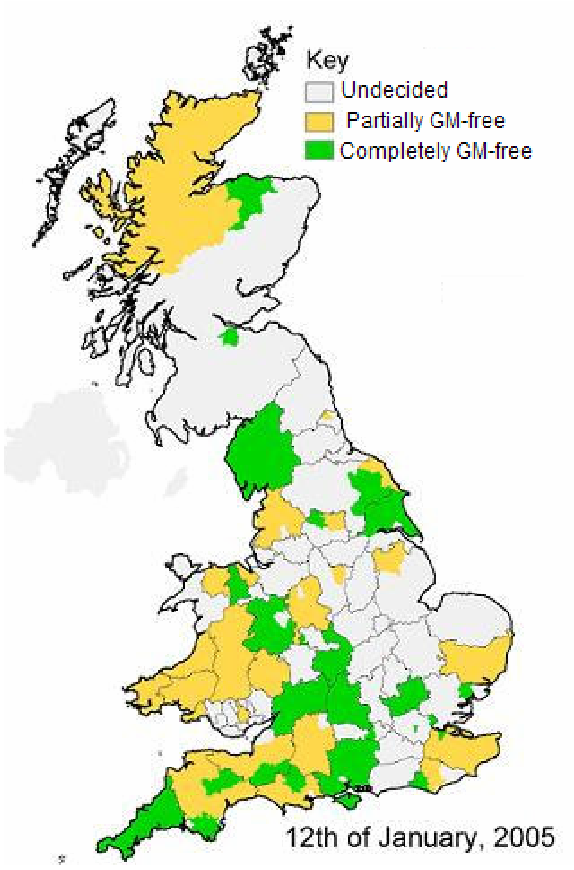
Scotland –

FIGURE 14 – SCOTLAND[31]

On the 18th of December 2003, the Highland Council's Land & Environment Select Committee recommended that '*active steps be taken to encourage the establishment of a GM free zone in the Highlands*', shortly thereafter the Highland council joined the European Network of GMO-free Regions, a group of regions opposed to GM crops[32]. Following this the councils of Moray and The Western Isles also declared themselves 'GMO-free' regions.

Figure 15 displays a map of the UK and the currently held views of councils on GMOs throughout the land.

<u>FIGURE 15 – GM STATUS IN THE UK</u>[33]



The laws of supply and demand dictate that when something is in demand it is more expensive to purchase, however when there is no market for that product the price is dramatically reduced. In the UK the demand for GM foods appears to be minimal, as judged from the actions of various councils and public opinion. This lack of demand also appears to be reflected by almost every supermarket in the UK who have adopted 'GM-free' polices (*table 1*).

TABLE 1 – GM POLICES OF UK SUPERMARKETS[34]

COMPANY	GM POLICY
ASDA [35]	‘*Asda has been working with its suppliers to ensure that Asda brand products are from a non-GM source of soya and maize*’. Asda’s policy is that no new products are to contain GM ingredients or derivatives; existing products should use certified non-GM sources and accept no new GM ingredients.
co-op [36]	‘*Aim to reduce, eliminate or exclude GM ingredients but where it is not possible we will clearly label*’. In 1999 the company withdrew from government sponsored field trials of GM crops on environmental grounds.
M&S [37]	Marks and Spencer believe that ’*genetic modification could have the potential to offer customers direct benefits in new products, which should be assessed on their own merits*’. But in 1999 the company banned all GM food saying ‘*we will be the only major retailer where customers can purchase any product on the shelves with full confidence that no GM ingredients or their derivates have been used*’.
MORRISONS [38]	Morrisons are in ‘*the process of clearly labelling any Morrisons own brand product which contains a GM ingredient*’. So far this extends to six products, it is also looking at the possibilities of sourcing GM-free foods in the future.
Iceland [39]	Iceland guaranteed that from May 1, 1998 no own-label production would contain any genetically modified ingredients and derivatives. Iceland is campaigning for crop segregation.

SAFEWAY [40]	Safeway's policy is to label all GM foods. It has developed sources of non-GM ingredients which it is using in certain own-brand products. The company has said that '*genetic modification has the potential to provide products with improved quality and flavour, and with reduced impact on the environment through the reduced use of pesticides and agrochemicals*'.
Sainsbury's making life taste better [41]	Sainsbury's is committed to eliminating all GM content from its own brand products. It has said it will abandon product lines altogether if it cannot establish a GM-free source or find alternatives.
Somerfield [42]	Somerfield '*guarantees consumers choice by labelling all products containing GM ingredients. We are also introducing labelling to indicate where GM derivatives are present as an additive such as oils. We have looked at all products in our own label range containing soya to see if alternative ingredients can be used. It is our intention to label all GM additives and to label them as soon as possible*'.
TESCO Every little helps [43]	Tesco started labelling products that contain GM ingredients and derivatives in 1998, '*Customers can then make an informed choice and decide if they want to buy them*'.
Waitrose [44]	Waitrose is looking to reduce the use of GM ingredients from all its own brand products.

The views of various supermarkets in the UK clearly reflect an overwhelming public rejection to GM foods, if there was no objection there would be no GM-free policies. In addition Monsanto closed its wheat development centre in Europe in 2003 stating '*our lack of success in hybrids means this is no longer a good strategic fit for Monsanto*'[45].

Spain –

FIGURE 16 – SPAIN[46]

In Spain several regions have reacted to approval by the central government to grow commercially certain varieties of GM crops, for example in May of 2000, the parliament of Castilla la Mancha asked the central government to declare a moratorium on commercial GM crops until a risk assessment was carried. The parliaments of Balears, Andalucia, Asturias among others have echoed the views of the Castilla la Mancha region supporting the proposed five year moratorium[47].

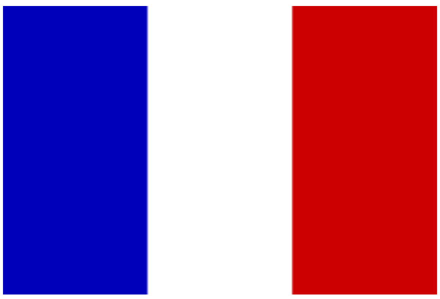
Portugal –

FIGURE 17 – PORTUGAL[48]

On August the 9th of 2004 the whole Algarve region declared itself a 'GMO-free zone' stating that '*GMOs must not be grown in the Algarve until their safety is 100% proven scientifically*'. The Algarve is a popular tourist destination for many Europeans, and it appears that this region of Portugal feels GM crops are neither wanted by the native population or visiting tourists[49].

France –

FIGURE 18 – FRANCE[50]



Pas d'OGM dans ma commune (No GMO in my municipality) was a French campaign launched in 2001 by several environmental groups including Greenpeace with the objective of stopping environmental contamination with GMOs; to date more than 300 majors have declared their municipality 'GMO-free'. A poll of French people found that more than half had serious reservations about the use of GMOs[51].

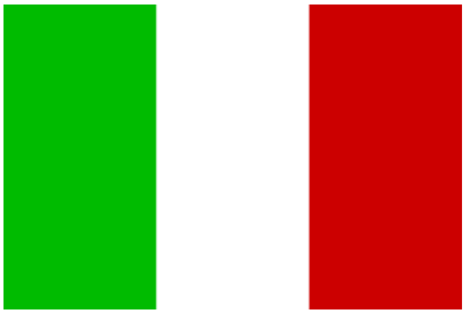
The Netherlands -

FIGURE 19 – THE NETHERLANDS[52]

A poll of Dutch people in 2001 by the University of Twente found that 65% of people rejected GM foods (an increase from 52% in the last poll). In 2002 the Terlouw Committee undertook a government sponsored survey to discover what the Dutch people felt about GM foods, they reported '*the general impression is that the public takes a very reserved stance on GM in food. The usefulness is undoubted, the risks are feared and alternatives are being asked for*'. 69% of Dutch people who took part in the survey stated that they found the use of GM in food '*unwanted*'[53].

Italy –

FIGURE 20 – ITALY[54]



In March of 2001 a poll carried out for the Ministry of Agriculture found that 67% of Italians were against the use of GMOs in agricultural production, 75% thought legislation on food safety was inadequate and 4 out of 5 Italians would spend more to get healthier food[55].

By the end of 2003 more than 500 cities in Italy had taken a position against the use of GMOs in agriculture, including Rome and Milan; nearly 80% of Italy is now declared 'GMO-free'[56].

Germany –

FIGURE 21 – GERMANY[57]

Friends of the Earth Germany launched a campaign in 2004 entitled 'Faire Nachbarschaft' (fair neighbourhood). In the first year of the campaign 50 'GMO-free' zones have been set up with an alliance of more than 11,600 organic and conventional farmers, representing 430,000 hectares of agricultural land[58]. Campaigns such as this have been launched throughout Europe often succeeding in establishing 'GMO-free' regions with the support of local farmers; this seems to reflect not only the concern of consumers but also those of producers.

Finland –

FIGURE 22 – FINLAND[59]

In November of 2000 the Nordic Industrial Fund carried out a survey in Denmark, Finland, Norway and Sweden on GM foods and applications of genetic modification. The survey found that it was regarded as a major benefit in itself that a product is non-GM and that when a product involved genetic modification this elicited numerous negative associations mainly '*unhealthy*' and '*uncertainty*'[60].

Greece –

FIGURE 23 – GREECE[61]

There is growing opposition to GMOs throughout Greece largely fuelled by fears that GM crops will compromise local ecosystems and interfere with efforts to develop organic products. 93% of Greeks questioned in a national poll stated they did not want GM crops on their land. The Greek National Bioethics Commission has recommended that Greece adopt a temporary moratorium on the cultivation of GM crops concentrating instead on '*integrated and sustainable agricultural practices*'[62].

Serbia & Montenegro –

FIGURE 24 – SERBIA & MONTENEGRO[63]

Serbia and Montenegro was the first country in South-East Europe to establish a regulatory system for controlling GMOs. In May of 2001 a law on GMOs came into force regulating the conditions for the deliberate release of GMOs and their placing on the market. Since then Serbia and Montenegro has had a policy of keeping its agriculture free from GMOs and has strict controls on import. Before the implementation of these regulations two permits had been issued for the commercial growth of Roundup Ready (RR) soybeans and maize[64].

Croatia –

FIGURE 25 – CROATIA[65]

The Croatian parliament has adopted several laws regulating GMOs, in July of 2003 a law came into force requiring authorisation for all GM food and animal feed placed on the market. The Health Ministry has to keep a register of all GM foods marketed and the Agriculture Ministry must maintain a register of all GM feed placed on the market.

The Nature Protection Law bans the release of GMOs in protected areas, areas of organic farming and in areas that are of importance to ecotourism. The law also bans the deliberate release of GM seeds except for areas specially designated by the Ministry of Agriculture and the Ministry of Environment and approved by the government[66].

Albania –

FIGURE 26 – ALBANIA[67]

Albania's Commission of Agriculture and Food in addition to the Commission of the Environment voted in favour of a 5 year ban on GMOs, no GM crops are currently grown[68].

WHAT EUROPE THINKS OF GM FOOD

Throughout Europe public opinion seems to be rather negative towards GMOs, this is best shown by the adoption of 'GM-free' policies in UK supermarkets. Four out of five Italians said they would be willing to spend more for healthier food, a view supported by findings of the Nordic Industrial Fund which found that '*being non-GM was a major benefit in itself*'.

Environmental groups representing citizens who object to the commercial growing of GM crops have launched campaigns such as the French Pas d'OGM dans ma commune (No GMO in my municipality) campaign and the German 'Faire Nachbarschaft' (fair neighbourhood) campaign latter joined and supported by alliances of organic and conventional farmers, reflecting concern in both consumers and producers. These campaigns have been so successful that Greece and Italy have declared a large majority of their land 'GMO-free' or have adopted 'GMO-free' policies. This is interesting as in these two countries religion is an important part of society and seem to reflect Prince Charles's view that '*this kind of genetic modification takes mankind into the realms that belong to God and God alone*'

In regions where tourism is an important factor to the local economy such the as Algarve of Portugal, GM crops have been banned completely due to fears of genetic contamination. All surveys conducted found, in most cases, an overwhelming majority of people did not wish to eat GM food and concerns regarding safety and effects on the environment were the most common objections.

Clearly there is resistance to GM crops in Europe, but why? The following sections attempt to address this question.

EUROPEANS AND SCIENCE

Science and technology are an integral part of our lives and effect almost every aspect of it, however due to the complex and intricate nature of the subject members of the general public lacking a scientific background may feel lost, confused and anxious about its developments. This may reflect a lack of ability by scientists to convey scientific discoveries to the general public in a way that can be clearly understood, regardless of whether the individual possesses a scientific background (*table 2)*.

TABLE 2 – THE EUROPEAN PERCEPTION OF SCIENCE[69]

	Do you feel well or poorly informed about the following subjects?		**Are you rather interested or not very interested in each of the following subjects?**	
AREAS	WELL INFORMED (%)	POORLY INFORMED	RATHER INTERESTED	NOT INTERESTED
SPORT	57.0	40.5	54.3	44.7
CULTURE	48.5	47.0	56.9	40.8
POLITICS	44.3	52.2	41.3	57.0
SCIENCE + TECHNOLOGY	33.4	61.4	45.3	52.2
ECONOMICS + FINANCE	31.9	63.5	37.9	59.8

This 'Eurobarometer' survey tested to what extent people felt informed or were interested in five areas. As a whole Europeans felt that they were best informed about sport (57%), culture (48.5%) and politics (44.3%), however when it came to interest culture came first (56.9%) then sport (54.3%) and science was is in third place with 45.3%. This shows that science is perceived to be an interesting subject however 61.4% of Europeans feel that they are poorly informed about it. This begs the question of who is informing the public and is the information being given accurate? (*table 3*).

TABLE 3 – HOW ARE EUROPEANS INFORMED ABOUT SCIENCE?[70]

	Agree	Disagree	Don't know
I prefer to watch television programmes on science and technology rather than read articles on the subject.	66.4	23.8	9.9
I rarely read articles on science and technology.	60.6	33.5	6.0
There are too many articles and programmes on science and technology.	18.0	65.8	16.1
Scientific and technological developments are often presented too negatively.	36.5	39.1	24.4
The majority of journalists treating scientific subjects do not have the necessary knowledge or training.	53.3	20.0	26.7

These results show that the majority of Europeans prefer to watch television programmes on science and technology rather than read articles on the subject, however are the various media outlets portraying the correct picture of GM crops? or is the subject 'spun' to seem more interesting and appealing to the viewer? In the UK phrases such as '*Frankenstein foods*' or '*killer tomatoes*' seem to suggest the latter. Therefore a key contributing factor towards the European objection to GM crops could simply be an issue of communication, whereby those who have a scientific background and access to scientific journals seem less apprehensive about the subject

However not all individuals with a scientific background are in favour of GM crops suggesting that whilst the media may play an influential role in shaping public opinion, other sources of information still lead people to hold a negative view. The following section shall examine in detail scientific grounds for concern and investigate possible reasons for strong objections to GM crops.

THE CASE AGAINST GM CROPS

Prior to the sequencing of the human genome it was a widely held belief that there were around 100,000 genes; however when it was revealed there were only 30,000 many scientists were shocked. This destroyed the idea of one gene producing one protein, instead it was discovered that a gene may serve multiple functions (i.e. produce multiple protein products) through processes such as alternative splicing.

FIGURE 27 – GM PROTEST[71]

Critics of Biotechnology (*figure 27)* say that such a basic miscalculation of the human genome casts doubts on the precision at which we can manipulate other genomes. This is a significant as genes do not work like Lego whereby you 'snap' in one gene and get one trait, rather there is a degree of uncertainty as genes interact with other genes sometimes causing the inserted gene to behave unexpectedly. Table 4 highlights some other uncertainties associated with this new technology.

TABLE 4 – THE UNPREDICTABLE BEHAVIOUR OF GM CROPS[72]

COMMON ASSUMPTIONS ON GENETIC ENGINEERING	SCIENTIFIC FINDINGS
Differing environments do not influence genes and genomes.	Genes and genomes are subject to and regulated by environmental feedback.
Genes and genomes are stable and unchanging.	They are dynamic and fluid change in response to the environment and mutate adaptively.
Genes stay where they are put.	Genes can jump horizontally between unrelated species and recombine.

These findings are also supported by experiences with early GM crops, for example in 1996 the first commercial growing season of Monsanto's Bt cotton, the engineered pesticide was not sufficient to kill of all pests throughout the season as the company had promised. Furthermore in 1997, 20% of RR cotton suffered deformed bolls and bolls dropping off early[73].

Whilst it could be argued that these were early generation GM crops, these examples do highlight how genes and genomes are subject to and regulated by environmental feedback, and for precisely this reason the exact behaviour of GM crops cannot be predicted with absolute certainty. This degree of uncertainty has also caused some to question the safety of the genes themselves, and what they may unexpectedly produce.

Allergenicity –

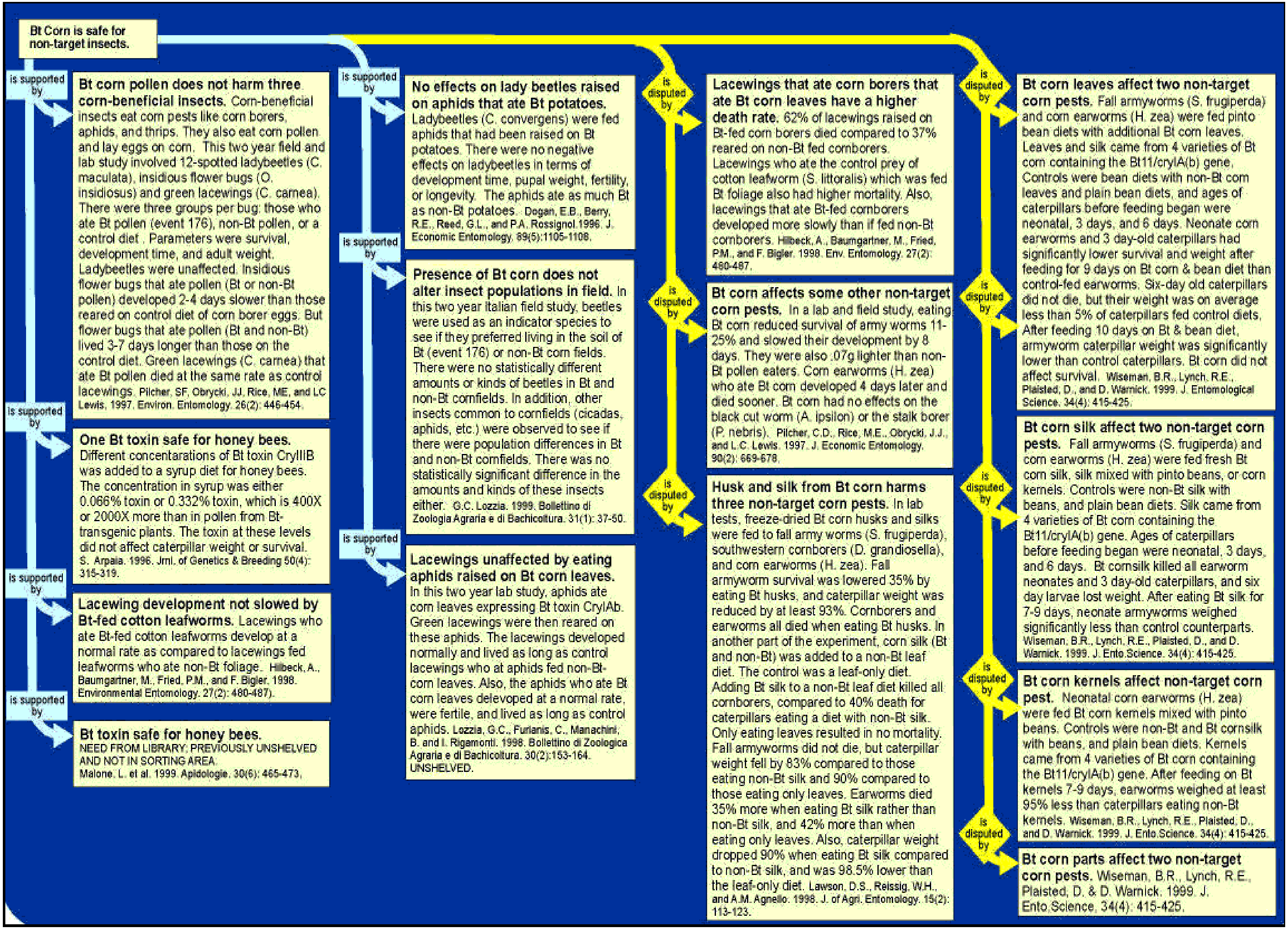
Genetic engineering is not a subject of isolation but one of integration, whereby species barriers are broken down allowing for the creation of hybrid organisms which would otherwise not naturally exist. Moving genes encoding proteins between species may result in allergic reactions as was found with Brazil nut albumin introduced into crop plants[75]. If these proteins have never before been found in our food supply how can we guarantee safety when a proteins allergenic characteristics are unknown? Of greater concern is the possibility of individuals experiencing reactions to foods which they had previously considered safe, after all how can you tell apart GM from non-GM foods when they look the same? (*figure 28*).

Figure 28 – Spot The GM Carrot[74]

Pesticide Resistance –

Whilst crops incorporating engineered pesticide resistance (such as Bt cotton) may provide advantages to farmers, concerns have been raised regarding possible effects on non-target organisms (*figure 29)*. For example pollen from early Bt crops was found to be deadly to the Monarch butterfly[76] (*figure 30)* (although later studies disputed these claims) prompting fears that pollen originating from other GM crops may have similar effects on other organisms; a fear heightened by GM field tests in Thailand where 30% of bees around the test site died[77].

FIGURE 29 – DO BT CROPS HARM NON-TARGET ORGANISMS?[78]



In 1999 Cornell University suggested that organisms beneath ground may also be affected, when it was discovered the Bt toxin can leach through plant roots and bind to soil particles where it remained active for up to 250 days, possibly harming soil micro-organisms and disrupting the soil ecology[79].

FIGURE 30 – GM CROPS, A DANGER TO WILDLIFE?[80]

There are also concerns regarding the long term consequences of Bt crops such as the development of insect resistance, a process which may be accelerated due to continual pesticide exposure.

Studies carried out by the 'Genetic Resources Action International' (GRAIN) organisation have demonstrated that resistance to Bt crops is developing much faster than Monsanto's scientists have claimed and that insects resistant to Bt are already present in the US and throughout the world. This may ultimately lead to the need for new and stronger pesticides possibly associated with greater negative environmental impacts than those currently in use. To help combat this issue farmers are now 'diluting' their Bt crops with strips of conventional varieties aiming to slow down the development of insect resistance[81].

Herbicides –

Glyphosate is manufactured by Monsanto and is the world's leading supplier of herbicides, claiming 95% of the global market. It is a systemic, broad spectrum herbicide whose mode of action leads to the inhibition of the biosynthesis of aromatic amino acids and products of the shikimate pathway (only targeting a pathway found in plants); crops tolerant to the herbicide incorporate a modified bacterial version of the enzyme EPSP synthase[82]. Monsanto claims that the use of herbicide tolerant crops will ultimately lead to a reduced use of toxic chemicals and the number of total sprays needed to provide effective weed management.

However an analysis conducted by the Pesticides Trust argued that the introduction of herbicide tolerant crops would alter the pattern of herbicide use but would not significantly change the overall amounts used. The report concluded stating that if it led to a greater use of glyphosate, other crops could be damaged and there may be adverse effects to beneficial organisms such as ladybirds[83].

FIGURE 31 – GLYPHOSATE; BAD FOR BIRDS?[84]

These findings were later supported by the publication of the largest ever scientific investigation into GM crops commissioned 'The Farm Scale Evaluations' , which looked at 201 field test sites over a period of four years. It was found that there were less weed and insect species such as bees and butterflies in areas with GM crop plantations and that two common weed species *Chenopodium album* and *Stellaria media*, faced extinction in 50 years. Birds such as the Sky Lark (*figure 31*) which use weeds to gather insects for food could also face extinction in 20 years[85].

In the US, analysis of four years of data from the US Department Of Agriculture found that contrary to Monsanto's claims herbicide use in the US has increased largely due to two factors. The first arises due to the nature of Glyphosate which allows it to be applied all year round, whereby previously herbicides were generally applied before the crop was grown. In addition were weed resistance is beginning to develop and the effectiveness of Glyphosate is decreasing, other more toxic and persistent herbicides are being used as well[86].

Another area of concern is the possible increased loss of biodiversity which may occur due to the over reliance on a single crop type, often called 'mono-cropping'. Widespread adoption of GM varieties could replace genetically diverse species with vast monocultures of single varieties subsequently reducing the available gene pool to protect against future pest and disease outbreaks.

The dangers of mono-cropping have already been demonstrated such as during the 1970s when US maize crop was devastated by Corn Blight disease, and also in 1975 when Indonesian farmers lost half a million acres of rice to damage caused by the rice hopper insect[87].

In fact there are many other objections to Glyphosate as summarised in table 5.

TABLE 5 – THE SAFETY OF GLYPHOSATE[88]

MONSANTO'S CLAIMS	INDEPENDENT RESEARCH FINDINGS
ROUNDUP DOES NOT CAUSE ANY ADVERSE REPRODUCTIVE EFFECTS	In laboratory tests on rabbits glyphosate caused long lasting harmful effects on semen quality and sperm counts[89]
ROUNDUP IS NOT MUTAGENIC IN MAMMALS	DNA damage has been observed in laboratory experiments in mice organs and tissue[90]
ROUNDUP IS ENVIRONMENTALY SAFE	Glyphosate is toxic to beneficial soil organisms and increases crops susceptibility to disease. The use of glyphosate in forestry and agriculture has indirect harmful effects on birds and small mammals by damaging their food supplies and habitat Doses of glyphosate may damage plant species up to 20 metres away by spray drift[91]
ROUNDUP IS RAPIDLY INACTIVATED IN THE SOIL AND WATER	Glyphosate is very persistent in soils and sediments Glyphosate inhibits the formation of nitrogen fixing nodules on clover for 120 days after treatment Glyphosate residues have been found in lettuce, carrot and barley a year after glyphosate was applied[92]
ROUNDUP DOES NOT CONTAMINATE DRINKING WATER WHEN USED BY LOCAL AUTHORITIES ON HARD SURFACES	In the UK levels of glyphosate above the EU limit have been detected by the Welsh Water Company every year since 1993[93]
IT IS NEARLY IMPOSSIBLE FOR GLYPHOSATE RESISTANCE TO EVOLVE IN WEEDS	In 1996 glyphosate resistant ryegrass was discovered in Australia[94]

Of most concern from the data provided in table 5 is the presence of glyphosate resistant ryegrass. Often the term ‘superweed’ is used by various media outlets when discussing the dangers of GM crops, the evidence of resistance in unintended organisms is surely a major cause for concern. Ultimately it could lead to the use of more toxic and persistent chemicals as is beginning to happen throughout the US and therefore these weeds could indeed one day become ‘super’. But it is also important to remember that essentially we are still dealing with technology or be it biotechnology and therefore a successor to Glyphosate is likely to be developed as its effectiveness wanes, but ultimately the cycle of resistance is likely to remain.

Promoters –

As touched upon previously in this report the insertion of genes into an organism also requires a promoter, and the example used was the viral 35s promoter sequence taken from the plant pathogen CaMV, resulting in constitutive expression of the gene. Concerns that antibiotic resistance genes may be passed to human gut bacteria also extend to the CaMV promoter, one such concern is the discovery of ‘recombination hotspots’ present within the CaMV promoter[95]. Furthermore these areas are prone to breaking and rejoining with non-homologous DNA and therefore do not require large similarities in nucleic acid sequence for these recombination events to occur. This is a daunting prospect as the CaMV promoter has been shown to recombine with host DNA including viral DNA. It is also classified as a Pararetrovirus making it similar to the Hepatitis B virus and related to the Human Immunodeficiency Virus (HIV) possibly leading to the creation of ‘superviruses’[96].

Antibiotic Resistance –

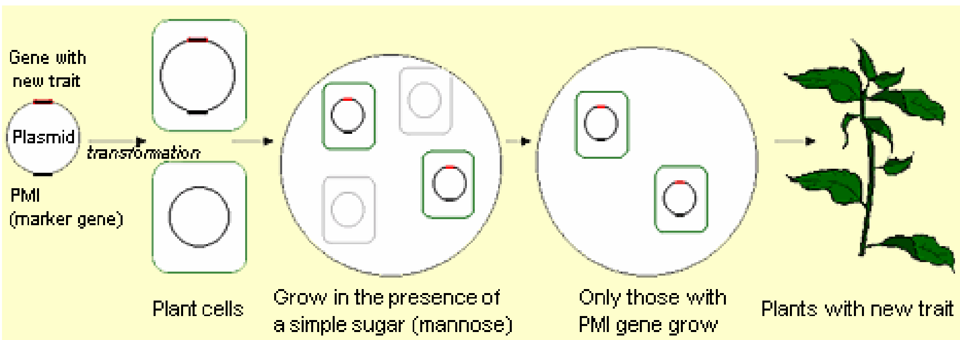
Methicillin resistant *Staphylococcus aureus* (MRSA), Severe Acute Respiratory Syndrome (SARS) and bioterrorism in general have lead to a heightened public awareness and fear of ‘superbugs’, the use of antibiotic resistance genes in GM crops has also contributed to this fear.

Antibiotic resistance genes have been used as markers in GM crops to identify which plant cells have successfully incorporated the desired foreign genes. However in 1996 the UK Advisory Committee on Novel Foods and Processes (ACNFP) blocked the approval of a GM variety of maize, this maize was later approved for cultivation in France however concerns regarding the use of an ampicillin resistance gene lead to a lack of market acceptance and the maize was never widely cultivated[97].

Later in 2002 a study commissioned by the UK's Food Standards Agency (FSA) showed that antibiotic resistance marker genes from GM foods can make there way into human gut bacteria after just one meal[98]. Two years previously the British Medical Association had warned that '*the risk to human health from antibiotic resistance developing in micro-organisms is one of the major public health threats that will be faced in the 21st century*'[99].

However some argue there is no need for alarm as resistance to antibiotics occurs naturally within bacterial populations via the exchange of plasmids. Others point to the fact that most of the antibiotic resistance genes commonly found in GM crops confer resistance to antibiotics that are not routinely used to treat disease in humans, such as kanamycin. Due to fears associated with the use of resistance genes other alternativeness such as genes which allow growth with certain sugars like mannose are being used (*figure 32*).

FIGURE 32 – AN ALTERNATIVE TO ANTIBIOTIC RESISTANCE GENES[100]



The importance of this example seems to be interlinked with the media and communication discussed in previous sections of this report. The use of the term 'superbug' could be described as an attention grabbing headline and previously it was questioned whether these headlines were indeed factual or 'spun' to make the subject seem more interesting. However this example along with the section discussing herbicides (and 'superweeds') reveals that behind the headline there is a scientifically backed ground for concern. Perhaps the reason why 61.4% of Europeans feel poorly informed about science could be due to these headlines which are short enough to spark interest but reveal little in terms of detail. However the media should be complemented for summarising a wealth of information and conveying the main concerns in a single word. This observation is significant as those in favour of GM foods often state that those against it are 'fear mongering'.

Yield –

FIGURE 33 – SOYBEANS[101]

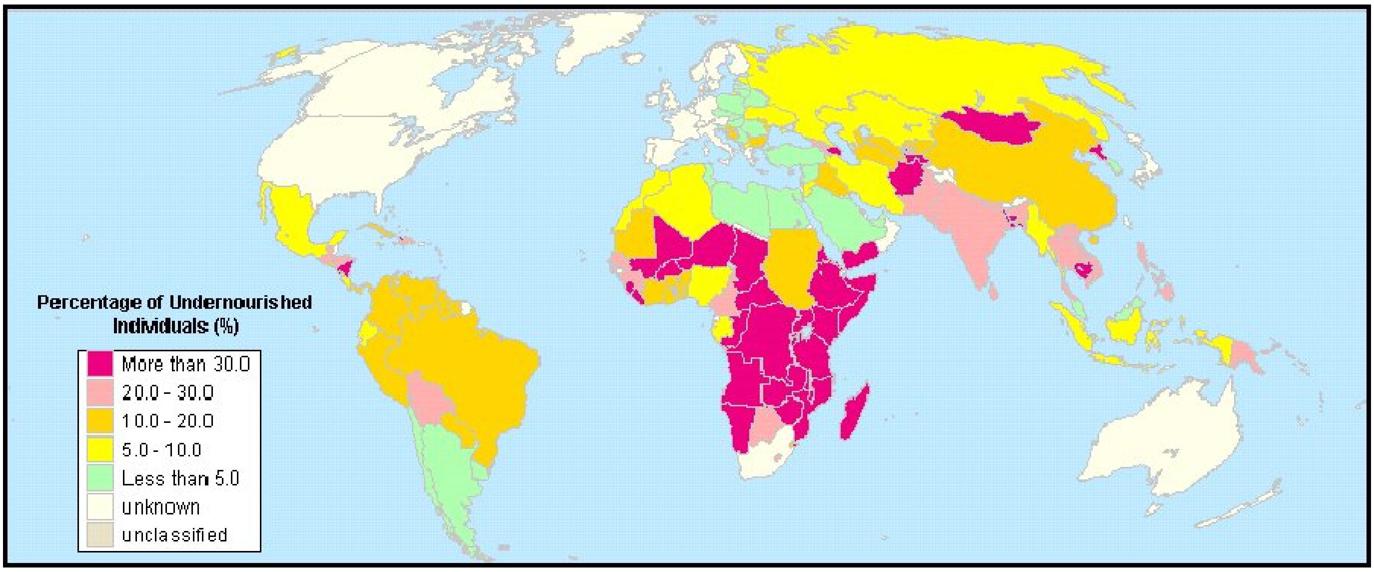
GM soya (*figure 33)* varieties account for the large majority of US soya plantations and were initially adopted by farmers with the expectation of increased yield, however many farmers have now become disappointed with their new crops. In 1999 and 2000 the US Department Of Agriculture conducted 10,000 comparative studies of GM and conventional soya in the US and found that GM soya produced a lower yield of 5-10%; this is in contrast to Monsanto's claims of a 5% yield increase[102].

Some possible explanations for this decrease may be due to the fact that many GM varieties have not been engineered specifically to produce greater yield but rather minimise loss to yield by incorporating protective traits, such as herbicide tolerance or insect resistance. This means that yield increases will only occur if the control achieved with the GM crops (i.e. weed or pest control) is needed and is greater than would be obtained with conventional crops. Other explanations may include the use of lower yielding varieties by the breeders, adverse effects of the engineering process or unexpected gene behaviour(s).

Feeding The World –

Those in favour of GM crops often point to the potential of the technology to solve the problem of global food security creating a so called 'gene revolution' similar to the 'green revolution' of the 1960's and 1970's. In essence food security means all individuals globally having constant access to safe and nutritious food however an increase in yield does not necessarily mean food for all. For example during the past two decades there has been a 15 percent increase in the amount of food available for the global population but despite this increase one in seven of the world's population remain chronically malnourished (*figure 34*).[103]

FIGURE 34 – WORLD HUNGER, 2004[104]



Global food demand is expected to increase by up to 50% in the next 30 years[105] and although it is generally recognised that food production must increase it is also recognised that equal distribution is an important factor. This increase must occur within an increasingly health and environmentally conscious society, therefore maximising yield on available land rather than expanding into new land is the preferred option. However many critics state that even if food production increases as a result of GM crops this will still not solve the issue of global food security pointing to the fact that there is already enough food surplus to feed the entire world, the problem is not production but distribution.

Criticisms also extent to the technology itself such as the 'terminator seed' which is sterile when replanted, and therefore requires new seed to be purchased each season along with the herbicide it is tolerant too. Many feel that this is of no benefit to third world farmers or to small farmers in the developed world who rely on saving seeds to minimise cost. Farming is also important for many local economies as it generates employment, however the benefits of GM crops such as a reduced need for attention and labour may ultimately result in unemployment for those who need it most.

Contamination –

The UK governments official advisor on GM foods, the 'Agriculture and Environment Biotechnology Commission' (AEBC) has said it would '*be difficult and in some cases impossible to guarantee*' that any British food was 'GM free' if commercial growing of GM crops went ahead[106]. This concern is also widely held by members of the public throughout Europe who felt that contamination was a major threat to biodiversity, the best example came from Greece and Italy where large areas of land were designated 'GM-free' or resolutions had been passed limiting the spread of GMOs into the environment. Critics of GM crops point to North American farmers who can no longer be certain the seed they plant does not contain and 'foreign genes'. The US organic certifier 'Farm Verified Organic' has stated that '*GM contamination of maize, oilseed rape and soya is now so pervasive that it is no longer possible for farmers in North America to source GM-free seed*'.[107]

FIGURE 35 – STARLINK MAIZE[108]

Critics say that it is not too late to prevent Europe from experiencing a similar fate to the Americans although instances still occur where unapproved GM products are sent to Europe as a result of contamination at the production end. For example in May of 2000 it was discovered that a large quantity of Canadian non-GM rapeseed which had been exported to Europe contained an unapproved transgene (GT-73). In 2002 US citizens also experienced contamination, Starlink maize (*figure 35)* which had only been approved for animal consumption and had been engineered to produce its own pesticide, became mixed with human maize supplies in grain silos; many individuals suffered allergic reactions, some severe[109].

Contamination may also occur at the gene level through the transfer of pollen from GM to non-GM plants either by wind or carried on the backs of insects such as bees, this is best illustrated by a study which found that oilseed rape pollen can travel up to 3 kilometres by wind. However current guidelines to limit gene flow require a distance of up to 500 meters between GM and non-GM crop varieties[110]. In May of 2002 the European Commission's Joint Research Centre (JRC) warned that if GM crops were widely adopted preventing contamination of organic food would be '*very difficult and connected to high costs, or virtually impossible*'.[111]

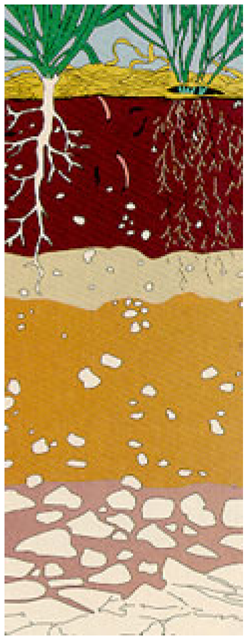
FIGURE 36 – SUGAR AND BEET WEED[112]

The danger of genetic contamination is not uniform and varies between regions, for example the introduction of GM soya into the US was considered to be of low risk as no native, sexually compatible 'weedy relatives' exist. However the introduction of GM Beet into the UK carries a greater risk due to the presence of native weed varieties (*figure 36*). A survey of European countries in 1981 found that 'weed beet' was regarded as a problem in Belgium, France, Ireland, Holland, Denmark, Germany, Sweden and the UK[113].

Weed Beet can result in reduced yields of Sugar Beet or the inability to grow it and is not easily controlled by standard herbicides, in 2000 60% of Britain's crops had a Weed Beet problem and is now considered a serious threat to the profitability of Sugar Beet. The commercial cultivation of herbicide tolerant Sugar Beet could potentially be catastrophic for almost the whole of Europe, major fears include the possibility of herbicide tolerant Beet Weed to Glyphosate, the reason this could be so catastrophic is that Beet Weed is not easily controlled and Glyphosate is one of the few herbicides which can kill it. Therefore should resistance be obtained a major aspect of control is lost, making Sugar Beet difficult or virtually impossible to grow.

'Soil Leakage' –

FIGURE 37- HOW WILL GM CROPS AFFECT OUR SOIL ECOLOGY?[114]



Many plants leak chemical compounds into the soil through their roots (*figure 37*), there are concerns that transgenic plants may leak different compounds than conventional plants do (such as the Bt toxin) as an unintended consequence of genetic manipulation. This could have adverse effects on soil micro-organisms and ultimately disrupt the soil ecology making the land unfertile for agricultural use, if this occurred on a widespread basis the farming industries of European countries could collapse leading to mass food shortage.

Can Conventional And GM Crops Co-exist?

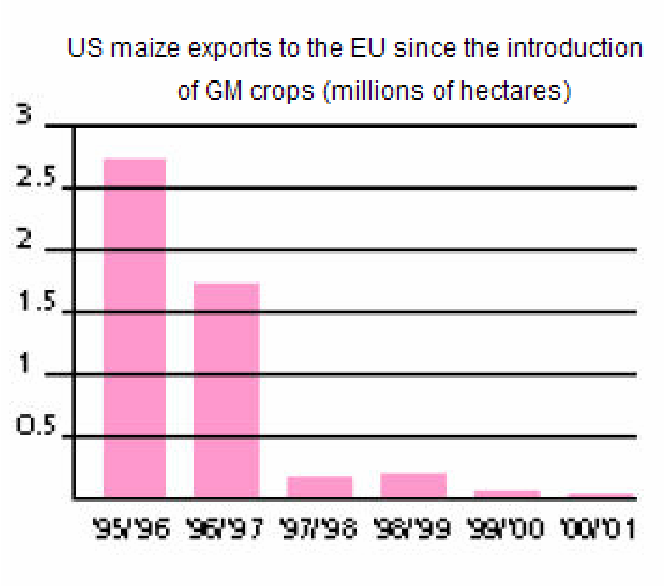
If and when GM crop varieties become commercially cultivated on a widespread basis they will need to exist alongside conventional crops without compromising their integrity. Co-existence is the term used to describe such a union, however many organic farmers feel that co-existence is unrealistic and GM crops threaten the genetic purity of their produce. Organic farming is a growing industry (*table* 6) and has continued to expand since the introduction of GM crops reflecting a trend of increasingly health conscious individuals.

TABLE 6 – LAND UNDER ORGANIC MANAGEMENT IN EUROPE[115]

COUNTRY	% AGRICULTURAL AREA (1999)	% AGRICULTURAL AREA (2004)
AUSTRIA	8.5	11.60
ITALY	6.5	8
DENMARK	5.5	6.65
UK	2.4	4.22
GERMANY	2.6	2.28
FRANCE	1.3	1.70

This increase in the organic market may be contrasted to the decrease in US exports of GM maize (*figure 38*).

FIGURE 38 – US GM MAIZE EXPORTS[116]



Organic farmers are now finding themselves in a position where they can charge more for their product as it is seen as a benefit for foods to be non-GM, evidence for this is given in figure 39 which shows the promotion of non-GM ingredients as a benefit (note the associations between the concept of 'no-GM' with vegetarians, children, health and quality).

FIGURE 39 – GM FOOD LABELS[117]

GM crops may therefore inadvertently result in a revival of the declining UK agricultural industry, by encouraging farmers to switch to organic crops in response to public demand. In Europe this will be most prevalent in countries with a strong overall majority against GM crops such as Italy and Greece. However in countries were objection is less or GM crops provide a clear benefit such as in Romania, farmers are likely to explore all technologies which result in increased yields and may therefore choose GM crops. Farmers who choose to go organic may risk contamination from GM crops resulting in a removal of their organic certificate, as occurred with several organic farms in Spain after the commercial cultivation of GM Maize was approved[118].

Other factors which may influence the type of crop grown include its use, whereby foods destined for human consumption are likely to be adopted the least and that destined for animal feed the most. In the UK one GM crop likely to have a slow uptake is Sugar Beet as 'British Sugar' the sole supplier of seed to farmers has a policy of not accepting GM Sugar Beet[119], possibly due to the threat of herbicide tolerant Weed Beet as previously discussed.

One issue purposely neglected until now is that of profit, overall farmers will decide upon the most economically viable option, as their livelihood and survival depends upon making the correct decision. Ultimately whatever approach is adopted farmers will still face a number of agricultural problems and depending on the type of crops grown, various solutions to these problems may be implemented (*table 7*).

TABLE 7 – GM VS ORGANIC AGRICULTURE[120]

SUSTAINABLE AGRICULTURE; THE DIFFERENT APPROACHES OF FARMERS AND BIOTECH COMPANIES		
PROBLEM	**GM APPROACH**	**ORGANIC APPROACH**
PESTS AND DISEASE	Single-gene resistance; engineered bio-pesticides.	Plant genetic diversity; indigenously improved varieties; intercropping; naturally insecticidal plants; crop rotation.
WEEDS	Herbicide tolerant genes.	Cover crops; early soil coverage.
WATER	Drought tolerant genes.	Moisture conservation practices; different plants for different micro climates; water retaining associated crops; contour ploughing.
PLANT NUTRIENTS	Engineered nitrogen fixing crops and microbes.	Multiple cropping with legumes; composting; integrated animal and crop farming; green manure; soil conservation strategies.
SOIL DEGRADATION	Saline and other tolerance genes.	Restore degraded soil: composting, crop rotation, green manure; avoid initial soil degradation.
YIELD	Yield increase from mono –cropping.	Multiple use crops; growing high yield crops and keeping livestock

In order to prevent organic farms from becoming contaminated by GM crops co-existence laws will be needed to ensure farmers do not loose their organic status.

Labelling –

Current EU policy dictates that co-existence laws must be decided by each member state, however a new EU regulation in April of 2004 the 'Traceability and Labelling Regulation'[121] was implemented to ensure the traceability of GMOs from producer to consumer. This would also serve to facilitate the withdrawal of GMOs from the market should any problems such as harm to the environment or health occur and requires all products containing more than 0.9% of modified DNA to be labelled, extending to both GM-derived products such as oils and also to animal feed.

As shown in previous sections of this report most Europeans welcome labelling as it provides them with a choice of whether to eat GM-foods or not, however some individuals feel this choice is undermined by the 0.9% labelling threshold and call for labelling of foods containing any amount of GM ingredients. Medicinal products for both human and veterinary use are excluded from the new regulation including crops grown for the production of pharmaceuticals, furthermore animal products such as meat, eggs and milk derived from animals fed on GM feed are also excluded.

Although most countries in Europe do not grow GM crops commercially, Spain and Romania do, the following section shall look at how these crops have performed and possible reasons for their uptake.

BT MAIZE IN SPAIN –

FIGURE 40 – CONVENTIONAL VS BT PROTECTED MAIZE[122]

Spain is one of the few areas in Europe where GM crop varieties are commercially grown, in 2001/2002 Spanish maize accounted for 11% of all EU maize plantations totalling 485,000 hectares, of which 25,000 was a GM variety. One factor which contributed to the uptake of GM crops in Spain was the loss of yield associated with the European Corn Borer and the promise of a technology which could minimise this loss and maximise profit (*figure 40*). Therefore all regions in which Bt Maize was planted experienced a medium or high level of Corn Borer pressure, as these were the regions where the benefits of the GM crop were most likely to be realised.[123]

It is also important to note that although up to 20% of Spanish Maize is treated with pesticides the large majority does not use any form of treatment due to difficulties associated with applying treatment which will be effective. For example effective spraying requires application of pesticide 2-3 days after Corn Borer eggs hatch, however difficulties in predicting when and where this will occur result in most treatments occurring to late[124].

Impacts –

Bt maize has largely had a positive impact in Spain although these impacts vary throughout the country, for example in regions with high infestation levels (such as the Sarinena region) there has been an average of 10% yield increase with Bt varieties and a 15% increase in regions with high infestation levels but where treatments had not previously been used. However in other regions with low Corn Borer pressures (such as the Barbastro area) and were pesticides were previously used yield increases were around 1%, table 8 provides a summary of yield increases with Bt maize throughout Spain.125

TABLE 8 – YIELD INCREASE WITH BT MAIZE[125]

REGION	BT AVERAGE YIELDS	CONVENTIONAL CROP YIELDS	% DIFFERENCE
ALBACETE	14.2	13.34	+6.4
GIRONA	13.63	12.07	+12.9
HUESCA	13.35	12.54	+6.5
LEIDA	13.72	13.13	+4.5
MADRID	14.70	14.28	+2.9
ZARAGOSA	12.01	11.32	+6.1
TOTAL	13.30	12.51	+6.3

On a national level the introduction of Bt maize has accounted for a 5-7% increase in yield over conventional maize, equivalent to an additional €10.82-€15.22 million increase in terms of value.[126, 127] This example highlights how under certain circumstances GM crops can provide great benefits, whereby crops previously susceptible to high pest pressures can be engineered to maximise yields under these conditions. Apart from yield there are many other benefits with arise both directly and indirectly with the use of Bt maize, for example a reduction in pesticide use (*figure 41*).

FIGURE 41 – NUMBER OF SPRAYS WITH BT AND CONVENTIONAL MAIZE[128]

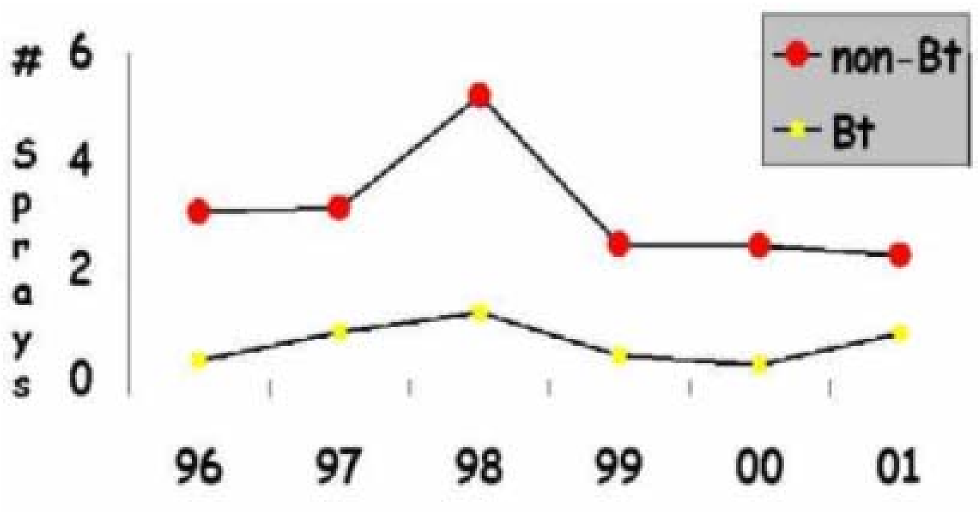


FIGURE 42 – THE SPIDER MITE[129]

Although Bt maize produces its own pesticide which results in the death of feeding insects, additional spraying may be required as the toxin is only effective once ingested and activated by the insects own digestive enzymes, additionally there may be other pests such as Spider Mites (*figure 42)* which are not affected by the toxin. Therefore spraying may occur in and around crop plantations depending on the level of pest pressure.

Associated with these benefits are other factors such as an increase in crop quality as Bt maize has lower levels of mycotoxins than conventional varieties, indirect benefits include more free time as less work is required to maintain the crops and there is also an added benefit of not having to worry about substantial yield losses due to Corn Borer attack. Overall Bt maize has been a success in Spain and most of the pesticides used are used almost exclusively for Corn Borer elimination, therefore the widespread adoption of this maize variety could potentially result in a substantial decrease of pesticide use.

ROUNDUP READY SOYBEANS IN ROMANIA –

FIGURE 43 – JOHNSON GRASS[130]

Weeds are a major problem in Romanian agriculture causing significant loss of yield and degradation of harvest quality, the weed problem has been largely caused by a limited use of herbicides since the 1990s. In addition there are some 'problem' weeds such as Johnson Grass (*figure 43*) that once established are difficult to control with standard herbicides.[131]

Romania has the third largest soybean area in Europe (75,000 hectares) behind Italy and

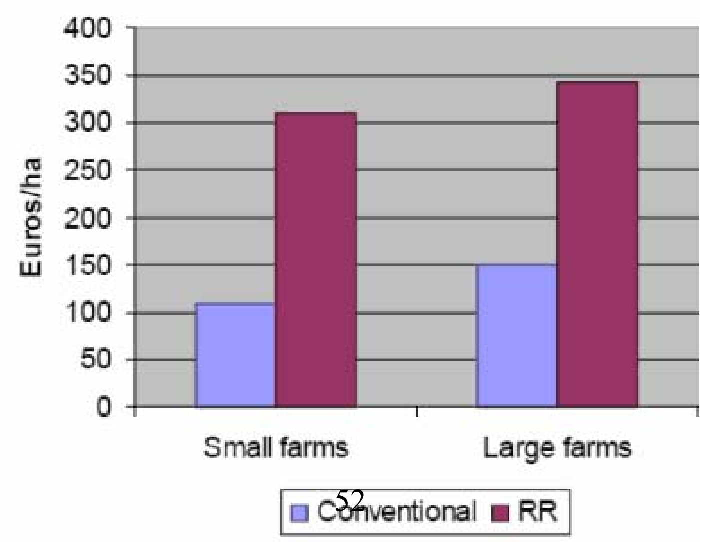
Serbia and Montenegro, and roughly equal to the area in France. RR soybeans are sold as a package deal from Monsanto which include herbicide tolerant soya seeds and Glyphosate, to date almost all farms in Romania subscribe to this package.

Impact –

RR soybeans have been a massive success in Romania increasing yields by up to 51% with an average increase of 31%, a larger increase than experienced with Bt maize in Spain. One reason for this success has been due to better weed management and the ability to kill Johnson Grass using Glyphosate. In other regions of the world where RR soybeans have been adopted such as Canada and the US yield increases have been largely neutral as weeds are less of a problem and therefore cause less reduction in yield.[132] This point illustrates a previous point discussed in this report whereby the technology was designed to increase yield indirectly by minimising yield lost to pests and disease. Therefore the application of GM crops seem to be most effective in areas where pests and disease are a problem, but less benefits are seen in areas where they are not.

However in countries such as Romania were weeds are a major agricultural concern the adoption of modern technologies to control these weeds has benefited the nation enormously, to the extent where RR Soybeans are now considered the most profitable arable crop grown in Romania (*figure 44*). These gains are largely derived from improved yields and improved quality of seed coupled with lower costs of production and reduced herbicide and application costs. On a national level the introduction of RR soybeans have resulted in an increase of €8.23-€8.62 million in terms of value.[133]

FIGURE 44 – THE PROFITABILITY OF RR SOYBEANS[134]



So far this report has concentrated on public perception and prospects associated with 'first generation' GM crop varieties, however the area of biotechnology is continually expanding and already technologies are present which could one day provide much greater benefits that those associated with current GM crop varieties. These coincide with Monsanto's prediction of three waves of beneficial GM products, namely the generation of 'quality traits' such as improved nutritional value and edible vaccines. The following concluding sections of this report shall examine these technologies in detail and later the future prospects of commercial GM crop cultivation in Europe.

FUTURE PROSPECTS

Much of the objection to GM crops stems from the view that they are of little benefit to the average individual, whilst at the same time are also regarded to be harmful and potentially dangerous to the environment. Perhaps the next generation of GM crops will experience less resistance as 'quality traits' become commonplace, this is especially relevant to today's society as more individuals are becoming health and environmentally conscious. Ultimately the aim of biotechnology will remain the same - to produce a plant that is considered better in some way than its wild type relative, one possibility involves the production of edible vaccines.

EDIBLE VACCINES –

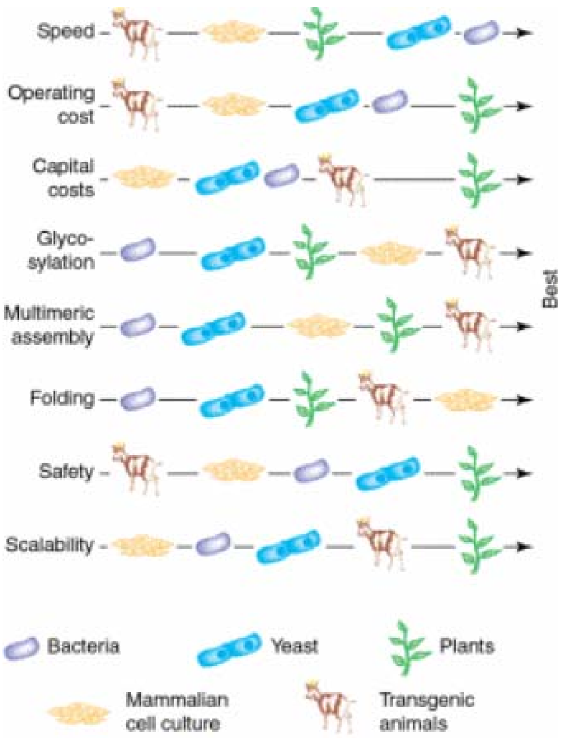
When food is eaten it is digested by the gastrointestinal tract resulting in the uptake of nutrients, antigens and pathogens by epithelial M cells found in the small intestine.[135] These cells present exogenous substances to either macrophages or dendritic cells resulting in the display of antigenic fragments on cell surfaces. These fragments are then recognised by helper T lymphocytes which induce B lymphocytes to secrete neutralising antibodies, resulting in protective immunity against future encounters with that antigen.[136]

FIGURE 45 –WHICH WOULD YOU PREFER?[137]

Edible vaccines involve the introduction of a desired gene into a transgenic plant and then its expression to produce the encoded protein, in this sense it could be said edible vaccines resemble subunit vaccines as they contain antigens but no genes which would allow the whole pathogen to assemble.

This provides an attractive prospect (*figure 45)* and has many advantages compared to production in other organisms (*figure 46).*

FIGURE 46 – ADVANTAGES OF USING PLANTS TO PRODUCE VACCINES [138]



They provide ease of administration, low cost and stimulation of both systemic and mucosal immunity[139] especially important in developing countries where diarrhoeal diseases are responsible for many deaths; two varieties of edible vaccines exist, those expressing either viral or bacterial antigens.

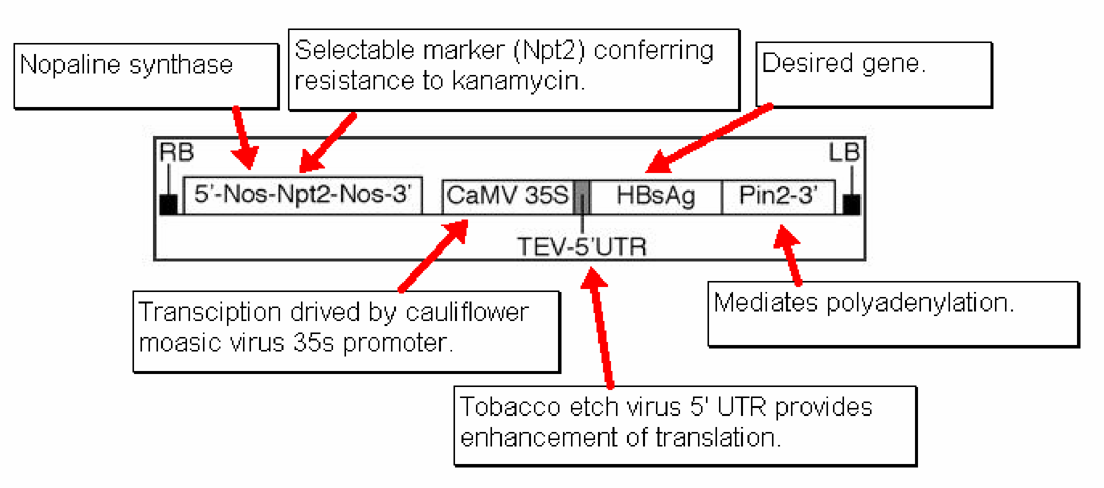
Viral Antigens –

FIGURE 47 – TOBACCO PLANT[140]

Hepatitis B affects around 400 million people globally resulting in possible liver damage and death. Although an effective vaccine exists it is expensive and a cheaper means of widespread distribution is needed for those in developing countries.

Tobacco plants (*figure 47)* were first used to produce a vaccine for hepatitis B due to their ease of genetic manipulation. Agrobacterium mediated transformation (*figure 48)* was used to introduce DNA encoding the hepatitis B virus major surface antigen (HBsAg) resulting in the tobacco plant leaf expressing HBsAg which was antigentically similar to that derived from human serum.

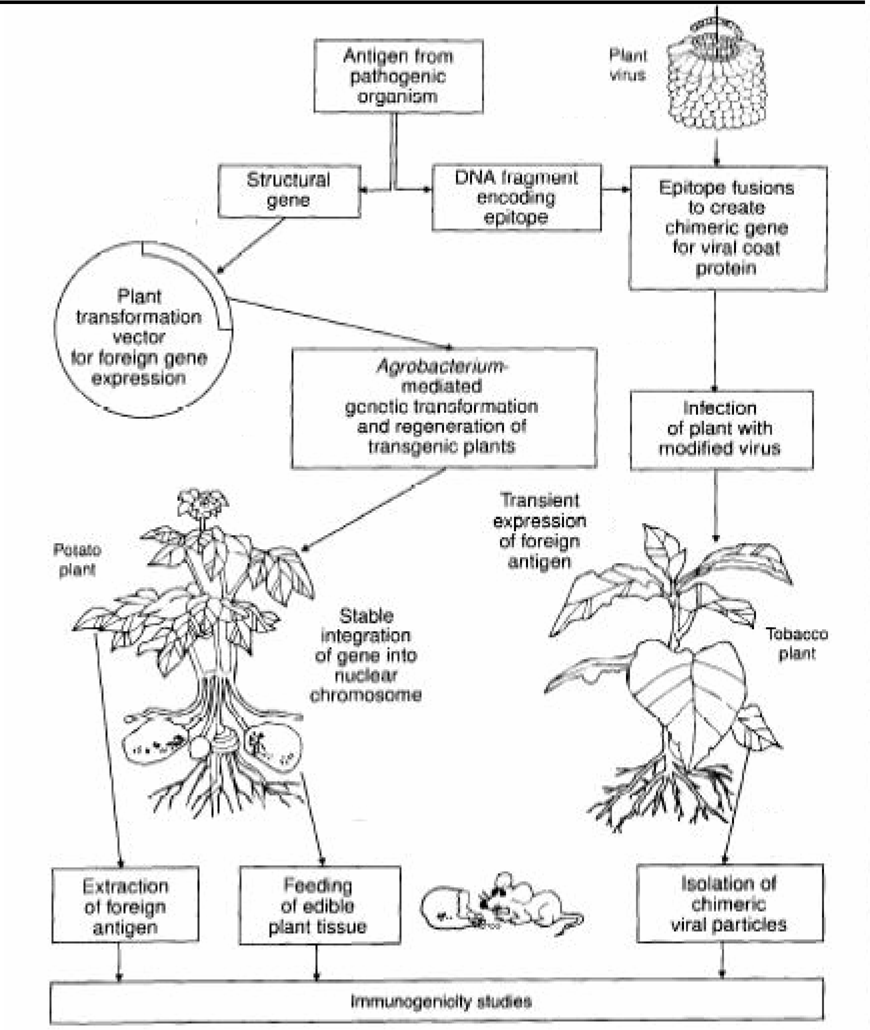
FIGURE 48 – T-DNA REGION USED DURING TRANSFORMATION IN TOBACCO[141]



These experiments were later repeated with edible transgenic varieties such as lettuce[142] and potato[143], evoking an immune response in those who had been administered the vaccine.

Figure 49 provides an alternative strategy for the production of viral antigens

FIGURE 49 – STRATEGIES USED TO PRODUCE VACCINES IN PLANTS[144]



These examples show how plants can be used to produce vaccines and are indeed an extremely attractive prospect. Plants offering beneficial products are likely to be accepted at a greater rate than has occurred with current GM varieties and could signal the end of widespread objection to all GM crops including those of first generation. This could also have major implications on health care throughout Europe and the world, as vaccines could be incorporated into everyday foods thereby increasing the pool of resistant and immune individuals whilst reducing the number of susceptible individuals to any given disease. Ultimately this could lead to better control and management of current and future diseases for the entire world, saving millions of lives.

Advances in plant biotechnology will not only help to protect humankind against disease by producing edible vaccines, but also by improving the nutritional value of foods. This aids an individual's ability to fight disease by strengthening the immune system and eliminating symptoms associated with vitamin deficiency.

IMPROVING THE NUTRITIONAL VALUE OF FOODS –

Unlike plants and bacteria, humans are unable to synthesise vitamins within the body (*except vitamin D)* resulting in malnourishment for individuals with a monotonous diet, however it is possible for plants to be engineered to express high levels of vitamins the following section describes one way this could occur.

Vitamin E –

FIGURE 50 – *Arabidopsis thaliana*[145]

Vitamin E (tocopherol) is a powerful antioxidant which can reduce the risk of heart attacks, cancers and strengthen the immune system; deficiencies lead to abnormal pregnancies and sterility in men.[146] Many oilseed crops like *Arabidopsis* (*figure 50*) contain a high level of γ-tocopherol which has only 10% of the vitamin E activity compared to α-tocopherol[147] (*figure 51*).

FIGURE 51 – TOCOPHEROL LEVELS IN CROPS AND PLANT OILS[148]

Plant and organ	Total tocopherol (μg/g fresh weight)	Percent α-tocopherol	Percent others and major types
Potato tuber	0.7	90	10% γ,β-tocopherols
Lettuce leaf	7.5	55	45% γ-tocopherol
Cabbage leaf	17	100	—
Spinach leaf	30	63	5% γ-tocopherol, 33% δ-tocopherol
Synechocystis sp. PCC6803	10	95	5% γ-tocopherol
Arabidopsis leaf	40	90	10% γ-tocopherol
Arabidopsis seed	350	1	95% γ-tocopherol, 4% δ-tocopherol
Oil palm leaf	300–500	100	—
Palm seed oil	500	25	30% α-tocotrienol, 40% γ-tocotrienol
Rapeseed oil	500–700	28	73% γ-tocopherol
Sunflower seed oil	700	96	4% γ,β-tocopherols
Corn seed oil	1000	20	70% γ-tocopherol, 7% δ-tocopherol
Soybean seed oil	1200	7	70% γ-tocopherol, 22% δ-tocopherol

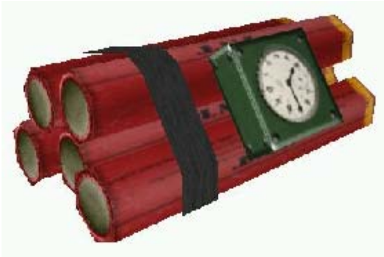
The biosynthetic pathway for tocopherol synthesis in plants was discovered during the 1970s, from which it was found γ-tocopherol is methylated to form α-tocopherol by the enzyme γ-tocopherol methyltransferase (γ-TMT). The low expression of this enzyme was infact the reason why many crops and oil seeds had low levels of α-tocopherol. By over expressing γ-TMT on a seed specific promoter in *Arabidopsis* seed α-tocopherol levels were increased by 80%.[149]

Antioxidants, such as vitamin E can protect against heart disease and cancer by ‘soaking up’ dangerous free radicals which damage our DNA. Sometime in the future it is quite possible that foods with enhanced vitamin contents are sold commercially in our supermarkets, this is especially important in Europe and the western world which in general eats a high fat diet, a factor linked to heart disease. The significance of this results from the fact that vitamin E can protect against heart disease, therefore if oils are genetically modified to contain large amounts of beneficial oils the number of heart attacks could significantly be reduced.

<u>BIODEGRADATION OF EXPLOSIVES –</u>

Traditionally technological advances have lead to the increased pollution of the world's air, water and soil which negatively impact both the duration and quality of our lives. With the dawn of a new genomic age efforts are now being made to clean up this polluted environment.

FIGURE 52 – TNT[150]



Many bacteria such as *Enterobacter cloacae* are naturally able to degrade explosive substances like glycerol trinitrate (GTN) and 2,4,6-trinitrotoluene (TNT) (*figure 52)* by expression of pentaerythritol tetranitrate (PETN) reductase[151]. This NADPH-dependant enzyme allows the bacterium to utilise nitrate ester and aromatic explosives as the sole source of nitrogen for growth. However these substances still persist in our soils indicating environmental factors such as competition with other bacteria for limited resources may reduce the effectiveness of their activity.

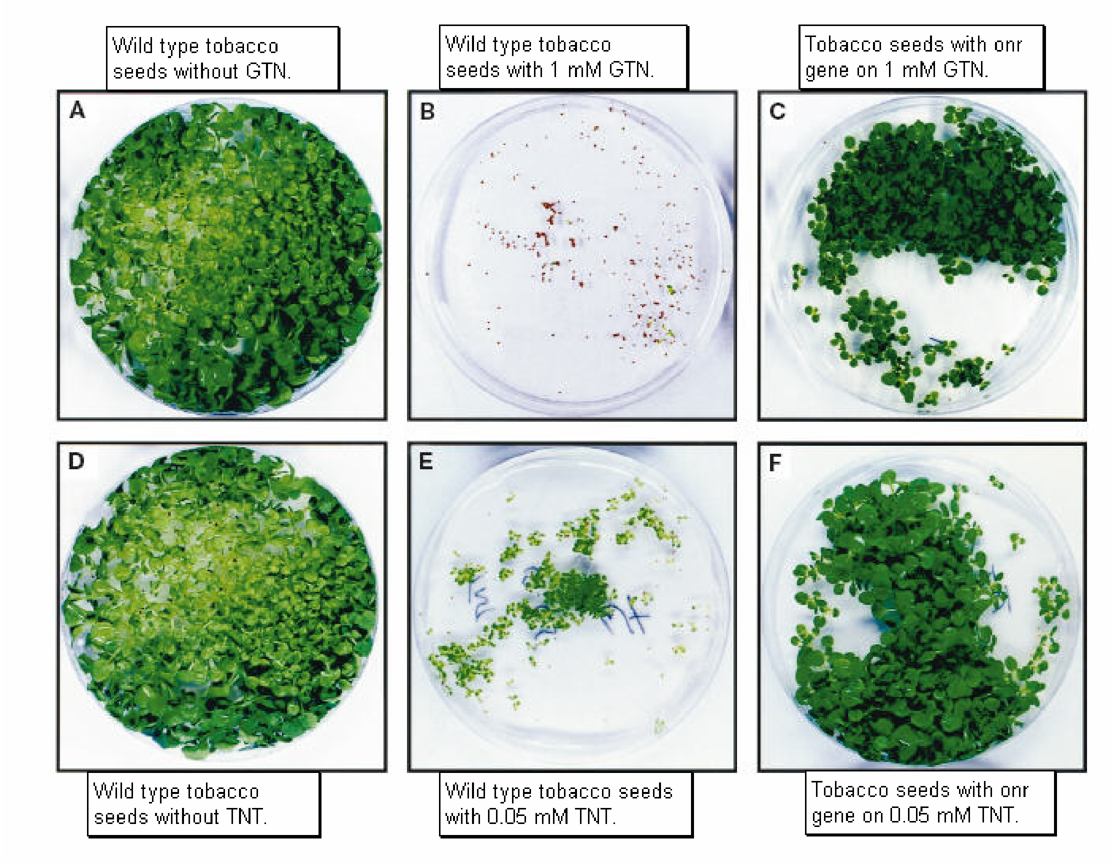
FIGURE 53 - *Myriophyllum spicatum*[152]

Some aquatic plants like *Myriophyllum spicatum*[153] *(figure 53)* are naturally able to degrade TNT but the resulting product aminodinitrotoluenes is more toxic[154], therefore by creating transgenic plants expressing PETN reductase the best characteristics of both plant and bacteria are combined.

<u>CREATING TRANSGENIC TOBACCO PLANTS EXPRESSING PETN REDUCTASE -</u>

The gene encoding PETN reductase (*onr)* was modified via the polymerase chain reaction (PCR) in order to include the plant consensus sequence AACAATGG, after which incorporation into a tobacco plant was preformed via agrobacterium mediated transformation. Seeds from the resulting transformed plants were then germinated on media containing GTN and TNT (*figure 54).*

FIGURE 54 – GERMINATION OF WILD TYPE AND TRANSFORMED TOBACCO SEEDS ON MEDIA CONTAINING GTN AND TNT.[155]



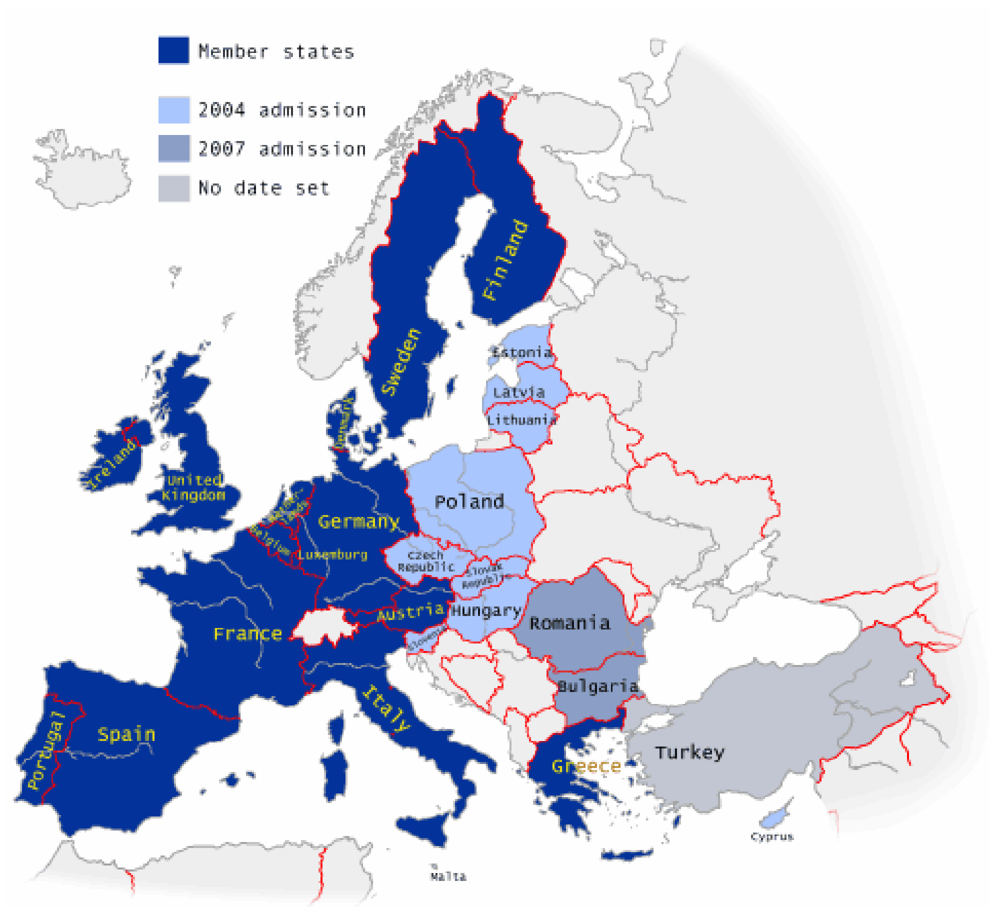
Transformed tobacco plants with the *onr* gene were able to germinate on media which was inhibitory to their wild type counterpart. These results also showed that GTN and TNT were absorbed and degraded by the transgenic varieties as PETN reductase is only active intracellularly.[156] Therefore the use of plants for the biodegradation of explosives has wider implications such as the removal of metals like mercury[157] from the soil, allowing previously unusable land to be reclaimed for productive and fertile future farming. Eventually this could lead to a knew form of environmental friendly 'mining' by using plants to 'suck up' precious metals from the earth.

The concluding section of this report shall concentrate on Europe's relationship with the EU and what that relationship could mean for the future of GM crops.

THE EUROPEAN UNION

The European Union is a body currently comprised of 25 member states (*figure 55*), and was designed with the goal of creating a single market often called the European Common Market.[158] All EU legislation is created through approval by the Governments of the member states and the European Parliament, the European Commission oversees the implementation of EU law and in certain areas also has an administrative role. In general the EU has adopted a policy which requires any new GMO to be individually approved by the Commission and the member states. Without such specific approval GMOs are banned within the EU they are neither allowed to be grown, sold or imported without such approval. Although it is up to individuals countries to decided whether to allow field trials of GM crops any product undergoing commercialisation requires authorisation at the European level as the functioning of a single market dictates that any product which can be sold in one country can also be sold in all other member states.

FIGURE 55 – EU MEMBER STATES[159]



The European Moratorium -

GM foods were first allowed into Europe in 1990, however in 1998 the EU agreed to improve laws governing the release of GMOs into the environment, whilst this was happening a number of European countries decided not to approve any new GMOs until the public and environment were better protected; this was called the 'de facto' moratorium and lasted for six years before it was broken by the approval Bt11 Maize in May of 2004. To date many countries have implemented bans on GM products they considered to be unsafe, table 9 provides a few examples.

TABLE 9 – GM BANS IN EUROPE[160]

COMPANY	GM PRODUCT	COUNTRY WHERE BANNED	DATE OF BAN	CONCERNS
Syngenta	Bt176 Maize	Austria	13/02/1997	Effects on non-target insects such as butterflies. Transfer of antibiotic resistance genes to humans and animals
Syngenta	Bt176 Maize	Germany	31/03/2000	Effects on non-target insects such as butterflies. Transfer of antibiotic resistance genes to humans and animals. Insects could develop resistance to Bt
Syngenta	Bt176 Maize	Luxembourg	07/02/1997	Transfer of antibiotic resistance genes to humans and animals.
Bayer	GM oilseed rape Topas 19/2	France	16/11/1998	Impact of genetic contamination and spread of herbicide tolerance
Bayer	GM oilseed rape Topas 19/2	Greece	08/09/1998	Impact of genetic contamination
Bayer	GM oilseed rape MS1xRf1	France	16/11/1998	Impact of genetic contamination and spread of herbicide tolerance
Bayer	T25 Maize	Austria	28/04/2000	Protection of sensitive areas. Lack of monitoring plans and fear of the spread of herbicide tolerance.
Monsanto	MON810 Maize	Austria	10/06/1999	Effects on non-target insects.

The US – EU Trade Dispute -

In May of 2003 the US, Argentina and Canada acting through the World Trade Organisation (WTO) launched a trade dispute against the EU complaining that the EU moratorium and national bans were a barrier to trade. On November 29th of 2004 European members states were asked to vote on whether or not these bans should be lifted, but failed to reach a 'qualified majority' (*figure 56*).

<u>FIGURE 56 – VOTES CAST ON NOVEMBER 29TH, 2004</u>[161]

☺ = keep bans
☹ = lift bans
— = abstentions

Country where ban in place	Austria	Austria	Luxemb'g Austria Germany	Greece France	France
banned GMO:	Maize T25	Maize MON 810	Maize Bt 176	Oilseed rape T19/2	Oils'd rape MS1Bn
Belgium	☺	☺	☺	☺	☺
Czech	—	☹	☺	—	—
Denmark	—	—	—	—	—
Germany	☺	☺	☺	☺	☺
Estonia	—	—	—	—	—
Greece	☺	☺	☺	☺	☺
Spain	—	—	☺	—	—
France	☺	☺	☺	☺	☺
Ireland	—	—	—	—	—
Italy	☺	☺	☺	☺	☺
Cyprus	☺	☺	☺	☺	☺
Latvia	—	—	—	—	—
Lithuania	☺	☺	☺	☺	☺
Luxembourg	☺	☺	☺	☺	☺
Hungary	☺	☺	☺	☺	☺
Malta	☺	☺	☺	☺	☺
Netherlands	☹	☹	☹	☹	☹
Austria	☺	☺	☺	☺	☺
Poland	☺	☺	☺	☺	☺
Portugal	☹	☹	☹	☹	☹
Slovenia	—	—	☺	—	—
Slovakia	—	☹	—	—	—
Finland	—	—	—	—	—
Sweden	—	—	—	—	—
Total ☹*	54	73	54	54	54
Total ☺*	178	178	221	178	178
Total —*	89	70	46	89	89

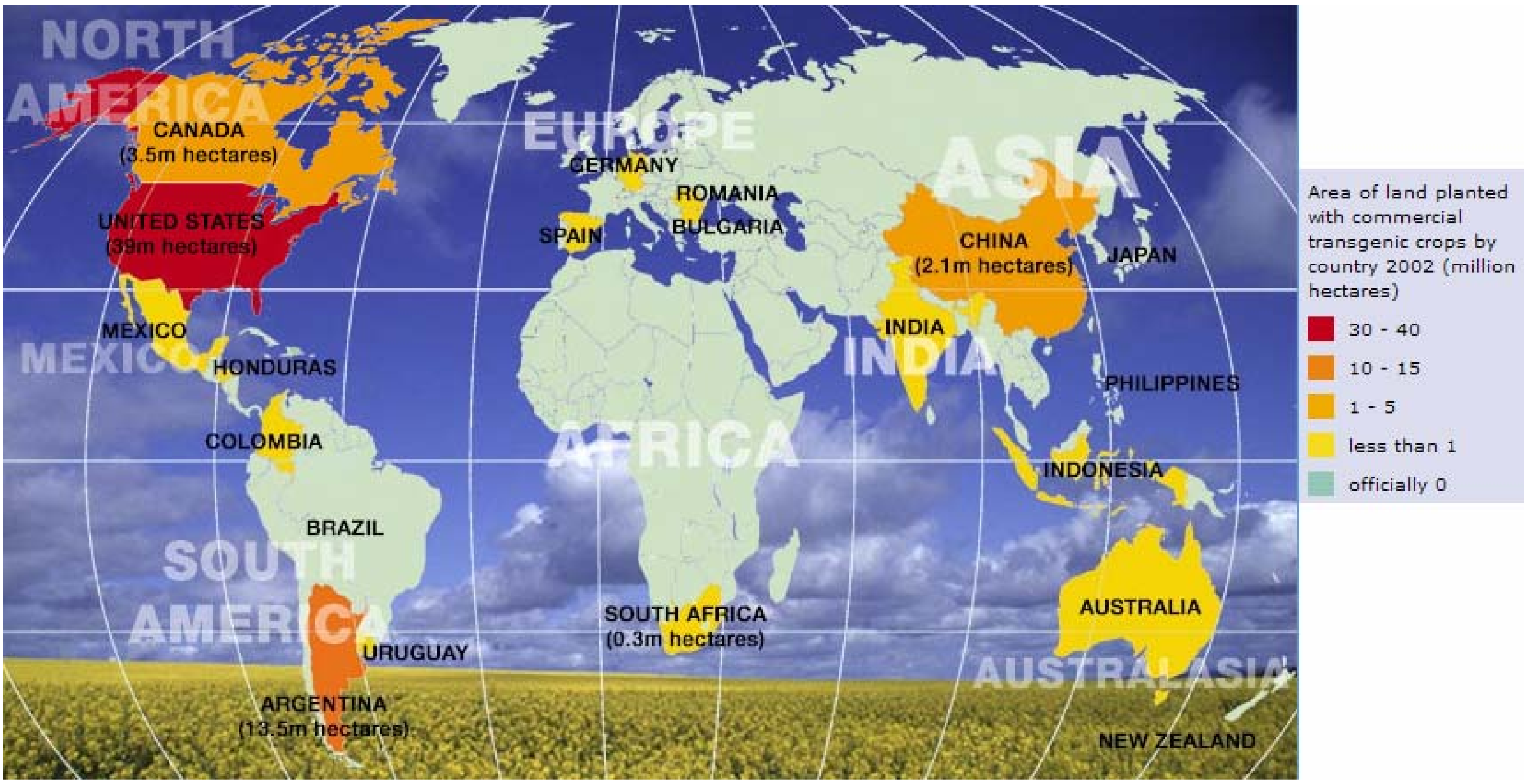
*Note that different countries have different numbers of votes.

FIGURE 57 – PRESSURE FROM ABROAD?[162]

Since this result the European Commission has decided to take the same proposal to the European Council of Environment Ministers in June of 2005 with the hope of lifting these bans, an interim report is expected towards the end of 2005.

If the proposal is successful this could result in the approval for many GM crop varieties to be cultivated commercially for sale in the European market, despite overwhelming public objection. Many individuals feel that Argentina, Canada but particularly the US (*figure 57*) are forcing open the European market to accept their products, driven by the power of multinational corporations such as Monsanto. Currently only four countries grow 99% of the worlds commercial GM crops, if the European Commission succeeds in overturning these bans the prospects of GM crops could one day result in Europe joining Argentina, Canada the US and China as the world leading commercial cultivators of GM crops (*figure 58*).

FIGURE 58 – WORLDWIDE COMMERCIAL GM CROPS[163]



CONCLUSION

Genetic engineering is still very much a young subject, one in which there is much to explore and much to do. As with any scientific development there are always risks associated with the potential benefit, however to obtain these benefits we must first learn to cope with the uncertainties no matter how daunting they may be. But this does not mean we should throw caution to the wind and set sails for full speed ahead, rather we should heed the warnings and seek to eliminate any potential problems which could appear on the horizon.

Whether it be a wheel, a plane or a computer humankind have always used the technology which is available to them in order to progress, both as individuals and as a society. However today's society is unique, for we as a species possess technologies which have the potential to destroy us, small errors could have big consequences, for example consider Chernobyl.

There are many concerns regarding biotechnology, however it should be remembered that GM crops are only a small part of this field and molecular genetic techniques have been used for decades to improve our quality of life, most notably in the field of medicine. GM enzymes have also been used to produce food for quite some time, for example chymosin (a type of enzyme which causes milk to coagulate) has been produced from GM bacteria as an alternative to another similar enzyme, rennet, to make vegetarian cheese since 1990. Tomato paste made from slow ripening GM tomatoes has also been on the market since 1996 although this was later withdrawn (*figure 59*).

FIGURE 59 – GM TOMATO PUREE[164]

Perhaps the most important determinant of whether GM crops will have a future is whether or not they are better than conventional crops and perceived to benefit everyone, not just the companies which produce them. If they are no better than conventional varieties the cost of the technology will outweigh the benefits and the technology will disappear. It should also be remembered that seed companies sell seeds to farmers, so it is they who must gain a benefit if the GM seed is to sell. Examples used in this report included Romania and Spain whereby farmers benefited from increased yield and better weed and pest management. These beneficial factors ultimately lead an accelerated uptake of the technology, to the extent where GM soybeans are now considered the most profitable arable crop for Romanian farmers.

Given these benefits it is not surprising herbicide tolerant and insect resistant crops have received such widespread and global uptake, however not all farmers, such as those in the US, have been pleased with their results showing how GM crops can be beneficial under some circumstance and less beneficial under others.

This could perhaps explain why many first generation crops were of herbicide tolerance as they would be recognised as a benefit by farmers, whereas quality traits such as improved nutritional value could only become a benefit if farmers felt they could charge more for their product. However in an increasingly health conscious society GM crops containing these 'quality traits' could be seen as a direct benefit to both farmers and consumers, thereby spearheading a wave of acceptance throughout Europe. For example products such as GM soybeans contain less saturated fat than conventional soybeans and require less trans fatty acids to be incorporated during processing, factors which are associated with a reduced risk of heart disease.

Many individuals are concerned about the safety of GM foods, but it should also be recognised that many foods we consider safe actually carry some risk. Many crops contain compounds that are potentially toxic or allergenic to humans (such as glycoalkaloids in potatoes) as a result of natural evolutionary processes serving to protect the crop from animal or pathogenic micro-organisms.

Another factor which may influence the uptake of GM crops involves who and what the crop will be used for, whereby crops grown for non-food uses could experience less resistance from the public. Examples could include crops modified to produce chemicals for pharmaceutical use which could be worth many more times the value of food crops.

The Monarch Butterfly is often used as an example of how GM crops could damage our wildlife when it was discovered that pollen from Bt maize could kill caterpillars. However it is important to remember that beside the fact these caterpillars do not normally eat pollen, conventional spraying of pesticides will also kill them and other insects. The use of engineered pesticide resistance, as in Spain, resulted in a reduced level of chemical inputs, therefore even if GM crops are damaging to wildlife the alternative must also be considered. Although this report stressed the possibility of unexpected negative consequences which may arise with GM crops, Bt maize has shown there may also be unexpected benefits. For example a reduced level of carcinogenic mycotoxins are found with Bt maize, ironically organic food which is considered to be healthier than GM food contains high levels of these mycotoxins as fungicides are not used.

However one must also consider the long term effects and whether or not greater problems will be created in the future than those initially solved by GM crops, such as the development of herbicide tolerance in wild type weedy relatives. In the UK Weed Beet is a major threat to the profitability of Sugar Beet and although herbicide tolerance may increase Sugar Beet yields, it may ultimately lead to Weed Beet developing resistance thereby making it harder to control. Another crop in which cross pollination could be a problem in the UK is rapeseed which could cross with Brassica species including cabbages and brussel sprouts, although the extent of this problem is largely determined by the type of gene transferred and whether or not it will convey a selective benefit to the new recipient.

To minimise this risk adequate separation distances will be required between GM and conventional varieties and should take into account factors such as pollen dispersal distances, both via wind and insects. However some crops such as wheat, maize and potato do not cross with any wild weed species in the UK and therefore carry a lower risk of ‘genetic contamination’. This shows that risks associated with GM crops are not uniform for all regions and therefore should be considered on a case by case basis.

Europe is currently in a unique position for it can examine how GM crops have preformed abroad and learn lesson about what to do and what not to do, thereby allowing regulations to be put into place before widespread commercial cultivation commences. Examples such as allergenicity associated with Brazil nut albumin show that harmful GM products can inadvertently be created but also detected and removed. Therefore whilst many dangers exist, learning lessons from those with past experience can minimise these risks and ensure we reap the benefits.

Word Count –

11, 952 (*excluding appendix*)

APPENDIX

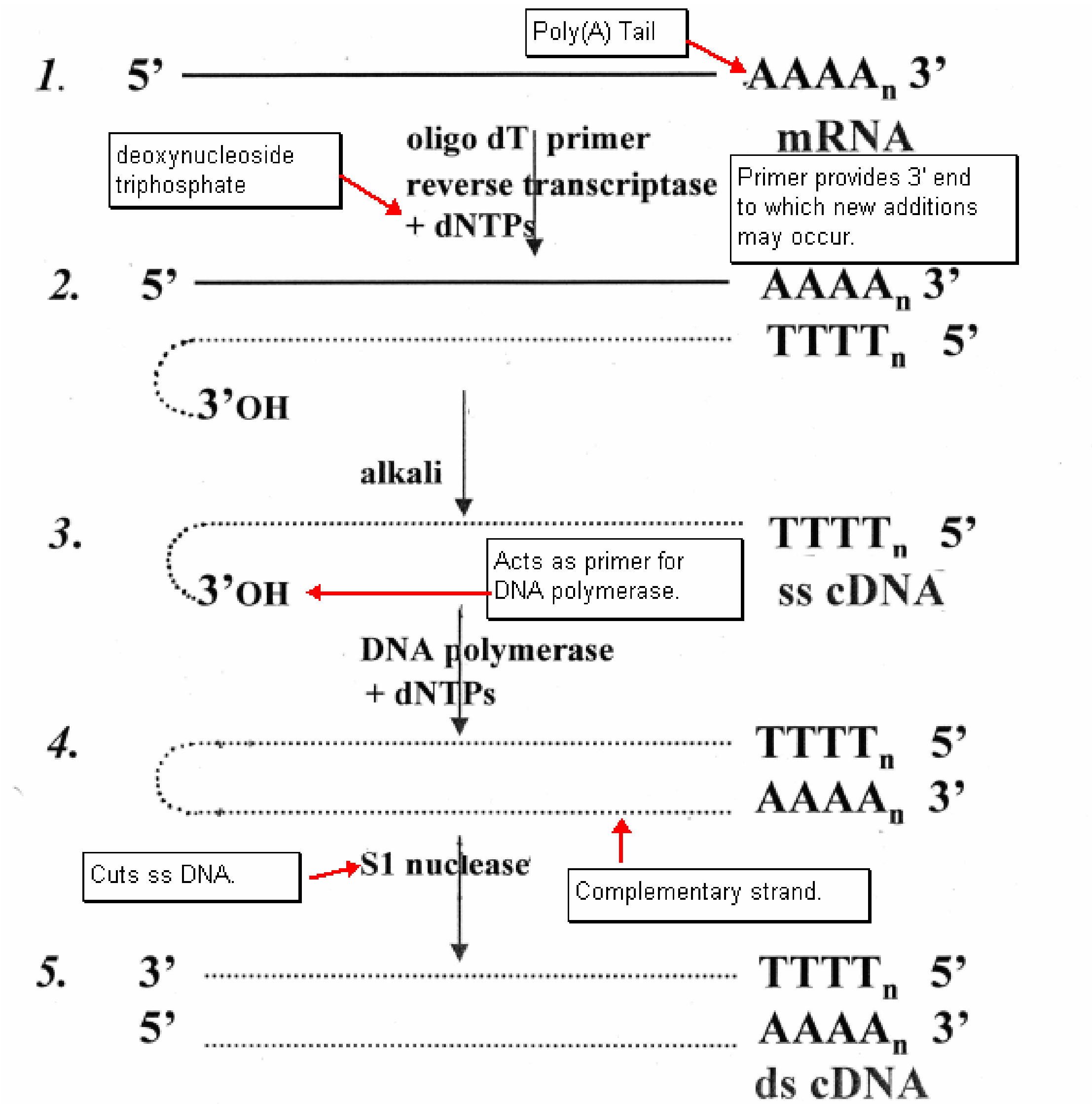
TECHNIQUES RELEVANT TO GENETIC ENGINEERING -

Transcribed genes produce messenger ribonucleic acid (mRNA) which is translated in the cytoplasm to produce proteins, by making DNA copies of these mRNA's called complementary DNA (cDNA)[1] it is possible to deduce the amino acid sequence of a protein from the corresponding cDNA.

CREATING CDNA –

Isolation of mRNA from a total ribonucleic acid (RNA) population is performed using an oligo-dT column[2] which binds the mRNA 3' poly (A) tail. Later reverse transcriptase is added to a separate mixture with the newly isolated mRNA creating a complementary DNA strand that is extended by DNA polymerase. Once single stranded (ss) cDNA has been produced RNA is removed by the addition of alkali and double stranded (ds) cDNA is generated by terminal transferase; a DNA polymerase which does not require a template (*figure 1).*

FIGURE 1 – PREPARATION OF CDNA[3]

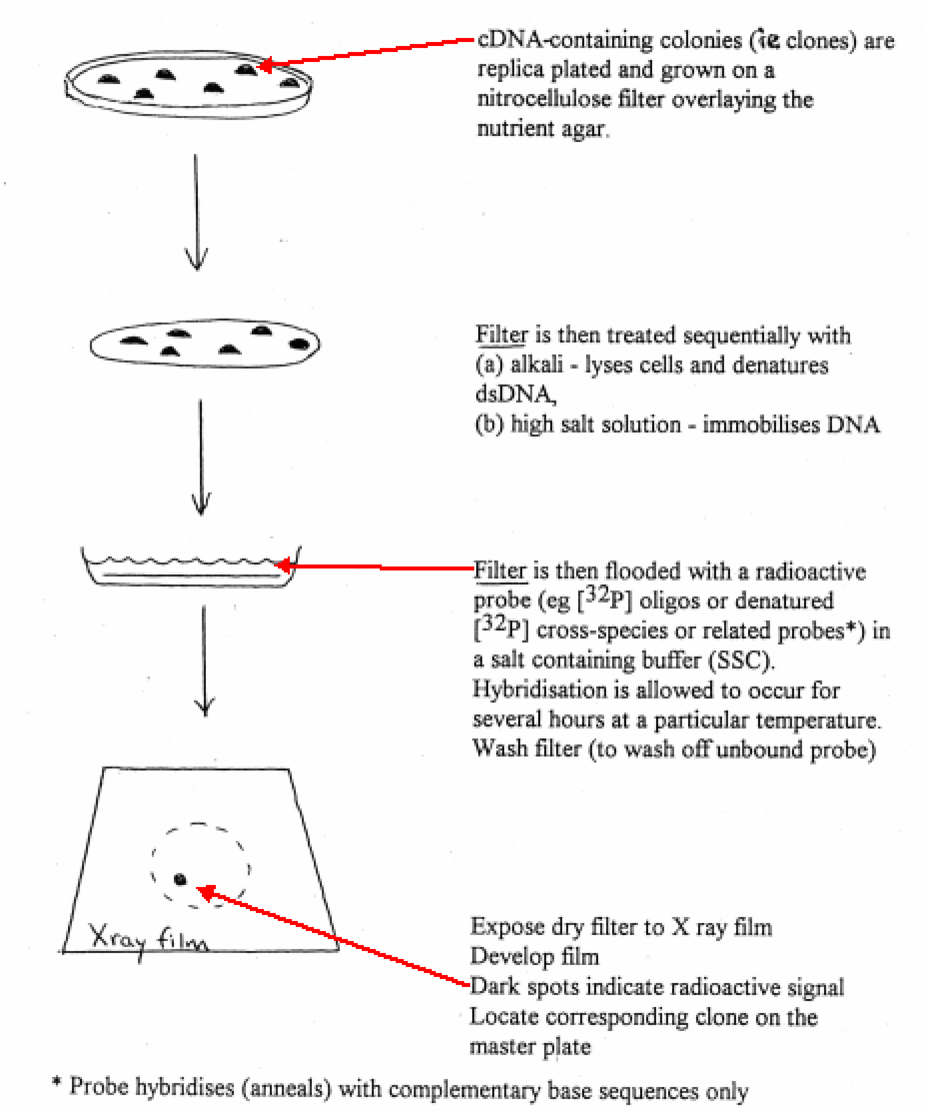


Resulting cDNA may then be ligated into a vector and introduced into Escherichia coli (*E. coli)* for the generation of cDNA clones.[4] These clones represent the protein coding DNA sequences expressed in the source tissue/cell at the time of mRNA extraction; further analysis will require selection of the clone via a screening process.

SCREENING FOR DESIRED CLONE -

cDNA clones will become part of a cDNA library that contains many clones, therefore a means of selection is required to isolate a gene of interest encoding a particular protein. One commonly used method is entitled colony hybridisation whereby the use of a radioactive probe detected by autoradiography reveals the location of a desired cDNA clone; summarised in figure 2.

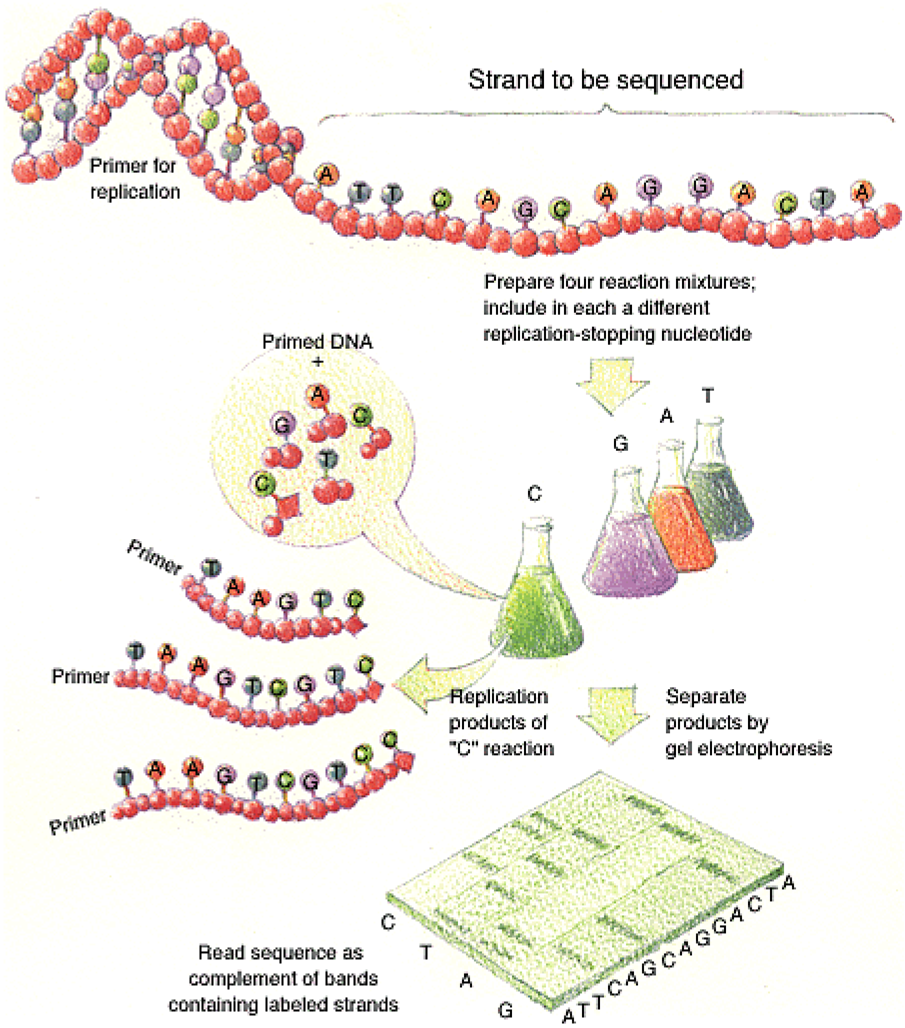
FIGURE 2 – COLONY HYBRIDISATION[5]



This process ultimately allows determination of the cDNA's nucleotide sequence and therefore the amino acid sequence of the encoded protein by performing a sequencing reaction.

DNA SEQUENCING -

FIGURE 3 – DIDEOXY SEQUENCING[6]



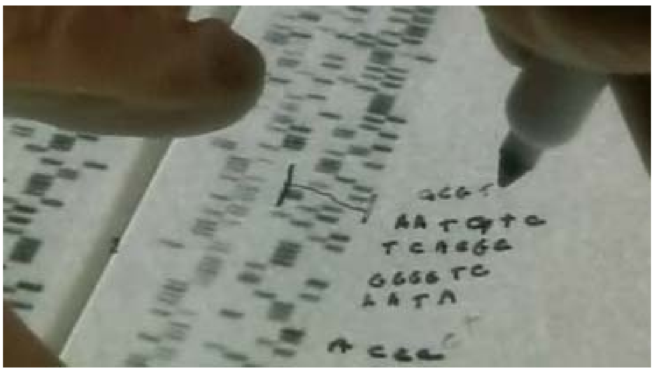
The Sanger method provides the basis of DNA sequencing. Chromosomes of varying length are first primed with a 5` oligodeoxynucleotide and cut into smaller fragments using restriction enzymes. The mixture is denatured to produce ss DNA which are then used as templates.

Chain elongation occurs by the addition of deoxynucleoside triphosphates (dNTPs) which are present at a higher concentration than the 2', 3'-dideoxynucleoside triphosphates (ddNTPs).

Incorporation of ddNTPs terminates chain elongation due to the absence of a 3' hydroxyl group, stopping the reaction mixture at either A, T, G or C (*figure 3)*.

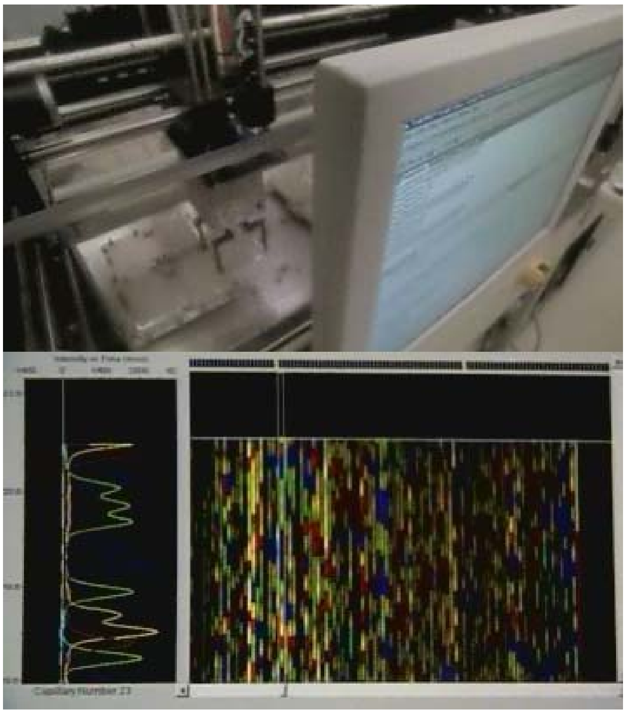
READING THE SEQUENCE -

FIGURE 4 – READING AN AUTORADIOGRAM[7]



Traditionally sequences were read by hand directly from an autoradiogram after the reaction mixture was separated by gel electrophoresis. For pioneer geneticists this meant genome sequencing was a long and tedious task (*figure 4)*.

FIGURE 5 – AUTOMATED SEQUENCING[8]

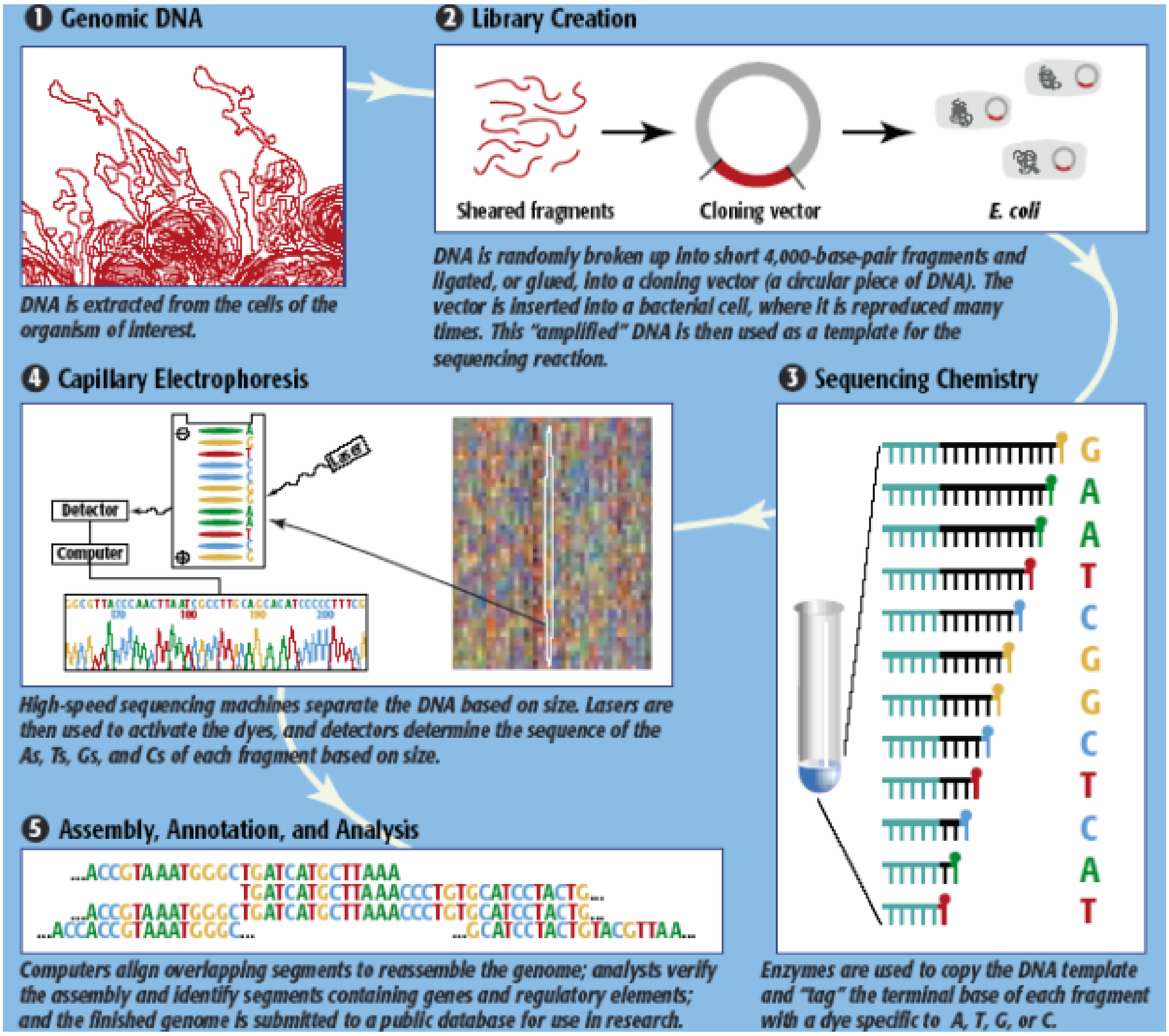


However with the introduction of a computerised system capable of sequencing thousands of base pairs day and night output escalated from 200 Mb for 1998 to 1.5 million bases per day in 2003.

This automated process detects each terminated chain fragment by wavelength corresponding to each base due to the incorporation of a fluorescent marker[9], heralding perhaps one of the most significant technological advances of our time (*figure 5).*

The entire sequencing process is summarised in figure 6.

FIGURE 6 – DNA SEQUENCING OVERVIEW[10]



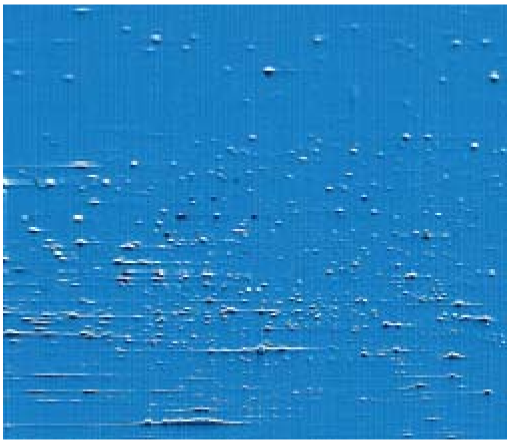
Sequenced genomes essentially provide a genetic blueprint to whatever organism it belongs to, however this does not mean an immediate understanding of that organism as the function of genes and proteins must first be investigated.

Whilst the genome provides the static genetic complement of an organism, the proteome provides the dynamic protein complement of that genome. This is perhaps one of the most important areas of research as proteins are essentially the expressed products of genes, whereby defective genes may result in defective proteins that lack a certain function(s) compared to its native counterpart.

<u>PROTEIN ISOLATION –</u>

A commonly used technique for protein purification is two dimensional (2D) gel electrophoresis whereby proteins are first separated according to charge, then by size resulting in a specific pattern of spots (*figure 7).*

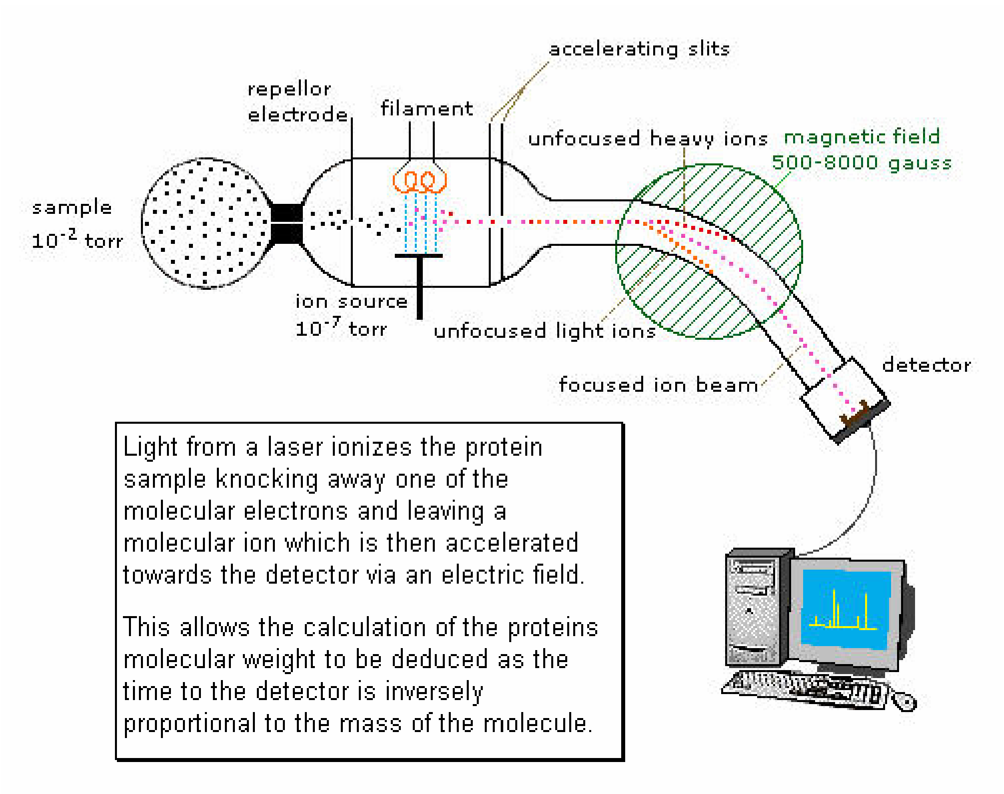
<u>FIGURE 7 –SORTING PROTEINS</u>[11]



Traditionally this approach has been restricted in its depth of study as it was difficult to determine which spot corresponded to which protein; therefore studies were limited to comparisons of the spot patterns between different samples.

Recently the existence of genomic databases have allowed for the identification of these proteins, after analysis has been preformed by mass spectrometry (*figure 8)* to determine molecular mass and amino acid sequence.

<u>FIGURE 8 – MASS SPECTROMETER</u>[12]



Although 2D gel electrophoresis has many advantages it also experiences limitations as do other techniques used to investigate proteins (*table 1).*

<u>TABLE 1 – METHODS OF PROTEIN ANALYSIS</u>

TECHNIQUE	DESCRIPTION	ADVANTAGES	DISADVANTAGES
2D GELS + MASS SPECTROMETRY	*Proteins separated on basis of charge + mass, analysis by mass spectrometry.*	*Established technology, 2D gel profiles incorporated into existing databases, large range for detection of expression levels.*	*Problems detecting very small/very large and membrane bound proteins, time consuming.*
MICROARRAYS[13]	*Silicon chips coated with known protein ligands, proteins from sample fractionated on chip, analysis by mass spectrometry.*	*Can detect all types of proteins, requires minimal technical skill, fast + reproducible results.*	*Range of proteins detected is less than 2D gels, no standardised format for organising data from chip.*
AUTOMATED YEAST TWO HYBRID SCREEN[14]	*Automated process to determine whether pairs or groups of proteins interact.*	*Protein behaviour*[15] *studied within living organism, quick results from proven and established technique.*	*Does not give structural information, possible false positive / false negative results. No information on biochemical function.*
HIGH-THROUGHPUT CRYSTALLOGRAPHY	*Proteins from sequenced genome are expressed, purified and crystallized to obtain 3D structure then tested for biochemical functions.*	*Tests directly for biochemical function, can uncover new protein functional families, provides structural information.*	*Can be time consuming, experimental technique.*

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ADDITIONAL COMMENTS –

Two articles discovered by the author of this report were felt to be worthy of inclusion, this is largely due to the amount of accusations encountered during research of this report that scientific publications were biased towards various company interests.

- One of every three articles has at least one author with a financial interest, and 15% of authors have a financial interest relevant to one of their publications

S. Krimsky, 1998, *Scientific Journals and their authors financial interests: a pilot study,* Psychotherapy And Psychosomatics, 67(4-5): 194-201

- Clinical trials with positive results are published more frequently and more quickly than those with negative results.

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