
ICSTI
IRELAND
Irish Council for Science,
Technology and Innovation
ICSTI Report on
Biotechnology
Forfás

Contents

Executive Summary

1. Introduction

The rapid pace of discovery in the last 30 years in biotechnology and genetics has given rise to public interest and, in some cases, concerns about how biotechnology impinges on medicine, agriculture, health and food and on the very essence of life itself. The Irish Council for Science, Technology and Innovation (ICSTI), in response to the Report of the Chairing Panel of the National Consultation Debate on Genetically Modified Organisms and the Environment, brought together a Task Force of scientists, clinicians and industrialists who have examined the information currently available on biotechnology and in particular genetic modification from a scientific, medical, political, economic and regulatory perspective. The results of their findings are the subject of this report.

2. Biotechnology

The Science

Historically, biotechnology has been used in selective breeding and in the production of bread, wine, and beer. Since the discovery of antibiotics in the 1940s, biotechnology has been used in process fermentations for large scale antibiotic production. Revelation of the structure of DNA and, in the 1970s, discoveries in molecular genetics have led to an understanding of gene function, expression and control, and to the ability to cut and paste genes into DNA using restriction enzymes. More recent genetic engineering techniques allow the DNA of an organism to be modified predictably and precisely by adding or subtracting DNA which codes for a particular trait or function.

The Application

To date, the most notable impact of biotechnology has been in the medical and pharmaceutical arenas. Important medical products such as human insulin and factor VIII are produced through genetic engineering.

Genetic engineering has the potential to modify physical characteristics of production crops, including their nutritional content, disease resistance and growing season. It can also be used to produce pharmaceuticals and nutraceuticals in farmed animals and to improve the growth and fitness of agriculturally important animal species. Genetic engineering has the potential to improve food production, industrial processes, waste and waste water treatment, bioremediation, renewable energy generation and biomining. Overall, this technology has the potential to improve the quality of life and to enhance conservation and preservation of the environment.

The Economics

A strategy for biotechnology is important to sustain Ireland's economic growth and to enhance Ireland's capacity to become a knowledge based economy. A Technology Foresight Fund, managed by Science Foundation Ireland (SFI), has been approved for the purpose of developing world class research excellence in Information and Communication technologies and in Biotechnology in Ireland.

3. Regulation of Biotechnology

National and International regulations exist to ensure the safety of food, drugs and medicines and to minimise negative environmental impact. Further regulations allow the development and application of new biotechnology while minimising the risks to human health and the environment.

US Regulation

In the mid 1970s in the USA, a Recombinant DNA Advisory Committee (RAC) was established to provide guidelines for research. Today, the USA Food and Drug Administration (FDA), the US Department of Agriculture (USDA) and the Environmental Protection Agency (EPA) share responsibility for regulating organisms, products and processes in the USA.

European Regulation

In Europe (including Ireland) there are 8 EU Directives and 5 EU Regulations governing recombinant DNA technology and the use of genetically modified organisms (GMOs). These cover use in medicine, veterinary medicine, horticulture and foodstuffs, contained use of GMOs and deliberate release of GMOs in field trials or onto the market. As of March 2001 there were 108 entries on the GMO register in Ireland, most involving contained use, and there were no direct notifications for GMO products to be placed on the market.

Environmental Liability

In 1999, the Chairing Panel of the National Consultation Debate on Genetically Modified Organisms and the Environment recommended responsibility for unforeseen damage to the environment rest with the body who obtained consent for release of the product. In line with this recommendation, the Report of the Interdepartmental Group (IDG) on Modern Biotechnology made a number of recommendations to strengthen the regulatory and policy framework at EU and national levels. ICSTI endorses those recommendations. The IDG on Modern Biotechnology has been placed on a permanent footing in order to monitor progress of implementation of the recommendations contained in their first report, including those dealing with regulation.

4. Some Applications of Biotechnology

Health

Current health benefits of biotechnology include the use of genetically engineered human insulin for the treatment of diabetes, human growth hormone for dwarfism, factor VIII for haemophilia and deoxyribonuclease for cystic fibrosis.

Agriculture

Genetic modification has the potential to further reduce the use of chemicals for disease and pest control in crop production, to increase crop yields, and to develop crops which are tolerant to drought, non-optimal temperatures and poor quality soils.

Food Products and Safety

Biotechnology has traditionally been used in producing alcoholic drinks, bread, cheese and yoghurt and has further potential for altering the level of nutrients and antioxidants as well as improving the texture, colour, flavour and shelf life of a variety of foods. Diagnostic DNA kits are a more accurate and cost effective method for testing food safety.

Environment

Biotechnology is currently used in the treatment of domestic and industrial waste and has increasing potential in bioremediation of sites contaminated with organic pollutants.

Industrial Biotechnology

Microbial enzymes are increasingly used in biological detergents as well as for biopulping in the paper industry and in textile processing.

Forensic Science

DNA testing, now acceptable practice in criminal investigations, is more reliable than traditional fingerprinting.

5. Important Public Concerns Related to the Application of Biotechnology

ICSTI has addressed a number of public concerns regarding genetic engineering.

Antibiotic Resistance Genes in Plants

ICSTI considers that the possibility that antibiotic resistance genes in GMOs will compromise the use of antibiotics in the treatment of diseases is insignificant compared to the risk of this occurring because of the overuse of antibiotics in medicine, animal feeds and crop farming, and the incidence of antibiotic resistant bacteria in nature. The genes most commonly used in genetic engineering code for resistance to kanamycin which is very rarely used and hygromycin which is not used in human medicine. Although vertical gene transfer between one generation to the next is normal in nature, horizontal gene transfer between species which occurs in genetic modification, does occur in nature and causes no intrinsic damage.

Biotechnology in Food Production

ICSTI considers that biotechnology in food production is considered the least beneficial application of genetic modification. The food industry currently benefits from biotechnology using genetically engineered micro-organisms to produce the enzyme chymosin used in cheese production. Further potential benefits include improved detection of pathogenic bacteria in foods allowing a reduction in the levels of chemical preservatives used, and the development of nutraceuticals and improved nutritional content of foods. Public concern exists over transfer of foreign genetic material, including antibiotic resistance genes, into other organisms including humans. However, despite all the DNA consumed daily, there is no evidence for the transfer of intact genes to humans, either from bacteria in the gut or from foodstuffs. In the opinion of the Food safety Authority of Ireland (FSAI) Sub-Committee, GM foods are as safe to eat as their traditional counterparts. All GM foods undergo rigorous safety assessment to minimise the risk of toxicity or allergenicity. The FSAI supports the consumer's right to know if food contains GM ingredients and that these foods should be clearly labelled.

Virus Genes in Genetically Modified Plants

The Cauliflower Mosaic 35S Promoter, a section of DNA that drives the expression of genes, is very effective in plants and has been used to drive expression of genes inserted into GM plants to maximise formation of the desired product. The concern is that more virulent viruses will arise from recombination of viruses in GM plants. However, these suggested dangers do not withstand detailed scrutiny.

Gene Therapy

Introducing genetic material into a patient's cells allows the cause of the disease, not just the symptoms, to be treated. Diseases suitable for gene therapy treatment will be considered on an individual basis and gene therapy will probably only be part of the overall treatment of the disease. *In utero* or pre-natal gene therapy will have to show therapeutic value before it is considered and will raise further concerns and issues. ICSTI considers that in Ireland, the Irish Medicines Board (IMB) should evaluate gene therapy protocols and the Environmental Protection Agency (EPA) should be involved in regulating gene therapy research. The public should be made aware of global developments in gene therapy and the regulations at research and clinical levels in Ireland.

Crop Production

ICSTI considers that GM crops use less agricultural chemicals thereby reducing environmental damage, and offer the potential for plant based oral vaccines. Concerns related to GM crop production include the potential for superweeds, the development of insects resistant to insecticide and an over reliance on pesticides. There are also issues of seed ownership and the option of organic farming. In Ireland important areas of research include improving nutritive value, output and increased varieties of grassland, and pest and disease resistance in cereals.

Remediation of Contaminated Sites

Micro-organisms can be used to degrade organic pollutants from contaminated soil and water into stable, non-toxic end-products. This works *in situ* by stimulating the biodegradative activity of competent endogenous microbial populations and *ex situ* by treating, under controlled conditions, soils and sediments removed from contaminated sites. Introducing GM bacteria into the contaminated site, bioaugmentation, has the potential to enhance bioremediation.

Genetic Testing

Genetic testing is currently available for a wide variety of disorders. ICSTI considers that molecular testing has to be applied appropriately and raises complex ethical issues as well as concerns regarding privacy, genetic discrimination and insurance.

6. Conclusions and Recommendations

Concerns over recombinant DNA technology include the safety of GM foods, the impact of GM crops on biodiversity, potential health risks in using antibiotic resistance marker genes in GM plants, acceptability of transgenic species, patenting of germ plasm, human reproduction applications, animal cloning and threats to third world farmers.

These concerns have to be addressed in order to maximise the potential benefits of the technology while minimising risks to humans, animals, and the environment.

A 'National Conversation on Biotechnology' was recommended in the Report of the Technology Foresight Health and Life Sciences Panel (April 1999).

ICSTI recommends the establishment of a balanced comprehensive information centre for science and technology providing information on current and proposed uses of GMOs.

ICSTI also supports:

- informed choice and mandatory labelling of GM foods
- that information be made available on applications for release or marketing of GMOs
- that research and clinical trials in gene therapy be regulated
- the establishment of a fully independent biotechnology ethics committee.

1. Introduction

Science and technology have transformed society during the 20th century. Isaiah Berlin, one of the most reflective and influential European humanists, described the development of the natural sciences and technology as "certainly the greatest success story of our time". While highlighting the many benefits to mankind of increasing scientific knowledge and technological development, Berlin also noted that these same scientific advances led to the development of "weapons of war" which wreaked devastation on mankind during the 20th century. As we enter the 21st century, society is being revolutionised by the impact of microelectronics and other branches of physics and engineering and especially by the extraordinary growth in information, communication and computer technology. We are literally surrounded by the products of modern technology, most of which could not have been developed without fundamental discoveries made primarily by chemists, physicists, mathematicians and biologists in the last hundred years. Biologists and medical specialists have played a major role in the development of modern medicine, which has allowed life expectancy to increase remarkably. Agricultural scientists, including plant and animal breeders, have been responsible for the spectacular increase in the productivity of food crops, although increased food production has not been equitably distributed throughout the world.

The pace of technological change is accelerating and so is the nature of the new technology. At the beginning of the 20th century, three great technologies were available, electrical, mechanical and chemical. For the first half of the 20th century, the emphasis was on using these technologies to build or make things. Today, the emphasis is on refining machines, devices and systems that derive their power from being more complex, much smaller and much smarter than their predecessors. In addition, an entirely new technology has emerged, which is not primarily based on chemistry, physics and mathematics, although it does indeed owe a great deal to these basic sciences. The new technology is biotechnology, a technology which, in its modern form, is based essentially on the advances made in the last fifty years in our knowledge of genetics, biochemistry and microbiology. The publication of the first draft of the DNA sequence (the genetic code) of the human genome in June 2000 is a dramatic sign of the potential impact of modern biology. Most of the genetic information of a human being is now in the public domain. As with all new technologies, the emergence of biotechnology has raised many questions of enormous public interest.

New discoveries in biology now have profound implications for society because of their potential use. Biotechnology is revolutionising the pharmaceutical industry and agriculture. Many drugs and medicines have been developed using biotechnological methods, including human insulin and the triple therapy against AIDS. The international pharmaceutical industry is being reorganised to make even more effective use of new biotechnological processes. In agriculture, many novel crops have been developed using biotechnology. In 1999, 39.9 million hectares (an area 5 times the size of Ireland) were planted under genetically engineered crops. This is an increase of more than twenty fold from the 1.7 million hectares planted in 1996. The International Service for the Acquisition of Agri-Biotech Applications reported that this adoption rate is the highest for any new technology by agricultural industry standards.

As biology is the science of life, people are intensely interested in the potential impact of biotechnology on their health and on their food in particular. As a result of the remarkable advances made both in our knowledge of biological processes and in the application of this knowledge, profound moral issues as well as important political concerns have emerged. Scientists are as concerned about the moral issues as members of the general public and are contributing to many discussions with the public and the various national and international authorities. For example, scientists, politicians, civil servants and philosophers contributed to the conference organised by Mr. Philippe Busquin, EU Commissioner for Research, in Brussels in November 2000 on "Genetics and the Future of Europe". Many excellent books and collections of essays have also been published[1]. Biotechnology is, undoubtedly, an extremely powerful technology and many of the moral concerns expressed are understandable and some are well founded. It is, therefore, extremely important that these concerns are carefully addressed taking into account the best available scientific information of how the technology might impinge on widely accepted norms of morality. Such considerations involving many scientists have led to a world-wide ban on reproductive cloning.

The scientists responsible for developing biotechnology in the 1970s appreciated its potential and requested appropriate regulation of its application. As a result, stringent regulations were put in place, starting in the USA in 1976. Since its inception in the 1970s, there have been many tangible benefits and no significant accidents or damaging incidents that can be ascribed to biotechnology *per se*. Most scientists who work in relevant disciplines believe that biotechnology is as safe as, if not safer than, many other technologies which are commonplace, and not feared. Despite this good safety record and good prognosis, many people feel uncomfortable with the application of biotechnology in agriculture, food production and processing, in healthcare and new methods of medical therapy, and in the patenting and ownership of living species.

It is widely accepted by professional scientists that public concerns should be given attention by scientists and by scientific organisations. In the first instance, there must be wide and informed discussion of the issues involved. Concerns about biotechnology have coincided with considerable international unease about the impact of science and technology in general. These concerns have led some commentators to fear for the future of science in our society and even for the future of modern society itself. Wolfgang Fruhwald, the distinguished historian and President of the Alexander von Humboldt Foundation, has become so concerned as to note that the emergence of anti-science has the capacity to destroy civilisation. Although science and technology have an incredible capacity to improve the circumstances of mankind, they have also provided us with the tools for our own destruction. Many scientists argue that the misuse of science is not the fault of the science but a much more fundamental failure of society to restrain itself. In the view of Fruhwald and many others, we will not be able to solve the huge problems of the modern world if we do not employ science. However, while scientists and their supporters argue that, far from being the problem, science is essential for the solution, the public have not been convinced of the positive role of science. Many members of the public suspect that the dreadful diseases

1 For example, "Designing Life, Genetics, Procreation and Ethics", edited by M. Junker-Kenny, Publ. Ashgate 1999.

of BSE and AIDS resulted from scientific manipulation in research laboratories. The converse is, in fact, true. BSE and AIDS are new diseases that arose naturally and spread internationally due to the complex structure of modern society. They were discovered and explained by scientists using biotechnological methods, and biotechnology is central, in both cases, to the ongoing efforts to control and cure these diseases.

Science and technology can only be fully harnessed for the benefits of society if all members of society have a high level of understanding of what is involved. All technologies have potential harmful effects, but risks and benefits have to be put into perspective. The public will better understand these risks and benefits, if they are able to participate at some level in the formulation and approval of national policy in science and technology. The final responsibility for such policy lies with the government but the government must endeavour to explain the policy to the public and to obtain its support. A society, in which the public, scientists and engineers do not interact in a constructive and open way, will not succeed in the modern era. Not only will industry and agriculture be inhibited, but the public will be less able to participate in appreciating the extraordinary richness of the natural world which is being revealed day by day through scientific research.

1.1 Provision of Independently Validated Information

Although extensive documentation exists on the development and application of traditional and modern biotechnology, the Irish Council for Science, Technology and Innovation (ICSTI) considers that there is a lack of independently validated and readable information for the general public. This issue was highlighted in the July 1999 *"Report of the Chairing Panel of the National Consultation Debate on Genetically Modified Organisms and the Environment"*[2]. The Panel recommended that a greater effort be made by the State to inform the general public about developments in modern biotechnology. Such information should be based on the needs of citizens and provided in language understandable to the general public.

General web-based searches indicate that cited literature is quite polarised and focuses primarily on Genetically Modified Organisms (GMOs) rather than on the broader topic of modern biotechnology. Coverage in the media can be inaccurate and misleading, leading to further polarisation of views on the benefits and risks of modern biotechnology.

In the absence of independent and credible information on biotechnology, the general public is not given the opportunity to fully understand, and therefore make informed decisions on, the enormously wide range of applications of traditional and modern biotechnology in the agricultural, industrial and healthcare sectors.

2 National Consultation Debate on Genetically Modified Organisms and the Environment – Report of the Chairing Panel; Department of the Environment and Local Government, Ireland, July 1999.

To address this issue, the *"Report of the Chairing Panel of the National Consultation Debate on Genetically Modified Organisms and the Environment"* recommended that:

- The Environmental Protection Agency (EPA) should take a more proactive role in disseminating information in relation to the environment.
- The issue of information dissemination should be referred to the Inter-Departmental Group on Modern Biotechnology for consideration in the context of its broader remit.

The report of the Inter-Departmental Group on Modern Biotechnology published in October 2000[3], made a number of recommendations, including "that the issue of co-ordination across agencies in relation to information and communication on biotechnology should form part of the on-going work programme of the Inter-Departmental Group".

1.2 Objective of the ICSTI Statement on Biotechnology

ICSTI decided to establish a Task Force on Biotechnology in order:

- to examine the current application of modern biotechnology
- to identify and consider certain issues that need to be addressed in a national context
- to prepare a report on Biotechnology that would take scientific, ethical and public concerns into account.

The aim of the ICSTI report is to provide a scientifically credible, balanced and clear document that will identify some of the main public concerns about modern biotechnology, while highlighting potential benefits and risks of its application. The statement is not intended to be fully comprehensive since not all current concerns have been fully addressed and other issues are likely to arise in the future.

3 Report of the Inter-Departmental Group on Modern Biotechnology, Government Publications, October 2000, Ireland.

2. Biotechnology

2.1 The Science

Biotechnology may be defined as the use of living organisms or their sub-cellular components to develop useful products, processes or services. Essentially, it is a group of technologies which involve the application of many biological systems that have evolved with the development of life itself. In essence, the definition illustrates the depth and breadth of this science which encompasses a wide range of disciplines, including the life sciences, agriculture, environmental science, medicine, chemistry, veterinary medicine, engineering and computer science.

The discovery of antibiotics in the 1940s and the need to develop "process fermentations" capable of large-scale antibiotic production during the World War II years led to striking new developments in fermentation technology and to the coining of the term "biotechnology". In the 1970s, biotechnology went into a remarkable new phase of expansion stimulated by discoveries in molecular genetics. These discoveries led to the extraordinarily powerful technology of genetic engineering and drew renewed attention to the whole field of "biotechnology".

OECD Definition (1982)

Biotechnology means the application of scientific and engineering principles to the processing of materials by biological agents to provide goods and services. These principles cover a wide range of disciplines but rely heavily on microbiology, biochemistry, genetics, biochemical and chemical engineering.

Although the term is relatively recent, man has used biotechnology for thousands of years. For most of human history, plants and animals have been selectively bred to improve particular traits, such as yield, disease resistance and hardiness. The making of bread, wine and beer by microbial fermentation processes are age-old activities, documented in our historical development even as far back as Egyptian times. Archaeological evidence suggests that the early Romans recovered copper leached by bacteria from natural copper sulphide deposits. The first recorded, large-scale bio-mining operation was initiated in the early 1700s in Rio Tinto, Spain.[4]

Biological processes have been used for many years, long before the role of microorganisms in these processes was understood. Appreciation of the enormous diversity of microorganisms and simultaneous development of the science of genetics greatly expanded the potential of traditional biotechnology and led to the development of what has been termed "modern" or "new" biotechnology.

4 Biomining, Theory, Microbes and Industrial Processes. Ed. D.E. Rawlings. Springer Verlag & Landes Biosciences (1997).

The discovery of the double helix structure of DNA (deoxyribonucleic acid) by Watson and Crick in 1953 resulted in an understanding of gene function, expression and control. Isolation of highly specific microbial enzymes, known as restriction endonucleases, by Hamilton Smith in 1970 and of ligase or "stitching" enzymes opened up the possibility of controlled gene manipulation and inter-species gene transfer. These discoveries revolutionised the potential of biotechnology in the health-care, food and other sectors.

The umbrella of modern biotechnology encompasses a broad array of technologies, both "traditional" and "new". However, the term biotechnology has, to the general public, become synonymous with **genetic engineering**. Genetic engineering, in turn, encompasses **recombinant DNA technology, genetic modification, gene technology and/or gene manipulation**. Genetic engineering makes it possible to cut DNA into its fundamental functional units, the "genes", and to splice (recombine) those genes into other DNA molecules. Thus, it is now possible to enhance the ability of an organism to produce a particular product, to prevent it producing a product, or to enable it to produce an entirely new product. While maintaining all or most of its original properties, a genetically engineered (GE) or genetically modified (GM) organism can do something it had not done before or ceases something which it did before.

The microorganism which was commonly used as a "host" for genes from other organisms at the onset of molecular genetics was the bacterium, *Escherichia coli (E. coli)*. There was no great deliberation, at the time, on the most suitable microbe of choice. *E. coli* was a common research laboratory organism that grew easily, was able to incorporate foreign DNA "vehicles" (in the form of phages and plasmids), and a considerable amount of information was available on its genetic make-up.

The ability to manipulate living organisms at the genetic level is one of the principal tools of modern biotechnology. Although the aim of traditional biotechnology, such as selective breeding, was to develop new traits or enhance existing functions (or to add or enhance a particular trait), new biotechnology (or genetic engineering) allows sophisticated manipulation of the genes in plants and animals which encode for particular characteristics in a more direct, precise manner. Genetic engineering is capable of providing an organism with a specifically chosen, designed and desirable "new" ability or property. In making such a specific manipulation, the outcome becomes much more predictable, precise and controlled than was feasible with traditional biotechnology techniques. This level of control is a tremendous asset in the application of modern biotechnology to sustainable development and improvement of the quality of life.

2.1.1 The Stages in Recombinant DNA Technology

The essential stages of recombinant DNA technology are briefly outlined below and diagrammatically represented for a microbial species in Figure 1. The stages involved include:

i. identifying, in a donor species, the gene that directs the production of the desired substance

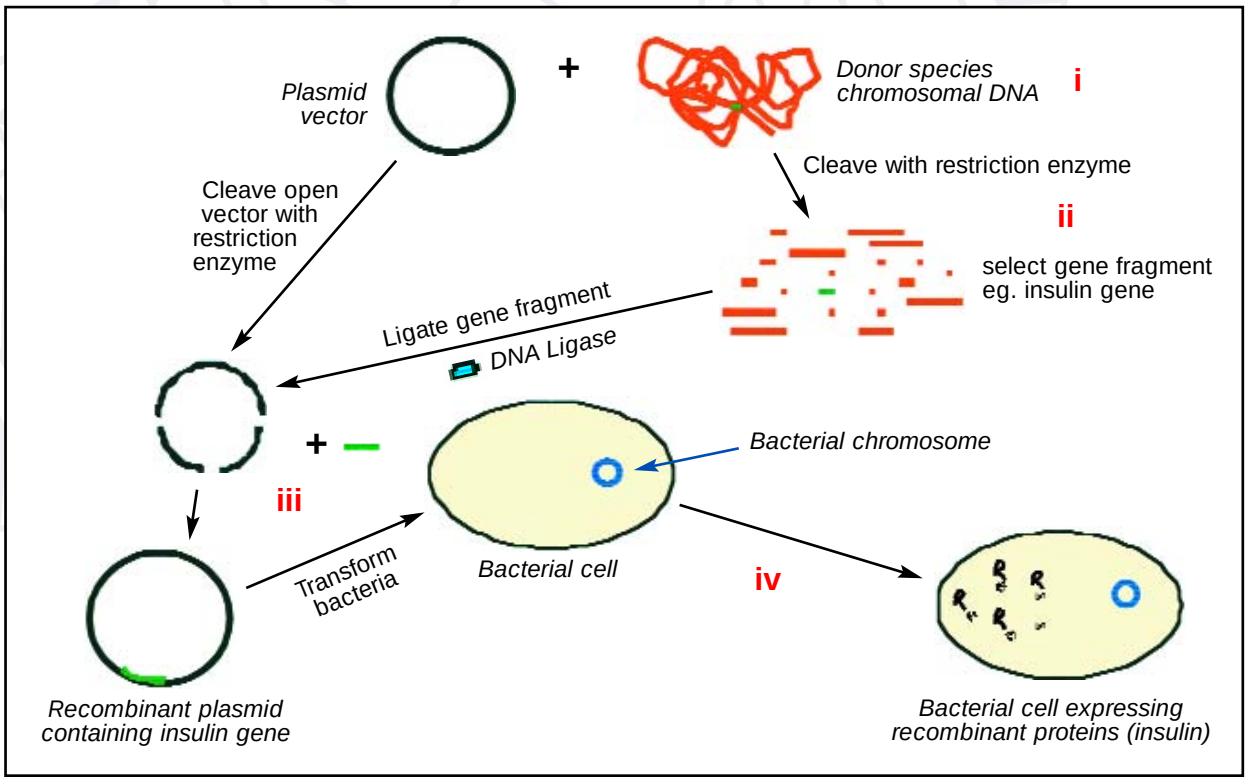
ii. isolating the gene from the donor using restriction enzymes

iii. splicing of the gene into a circular piece of DNA, called a vector, which can replicate in the host

iv. transferring the recombined DNA into a bacterium or other suitable host.

The overall process is referred to as cloning since the genetically-engineered organism becomes the parent of a population of identical organisms, which are literally clones of each other in the sense that they are genetically identical. Plants, animals and micro-organisms, which have been subjected to genetic manipulation artificially using these techniques, are referred to as **genetically modified organisms** (GMOs). Species that have artificially received a gene or genes from a different genus (plant, animal, microbial) are described as **transgenic**.

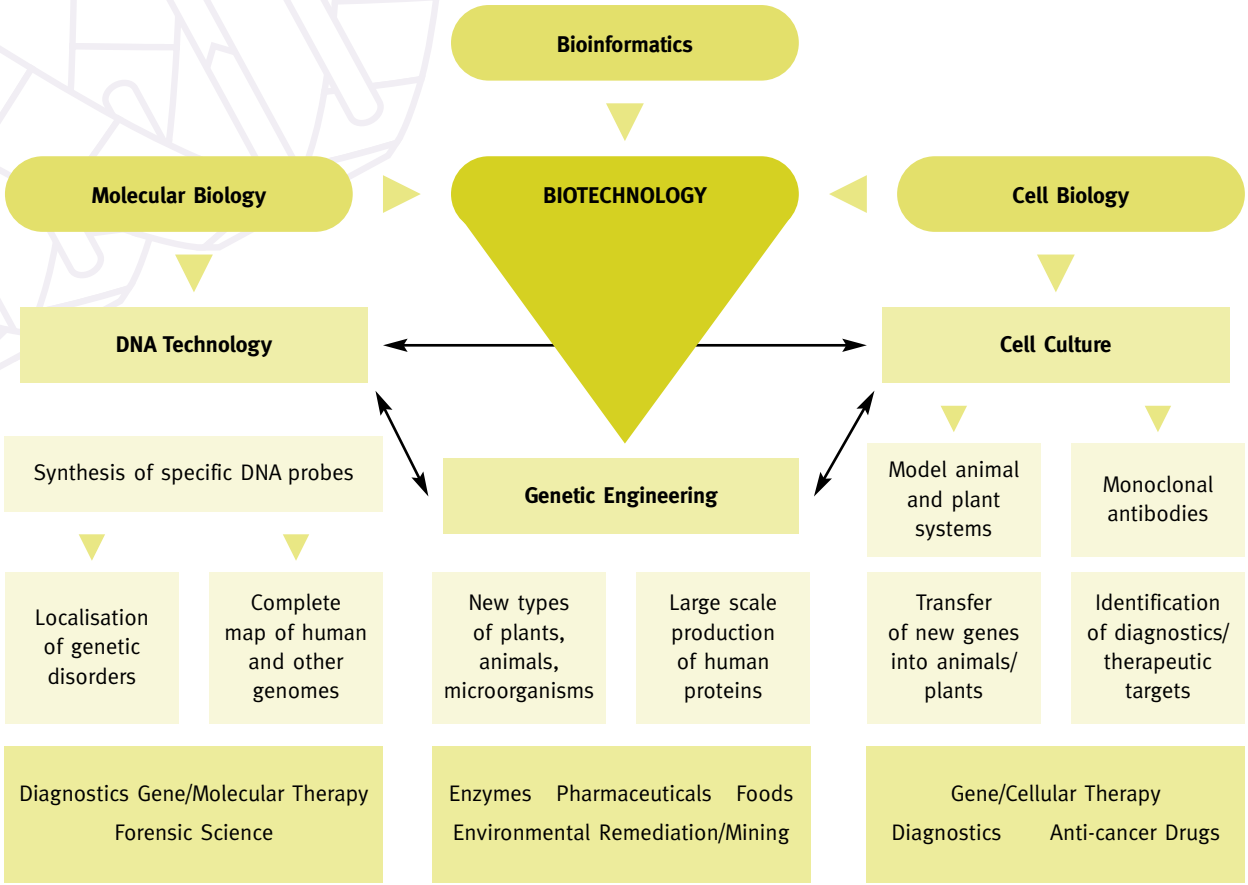
Figure 1: An Example of DNA Cloning Processes



2.2 The Application

The potential of biotechnology, together with the "new" sciences required for its current and future development and application, are illustrated in Figure 2. Chapter 4 provides some examples of the current applications of traditional and modern biotechnology in a number of industrial, agricultural, healthcare and environmental sectors.

Figure 2: Overview of Scientific Disciplines Involved in Recombinant DNA Technology



Genetic engineering using recombinant DNA techniques is currently widely used in the pharmaceutical industry and in human medicine. Drugs produced by biotechnological processes are used to treat invasive fungal infections, pulmonary embolisms, kidney transplant rejection, infertility, growth hormone deficiency, diabetes, AIDS and other serious disorders. In the future, drug therapy will become more personalised through the use of genomics and pharmacogenomics. Many of the products we eat, wear and use are made using the tools of modern biotechnology. Using genetic engineering, scientists are able to enhance the nutritional content, texture, colour, flavour, growing season, yield, disease resistance and other properties of production crops.

Transgenic techniques are being applied to farmed animals to produce pharmaceuticals and nutraceuticals, and to improve the growth, fitness and other qualities of agriculturally important mammals, poultry and fish.

The public are generally unaware of the extent of application of traditional biotechnological processes in food production, industrial processes, waste and wastewater treatment, bioremediation, renewable energy generation and biomining. These applications will undoubtedly continue but are likely to be improved by using recombinant DNA technology, for example, in the more informed, more specific and more controlled use of microbes or microbial enzymes. Used efficiently, after appropriate risk assessment and with effective and enforced regulation, biotechnology has enormous potential to improve the quality of life and to enhance our capacity to conserve and protect the environment.

2.3 The Economics

Biotechnology is of strategic importance to the Irish economy in order to sustain current economic growth and to enhance the ability of Ireland to become a knowledge-based economy.[5]

Table 1: Biotechnology in Perspective (€millions) (1999)

EUROPE	Public Companies			Industry Total		
	Current Year	Prior Year	Percent Change	Current Year	Prior Year	Percent Change
Financial						
Revenues	2,612	1,032	153%	5,368	3,709	45%
R&D expense	1,504	762	97%	3,164	2,334	36%
Net Loss	367	410	-10%	1,189	2,107	-44%
Industry						
No. of Companies	68	68	0%	1,351	1,178	15%
Employees	15,444	11,449	35%	53,511	45,823	17%

The current market value of biotechnology companies world-wide is estimated to be in the region of $500 billion. Ernst & Young estimate that in 1999 the European entrepreneurial life sciences included over 1350 companies and employed nearly 54,000 people[6]. The table below shows the state of the market in 1999, as reported by Ernst & Young.[7]

World-wide, the pharmaceuticals, chemicals, agri-food and medical device sectors, which have contributed significantly to industrial development in Ireland in the past 20 years, and account for a high proportion of Irish high technology jobs and exports are being revolutionised by biotechnology. In Ireland, over 76,000 people are employed in biotechnology-related sectors –

5 Technology Foresight Ireland 1999: An ICSTI Overview, Forfás, April 1999.
6 Evolution: Ernst & Young's Seventh Annual European Life Sciences Report 2000
7 Evolution: Ernst & Young's Seventh Annual European Life Sciences Report 2000.

pharmaceuticals and chemicals (23,000) and food and beverages (53,000)[8]. Turnover in 1997 in these sectors was €21 billion of which food accounted for €15 billion. Exports were worth €16 billion with food accounting for €10 billions[9].

Developments in biotechnology will have a profound effect on a number of sectors that are vital to the future development of the Irish economy. While employment in the food and beverages sector is unlikely to grow significantly, substantial growth is expected in the pharmaceuticals and chemicals sector, with an approximate doubling of permanent employment expected by 2010.[10] A recent study by Forfás and Enterprise Ireland concluded that there was potential for 6,200 jobs in Irish-owned biotechnology companies with associated revenues of €490 million by 2010. From a wider perspective, it is estimated that there will be up to 40,000 jobs in the rest of the economy that will have a biotechnology component (in many cases this will be significant).

Ireland's biotechnology capability is thus a major issue. If companies based in Ireland do not capitalise on the potential and deal with the possible risks arising from biotechnology developments, not only will the significant potential of high quality new jobs be at risk, but there would also be a significant threat to a high proportion of the existing job base.

To enable Ireland to:

- develop world class research capability in strategic technologies for the future competitiveness of indigenous industry
- facilitate the undertaking of R&D in this country by multinational companies
- attract more high tech companies to Ireland in the future

it is necessary to have well focussed and significant investment in upgrading the technological infrastructure of the economy. This includes significant investment in biotechnology.

The Technology Foresight Ireland Reports, published in 1999 by ICSTI and Forfás, recommended that the Government establish a major fund to develop Ireland as a centre for world class research excellence in strategic niches of Biotechnology and ICT (Information and Communication Technologies). As part of its response the Government approved a Technology Foresight Fund of over €711 million for investment in research, initially in the niche areas of ICT and Biotechnology in the years 2000-2006. Science Foundation Ireland (SFI) is responsible for the management, allocation, disbursement and evaluation of expenditure of the Technology Foresight Fund.

8 Forfás Employment Survey, 1997.
9 Trade Statistics, 1998.
10 "Enterprise 2010 – A New Strategy for the Promotion of Enterprise in Ireland in the 21st Century", Forfás, January 2000.

3. Regulation of Biotechnology

Traditional biotechnological processes and products are subject to a wide variety of national and international regulations designed to ensure the safety of food, drugs and medicines, and to minimise negative environmental impact. The development of genetic engineering techniques, with the consequent ability to produce genetically modified organisms and transgenic species, necessitated the development of additional guidelines and regulations that would allow development and application of the "new" biotechnology, while minimising the risks to human health and safety, and avoiding environmental damage.

The desire by leading researchers for appropriate regulation of recombinant DNA technology was evidenced in 1974 by a call for a moratorium on genetic engineering research based on the findings of the US National Academy of Sciences (NAS) Committee on Recombinant DNA Molecules. This led to the landmark Asilomar Conference in 1975, which was attended by eminent specialists in biotechnology and risk assessment and which explored all foreseeable implications of recombinant DNA research. The outcome of the conference was the development of a series of guidelines designed to ensure the safety of genetic engineering research. It also led to the establishment of the Recombinant DNA Advisory Committee (RAC) by the US National Institute of Health (NIH) and the eventual publication in 1976 of what subsequently became known as the RAC Guidelines. To ensure compliance with the RAC Guidelines, Institutional Biosafety Committees (IBCs) were set up to assist the RAC in reviewing recombinant DNA research programmes at institutional level.

Procedures to ensure the safety of genetic engineering research in other parts of the world generally followed the US guidelines. Over the 25 year period from 1975 to 2000, the vast amount of information that has accumulated on risk assessment of GMO research has allowed some relaxation of the initial guidelines without compromising safety.

Commercialisation of the "new" biotechnology processes and products required development of a regulatory framework, rather than reliance on research guidelines. The objective of regulation is to ensure maximum consumer protection, while minimising negative environmental impact. However, it is important to prevent over-regulation to the extent that it may inhibit the development of GM products and processes that are of benefit to the public at large and to the environment.

3.1 US Regulation

In the present US regulatory environment, three agencies share responsibility for regulating the organisms, products and processes of recombinant DNA technology. The agencies involved are the Food and Drug Administration (FDA), the United States Department of Agriculture (USDA) and the Environmental Protection Agency (EPA). The regulations cover the contained use and deliberate release of GMOs.

3.2 European Regulation

The current EU Directives and Regulations governing the application of recombinant DNA technology and use of GMOs are outlined in Table 2. While the EU has given strong commitment to the development of the biotechnology sector, for example through the Framework Programmes of research, technological development and demonstration, these EU Directives and Regulations give a clear priority to human and animal health and to environmental protection and sustainability.

European authorisation of medicinal products for human and veterinary use is carried out by The European Agency for the Evaluation of Medicinal Products (EMEA) in co-operation with national authorities. Table 2 indicates the relevant EU Directives and Regulations governing the use of GMO products in human and veterinary medicine.

3.3 Irish Regulation

The EU Directives and Regulations provide the regulatory framework that is currently in place in Ireland governing genetically modified organisms and medicinal products for human use. These regulations and directives have been transposed, or are in the process of transposition, into Irish law.

3.3.1 Medicinal Products

EU directive 65/65 covers all medicinal products for human or animal use. The Irish Medicines Board (IMB) is the competent authority for the licensing and sale of medicinal products for human use by means of the Medicinal Products Regulations (S.I. 142 of 1998) and relevant EU directives.

Before a medicinal product can be authorised for use, an application must be made for a product authorisation to the IMB. In the case of centrally licensed products, the application must be made to the EMEA. The granting of such authorisation ensures that a product complies with required standards of quality, safety and efficacy. It is the responsibility of companies and agencies marketing medicinal products to comply with the relevant legalisation and to ensure that products are marketed in accordance with relevant legislation.[11] Medicinal products derived by pharmaceutical methods or by biotechnology processes are regulated in a similar manner.

3.3.2 Genetically Modified Organisms (GMOs)

Table 2 lists the EU Directives and Regulations currently governing contained and field use of genetically modified organisms in crops, foodstuffs and medical, veterinary and plant protection products and highlights the relevant Competent Authorities in Ireland.

The EU Directives dealing with contained use (Directive 90/219/EEC) and deliberate release of GMOs (Directive 90/220/EEC) were introduced into Irish law in December 1994 by the Genetically Modified Organisms Regulations 1994 (S.I. No. 345 of 1994). The Environmental Protection Agency (EPA) was nominated as the competent authority to administer the Regulations in Ireland. Amendments to Regulation 345 of 1994 were made in 1996 and 1997. Directive 90/219/EEC was amended on 26 October 1998 and Directive 98/81/EEC amending Directive 90/219/EEC was transposed into Irish law on 15 March 2001 (S.I. No. 73 of 2001).

11 Source: Irish Medicines Board web-site, www.imb.ie

As of March 2001 there were 108 entries on the GMO Register in Ireland, with the majority of these involving contained use. There have been six notifications for deliberate release to the environment for R&D purposes, two of which were withdrawn. To date, there have been no direct notifications for placing products containing or consisting of GMOs on the market in Ireland under S. I. No. 345 of 1994[12].

Table 2: European Union Legislation Regulating Genetically Modified Organisms

Directive/Regulation	Purpose	Competent Authority	Aspects Regulated
Directive 98/81/EEC amending Directive 90/219/EEC	Regulates the contained use of Genetically Modified Micro-organisms (GMMs)	Environmental Protection Agency (EPA)	• Contained use of GMMs and GM animals and plants
Directive 90/220/EEC	Regulates the deliberate release of GMOs into the environment for: • R&D purposes (field trials) • Placing GMO products on the market	Environmental Protection Agency (EPA) Department of Environment & Local Government are responsible for certain functions e.g. decisions to place GMOs on the market under Article 21 of 90/220	• Environmental assessment for the cultivation and importation of GMOs in the EU • Animal feed aspects (including allergenicity and toxicity) relating to the cultivation of GM crops in the EU
Directive 90/679/EEC	Regulates biological agents in the workplace	Health & Safety Authority (HAS)	• Workplace contact
Directive 94/55/EEC	Regulates the transportation of certain GMOs	Department of Enterprise Trade & Employment	• Transportation
Regulation 258/97/EC	Regulates novel food and novel food ingredients including GMOs	Food Safety Authority of Ireland (FSAI)	• Food and food ingredients containing or consisting of GMOs • Food and food ingredients produced from but not containing GMOs e.g. oil from GM soyabeans
Regulation 1139/98/EC	Regulates the labelling of certain foodstuffs produced from GMOs	Food Safety Authority of Ireland (FSAI)	• Labelling of foods from GM soyabean and GM maize
Regulation 49/2000/EC	Establishes a threshold below which the labelling of genetically modified food or ingredients is not required	Food Safety Authority of Ireland (FSAI)	• Regulates the labelling of GM food and food ingredients
Regulation 50/2000	Regulates GMOs for food additives and flavourings	Food Safety Authority of Ireland (FSAI)	• Regulates additives and flavourings that have been genetically modified or have been produced from GMOs

12 Source: EPA (June 2001).

Table 2: European Union Legislation Regulating Genetically Modified Organisms *continued*

Directive/Regulation	Purpose	Competent Authority	Aspects Regulated
Regulation 2309/93/EEC	Regulates GMOs for medicinal and veterinary uses	Irish Medicines Board	• Regulates medicinal and veterinary products including those products which contain or consist of GMOs
Directive 91/414/EEC	Regulates the use of plant protection products	Department of Agriculture & Food, Pesticide Control Service	• Regulates the use of herbicides, insecticides and fungicides on crops including GM crops
Directive 98/95/EEC	Regulates the marketing of GM plant varieties and amends current Directives relating to seed	Department of Agriculture, Food & Rural Development	• Regulates seed, including GM seed, to be placed on catalogues for use in agriculture
Directive 70/524/EEC as amended	Regulates the authorisation, marketing and use of additives in feeding stuffs	Department of Agriculture, Food and Rural Development	• Authorisation procedures, conditions of use • Labelling and distribution of additives in animal nutrition • Establishes and EU list of approved additives
Directive 87/153/EEC	Regulates guidelines for the assessment of additives in animal nutrition	Department of Agriculture, Food and Rural Development	• Sets out the studies to be undertaken and information provided in an additive dossier submitted for assessment
Animal feed	The proposed Directive will amend current Directives relating to animal feed	Department of Agriculture, Food and Rural Development will be responsible	• Regulate animal feeding stuffs containing or consisting of GMOs and feed derived from GMOs

Further details on EU Directives and Regulations can be obtained from the competent authorities listed in Table 2.

3.3.3 Council Directive 98/81/EEC (Contained Use of Genetically Modified Microrganisms)

This covers any GMO operation where organisms are genetically modified or where GMOs are cultured, stored, used, transported, destroyed or disposed. Containment is provided by physical barriers, or by a combination of physical, chemical and/or biological barriers. Containment is used to limit the contact of the GMO with the general population and the environment. For some Group II GMMs (genetically modified microorganisms), there is a requirement to prevent release of the GMM from the physical containment facility.

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

This covers any intentional release into the environment of a GMO without provision for containment. It excludes any plant, animal or microbial species that is the product of techniques such as cell fusion, *in vitro* fertilisation or conjuction. There are two different types of release covered by the directive:

1. R&D purposes – Field Trials
2. Placing GMO products on the market.

3.3.5 R&D purposes – Field Trials

Applications to the Environmental Protection Agency (EPA) for deliberate release must include a technical description of the proposed deliberate release, a statement evaluating the impacts and risks posed by the GMO to human health or to the environment and information on previous releases of the GMO either inside or outside the EU.

The EPA does not consent to a deliberate release unless it is satisfied that the release will not result in adverse effects on human health or the environment. A post release procedure is also in place which requires the notifier to submit the results of the deliberate release to the EPA.

Between October 1991 and September 1999, 1500 GM crop release SNIFS (summary notification information formats) relating to GM plants (more than 70 varieties) were circulated in the EU under part B of Directive 90/220/EEC for purposes other than being placed on the market (i.e. for field trials). The first field trial in Ireland took place during the 1997 growing season and involved two varieties of GM sugarbeet. There were five field trials in five locations (one GM sugarbeet) during the 1998 growing season. All subsequent trials also involved GM sugarbeet and were carried out at four locations in 1999 and at two locations in 2000. More detailed information on deliberate release of GMOs to the environment can be obtained by contacting the EPA headquarters at Johnstown Castle, Wexford.

3.3.6 Placing GMO Products on the Market

A person cannot place a product on the market in Ireland which contains or consists of a GMO unless consent is either given in writing under Part 1V of the Genetically Modified Organisms Regulations, 1994, or obtained from the Competent Authority of another EU Member State in accordance with Part C of Directive 90/220/EEC.

No notifications for licensing of GMO food products have been received by the EPA since Directive 90/220/EEC was transposed into Irish law[13].

In the case of crop plants, it is only the 'live' seed (able to germinate or transfer its genetic material to other plants) that is regulated under Directive 90/220/EEC. Once the seed is processed (at certain temperatures), the DNA is denatured (non-viable) and therefore the product is not

13 Source: EPA.

classified as a GMO, e.g. oil derived from genetically modified soyabeans. Such products, as well as 'live' GMOs to be used for human food consumption, are regulated under EU Regulation 258/97 (concerning novel foods and novel food ingredients).

In order to place a GMO product on the market in the EU, the manufacturer of the product must deal with the competent authority from the Member State where the product will be marketed for the first time.

Eighteen GM products have been approved under Directive 90/220/EEC, including a number of plants which have been modified for herbicide resistance. It is anticipated that more plant products will be submitted under Part C of 90/220/EEC in future years. Table 3 lists the GMO products approved under Directive 90/200/EEC.

Table 3: Examples of GMO Products Approved Under Directive 90/220/EEC (May 2000)

- Vaccine against Aujeszky's disease
- Vaccine against rabies
- Tobacco-herbicide tolerant
- Vaccine against Aujeszky's disease (further use)
- Hybrid oilseed rape-herbicide tolerant (variation)
- Soybeans-herbicide tolerant
- Male sterile chicory-herbicide tolerant (variation)
- GM maize-insect & herbicide tolerant (variation)
- Hybrid oilseed rape-herbicide tolerant
- Hybrid oilseed rape-herbicide tolerant (variation)
- GMMs – test kits to detect antibiotic residues in milk
- GM carnations (variation)
- GM-maize-herbicide tolerant
- GM maize-insect tolerant
- GM-maize-insect & herbicide tolerant (variation)
- GM oilseed rape-herbicide tolerant
- GM carnations (variation)
- GM carnations (variation)

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

This regulation concerns the placing on the market of novel foods and novel food ingredients and contains provisions for labelling. A number of categories of novel foods are specifically mentioned including:

- foods and food ingredients containing or consisting of genetically modified organisms
- foods and food ingredients produced from, but not containing, genetically modified organisms.

It should be noted that those products that are produced in whole or in part from GM soya or GM maize and that are to be placed on the market for human consumption are regulated under EU Regulation 1139/98. The Novel Foods and Food Ingredients Regulation (258/97) came into force after the EU had sanctioned growth of these GM crops, thereby requiring separate EU regulation of their food products.

3.4 Environmental Liability

Environmental liability including damage resulting from the release of GMOs is an emerging issue. Liability in terms of damage to health or property is already addressed under Directive 85/374/EEC, as modified by Directive 99/34/EC, which concerns liability for defective products.

The European Union intends to submit a proposal on general environmental liability rules as a follow up to the White Paper on Environmental Liability before the end of 2001, as requested by the European Parliament. This will deal specifically with damage caused to the environment by GMOs.

The Chairing Panel of the National Consultation Debate on Genetically Modified Organisms and the Environment[14] briefly considered the issue of environmental liability. The Panel recommended that responsibility for any damage to the natural environment, which was unforeseen when consent to release was granted, should rest with the body who sought and obtained consent for the release of that product. In the Policy Statement[15] by Mr. Noel Dempsey, T.D., Minister for the Environment and Local Government, the Minister agreed with the concept of strict liability for environmental damage resulting from the release of GMOs and undertook to press for acceptance of this principle in EU level negotiations in this regard.

3.5 Risk Assessment and Management

With many of the GM products and processes under development, there are a number of benefits to the public at large and to the environment but there may also be a number of risks.

As stated in the Report of the Interdepartmental Group on Modern Biotechnology (October 2000) some of the issues surrounding the public debate on biotechnology arise from the fact that scientists have not been able to offer absolute guarantees that there are no risks of adverse effect. The report goes on to state that *"though science does not deal in certainties, it remains the most reliable and rigorous form of knowledge we have and offers the only possible basis for assessing the safety of new products and processes"*.

The Chairing Panel of the National Consultation Debate on GMOs and the Environment placed primary emphasis on a position of precaution, well grounded in scientific risk assessment and management. In line with this recommendation, the Report of the Interdepartmental Group on Modern Biotechnology made a number of recommendations to strengthen the regulatory and policy framework at EU and national levels.

ICSTI endorses these recommendations and believes that examination of risks of any GM product or process should be assessed on a case-by-case basis and should be evaluated in the light of risks imposed by their traditional counterparts. In the case of GM crops, the combined impact of several GM crops on the environment and the food chain should also be properly assessed.

14 Report of the Chairing Panel of the National Consultation Debate on Genetically Modified Organisms and the Environment, Department of the Environment and Local Government, July 1999.

15 Policy Statement by Mr. Noel Dempsey, T.D., Minister for the Environment and Local Government, October 1999.

4. Some Applications of Biotechnology

By its nature, biotechnology is a generic underlying technology that has many applications and benefits for almost all sectors of the economy. Biotechnology encompasses a wide range of fields, including the life sciences, chemistry, agriculture, environmental science, medicine, veterinary medicine, engineering and computer science. Some applications of biotechnology are outlined in the following sections. It should be noted that this is not an exhaustive list.

4.1 Health

To date, the most notable impact of biotechnology has been in the medical and pharmaceutical arenas. Over 200 million people world-wide have benefited from the $13 billion biomedical biotechnology industry. One of the major discoveries within the biomedical industry has been the use of biotechnology to produce human insulin for the treatment of diabetes. Today, all diabetics world-wide who need to take insulin receive genetically engineered human insulin. Before this hormone was produced using modern biotechnology, it was isolated from the pancreas of pigs and cows. This was both costly and inefficient and sometimes the extracted hormone caused an allergic reaction in humans. Through genetic engineering, the production of insulin for the treatment of diabetes has become less costly and safer to use. Other medical products produced using biotechnology include human growth hormone to treat dwarfism, factor VIII for the treatment of haemophilia and deoxyribonuclease in the treatment of cystic fibrosis. Biotechnological advances have also led to developments in gene therapy, which has the potential to treat the cause of the disease rather than the symptoms.

4.2 Agriculture (Crop & Animal)

The use of biotechnology has potential in agricultural crop productivity in reducing chemical inputs for disease and pest control, and in developing crops that are more tolerant of abiotic stresses such as drought, non-optimal temperatures, marginal quality soils and in increasing yields. Large areas of genetically modified (GM) soyabean, maize, cotton and canola have been successfully grown in the Western Hemisphere. In the United States in 1999, of the 72 million acres (29 million hectares) planted with soyabeans, half were planted with GM herbicide-resistant seeds. These advances in plant technology have major implications for crop production in the developing countries where there are extreme conditions and even when crops are successfully grown they do so with low yields. Using biotechnology, the yield of these crops can be dramatically increased.

Another promising area is in the health care of animals, primarily in the development and production of pharmaceuticals, therapeutics and diagnostics for disease detection and treatment. Biopharming, i.e. the production of pharmaceuticals or medically important proteins in cows' milk to enhance human health, also has potential. The use of GM animals offers a viable economic approach for large scale production of recombinant proteins in addition to therapeutics.

4.3 Food Products

Historically, biotechnology has been used in food production, both in the selective breeding of plants and animals and in food processing using microorganisms or microbial enzymes. Examples of traditionally processed foods using biotechnology include alcoholic beverages, cheese, bread, yoghurt, fruit and vegetable products such as pickles and soya sauce. A wide variety of food flavouring agents and additives are also produced using biotechnology. Advances in enzyme technology have allowed sourcing, development and production of a wide range of microbial enzymes that currently play key roles in food processing. For example, the enzyme rennet, which is used in the clotting of milk during cheese production, was originally sourced from the stomachs of calves. Rennet has now been replaced by the microbial enzyme, chymosin, which is produced by conventional fermentation technology.

Using biotechnology, it is now possible to alter quality traits of food products, such as nutritional content, antioxidants, vitamins, minerals, texture, colour, flavour and shelf life, all of which are of direct importance to the consumer.

Growing consumer awareness of the relationship between diet and health is now a major factor in advancements in food technology, particularly in the field of functional foods and probiotics. For example, between 140 and 250 million infants in developing countries, under the age of five suffer from vitamin A deficiency. Through genetic engineering, scientists have succeeded in modifying rice – the staple diet of 2 billion humans – to produce ß-carotene. The result is a new yellow rice rich in vitamin A. This contribution of biotechnology could potentially reduce related infant mortality by 23%, as well as deaths from measles and diarrhoeic diseases by 50% and 33%, respectively.

4.4 Food Safety

The safety of food is an absolute priority which must be assured in order to maintain and expand food markets. Approximately 9,000 Americans die each year from food-borne illness caused by micro-organisms such as *E. coli* in meat and *Salmonella* and *Campylobacter* in poultry. The role of biotechnology in quality assurance is of great importance. DNA probe kits have been developed to detect *Salmonella*, *Campylobacter*, *Listeria* and *E. coli 0157*. Compared to traditional culture plating methods, these new diagnostic kits offer greater precision, shorter turn around times, and cost savings and reduce the need for highly trained personnel. Biotechnology is enabling manufacturers to ensure the safety of their foods, meet legal standards, and provide reassurance to customers.

4.5 Environment

The environmental benefits offered by biotechnology are enormous, particularly in the fields of waste treatment and bioremediation of contaminated sites. Traditionally, biological treatment systems have been used to reduce the organic pollution potential of domestic wastewaters (sewage) and of wastes and effluents from food-processing, chemical, pharmaceutical, electronics, textile and leather-processing industries, and even from oil refineries. Increasingly, biotechnology is being used to also remove the nitrogen (N), phosphorous (P) and sulphur (S) contaminants of domestic and industrial wastewaters.

Bioremediation represents an exciting and rapidly growing technology for the remediation of soils, sediments, aquifers and marine environments contaminated by organic pollutants. These pollutants include hydrocarbons, chlorinated solvents, insecticides, pesticides, dyes, plasticizers and a wide variety of other potentially highly toxic and recalcitrant organic compounds. The use of bacteria in bio-mining is also beneficial to the environment in that it reduces energy and chemical costs. Biomining is currently used world-wide for copper extraction. It is estimated that over 90% of the copper currently mined world-wide is biomined. The largest copper mine using bacterial leaching is in Quebrada Blanca in Chile, which processes more than 17,000 tonnes of chalcocite ore per day and produces 75,000 tonnes of high grade copper per year. Another environmentally favourable use of biotechnology is the bacterial removal of inorganic sulphides from coal. This reduces the discharge of sulphur dioxide (SO_2), a causative agent of acid rain, to the atmosphere during coal-based electricity generation.

4.6 Industrial Biotechnology

Industrial biotechnology applies the techniques of modern molecular biology to improve the efficiency and reduce the environmental impacts of industrial processes. Just as advances in modern molecular biology and in enzyme technology have transformed the pharmaceutical and food processing sectors, biotechnology is increasingly being applied to other industries, such as the textile, pulp and paper, tanning, detergent, and even the energy sector.

One of the earliest applications of microbial enzymes in the cleaning industry was their incorporation into “biological” detergents. The principal advantage of using enzymes is their ability to remove protein stains, such as grass, blood, etc., as well as oily and fatty stains at low temperatures. Using enzymes in “biopulping” processes in the paper industry offers the potential of a less polluting technology while improving product quality. Microbial enzymes are also used in the processing of hides and skins prior to tanning in the leather industry.

Enzymes are increasingly being used in textile processing, mainly in the finishing of garments and goods. Many casual garments are subjected to a wash treatment to give them a slightly worn look. In traditional stonewashing techniques, blue denim garments were faded by the abrasive action of pumice stones on the garment surface. The use of cellulase enzymes ("biostoning") accelerates the abrasion, reduces the quantity of pumice stone required and results in less damage to the garments, less wear on machines and a reduction of pumice dust in the laundry environment.

4.7 Forensic Science

Advances in mapping and sequencing the human genome have immense importance in the field of forensic science. DNA testing is now acceptable practice in criminal investigations and is far more reliable than traditional fingerprint evidence. A single hair root has enough DNA to give a reliable DNA fingerprint. In the US, 46 States admit DNA evidence in criminal proceedings; 43 State courts have ruled on the technology and in 3 states, statutes require admission. The UK database, which holds DNA profiles of all those previously convicted of violent crimes, is achieving large numbers of "hits" with new scene-of-crime samples leading to rapid identification of suspects.

5. Important Public Concerns Related to the Application of Biotechnology

Public concerns related to the application of biotechnology focus primarily on genetic engineering, gene cloning and DNA manipulation. It perhaps is unfortunate that these are the terms generally used to refer to "*in vitro* recombinant DNA techniques" since they have connotations of interfering with the natural processes of reproduction, heredity and growth and even initially raised visions of Aldous Huxley's Brave New World and the spectre of eugenics.

Eurobarometer surveys conducted since 1973, on behalf of the EU Directorate General for Education and Culture, have highlighted a growing public concern about the applications of biotechnology. Concerns expressed by the general public relate particularly to the use of recombinant DNA techniques. By comparison with the 1996 Eurobarometer survey, the perception of the utility and the moral acceptability of four selected biotechnology applications (introducing human genes into bacteria to produce medicines and vaccines, developing transgenic plants, using genetic testing and producing genetically modified food) had decreased considerably in the 1999 survey[16]. While considerable anxiety was felt by consumers regarding the placing of genetically-modified foods on the market, the same individuals responded much more favourably to the use of genetic engineering techniques for developing new drugs and medicines.

Most controversy in the media relates to the production of genetically modified crops and the marketing of foods derived from these crops. Consumers have expressed concerns about toxicity, allergenicity and other unforeseen long-term adverse effects. There is also concern about the regulations governing labelling of GM foods, abuse of labelling regulations, and the guarantee of consumer choice.

Wider issues of public concern regarding the application of recombinant DNA technology include:

- ethical/moral arguments regarding the development of transgenic species – i.e. is the transfer of a gene from an animal to a crop or microbial species an acceptable interference with nature?
- environmental considerations such as, for example, the potential spread of introduced genes from a GM plant to other plant species
- the potential human health impact of introducing antibiotic resistance genes to GM plants
- reduction of biodiversity
- the patenting of germ plasm or the "ownership of life"
- the perceived threat to third world farmers

16 Eurobarometer 52.1, "The Europeans and Biotechnology". European Commission, March 2000.

- application in human reproduction – i.e. “designer” babies and human cloning
- control of scientific development and application by multinationals
- excessive focus of research funding towards biotechnology
- the trade war between the US and Europe
- enforcement of environmental liability with respect to GMO release
- misuse of genetic information in the insurance sector

ICSTI has identified a number of public concerns related to the application of modern biotechnology that are important in a national context. These will be addressed, together with the potential of the technology, in the following examples:

1. Antibiotic resistance genes in GM plants
2. Biotechnology in food production
3. Biotechnology in crop production
4. Virus genes in GM plants
5. Gene therapy
6. The application of biotechnology for bioremediation of contaminated sites
7. Genetic testing

ICSTI accepts that the above list is not comprehensive and that some concerns are not addressed in detail in the following sections.

5.1 Antibiotic Resistance Genes in GM Plants

Much concern has been expressed about antibiotic resistance genes in GM plants. Concern has arisen because antibiotic resistance in bacteria is a major health problem of which microbiologists and doctors as well as the general public are very much aware. The scientific community, worldwide, has taken these concerns very seriously.

Concerns about antibiotic resistance genes were raised on page viii of the summary of the Consultation Paper on “Genetically Modified Organisms and the Environment”, published by the Department of the Environment and Local Government, August 1998.

The four concerns that are described are related to each other:

i. Reduction in the usefulness of antibiotics in human and veterinary medicine

ii. The theoretical possibility of antibiotic resistance genes being transferred to soil and non-soil microorganisms (and to other organisms), thus increasing the pool of antibiotic resistance genes in nature

iii. The possibility of antibiotic resistance genes being transferred to pathogenic organisms

iv. Whether the use of antibiotic resistance genes in GM plants is necessary at all and whether the genes could be deleted once they have served their primary function.

The first three concerns are essentially the same – i.e. the possibility of compromising the use of antibiotics in the treatment of human, animal, and plant diseases.

There is a consensus world-wide among microbiologists that antibiotic genes used in making GM plants will not pose any significant risk to human or animal health for the following three reasons:

1. The genes are very unlikely to be transferred to and expressed in pathogenic bacteria

2. If the genes are transferred and expressed, the bacteria will not pass on the gene because there is no advantage in having antibiotic resistance unless the antibiotic is present.

3. There is a huge background of antibiotic resistance genes in the natural bacterial population. These genes are a cause for great concern and dwarf the dangers posed by GM crops, which should be considered in relative terms as minimal.

Antibiotic resistance genes in GM plants will not affect the usefulness of antibiotics which are important in human or animal health. The theoretical possibility of such genes transferring from plants in the fields to microorganisms, which are pathogenic and which may infect man or animals and cause disease, is practically zero. However, there is a theoretical possibility that such genes might transfer to bacteria in the digestive system from GM crops used as animal feed, but the chances of propagation are insignificant in the absence of selective pressure.

The risk from GMOs of transferring antibiotic resistance genes and propagating antibiotic resistant bacteria is insignificant compared to the risk of this occurring from the widespread use of antibiotics in medicine, veterinary medicine, animal feeds and crop framing. Farmers in the US currently spray certain crops with antibiotics (to control *Erwinia*, *Pseudomonas* and other microbial pathogens of plants). This practice is unwise since it will increase the number of antibiotic resistant bacteria. Moreover, it could provide a selective pressure without which antibiotic resistance genes in GM plants could not spread (see below). There is a strong case that it should be illegal to spray antibiotics on plants or to add antibiotics to animal feed.

The possibility of transfer of antibiotic resistance to pathogenic microorganisms can be assessed by comparison to the "natural background" population of antibiotic resistant bacteria. Genes for antibiotic resistance are widespread in nature and are especially frequent in places where antibiotics are used. The risk of antibiotic resistance occurring in bacteria is higher on farms and in hospitals where antibiotic use is high. The number of antibiotic resistance genes in GM plants will always be minuscule by comparison to their numbers in the natural microbial population.

Genes in plants are not readily transferred to bacteria. Even under the most favourable laboratory conditions, antibiotic resistance genes in plant DNA very rarely transfer to bacteria. These laboratory conditions included the use of purified genetic material (DNA) from GM plants, specially chosen bacteria as recipients, and selection for transfer by exposure of the recipient bacteria to the test antibiotics.[17]

If an antibiotic resistance gene does transfer in the field from a plant to a bacterium, this gene will not spread through the bacterial population because it will not confer any advantage to the bacterium in the absence of the selective pressure of the antibiotic itself. Antibiotics, such as penicillin (or ampicillin), kanamycin, hygromycin or streptomycin, are not spread on fields of crops (except, as indicated above, for control of *Erwinia*, *Pseudomonas* and other plant pathogens in the US). Consequently, there is normally no selective pressure to select for microorganisms which have picked up the gene for antibiotic resistance. The genes for hygromycin-resistance or kanamycin-resistance are usually under the control of promoters (genetic switches) which are not active in bacteria. If, by chance, such a gene does transfer to a bacterium, it will most likely just be transferred to the descendants of that single bacterium (and rarely if ever to any other bacteria, especially not to bacteria of other species). Most lines of bacteria (and other microorganisms) become extinct in a relatively small number of generations (which can be seen, for example, in the studies of the evolution of flu viruses).

In any case, an antibiotic resistance gene, which is either not active (because it does not carry the correct genetic switch), or which confers no selective advantage, will be useless to the bacteria and will gradually decay by random mutation, and be deleted by chance or disintegrate into a pseudogene.

The antibiotic resistance genes used in plant genetic engineering are generally not relevant to the antibiotics used in clinical or veterinary medicine. The exceptions are streptomycin and ampicillin. There is no need to use streptomycin or ampicillin in plant genetic engineering experiments and these antibiotics are not now being used in the generation of GM crops intended for release. Genes encoding resistance to these two antibiotics were incorporated into some of the first GM crops as passengers, where they were and are harmless. However, due to public concern, it has now been accepted that these two antibiotic marker genes will not be used in plant genetic engineering in the future. This sort of response only serves to vindicate public concern. If a process that is safe is made illegal, the public are led to believe that the process was unsafe from the outset.

17 Gebhard and Smalla (1998). *Applied and Environmental Microbiology* 64, 1550-1554.

The two genes which are currently used in the majority of plant genetic engineering processes encode resistance to kanamycin (nptII) and hygromycin (hpt). Kanamycin is very rarely used and hygromycin B is not used in human medicine.

Horizontal Gene Transfer

Concern has been expressed about the phenomenon of horizontal gene transfer, that is the transfer of genes from one species to a different species. Genes are normally transferred vertically from one generation to the next within the same species. One of the remarkable achievements of genetic engineering has been the invention of novel and efficient, experimental mechanisms for horizontal gene transfer. For example, the human insulin gene has been transferred to bacteria and yeasts, and today all diabetics can be treated with human insulin made in bacteria or yeasts under the direction of the human insulin gene. This and similar systems are important contributions of genetics to medicine.

It has been alleged that horizontal gene transfer is unnatural and therefore dangerous. Specifically, people have been concerned about the horizontal transfer of bacterial genes for antibiotic resistance into plants. It has been alleged that this process is somehow likely to unleash a plague of antibiotic resistance genes because we have crossed a critical boundary which demarcates bacteria from plants. In other words, horizontal gene transfer might cause a catastrophe because it is intrinsically dangerous. This kind of assertion causes anxiety because it refers in a striking way (consider the impact of the words “horizontal gene transfer”) to something which the public know little about. In fact, horizontal gene transfer has been known since the discovery of resistance transfer factors by Watanabe and others in Japan in the 1950s. It occurs widely in nature[18], though not so widely as to prevent the phenomenon of speciation (which Darwin rightly identified in **“The origin of species”** as a remarkable feature of the kingdom of living organisms). Vertical gene transfer is the norm but horizontal gene transfer is an important natural phenomenon which carries no general intrinsic dangers.

Conclusion

Antibiotic resistance genes are very unlikely to be transferred from GM plants into other organisms. If they do, they will not spread in soil or gut organisms because they are not being selected, and will therefore disappear or decay. The pool of antibiotic resistance genes in pathogenic microorganisms and their close relatives is so large that the impact of occasional and temporary transfer of such genes from GM plants will be vanishingly small and presents no cause for concern.

18 Droge et al. (1998). Journal of Biotechnology 64, 75-90.

5.2 Biotechnology in Food Production

In the 1999 Eurobarometer[19] survey carried out by the European Commission, respondents were asked to rank the benefits of seven biotechnology applications. The most beneficial application of biotechnology was considered by respondents to be detection of hereditary diseases. The least beneficial was the production of GM foods. This survey highlights the increasing level of concern within the EU about food safety.

This concern is of relatively recent origin. It arose initially as a result of the debate, within Europe, on the use of growth hormones in cattle, and was exacerbated by the emergence of BSE and by the proven link between BSE in infected cattle and new variant CJD in humans. The result has been an erosion of the public's trust in regulatory authorities, scientists and politicians. Since the advent of GM foods coincided with this growing concern about food safety, it is not surprising that the public views GM foods with suspicion and requires reassurance about their safety. In the recent Eurobarometer survey, 26% of EU citizens questioned were of the opinion that consumer organisations were most likely to tell the truth about GM food safety, followed by the medical profession (24%) and environmental protection organisations (14%).

If GM foods are to be accepted by the European public, there is an evident need for open and informed debate about their benefits and risks. The potential benefits of the use of GM foods are addressed in section 5.2.1. Public concerns are considered in section 5.2.2.

5.2.1 Benefits of the Application of Biotechnology in Food Production

Biotechnology has been used in food production since ancient times. As illustrated in section 4.3, the selection and breeding of improved animal and plant strains, fermentation of milk to produce cheese, yoghurt and other dairy products, alcoholic fermentation to produce beers and wines, use of yeast in bread leavening, are all examples of applications of traditional biotechnology. In more recent times, advances in fermentation technology, availability of defined microbial starter cultures, developments in protein separation techniques, and use of purified enzymes in alcoholic beverages, cheese and other processed foods have greatly increased the role of traditional biotechnology in food production.

The use of recombinant DNA technology in food production and food processing reflects the application of our growing knowledge of biological systems to traditional biotechnological processes. One of the best known examples of recombinant DNA technology is provided by the cheese-making industry. Rennet is an enzyme that has traditionally been extracted from the stomachs of calves and used in the clotting of milk proteins to produce cheese. More recently, the enzyme chymosin has been produced from genetically engineered moulds, yeast and bacteria into which the bovine gene was introduced. Cheeses made using chymosin do not differ from traditional products with respect to flavour, texture or appearance. Since only the purified enzyme is used, cheeses produced using chymosin do not contain any trace of GM DNA. The guaranteed availability and cheaper cost of chymosin has been welcomed by cheese manufacturers and accepted by animal rights and vegetarian groups because of its replacement of calf rennet.

19 Eurobarometer 52.1, "The Europeans and Biotechnology". European Commission, March 2000.

In the food sector, biotechnology is not solely applied to food production and food processing. It has many other uses, such as evaluation of food safety, improvement of nutritional quality and generation of food ingredients.

(i) Food Safety

The safety of human food and animal feed is an absolute priority which must be assured in order to maintain or expand food markets. In recent years, there has been a dramatic increase world-wide in food-borne diseases which has, to some extent, been linked to new food processing techniques which may compromise food safety. This increase has been linked to the production of "ready-to-eat" convenience foods which may contain a wide variety of diverse ingredients, and to the current availability of minimally processed foods and food products containing reduced levels of preservatives. Storage and display of these foods, particularly at incorrect temperatures, may also provide opportunities for growth of any pathogenic bacteria present in these foods.

The application of molecular biotechnology techniques may offer greater sensitivity in the rapid detection of pathogenic bacteria in food. Genetic characterisation of food-borne bacterial pathogens will help us to understand why certain bacterial pathogens survive and grow in individual foods, and may also unravel the complexity of pathogen/host interactions. Research is also ongoing on the role of inhibitors, such as bacteriocins, and on the potential use of protective bacterial cultures with the ability to competitively inhibit growth of bacterial pathogens. These research initiatives represent a proactive use of biotechnology to ensure food safety and reduce dependence on chemical preservatives in some foods.

The safety of foods may also be compromised by a range of threats over and above those posed by pathogenic bacteria. Contamination of grains and other dry foods by pathogenic fungi results in the production, within the food, of highly toxic and carcinogenic aromatic compounds (aflatoxins). Viral contamination of foods is currently considered to be responsible for the majority of gastroenteritis incidents world-wide. Biotechnology research is also focussed on developing sensitive techniques for the detection of aflatoxins and viruses in foods.

(ii) Health and Nutrition

In response to the growing consumer awareness of the relationship between diet and health, there is a need for increased biotechnological research towards improving the nutritional status of many foods. Research is unveiling the existence within milk and meat of novel health promoting components, some of which are currently being exploited for the development of added value 'Functional Food' ingredients or "Nutraceuticals". This is an area where biotechnology may provide new opportunities for the food industry. For example, the application of biotechnology to this area will allow the enrichment of foods with health promoting components, such as vitamins, bioactive peptides and certain fatty acids.

Probiotic foods are currently the best known examples of functional foods in Europe, with health claims ranging from alleviating symptoms of lactose intolerance, treating diarrhoea, suppressing cancer and reducing blood cholesterol. Dairy foods such as cheese and yoghurt provide the ideal food system for delivering these health-promoting bacteria to the human gut. However, research is needed to improve the technological properties of these bacterial strains and to confirm the health claims associated with their products. The enhancement of the health status of food by such innovative approaches should aid in industrial diversification into high value added food markets, in addition to improving overall public health.

(iii) Improvements in Food Processing

The quality of food rather than the price is becoming the dominant feature of competitiveness in the food products and food ingredients markets. In this respect, there are a number of examples where biotechnological approaches are being adopted to improve and guarantee food quality.

Biotechnology can be used to great effect in the development of novel starter cultures required for the production of fermented foods. Over the last 20 years, there has been an intensive world-wide effort into the genetic characterisation of starter and probiotic bacteria used in the food industry. The results of this research have included development of efficient systems for their genetic improvement and characterisation of the genetic determinants which govern much of their industrial traits. Consequently, the exploitation of biotechnology for starter culture improvement can produce strains which produce acid more consistently, which are less sensitive to bacterial viruses (phage) and which produce anti-microbial compounds, thereby improving food safety. Moreover, the analysis of the total genetic make-up of these strains will facilitate their further modification through a process referred to as metabolic engineering where cellular metabolism can be directed towards the increased production of desirable end-products, such as certain flavour compounds and amino acids.

Other applications include developing novel enzymes for meat and dairy food processing and using molecular techniques to define the key determinants of food flavours and aromas. The availability of new enzymes from novel sources will enable the food sector to develop a more diverse product range, and may also allow application of less severe processing technologies.

5.2.2 Concerns Relating to the Use of Biotechnology in Food Production

It is accepted that many consumers have concerns, queries and objections to the use of GM organisms in food production and food processing. These concerns include:

- the potential transfer of foreign genetic material into other organisms, including humans
- the use of antibiotic resistance genes in the development of GM bacterial and plant species used in the production of GM foods

- potential toxic or allergenic effects resulting from introducing new genes, and their products, to GM foods
- patenting of germ plasm by multinational companies; threats to third world farmers; "ownership of life"; environmentally damaging effects on biodiversity.

(i) Is There the Possibility of Transfer of Foreign Genetic Material Into Other Organisms Including Humans?

Horizontal gene transfer is the movement of genetic information (DNA) between different species. Concerns have been expressed regarding the possibility of DNA introduced into GM species transferring into other bacteria, human or animal cells and whether there might be risks associated with such a transfer.

Experiments have shown that DNA remaining after digestion consists of very small fragments and have failed to show survival of intact DNA in stools or blood of animals fed with large quantities of DNA. There is no reason to believe that DNA in GM plants would behave differently. According to the Royal Society, UK, there is no evidence to date for transfer of intact genes to humans, either from bacteria in the gut, or from foodstuffs such as potatoes, wheat or chickens, despite daily consumption of DNA in the diet.

It should also be noted that DNA from GM crops is, in many cases, not present in the part of the plant that ends up on the supermarket shelf. Transgenic GM soya plants contain foreign genes introduced to confer resistance to particular herbicides. However, the process used to refine the oil produced from GM soya ensures that the product placed on the market has no detectable trace of the genetically modified DNA or of the foreign proteins expressed in the GM soya plants.

(ii) Is There a Possibility that Antibiotic Resistance Marker Genes Used in GM Foods Could be Transferred to Humans?

This issue has already been discussed in section 5.1. The general consensus is that antibiotic resistance genes are unlikely to be transferred from GM plants into other organisms. Recent developments have also made it possible to use alternative "marker" gene systems, which do not use genes for antibiotic resistance.

(iii) Are Genetically Modified Foods Safe to Eat?

There is no evidence to date that GM foods pose a greater risk to human health than their traditional counterparts. The independent GMO and Novel Foods Sub-Committee of the Food Safety Authority of Ireland (FSAI) reviews each new food separately to ensure that it complies with specified safety criteria. If this Sub-Committee is of the opinion that a GM food is not safe, or if it requires further information before reaching a decision, an objection can be raised at EU level.

It is the opinion of the FSAI Sub-Committee that GM ingredients currently on the market in Ireland are as safe as their traditional counterparts. The report[20] of a workshop organised by the European Federation of Biotechnology (EFB) and the European Molecular Biology Organisation (EMBO) in Dublin in April 1999, also confirmed that risks to human health from GM foods are minimal and are no different from those associated with traditional foods.

(iv) Is There the Possibility that the Introduction of Genes from Other Species May Cause Toxic or Allergenic Properties in GM Food Products?

Concerns have been expressed[21] that:

- the introduced gene product may itself be toxic
- the introduced gene may lead to production of toxins in the GMO
- the introduced gene may modify allergenic properties of crops used for human food and animal feed production or may enhance the allergenic properties of the pollen of flowering plants.

All GM food products undergo a rigorous safety assessment before being released onto the supermarket shelf. In Ireland, the Food Safety Authority of Ireland is the compotent authority for the safety assessment of GM foods.

Before any GM food or food ingredient can be sold in the EU it has to be scientifically assessed by specialist scientific committees in each Member State. If any of these committees have objections based on scientific grounds, the product is rejected and referred to the European Commission Standing Committee for Foodstuffs where it is re-assessed. In order to obtain clearance to the market, the Committee must vote by a qualified majority in its favour.

(v) Should Foods Derived from GM Crops or Containing GM Ingredients be Labelled?

Many consumer organisations consider that labelling is essential for ascertaining the origin of foods, and in particular for separating GM from non-GM foods and for monitoring possible adverse effects of ingredients. The current labelling position in Ireland is outlined in Table 1, under Regulations 258/97, 1139/98 and EU Directive 49/200 and 50/2000. This situation is currently being reviewed at EU level.

The Food Safety Authority of Ireland supports the consumer's right to know whether or not a particular food contains GM ingredients. This support for labelling is based on the Authority's belief in consumer choice rather than on any food safety concerns.[22]

It is the view of ICSTI that foodstuffs containing GM material, where the new foodstuff is substantially changed from that of its conventional counterpart, should be labelled in order to allow consumer choice.

20 Focus on Future Issues of Biotechnology (1999), published by Cambridge Biomedical Consultants, Oude Delft, The Netherlands.
21 Food Safety Authority of Ireland, "Food Safety and Genetically Modified Foods".
22 Food Safety Authority of Ireland, "Food Safety and Genetically Modified Foods".

Conclusion

There is no evidence to date that foods derived from GM crops or foods containing GM ingredients pose any greater health risks to man and animals than those posed by traditionally produced and processed foods. In order to allow consumer choice, foods placed on the market, that are produced or processed using recombinant DNA technology, should be clearly labelled. As with all foods, rigorous safety assessments should be carried out before release of GM foods to the marketplace.

5.3 Biotechnology in Crop Production

In the next decade, the arable crop sector and the agri-food industry will operate in a rapidly changing world environment due to increased competitiveness, globalisation of prices, and consumer demands for food quality, safety, health enhancement and convenience. It is, therefore, imperative to adopt new and innovative techniques to improve the competitiveness and efficiency of the crop and agri-food sectors. Innovation is essential for sustaining and enhancing crop productivity, and has always involved new, science-based products and processes which have, in the past, contributed to increased crop productivity. Ireland's capacity to compete in the future is dependent on the quality of its technology and the capacity of its producers and processors to apply that technology. The enabling technologies that constitute biotechnology have introduced a new dimension to crop productivity improvement. Key core technologies will need to be developed to supply the appropriate crops and ultimately food products for an increasingly discerning and well-educated consumer.

The main initial focus of the use of biotechnology to produce the first generation of genetically modified crops was to reduce input costs for control of insect pests and plant diseases. This was achieved by a combination of efficient breeding, exploitation of resistance factors, and by development of GM crops with traits which reduce or eliminate the need for pesticides. A consequence of using GM crops is a reduction in environmental risk due to decreased application of agricultural chemicals. Biotechnology, combined with efficient plant breeding is, in fact, a low-risk alternative to previous conventional practices and is the most cost-effective method for controlling pests and disease. This approach has already led to a reduction in the use of sprayed chemical insecticides and to decreased environmental impact. Failure to control fungal disease in plants allows generation of fungal toxins, such as aflatoxin and fumonisin, which have severe negative consequences for human and animal health. Biotechnology can overcome these problems leading to safer and more nutritious food products which will be longer lasting and probably less costly. The development of plant-based oral vaccines, which will allow disease immunity to be achieved through dietary supplementation, will also give safer food products.

Environmental Concerns

Among the ecological issues associated with transgenic crops is the possibility that some newly introduced traits, such as pest or pathogen resistance, could confer added fitness to the crop. As a result, the crop may gain weedy characteristics if its ability to survive and spread outside of cultivation is enhanced. A second issue arises if such crops are grown in the vicinity of compatible wild or weedy related species. Transfer of the trait by natural hybridisation may produce a hybrid progeny that is more aggressive or more difficult to control.

Response: There is general recognition that conventional agricultural activity entails environmental and ecological risks. Genetically engineered pest resistance traits, currently being field tested or commercially released, present no fundamental differences from similar traits bred into crops using traditional techniques. Some scientists and plant experts disagree with this hypothesis and contend that transgenes will have more profound effects on crop phenotype than traditional genes, and thus may have potentially greater impact on weed species. There is no evidence to-date to support this view. However, the way in which future crops are engineered with multiple pest resistance or other fitness traits presents more complex ecological questions. Such "gene stacking" to confer resistance against a broad spectrum of pests may give recipient plants a greater selective advantage and lead to ecological consequences that are less predictable than the single-gene pest resistance traits which constitute much of our experience to date.

On the other hand, insecticides currently used in conventional agriculture kill some beneficial insects in addition to the target pest. However, the use of Bacillus thuringiensis (Bt) crops should lead to a reduction in the use of insecticides, thereby decreasing the impact on these beneficial insects and leading to greater sustainability.

Effectiveness of Pest Resistance Genes

Pest and disease resistance has been a primary objective of farmers and breeders throughout the history of agriculture. Using traditional breeding techniques, pest resistance genes identified in wild germplasm have been incorporated into cultivated varieties of many major crop species. This process is now being supplemented by the techniques of genetic engineering and dozens of crop species are being engineered for improved pest resistance. In genetically engineered crops, most insect resistant cultivars express cry genes from **Bacillus thuringiensis**, *a gram positive soil bacterium which is noted for its abundant production of insecticidal proteins. One of the obstacles to approval for commercial growth in Europe of GM crop species is the potential for insects to become resistant to the Bt toxin.*

Response: It is possible that insects could become resistant to the Bt toxin. This is also the case when pest resistance genes are introduced into plants using conventional plant breeding techniques. Resistance is a natural process of evolution and is inevitable regardless of whether the Bt is produced naturally in the plant or sprayed directly onto plants as currently happens in organic production systems. In order to reduce the likelihood of resistance taking place, there is certainly a need to develop strategies which would reduce the overall selection pressure. One such approach involves maintaining non-Bt refuges to thwart the emergence of the resistance

phenomenon. Other strategies are also being developed which would reduce the possibility of resistance taking place – e.g. developing plants which would synthesise the Bt protein at a particular time when the crops are most at risk from the pathogen. Such an approach would also reduce the selection pressure and greatly reduce the possibility of resistance developing.

Over-Reliance on Pesticides

Concern is often expressed that the development of plants with built-in resistance to certain herbicides could lead to the over-use of these herbicides leading to possible damage to plants, insects and a range of soil organisms.

Response: The reality is that crop biotechnology has the potential to reduce the dependency of agriculture on chemicals, and the development of herbicide tolerant crops should lead to an overall reduction in the total amount of herbicide used. In trials carried out by Teagasc at the Crops Research Centre in Carlow, herbicide tolerant sugar beet reduced the level of herbicide usage by 50%. It also allowed substitution of chemical herbicides that persist in the soil with environmentally friendly alternatives, leading to more sustainable farming systems. For example, Glyphosate is one of the most environmentally friendly herbicides ever developed and is widely regarded for its lack of persistency, low risk of groundwater contamination and safety towards fauna. The World Health Organisation classifies Glyphosate as having minimal toxicity to humans, animals, birds and bees.

Herbicide Tolerant Plants and Superweeds

It has been contended that herbicide resistance could be transferred to weeds in hedgerows and ditches leading to the creation of superweeds resistant to herbicides.

Response: The possibility of transfer of herbicide resistance genes to weed species would depend on whether or not there is a closely related weed species present. If such related weed species are present, gene transfer could take place. The consequence of such an occurrence is not considered to have any great significance, as herbicides are not sprayed onto hedgerows and, consequently, herbicide-tolerant weeds would have no survival advantage over other plants in the ecosystem. Herbicide tolerant weeds could cause difficulties if they grow in fields where they need to be controlled. Under these circumstances, farmers would have to use a different herbicide. At present, farmers mix different herbicides and practice crop rotation to control various weed problems and could do the same with GM crops if weed herbicide tolerance became an issue. Farmers could also grow another GM crop that was tolerant to a different herbicide, thereby solving any difficulties which might arise. It is difficult to predict if herbicide tolerance is likely to develop in weeds in the future. Herbicide tolerant crops have been bred and used in conventional agriculture for many years and, to date, no adverse effects have been shown. Nevertheless, it is important that research is continued to assess the potential for transgenic pest resistant crops to become problem weeds, or to enhance the weediness of nearby sexually compatible relatives. This is a complex task, and information is required from many disciplines – e.g. weed science, agronomy, population biology, genetics, entomology, plant breeding, ecology, plant pathology, molecular biology, and others. Scientific evidence in support of informed risk assessment and decision-making thus lies in the collective knowledge of experts from these fields.

Could Genetic Engineering Result in Unforeseen Problems?

It is often argued that information on the science of genetic engineering is incomplete and that genes could inadvertently be altered which might lead to unforeseen problems later.

Response: Classical plant breeding has been the norm for over 100 years. While very significant progress has been made, the procedures have been very much hit and miss. For example, the process of hybridisation involves the mixing of millions of genes with no complete control over the outcome. Molecular methods, on the other hand, are more specific, and users of these methods will be more certain of the traits they introduce into plants facilitating greater precision and safety. Since the technology allows for a specific gene controlling a specific trait to be identified and copied, it is a far more precise technique than the trial and error approach of traditional plant breeding. In addition, marker assisted selection, a new molecular technique for confirming the presence of traits, is also a powerful new tool for improving crop quality, fertiliser use efficiency, disease resistance and the plant's ability to withstand a range of biotic and abiotic stresses.

Seed Ownership/Patenting

Genetic diversity has always been an important component of plant breeding programmes, both nationally and internationally. Concern has increasingly been expressed regarding the involvement of large multinationals in the take-over of many plant breeding companies world-wide and the possible control and patenting of the world's germplasm.

Response: While there is some substance to this view, the present reality is that only 17% of the current world seed supplies are controlled by large multinational companies, with 66% of seeds coming from state owned and farmer controlled companies. Local adaptation will become more and more important in the varieties of the future. Consequently, it is imperative to support local crop breeding programmes both in the developed and less developed regions of the world. The continued support of World governments to international plant breeding institutes such as the International Maize and Wheat Improvement Centre (CIMMYT) in Mexico and the International Rice Research Centre (IRRI) in the Philippines is warranted. The provision of varieties that are finely adapted to the "Irish production environment" should be a central theme for this country.

Patents for genetically modified plants are available in the US, Europe and Japan. If the possibility of patenting was denied, the absence of a financial incentive to develop new products would make it difficult for companies to make large investments in research, since the results would be available for anybody to copy. However, the patenting of a particular GM crop only means that the company concerned has the right to benefit from a specific application for a specific period of time, and has no automatic right to use the invention as it may be blocked by health, safety or environmental regulations.

Conventional Versus Organic Farming

Conventional farming methods are regarded by many as undesirable because of potential negative effects on the environment, biodiversity and sustainability. A move to organic production systems is seen as the ideal.

Response: All types of farming have some impact on the environment and new techniques are continually being developed to minimise any negative effects. Organic farming is no different – e.g. copper sulphate applied to organic crops as a disease control measure can cause toxicity to beneficial soil organisms, such as earthworms. GM crops, on the other hand, could solve many problems currently faced by farmers while at the same time bringing environmental and agricultural benefits.

Research Areas of Importance in an Irish Context: Cost Reduction and Decreased Environmental Impact

(i) Grassland

Since grassland occupies nearly 90% of the total land area in Ireland, grass productivity is of crucial importance nationally. Consequently, it is imperative that we use whatever techniques are available to increase the nutritive value of grass, as well as increasing output. It is certain that biotechnology will make a significant contribution to achieving these goals. Since many gene sequences are common to both wheat and grasses, comparative mapping can be used to elucidate traits which require targeting and incorporation into new and improved cultivars which will be very important nationally.

The development of marker genes (in ryegrass species) for early growth, leafiness, seed ripening, tolerance to low temperature and secondary compounds, including tannins, lignins and phenolics, should lead to improved varieties with the potential to produce higher yields of digestible dry matter. The overall net benefit of improved grass varieties could be as high as €130 million annually to the Irish economy.

The elucidation of the functional relationship between traits, such as high sugar content, and underlying metabolic pathways could increase grass sugars by at least half their current concentration. This should remove the need for silage additives, which currently are required to ensure good grass preservation, and lead to potential annual savings of €6.35 million. Grass intake should also be improved leading to increased milk and beef production with consequent improved efficiencies amounting to €45 million annually.

In clover breeding, optimisation of growth and increased nitrogen fixation rates, together with greater disease resistance, are likely to increase the potential of legumes for reducing fertiliser inputs and boosting quality. Reducing the likelihood of clovers to cause bloat in grazing animals is another long-term target which could be greatly enhanced with modern tools of biotechnology. Developments in clover breeding, utilising new molecular techniques, could reduce the need for artificial nitrogen fertiliser by approximately 50 kg/ha, leading to savings of at least €26 million per annum and a significant reduction of the current negative environmental impact of synthetic fertiliser use.

(ii) Pest and Disease Resistance in Cereals

Pest and disease resistance in plants can be maximised in breeding programmes for the major arable crops of national strategic relevance, particularly barley and wheat. Disease resistance in modern cultivars has a relatively short life span unless protected by frequent spraying with fungicides. This type of resistance is often unstable, breaking down as the pathogen adapts to the change in selection pressure. Consequently, the identification of markers to improve the selection efficiency for resistance to *Septoria spp*. is of high priority. Success in this area could significantly reduce the need for fungicides and save farmers 13 million euros annually in fungicide costs.

Plant viruses have developed many novel ways of moving from one infected plant to another using vectors, such as aphids. Consequently, the control of barley yellow dwarf virus (BYVD) in cereals requires the routine application of insecticides to control the vector. Unfortunately, other beneficial insects are also killed. Using molecular techniques to introduce virus resistance into new varieties would have significant benefits for both the grower and the environment, as the need to routinely apply aphicides would be greatly diminished.

Conclusion

If GM technology is considered to be hazardous in introducing new gene combinations in the development of new crop plants, then it is likely that the same or perhaps even greater hazards arise from the use of conventional plant breeding.

5.4 Virus Genes in GM Plants

Viruses consist of either DNA or RNA surrounded by a coat of proteins called a capsid. They reproduce by entering the cells of animals, plants or microbes, taking control of the host cellular activities to make more viruses and usually killing the host cell in the process. The genetic material of the infecting virus dictates the structure of the newly formed viruses. The capsid proteins help to protect the genetic material and assist with the entry of the virus into a host cell.

Most plant viruses have RNA (rather than DNA) as their genetic material. However, some of the DNA-containing plant viruses, such as the Cauliflower Mosaic Virus (CaMV), are economically important and have been widely studied. After infection of a plant cell with CaMV, the viral DNA is transported to the nucleus and, following some processing, is used as a template for making RNA copies of the DNA (transcription). The RNA is exported from the nucleus to the cytoplasm where it is used both as an information source for making the enzymes and capsid proteins necessary for assembling new viruses (translation) and as a template for making new virus DNA using the reverse transcriptase enzyme.

Many GM plants have viral capsid protein genes or viral regulatory sequences deliberately incorporated into their genomes. The insertion of viral capsid genes in some GM plant genomes results in the production of capsid proteins by the plant cell, thereby often rendering the cell resistant to the particular virus from which the capsid gene was obtained.

The regulatory viral gene most often incorporated into GM plants is the Cauliflower Mosaic 35S promoter (CaMV promoter). A promoter is a section of DNA that promotes the expression of genes associated with it. The CaMV promoter is a very effective promoter in plants and has consequently been used to drive expression of genes inserted into GM plants. This is very important for maximising product formation in GM crops. The products either directly or indirectly under control of the CaMV promoter may include medically useful products such as vaccines or antibodies, nutritionally important products such as vitamins, or products to protect the plant against pests or disease.

Exchange of Genetic Information Between Viruses and Plant Viral Genes

There is some evidence that when two different viruses infect a plant cell simultaneously, the viruses can exchange genetic information – a process known as recombination. There is also some evidence that viral genes in GM plants may recombine with the genetic material of incoming viruses.

Suggested Dangers Arising from Interaction of Viruses with GM Plants

Suggested Danger No. 1: It is suggested that new, more virulent viruses might arise from the type of recombination event described above.

Assessment of Suggested Danger No. 1: The factors to consider here are the frequency of recombination events, the likelihood of producing a new virus with more severe symptoms and the fitness of any such new virus to survive in competition with existing viruses.

With respect to frequency, this is rather low but further research needs to be carried out to determine whether there is a significant difference between recombination frequencies in GM plants and non-GM plants. It is important to realise, however, that research has shown that natural co-infection by different viruses is extremely common so that in the natural order of things there is every reason to believe that most new combinations of viral genes will have already arisen naturally.

In laboratory experiments, new viral combinations with more severe symptoms can be found on rare occasions but usually only under conditions of active selection for such combinations. Although such strains may induce more severe symptoms, the new strains are almost invariably less competitive than existing viruses. There is only a single case where such a rearranged virus was found to have acquired increased infectivity. In this case, the virus had been repeatedly inoculated into host plants in a greenhouse situation, with the deliberate intention of increasing its infectivity. It is difficult to see how such a series of events would occur in a field situation.

Suggested Danger No. 2: Transcapsidation. This is a process that might occur when the virus coat proteins from a GM plant cell are used by an invading virus. It has been suggested that the new type of virus formed might have enhanced infectivity and may infect an extended range of hosts.

Assessment of Suggested Danger No. 2: While such a virus might initially infect a new host, it would be a dead end for the virus as the capsid proteins of the viruses arising from such an infection would be of the normal type specified by the virus genetic material.

Suggested Danger No. 3: Synergism. It is suggested that a virus gene in the GM plant cell might potentiate the effect of an incoming virus, thereby increasing the severity of its effects.

Assessment of Suggested Danger No. 3: While, in principle, it is possible that this might happen, the only plants affected would be the GM crop plants themselves as any non-GM crops or any GM crops with different virus genes would not potentiate the effect of any virus resulting from such an infection.

Suggested Danger No. 4: Outcropping of virus resistance genes to weeds. It is suggested that GM crops with virus resistance genes might outcross to weeds, making these resistant to the particular virus and therefore more prolific.

Assessment of Suggested Danger No. 4: This proposal is based on the conjecture that virus infection is a major controlling factor in weed proliferation. There is little or no evidence that viruses act as biological control agents for weeds. Furthermore, viruses are very host-specific and even if viruses could be shown to keep weed populations under control this could only apply to weeds very closely related to the crop plant itself.

Suggested Danger No. 5: "Naked" CaMV promoter from GM food plants may gain access to human cells when these foods are eaten. The CaMV promoter has a recombination hotspot that may cause it to recombine into the genome of a human cell. This insertion of the CaMV promoter into the human genome could potentially activate or inactivate genes, which could lead to cancer.

Assessment of Suggested Danger No. 5: The CaMV promoter gene is not, in fact, "naked". It is part of the plant genome just like any other promoter gene in the plant. The possibility for uptake of CaMV promoter into humans is no different from any other plant gene. With fresh foods, the processes of digestion make it very unlikely that DNA pieces are taken up by human cells. With processed foods, this is even less likely. Cells have mechanisms for destroying foreign DNA that enters the cells. The CaMV promoter recombination hotspot is restricted to recombination within plant cells. What is more, it has been shown that 10% of the non-GM cauliflower and cabbage sold in a UK market was infected by CaMV. The cells of these plants contained up to 100,000 copies of the virus. It is likely that very large quantities of CaMV DNA have been consumed for as long as we have eaten cauliflowers and cabbages.

Conclusion

While there are many suggested dangers of using viral genes in GM crop plants, most of these do not withstand detailed scrutiny. The so-called dangers are little different from those that are presented by the natural presence of viruses and viral genes in the non-GM food that we consume. That does not mean we should abandon all caution in this respect. Development of GM technology employing virus genes should proceed judiciously in the light of current scientific knowledge. Where there are gaps or insufficiencies in our knowledge, research to eliminate these should be encouraged. At this time, it would be important to encourage research into:

(i) Virus recombination frequencies in co-infected GM and non-GM plants.

(ii) Frequency of recombination events between plant viruses and viral genes in plant genomes.

(iii) The part played by viruses in natural control of weed species.

5.5 Gene Therapy

Definitions

Gene therapy may be defined as the introduction of genetic material into the cells of a patient in an effort to help cure a disease, either by providing a protein which is missing from the patient due to a genetic mutation (e.g. Factor VIII protein for haemophilia) or by the introduction of new genetic material which either directly or indirectly will help to combat the disease (e.g. genetic vaccination). Therapeutic genes are delivered using a carrier (vector) which may be a non-functional virus vector or a non-viral vector such as liposomes. Current gene therapy protocols involve the introduction of genetic material into somatic tissue, such as blood cells, liver cells, etc. Somatic cell gene therapy precludes passage of the introduced gene to the next generation. This contrasts with germ line therapy which involves the introduction of a gene or genes into sperm, ova, or gonadal tissue, resulting in the possible inheritance of the gene(s) by the children of the patient. Germ line therapy is currently subject to an international moratorium.

Somatic Gene Therapy: Introduction of a gene into a specific tissue or tissues to provide a therapeutic benefit to the patient.

Germ Line Therapy: Introduction of genetic material into the egg or sperm cells of an individual such that the gene will also be passed on to the next generation.

Ex Vivo Gene therapy: Collection of the patient's cells, introduction of therapeutic genetic material into these cells and reintroduction of these cells into the patient.

In Vivo Gene therapy: Direct injection of therapeutic genes to the relevant tissue via a vector.

The promise of gene therapy lies in its proposed ability to treat the causes of disease rather than the symptoms. The first decade of gene therapy has been somewhat of a 'roller coaster' ride, with early excitement of the potential of this approach being tempered by disappointing clinical results. It is important to note that for any therapy that is tailored to a molecular defect in a disease, the timeframe between identification of the gene defect and the potential application of a therapy which is specifically targeted to that defect may be greater than 10 years. However, two recent examples in the treatment of cancer show the promise of molecular medicine and targeted therapy. In breast cancer, overproduction of a particular oncogene product called *her 2* leads to a form of breast cancer that is very resistant to treatment. The development and use of a monoclonal antibody (herceptin) to this protein has shown significant reduction in tumours in phase I and II clinical trials. In Chronic Myeloid Leukaemia (CML) a leukaemia specific tyrosine kinase protein called P210 is implicated in the disease and makes patients resistant to chemotherapy. The use of a tyrosine kinase inhibitor STI571 to directly affect the key molecular change in CML has shown dramatic clinical results and holds great promise for the treatment of this therapy resistant leukaemia. Furthermore, in the gene therapy setting, improvements in vector construction and vector delivery to the appropriate tissue have led to better pre-clinical and clinical results. One of the more important contributions of gene therapy to date has been in the use of viral vectors in laboratory research to help elucidate the function of genes and provide proof of principle of possible therapies.

Where Did Gene Therapy Begin?

The development of gene therapy, as we know it today, resulted from two significant advances in science and medicine in the 1960s and 70s – the advances in cellular and transplantation biology leading to effective bone marrow transplant treatment for leukaemia and advances in molecular biology and genetic engineering leading to the cloning of therapeutic proteins for the treatment of human disease. On 14 September 1990, the first patient was entered into a somatic gene therapy protocol. The 4 year old girl had a rare autosomal recessive disease, known as adenosine deaminase (ADA) deficiency, where copies of the gene for ADA in each cell did not function. As ADA deficiency leads to an immune deficiency syndrome patients are very susceptible to infection, and have to live in a carefully controlled environment. Blood and bone marrow cells were taken from the girl and an artificial copy of the ADA gene was introduced into these cells which were then returned to the patient. Despite an improvement in clinical symptoms, there is no evidence to date of a patient with ADA deficiency having long term 'cure' of their disease solely by gene therapy.

Relationship Between Gene Therapy and Currently Accepted Clinical Protocols

In some respects, gene therapy has strong connections to cell therapies such as bone marrow transplantation, and indeed many of the gene therapy protocols involve the use of bone marrow transplant techniques. One of the reasons for choosing ADA deficiency as the first disease to be treated by gene therapy was that it had already been demonstrated that allogenic bone marrow transplantation from a donor who was a brother or sister and showed a similar tissue type could cure this disease by providing the missing enzyme in the infused donor marrow. Particularly for enzyme deficiencies, allogenic bone marrow transplantation could, therefore, be considered as a

'natural' form of gene therapy. In a gene therapy type approach, the bone marrow or peripheral blood stem cells are taken from the patient and the missing gene is introduced into these cells. The gene-corrected cells are then returned to the patient where they begin to produce the therapeutic protein. While gene therapy has a long way to go, it may be relevant to draw a comparison with heart transplantation which went through initial cycles of enthusiasm tempered by the problems of the immune response/rejection issue; there followed years of basic research in an environment of great disappointment and finger pointing. Painstaking research and a degree of good fortune led to the resolution of the rejection issue through immune suppression and a procedure which has widespread acceptance today.

Gene Therapy: Status to Date

Gene therapy is just over 10 years old and is still in its infancy. However, more than 350 phase I and phase II clinical trials utilising gene therapy type approaches have been used world wide in the treatment of cancer and genetic disease. Cancer gene therapy protocols predominate, partially due to the fact that retroviral vectors are well suited for introducing material into cancer cells. In addition, approximately 30 gene therapy protocols for AIDS are currently in progress and several cardiovascular gene therapy studies are underway. The principles of gene transfer that have been developed are now being applied to the development of genetic vaccines which are currently being used in patients with AIDS. Preventive or therapeutic vaccines may soon be developed against malaria, tuberculosis, hepatitis A, B and C viruses, influenza virus and Ebola virus. Preclinical studies are also addressing the possibility of initiating new gene therapy programmes for autoimmune diseases, allergies and neurological disease.

Concern over the matter of safety of gene delivery has meant that this approach has been subject to peer review and open debate, which has helped to make it a safer clinical treatment. One area that is of concern is the use of viral vector delivery systems and the potential danger of damaging existing genes or promoting interaction between viral vectors and existing or new viral pathogens. Due to these concerns, many researchers are now developing safer non-viral delivery methods using established or experimental drug delivery methodologies. National legislation in several EU countries is favouring a non-viral approach in certain circumstances. While gene therapy has been accepted in the treatment of disease in children and adults, controversy has arisen over the proposal to begin *in utero* gene therapy clinical trials for the treatment of inherited genetic disorders.

Questions to be Asked About Gene Therapy

(i) Is Gene Therapy Different from Current Techniques?

While gene therapy is a novel protocol for treating patients with disease, it does have some parallels with conventional treatment which has led to important development and application of the technology. As indicated above, the comparison with bone marrow transplantation is a good one – particularly in the treatment of enzyme deficiency syndromes. Also in Cystic Fibrosis (CF), many patients are now being treated with lung transplants. One might say that somatic gene therapy is a less invasive procedure than the transplantation of a major organ, although at present the gene therapy protocols for CF are somewhat disappointing.

(ii) What Diseases are Suitable for Treatment? What are the Current Alternatives – i.e. Why Gene Therapy?

The question of what diseases should be considered for gene therapy is not an easy one and it is important that different diseases are considered on an individual basis for the pros and cons of a gene therapy type approach. Benefits of new treatments can have many different measurements; cure, partial cure, improvement of quality of life etc. Also particularly in diseases such as cancer, clinical advance will come from co-operation with other more established disciplines – such as chemotherapy, radiotherapy and immunotherapy. This is inevitable and necessary in order to prove that gene therapy can have efficacy as part of a combinatorial therapy, before hoping to move clinical mountains alone. There will have to be a thorough understanding of the clinical situations in which gene therapy will be used in order both to understand its own limitations, and to exploit its full potential. Inevitably, the issues of cost of treatment will also have to be taken into consideration. It must be realised that for early gene therapy protocols in particular diseases, the first patients entering such trials may provide much information that will help to guide future treatments but may not benefit personally from the treatment. Unfortunately, the experience in clinical medicine is that new therapies are not immediately 100% effective and this must be recognised both by the clinician and by the patient. Also the 'newspaper breakthrough' mentality should be approached with caution as with access to the Internet etc, many patients are now extremely up to date on new technologies and care must be taken to avoid offering false hope.

Issues to consider include:

- How representative are preclinical studies?
- Small benefits versus big benefits
- Gene therapy and current treatments versus gene therapy alone
- Gene therapy as last ditch therapy or gene therapy at an earlier stage where it may be more effective

(iii) Is There a Need for In Utero or Prenatal Gene Therapy?

Several diseases where some of the pathological changes manifest themselves during foetal life might benefit from an *in utero* gene therapy approach e.g. Cystic Fibrosis or Tay Sachs disease (B hexosaminidase A deficiency). However, one must realise that prenatal gene therapy concerns both the mother and the foetus. There must be a firm demonstration of therapeutic value before any protocols can be considered.

Concerns over *in utero* gene therapy include:

- Accidental foetal germline gene transfer
- Accidental maternal gene transfer

- Immunological status of the foetus – could mount an immune response against the viral vector leading to problems with infection later in life
- Access to the target organ in a reasonable and reliable developmental window

(iv) What are the Risks Associated with Gene Therapy?

As with any new therapeutic approach, it is important to identify and quantify the risks associated with the approach, taking into account both actual and perceived risks and counterbalancing them against perceived benefits.

Questions that we must address include:

- Is the vector used to deliver the gene to the appropriate tissue safe (i.e. no risk of replication competent retrovirus)?
- Is there a risk of the vector integrating with a gene activating an oncogene leading to the development of cancer.
- Is there a risk of the vector combining with other naturally occurring viruses which may infect the host?

The first two scenarios are quantifiable risks but need to be addressed stringently in *in vitro* and pre-clinical studies and should form part of the regulatory process before any patient receives any gene therapy product. The third scenario is an important one and researchers are currently investigating non-viral strategies to improve the safety of gene therapy approaches.

(v) Risk of Vector Going to a Different Organ and Causing Damage

This is an increasingly important area, particularly if *in vivo* gene therapy is being considered, since inappropriate expression of a particular gene product in a non-target tissue could have a detrimental effect.

(vi) Risk of an Immune Reaction to the Vector

This has been documented with a number of vector constructs, most notably adenoviral constructs.

Regulation of Gene Therapy

The US Recombinant DNA Advisory Committee (RAC) was established in 1975 and has advocated open and public discussion of advanced therapeutic products and protocols. Stringent vetting of proposals is performed and they stress the need for full disclosure of positive and negative results and potential side effects of gene therapy. The US Food and Drug Administration (FDA) issued a Note for Guidance on the use of human somatic cell therapy and gene therapy in March 1998. The European Commission communication (OJ EC C229/4 issued on 22/07/1998) provides details on human gene therapy and regulations but is currently being revised. The European Agency for the Evaluation of Medicinal Products (EMEA) has recognised the need for consistent regulations in relation to gene therapy. In February 1999 it published a concept paper (CPMP/BWP/2257/98) of its Biotechnology Working Party entitled "Concept paper on the development of a committee

for proprietary medicinal products (CPMP) points to consider on human somatic cellular therapy". This has led to the release of two papers, CPMP/BWP/41450/98 and CPMP/BWP/3088/99, for discussion and consultation which form the basis of current regulation of gene therapy and gene therapy products in Europe. In Ireland, the Irish Medicines Board (IMB) would use these directives and discussion papers in the evaluation of gene therapy protocols. The Environmental Protection Agency (EPA) would be the regulatory body in relation to research in this area but does not have any specific guidelines regarding gene therapy research – guidelines relate to GMOs and their release in general. Nevertheless, despite these regulations and proposed regulations in Europe and North America, in September 1999 the first death directly attributable to gene therapy occurred. The patient was being treated for an enzyme deficiency called ornithine transcarbamylase deficiency (OTC) as a part of a phase I clinical study. The patient was in the group that received the highest dose in the trial protocol of an adenoviral vector containing the OTC gene. He developed acute respiratory distress syndrome (ARDS) shortly after the gene therapy infusion and died two days later from organ failure. Measurement of cytokine levels indicated that he had systemic inflammatory response syndrome; all erythroid precursor cells were wiped out from his marrow and the vector had gone to other organs besides the liver. Subsequently the FDA found procedural problems and shut down all seven clinical trails at Penn's Institute for Human Gene Therapy. Problems related to consent and death of two animals in a similar preclinical procedure, indicating that as in all other therapeutic approaches, there should be full and frank disclosure of any problems. There is a perception that there remains too much secrecy about gene therapy trials (Lancet, Jan 29 2000) and this needs to be addressed as a matter of urgency.

Other issues that are of similar importance relate to the consent of the individual undergoing the protocol, particularly in an experimental protocol, and the privacy of the patient.

It is imperative that the public are aware of global developments in gene therapy and that there is community wide discussion on this potentially important new therapeutic approach to disease.

It is important that gene therapy is regulated both at the research level and at the clinical level in Ireland. At the clinical level, the relationship between the EMEA and CPMP is an important one which ensures that any gene therapy trials that may take place in Ireland will be subject to European Guidelines. Regulation at the research level is less clear. It is recommended that a special committee should be established to regulate research in this area. Guidance and membership should be drawn from the Irish Medicines Board, the Health Service, the Environmental Protection Agency, Third Level Institutions, the Private Sector and other relevant agencies and interests.

Conclusion

Somatic gene therapy is ending its first decade. Research and technological advances have led to gene therapy protocols entering the clinic and being tested in various diseases. New and substantially improved vector systems and related technologies are undergoing development. Many have shown promise in animal studies, and some are now being used in clinical trials. However, further developments in gene-transfer vectors, gene-delivery techniques and identification of effective treatment genes will be required before the full therapeutic potential of gene therapy can be assessed. Safety issues should be considered and stringent controls put in place. More discussion and education in relation to gene therapy is an important part of its development as a useful clinical treatment. Appropriate authorities should be put in place to regulate research and clinical studies in this area.

5.6 The Application of Biotechnology for Bioremediation of Contaminated Sites

Bioremediation refers to the use of microorganisms, either *in situ* or *ex situ*, to remove pollutants from contaminated soil, sediment, aquifer, freshwater and marine environments. Bioremediation is usually applied for the treatment of sites contaminated by organic pollutants (hydrocarbons resulting from oil spillages or storage tank leachates; xenobiotic insecticides, herbicides, pesticides; pharmaceutical drugs, disinfectants, antiseptics; wood preservative agents, plasticisers, flame retardants, paint constituents, etc.). More recently, *ex situ* bioremediation techniques have been applied to inorganic (metal) contaminant removal from soils, sediments, aquifers and acid mine drainage wastewaters.

Traditional Methods of Remediation of Organic Pollutant-contaminated Sites

The requirement, under National and International law, to adopt a hierarchy of waste management that promotes: (i) waste minimisation, (ii) waste recycling/re-use, (iii) waste treatment and (iv) waste disposal, is of recent origin. The advent of the Industrial Revolution initially led to uncontrolled dumping of recalcitrant and potentially toxic organic wastes; hydrocarbon spillages; coal tar and heavy fuel oil residue dumping at district heating gas generation plants; leachate generation in poorly operated municipal and toxic waste landfill sites; unlicensed disposal of outdated chemical explosives, chemical and biological warfare weapons; the discharge of untreated chemical/pharmaceutical wastewaters, etc. The scale of historical organic contamination is of greater magnitude in those countries (i.e. former Soviet Union) where environmental legislation was slow to develop and where enforcement was rarely practised.

Although remediation techniques have focused on our legacy of historical organic contamination, it is worth pointing out that, even in the context of more enlightened environmental legislation and enforcement, illegal dumping and accidental spillage will inevitably occur, leading to future contaminated sites requiring remediation.

Earlier, non-biotechnological techniques for remediation of sites contaminated by organic pollutants employed incineration or extraction/treatment/safe disposal procedures. Incineration involves removal of the contaminated soil and sediment, followed by waste-to-energy combustion at high temperatures (› 1,500°C) and disposal of the ash residue in a controlled toxic waste landfill site. The operational and monitoring costs involved are extremely high and legislation preventing the trans-boundary shipment of toxic waste is currently limiting the application of this technology – i.e. the contaminated soil/sediment must be transported to an existing incinerator as the costs involved in commissioning an on-site incinerator would be prohibitive. Extraction of the pollutant from the contaminated site involves flushing with hot water, detergents or solvents, followed by either incineration or safe disposal in toxic waste sites. These traditional treatment methods will continue to be required for heavily contaminated soils and sediments and for organic pollutants that are not susceptible to microbial breakdown and mineralisation.

Non-biological remediation of contaminated marine environments has focused primarily on major hydrocarbon spillages resulting from tanker accidents (i.e. Mega Borg, Exxon Valdez, Torrey Canyon, etc.). Techniques used involve dispersal using detergents; off-shore containment and collection; shoreline recovery followed by incineration or landfill disposal.

In Situ Bioremediation of Sites Contaminated by Organic Pollutants

The objective of bioremediation is to degrade organic contaminants to stable, non-toxic end-products, such as carbon dioxide (CO_2), methane (CH_4), water (H_2O), etc. *In situ* techniques involve stimulation of the biodegradative activities of competent, endogenous microbial populations in the affected sites by:

1. adding limiting inorganic nutrients (N/P) or trace metals
2. providing external oxidants, such as oxygen(O_2), nitrate, sulphate, ferric iron, etc., required by species involved in aerobic or anaerobic respiration, or CO_2 required by bacteria catalysing methanogenesis or homoacetogenesis
3. altering pH or temperature
4. providing non-toxic organic compounds required for co-metabolic degradation

In situ bioremediation may be enhanced by introducing bacterial inocula (natural or genetically engineered) to the contaminated site (bioaugmentation). Bioaugmentation is usually accompanied by nutrient and external oxidant supplementation in order to increase *in situ* mineralisation rates. If the site conditions permit, "land-farming" may be practised – i.e. removal of surface vegetation, followed by ploughing, tilling and raking of the soil in order to enhance aeration and ensure efficient distribution of inocula and nutrients. When carrying out bioremediation *in situ* it is important to ensure that nutrients, oxidants, other introduced chemicals, inocula or the organic pollutants being remediated do not migrate from the test site or cause eutrophication of marine or freshwaters. In practice, bioremediation *in situ* is a multidisciplinary biotechnological application, involving microbiologists, geneticists, chemists, hydrologists, geologists and environmental engineers.

Bioremediation *in situ* has been used successfully to clean up soils and sediments contaminated by hydrocarbons, coal tar, solvents, organic explosives (TNT), poly-chlorinated biphenyls (PCBs), poly-aromatic hydrocarbons (PAHs), creosote, DDT, etc., and marine and shoreline environments affected by oil spillages and groundwater aquifers contaminated by landfill leachates.

Ex Situ Bioremediation of Sites Contaminated by Organic Pollutants

Ex situ bioremediation is more usually applied to contaminated soils and sediments, rather than to aquifers, freshwater bodies or the marine environment. A number of options for soil and sediment *ex situ* bioremediation have been developed:

i. physically removing of the soil followed by composting under controlled conditions on specially-constructed platforms or after transfer to composting sheds. If necessary, bulking agents (straw, woodchips, etc.) are added to improve oxygen entry. Nutrients and bacterial inocula (natural or GMO) can also be introduced in order to speed up the composting process.

ii. removing the soil followed by its treatment (aerobically or anaerobically) under controlled and optimised conditions in bio-reactors.

iii. extracting the organic contaminants from the soils and sediments (with or without removal from the site) using hot water, detergent solutions or solvents, followed by degradation of the contaminant(s) in bioreactors under optimised conditions.

Bioremediation *ex situ* of contaminated groundwater has been practised in a limited number of cases. This involves extraction of the groundwater followed by biological treatment in bioreactors or by re-circulating the contaminated water through the topsoil using landfarming techniques. Natural or genetically-engineered bacterial inocula, nutrients, etc. may be introduced during recirculation of the groundwater through topsoil.

Use of Natural or Genetically-modified Bacterial Inocula for Bioremediation

Bioaugmentation, using natural or GMO species, during *in situ* bioremediation, does not necessarily ensure more rapid rates of organic pollutant degradation. To date, bioaugmentation in the field has involved natural inocula only and the use of GMOs *in situ* has not been sanctioned. The success of introduced, competent bacteria to contaminated sites may be limited by their inability to compete with indigenous species under the prevailing environmental conditions; their susceptibility to predation by protozoans; their preferential use of non-pollutant organic substrates present in the eco-system and their sensitivity to toxic compounds present in the contaminated site.

Although bioaugmentation using natural inocula has been reported to achieve successful remediation of marine oil spillages, the findings in contaminated soils and sediments are conflicting and do not provide proven support for the beneficial effects of bioaugmentation. In many cases, insufficient controls were used to determine the effect of the introduced inoculum. In other cases, it was shown that the simultaneous addition of inorganic nutrients and oxidants (practised in virtually every case) led to enhancement of the activity of indigenous degradative

species rather than to the growth and activity of the introduced non-indigenous species. For example, bioremediation of Hudson River sediments heavily contaminated by PCBs (printed circuit boards) involved introduction of hydrogen peroxide (H_2O_2, as a source of oxygen via biological and chemical oxidation), inorganic nutrients, biphenyl to stimulate co-metabolism and an inoculum of *Alcaligenes eutrophus*, strain H850 (a known PCB degrader). The results obtained suggested out-competition of the introduced *Alcaligenes* strain by endogenous bacteria in the sediment and its gradual die-off and disappearance from the test site. These findings are not surprising since the endogenous bacteria present in a given ecosystem have adapted over the millennia to the environmental characteristics of their habitat and are, therefore, much more likely to grow and multiply under favourable nutrient and oxidant conditions than an introduced species from a different ecosystem and cultivated, prior to inoculation, in a laboratory environment.

Ex situ bioremediation of contaminated soil/sediment slurries or extracted pollutants in bioreactors provides a more realistic use of competent natural inocula or GMOs. Aerobic, anaerobic or combined anaerobic/aerobic bioreactor treatment processes generally utilise complex mixtures of many different microbial trophic groups. Many of the microbial species involved have not, so far, been isolated and may be non-culturable using current procedures. Genetic analysis, using DNA or RNA probes, is presently providing an insight into the rich biodiversity of the microbial populations of organic waste treatment bioreactors. Consequently, it is likely that introduced inocula will also be subject to competition in bioreactors. However, the ability to control operating temperature, nutrient and oxidant supplementation and other operational parameters can be exploited to ensure that introduced inocula are favoured and that pollutant degradation rates are enhanced.

Concerns Regarding the Use of GMOs for Bioremediation

In Situ Bioremediation:

Concerns regarding the introduction of GMOs for *in situ* bioremediation include:

(i) possible persistence of the introduced species in the environment and potential negative impacts on the natural functioning of the ecosystem

(ii) transport of the introduced GMO(s) away from the original site of application with potential impact on other ecosystems

(iii) gene transfer from the introduced species to the indigenous population

(iv) difficulties in following the fate of the introduced species or genes within and without the test site.

Ex Situ Bioremediation

The use of GMOs during *ex situ* bioremediation in bioreactors offers the possibility of controlled application, containment and safe disposal. In many contaminated sites, indigenous species with the metabolic versatility required for biodegradation of complex xenobiotic organic pollutants are not present. *Ex situ* treatment, under controlled and optimised conditions in bioreactors, allows the use of genetically-modified organisms developed specifically for the degradation and

mineralisation of specific xenobiotic pollutants. The persistence of many xenobiotic organics in the environment has recently been linked to the requirement for cycling of these compounds between anaerobic and aerobic environments for degradation to proceed efficiently. For example, azo-dyes must first be cleaved by anaerobic species that are incapable of further degradation of the cleavage products. However, aerobic species, that cannot catalyse the initial cleavage reaction, can fully degrade the resultant monomeric aromatic products. A similar situation exists with respect to polychlorinated aromatic compounds (insecticides, pesticides, germicides, etc.). Reductive dechlorination by anaerobic species results in the generation of mono- or di-chlorinated derivatives. While these derivatives cannot be further metabolised by anaerobic bacteria, they are readily mineralised by anaerobic bacteria that are incapable of dechlorination of the initial polychlorinated compounds. *Ex situ* bioremediation offers the feasibility of utilising sequential anaerobic/aerobic biological treatment systems under optimised conditions in order to facilitate the degradation of these persistent pollutants. It also provides an opportunity to utilise GMOs with specifically designed degradation capabilities under controlled and environmentally-acceptable conditions.

Benefits of Biotechnology for Remediation of Contaminated Sites

Although non-biological remediation techniques will continue to be required for restoration of heavily contaminated sites, bioremediation currently offers a valid biotechnological alternative for sites contaminated by an increasingly diverse array of recalcitrant and xenobiotic pollutants. It is unlikely that GMOs will be utilised or permitted for *in situ* bioremediation purposes. However, their use, *ex situ*, in bio-reactors for slurried soils or extracted pollutants under optimised and contained conditions provides a biotechnological application that can address and remediate the problem of xenobiotic compound accumulation, with resultant toxicity, in aerobic and anaerobic environments.

Many contaminated sites do not lend themselves to *in situ* bioremediation – i.e. cold environments where the ambient temperature does not allow stimulation of bacterial pollutant degradation, or high temperature desert environments where lack of water or excessive temperatures prevent *in situ* bioremediation. In these cases, pollutant removal requires *ex situ* treatment under optimised conditions in bioreactors, thereby permitting contained use of GMOs or natural competent degradative species.

Conclusion

Incineration, chemical treatment and landfill have been the methods of choice, until recently, for remediation of environmental sites contaminated by organic chemicals as a result of accidental or deliberate discharges. Although these procedures will continue to be required for very heavily contaminated sites, biotechnology offers more benign and environmentally sustainable remediation systems for less contaminated sites. Application of bioremediation processes results in degradation of the pollutant organics to non-toxic, stable end-products, without adverse impact on terrestrial or atmospheric environments. Use of GMOs with designed abilities to degrade key pollutants will enhance the potential application of bioremediation and should be confined to *ex situ*, rather than to *in situ*, applications.

5.7 Genetic Testing

Definitions

Between 2% and 5% of all live born infants have genetic disorders or congenital malformations. Genetic disorders are inherited in two main ways. In dominant diseases, mutation of the copy of the gene inherited from **either** the father **or** the mother is sufficient to lead to the development of the disease (examples include Huntington's disease and inherited breast cancer). In a recessive genetic condition, such as cystic fibrosis (CF) or phenylketonuria (PKU), the copies of the gene inherited from both parents must be damaged for the child to develop the disease. This implies that both parents are carriers for the disease as they have 1 normal copy and 1 mutant copy of the gene. A special type of recessive condition termed X-linked recessive disease (e.g. Haemophilia or Duchenne Muscular Dystrophy) involves a mutated gene on the X chromosome; if the mother is a carrier for the disease (with one mutant and one normal X chromosome), her sons will be at increased risk of developing the disease.

In addition, many common diseases, such as heart disease, diabetes and cancer, have an important genetic component. Increasing awareness of this contribution to disease, allied to the emotional health and economic burden on patients, their families and the community have led to an increasing demand for clinical genetic services.

Genetic testing is a multidisciplinary area, involving a range of medical, scientific and counselling specialities including general practitioners, clinicians, clinical geneticists, molecular biologists, clinical scientists, nurse practitioners and genetic counsellors. The technical part of the genetic testing procedure, which will be referred to in this section as the gene test, chromosome test or DNA test where appropriate, involves the use of either chromosomal analysis or DNA analysis. Chromosomal analysis (often called karyotyping) allows the entire set of chromosomes of an individual to be looked at in a single test and permits detection of relatively large changes in our genetic make up – e.g. the presence of an extra chromosome 21 (termed trisomy 21 as seen in Down's syndrome). DNA analysis allows the fine structure of specific genes on these chromosomes to be examined, permitting determination of the presence of an abnormal gene in an individual's genetic blueprint. Using DNA analysis, it is possible to detect a mutation even if it only affects a single building block (termed a base) of a gene.

However, although the technology has made it possible to perform genetic testing in many countries throughout the world, it is important to stress that genetic testing must involve pre and post counselling visits, education of the community (both medical and lay) as well as the taking of a blood sample and performing the test. It is also crucial that non directive counselling is performed such that the final decision to take or not take a genetic test is made by the patient and is not influenced unduly by an over zealous clinician.

Originally genetic testing referred to diseases that were caused solely by a defect or mutation in a single gene giving rise to the disease or making an individual a carrier for the disease. Increasingly this definition is broadening to include gene testing for multifactorial diseases, such as cardiovascular disease where a gene defect may place an individual at increased risk

of developing the disease, but where factors such as diet or the environment may also play a role. In addition, karyotyping and DNA testing are very important both in the diagnosis and prognosis of leukaemia and other cancers.

Genetic Testing for Single Gene Disorders

The advances in the application of molecular biology in the health service has led to an increase in the number of genetic tests that are now available. However, it is important to stress that each disease should be considered separately in relation to whether a genetic test best serves the need of the patient, whether it be to aid diagnosis, prognosis or reproductive choices. While technical advances have meant that taking the blood sample and performing the gene test are now routine procedures, the development of a new gene test should not be considered in isolation. Below are some examples of tests that have been or are being developed that show clear benefit to the community.

Genetic testing has, in reality, been performed for many years – a good example is the case of **PKU**, a deficiency in an enzyme that metabolises phenyalanine, an amino acid which we use as a building block to construct the various proteins and enzymes our body needs. High concentrations of phenylalanine lead to mental retardation, seizures and eczema. Even before DNA testing procedures had been developed, a biochemical test could be performed to determine this deficiency at birth. Community screening programmes are active world-wide involving taking a drop of blood from the heel of an infant and placing it on a card (a Guthrie card) for analysis. Children with the disorder simply need to limit their intake of phenylalanine in their diet to correct the disease. Thus, genetic testing of this and other enzyme deficiency disorders is crucial to designing simple approaches to prevention of the disease symptoms.

Tay-Sachs Disease (TSD) is a recessive, progressive, and ultimately fatal neurodegenerative disorder. Within the last 30 years, the discovery of the cause of the disease (hexosaminidase enzyme deficiency), allied to cloning of the HEXA gene and identification of more than 80 associated TSD-causing mutations, has permitted molecular diagnosis and determination of carrier status in many instances. TSD was the first genetic condition for which community-based screening for carrier detection was implemented. As such, the TSD experience can be viewed as a prototypic effort for public education, carrier testing, and reproductive counselling for avoidance of fatal childhood disease. The outcome of TSD screening over the last 28 years offers convincing evidence that such an effort can dramatically reduce incidence of the disease. Similar studies have been performed for **ß thalassaemia**, particularly in Mediterranean populations, and the outcome has also been a positive one, reducing the incidence and clinical and economic burden of this disease in the community.

Hereditary Haemochromatosis (HH) is a common iron overload disorder (with a population prevalence of 0.3%-0.8%). It is a common cause of preventable liver, heart, joint, and endocrine disease. An accurate HH diagnosis demands both a high index of suspicion and direct laboratory demonstration of elevated iron parameters. The substantial public health burden of HH as a common, deadly, detectable, and treatable chronic disease has led the College of American

Pathologists to recommend that "*systematic screening for haemochromatosis is warranted for all persons over the age of 20 years*." The recent discovery that most HH cases are the result of a single mutation within a transferrin-receptor binding protein (HFE) has given rise to diagnostic tests for the DNA-based detection of this pathologic mutation. This test can now be used, not only to confirm the diagnosis of HH in those with symptomatic disease, but also and perhaps more importantly, to detect those with presymptomatic iron overload in whom future disease manifestations may be prevented with phlebotomy therapy. Thus, genetic testing for this disorder can aid in clinical diagnosis and management of this common genetic disease.

Genetic Testing for Inherited Cancer Susceptibility

Recent studies have indicated that there are inherited forms of various types of cancer, including breast cancer, ovarian cancer and colon cancer. Although these cancers only collectively account for 5-10% of all cancers, inherited breast and colon cancer have higher frequencies in the population than other common single gene disorders – thus a large group of people are at risk of developing inherited cancer. The study of cancer-prone families is a powerful approach to cancer control, particularly when the germ-line mutation is identified in the family and individuals at high risk can be tested, once they provide informed consent, and receive DNA-based genetic counselling. Discovery of the germ-line mutation provides an opportunity to predict patients' lifetime risk for cancer and, in combination with current therapeutic advances, can help to save lives. There is also a huge demand from families with an increased incidence of inherited cancers for genetic testing and genetic counselling to be available. Motivations for genetic testing include the following: to know if more screening tests are needed, to learn if one's children are at risk and to be reassured. Barriers to testing included concerns about insurance, test accuracy and how one's family would react emotionally.

Hereditary breast cancer accounts for 5-10 per cent of all breast cancer cases. About 90 per cent of hereditary breast cancers involve mutation of the BRCA1 and/or BRCA2 genes. Risk estimation is the most important clinical implication. Management options for the high-risk mutation carriers include cancer surveillance and preventative strategies (prophylactic surgery or chemoprevention). Despite inadequate knowledge about the genetic predisposition to breast cancer and its clinical implications, the demand for genetic testing is likely to expand rapidly. In addition to risk estimation, cancer surveillance and preventative strategies, gene therapy may offer a new and theoretically attractive approach to breast cancer management. However, there are a significant number of patients for whom genetic testing may not provide any benefit, as treatment strategies may not be effective or may not be seen as a viable option from the patient's point of view and so genetic testing should be considered on an individual basis.

In hereditary colon cancer, several studies have indicated that those who sought counselling overestimated their risk for inheriting the mutation, showed a high rate of interest in prophylactic surgery, and were greatly concerned about insurance discrimination. Knowledge about the disease, its molecular genetic diagnosis, surveillance and management opportunities, and genetic counselling implications is still emerging, all in the face of a greater need for physician education regarding all facets of hereditary cancer.

Genetic Testing for Acquired Cancers

The case for genetic testing for acquired cancers is probably less controversial, particularly in the case of leukaemia, where the use of chromosomal or DNA analysis allows easier diagnosis of certain forms of leukaemia and increases our understanding of the mechanism of development of the disease which may help us to develop new therapies. A good example of this is acute promyelocytic leukaemia, where over 98% of patients have an acquired genetic change (called a translocation) involving chromosomes 15 and 17 at diagnosis. One of the genes that is mutated is the retinoic acid receptor gene. Knowledge of this abnormality in a patient immediately allows a clinical decision to be made – clinical remission (reduction of the leukaemia "load") in these patients can be induced by treatment with retinoic acid. Thus, direct knowledge of the acquired genetic abnormality allows the appropriate therapy to be commenced. The burgeoning influence of chromosomal and DNA analysis in leukaemia health care can be judged by the recent statement from the Medical Research Council in the UK that molecular analysis is the **single most important parameter** in assessing prognosis.

Genetic Testing for Multifactorial Disorders

Coronary artery disease (CAD) has a strong genetic component, but is also greatly influenced by environmental factors such as diet and smoking, and disorders such as diabetes mellitus and hypertension. In familial hypercholesterolaemia (FH), risk of early CAD is considerably increased by the mutation of a single gene, and genetic testing may be appropriate. We already know that the interaction between environment and particular genotypes may amplify the effect of a particular genotype (e.g. the increased risk of heart disease in patients who smoke and have particular genotypes for certain haemostatic genes). However, for many common diseases we have very little knowledge of how changes in single genes will influence the disease and the response to drugs and very large studies are required to try to tease out these complex relationships.

Issues and Controversies in Genetic Testing

Genetics and Insurance

Questions regarding insurance companies' access to and use of genetic test results and genetic information have been raised since the advent of the Human Genome Project. The ability to place applicants of similar risks in groups, a process known as underwriting, is critical to the availability and affordability of individually underwritten life, disability income, and long-term care insurance. The availability of presymptomatic and predisposition genetic testing has spawned the need for legislation prohibiting health insurance discrimination on the basis of genetic information. Legislation should be enacted in order to prevent health insurance companies from denying coverage or setting insurance rates on the basis of genetic information. It should also protect the privacy of genetic information and prohibit performance of genetic tests without specific informed consent.

One of the main questions is whether the use of genetic tests and genetic information by life insurance companies should differ from the use of routine medical information. These issues are particularly complex and, in diseases such as Huntington's disease and Alzheimer's Disease (AD)

where long-term care may be needed, the issues surrounding predictive genetic testing and the use of test results in determining insurance premiums and eligibility are of great concern to patients, clinicians, insurers, ethicists, and patient advocate groups. We must avoid any possibility of genetic discrimination, particularly in presymptomatic persons who test positive for diseases such as Huntington's disease.

Genetics and Privacy

One of the issues in relation to privacy that is particular to genetic testing is the dilemma of the doctor in keeping a patient's genetic information confidential as weighed against third parties' needs to know genetic information regarding their family members. This is a difficult issue to which there are no simple answers. Equally important is the issue of *informed consent*. An important caveat in relation to genetic testing relates to the large number of families who have participated in research studies in order to help our understanding of how diseases develop. Ireland is a particularly good example in this regard, with close interaction between scientists, patient support groups and the patients and their families. It is important that the strong bond that exists should not be compromised by issues of insurance and privacy and that patients should be adequately protected in this regard.

Community Screening

The increasing availability of DNA-based diagnostic tests has raised issues about whether these should be applied to the population at large in order to identify, treat or prevent a range of diseases. DNA tests raise concerns in the community for several reasons. There is the possibility of stigmatisation and discrimination between those who test positive and those who do not. High-risk individuals may be identified for whom no proven effective intervention is possible, or conversely may test "positive" for a disease that does not eventuate. Controversy concerning prenatal diagnosis and termination of affected pregnancies may arise. It is important that the community itself should be actively involved in evaluating these issues. This allows the collective implications of testing to be evaluated by all interested parties. How genetic screening is socially constructed using a community's existing dichotomy may be central to its success.

The ability to test for mutations in cystic fibrosis (CF) patients at the molecular level has already improved the diagnosis of symptomatic patients and expanded the reproductive options of family members of CF patients. The same technology also holds promise of identifying asymptomatic carriers and at-risk couples without family history in the general population. However, a number of key issues need to be addressed before a widespread national screening programme can be put into practice. These include the target population to be offered testing (the entire population vs. high-risk ethnic groups), the optimal testing technology, appropriate standards for laboratory quality assurance, and the development of sufficient educational materials and genetic counselling resources for test delivery, reporting, and interpretation. The answers to these questions will be relevant not only to CF testing but also to many other large-scale molecular genetic screening programmes being considered in the future.

Commercial Gene Testing

Commercial gene tests are currently available in many countries and the range of tests offered is likely to increase. As already discussed, genetic testing also brings its own unique problems. Commercial ventures may do little to resolve these and adequate safeguards are needed to ensure that clients undergoing testing are not disadvantaged. In the US there are private companies which are attempting to provide patients with results of gene testing without any counselling or any clinical context and this should be avoided. The availability of gene tests can only serve to heighten public awareness of the relevance of genetics to health care, and there is likely to be an increased demand for information and advice from healthcare professionals before, and following, testing. However, for many individuals, increased knowledge about their genes will present ethical dilemmas which are difficult to resolve. There are also wider ethical issues which concern the use of genetic information by insurers and employers and which concern ownership and access to genetic test data. Provision of information in relation to genetic testing is very important and a web based system that would allow both access to the information and questioning of the issues involved could be a very important resource.

Education and Genetic Testing

Technical advances in genetic testing in the absence of effective treatment have presented the health profession with major ethical challenges. A compelling need exists for adequate education about medical genetics to raise the “literacy” rate among health professionals. As numerous new gene tests are introduced into clinical practice, patients have a growing need for accurate and comprehensive information about the risks and benefits of gene testing. However, in the changing healthcare environment, it is not clear who will provide such information because genetic counsellors are scarce and their services are not widely utilised, and primary care providers lack expertise in genetics and are already over-burdened. One approach that may assist is the use of interactive computers which may help fill the information gap if used appropriately with pre and post counselling sessions. One cannot overemphasise the importance of educating patients about the potential risks, benefits and limitations of genetic testing, with particular emphasis on the possibility of adverse psychological effects and implications for health insurance. Health professionals need to be aware of the technical and ethical implications of these new methods of testing, as well as the complexities in test interpretation, as molecular approaches are increasingly integrated into medical practice.

Conclusion

Genetic testing is currently used to provide prenatal or postnatal diagnosis for a wide range of single gene disorders including inherited cancer syndromes. The meaning of the term needs to be vastly broadened to include the uses of genetic information in mainstream medicine for common multifactorial diseases. Widespread genetic testing must be supported by adequate genetic counselling and by education of healthcare professionals in order to ensure appropriate application of this information for the benefit of patients and their families. Molecular testing raises a number of complex ethical issues, including those associated with prenatal or presymptomatic diagnosis. In addition, there are concerns about informed consent, privacy, genetic discrimination and insurance.

6. Conclusions and Recommendations

Although biotechnology is a term that was introduced in the 1940s, microorganisms have been used in food production and food processing since Roman and Egyptian times. Equally, extracts from plants have been used for centuries to treat various diseases, e.g. extract of cinchona bark for the treatment of malaria. These traditional biotechnologies predated knowledge of the existence of microorganisms by thousands of years and of the chemical constituents of plant medicinal products by many centuries.

Recognition of the existence of microorganisms in the 19th century, followed by the development of pure culture techniques, allowed identification of the microbes involved in food fermentations and made it possible to control food fermentation processes, and ensure more consistent food and beverage production. The discovery of antibiotic-producing fungi and bacteria in the 1940s/1950s revolutionised the treatment of both human and animal disease and illustrated the potential of the use of microorganisms in the health-care sector. Understanding of the role played by microorganisms in the global carbon, nitrogen and phosphorus cycles facilitated the use of these organisms to remove organic and inorganic pollutants from domestic, industrial, and agricultural wastes and wastewaters. Use of anaerobic bacteria for organic pollutant conversion also enabled recycling of the energy content of organic wastes to a usable fuel, methane (natural gas), i.e. renewable energy generation.

It is not surprising, therefore, that the dramatic advances in our knowledge of the genetics and biochemistry of living systems (microorganisms, in particular), during the latter half of the 20th century, has resulted in rapid development of new biotechnological applications in the agriculture, food production/processing, health-care and waste treatment sectors. Many of these new applications differ from traditional biotechnological processes in utilising genetically modified (GM) microbes and plants which contain artificially-inserted genes from other species (transgenic).

It is widely accepted by the scientific community that biotechnology has great potential for contributing to the solution of many existing problems and to greater productivity in a wide range of industries. However, the power of modern biotechnology and the pace, scale and range of its application has raised justifiable concerns within the general public. As indicated in previous sections, these concerns include the safety of GM foods; the impact of GM crop production on biodiversity; potential health risks of using antibiotic resistance genes as markers in GM plants; ethical and moral issues, such as the acceptability of transgenic species, patenting of germplasm, human reproduction applications, animal cloning, threats to third world farmers, etc.

These concerns must be addressed in an open and transparent manner in order to ensure that the potential benefits of modern biotechnology can be realised, while ensuring minimal risk to humans, animals, biodiversity and the environment.

The Report of the Technology Foresight Health and Life Sciences Panel (April 1999)[23] advocated the need to have a communications strategy in biotechnology that uses a partnership approach with ongoing, transparent and open dialogue. The report recommended that a "National Conversation on Biotechnology" should be an integral part of the Irish Biotechnology Investment Programme proposed.

The report of the Inter-Departmental Group on Modern Biotechnology highlighted the need to foster dialogue between all those involved in science and technology and the public.

BioResearch Ireland recently called for the establishment of an independent information agency on biotechnology[24]. However, the Chairing Panel Report of the National Consultation Debate on GMOs and the Environment, considered that a specific agency dealing solely with information dissemination was unnecessary. The need for a separate information agency on biotechnology was not endorsed by the Inter-Departmental Group whose report recommended that the EPA (Environmental Protection Agency), FSAI (The Food Safety Authority of Ireland) and FSPB (Food Safety Promotion Board) should be responsible for a programme of information dissemination on environmental and food safety aspects of genetic engineering.

6.1 Recommendations

- In order to promote a dialogue in biotechnology between those who work in the field and the general public, ICSTI strongly endorses the concept of a "National Conversation in Biotechnology". To achieve this, ICSTI recommends the establishment of an independent, balanced, credible and comprehensive information centre for science and technology, which should be linked to the proposed Science Centre recently announced (September 2000) by The Tánaiste, Ms. Mary Harney. Access to information on biotechnology should be available at all major population centres. Given the pace and scale of biotechnological development, it is essential that the information centre should have sufficient resources to provide up-to-date, balanced and comprehensive information on new biotechnological applications.

  The centre should provide unbiased information for the general public on current and proposed uses of GM organisms in agriculture, food processing, health-care, waste treatment, and other sectors.

- ICSTI supports the demands of individuals, consumers' organisations and environmental NGOs for mandatory labelling of GM foods and accepts the rights of consumers with respect to informed choice and acceptance, or rejection, of GM foods. The ICSTI view coincides with that of the Food Safety Authority of Ireland.

23 Report of the Health and Life Sciences Panel, Technology Foresight Ireland, Forfás, April 1999.
24 EU BioDivulga Project: Irish Case Report, June 2000.

- ICSTI supports the recommendation of the Inter-Departmental Group that, in the interests of transparency and public awareness, the fullest possible level of information about applications for release or marketing approvals for GMOs should be made available as a matter of standard practice by all of the relevant regulatory bodies.
- ICSTI recommends that an appropriate authority should be put in place to regulate research and clinical trials in the field of somatic gene therapy.
- Although ethical and moral considerations are clearly of importance with respect to the application of biotechnology, these issues are not easily addressed by legislation. ICSTI supports the recommendation of the Inter-Departmental Group on Modern Biotechnology that a fully independent national biotechnology ethics committee should be established under the auspices of the Royal Irish Academy.

Annex 1 Glossary of Terms Commonly Used in Biotechnology

Glossary of the most commonly used terms that appear in reports about biotechnology and genetic engineering. The explanations are kept as simple as possible.

Acclimatisation
Adaptation of an organism to a new environment.

Active immunity
A type of acquired immunity whereby resistance to a disease is built up by either having the disease or receiving a vaccine against it.

Active site
The part of a protein that must be maintained in a specific shape if the protein is to be functional, for example, the part to which the substrate binds in an enzyme. The part of an enzyme where the actual enzymatic function is performed.

Adaptation
In the evolutionary sense, some heritable feature of an individual's phenotype that improves its chances of survival and reproduction in the existing environment.

Additive genetic variance
Genetic variance associated with the average effects of substituting one allele for another.

Adjuvant
Insoluble material that increases the formation and persistence of antibodies when injected with an immunogen.

Aerobic
Needing oxygen for growth.

Affinity chromatography
A technique used in bioprocess engineering and analytical biochemistry for separation and purification of almost any biomolecule, but typically a protein, on the basis of its biological function or chemical structure. The molecule to be purified is specifically and reversibly adsorbed by a complementary binding substance (ligand) that is immobilised on a matrix, the matrix usually being in the form of beads. The matrix then is washed to remove contaminants, and the molecule of interest is dissociated from the ligand and is recovered from the matrix in purified form by changing the experimental conditions.

Agglutinin
An antibody that, is capable of recognising and binding to an immunological determinant on the surface of bacteria or other cells and causing them to clump (agglutination).

Agrobacterium
A bacterium normally responsible for production of crown gall disease in a variety of plants. A plasmid has been isolated from this bacterium that is useful in plant genetic engineering. This plasmid, called the Ti plasmid, has been modified so that it does not cause disease but can carry foreign DNA into susceptible plant cells.

Allelle
Any of several alternative forms of a given gene.

Allele frequency
Often called gene frequency. A measure of how common an allele is in a population; the proportion of all alleles at one gene locus that are of one specific type in a population.

Allelic exclusion
A process whereby only one immunoglobulin light chain and one heavy chain gene are transcribed in any one cell; the other genes are repressed.

Allogenic
Of the same species, but with a different genotype.

Allopolyploid
Polyploid produced by the hybridisation of two species.

Allotype
The protein product (or the result of its activity) of an allele which may be detected as an antigen in another member of the same species.(e.g. histocompatibility antigens, immunoglobulins), obeying the rules of simple Mendelian inheritance.

Alternative splicing
Various ways of splicing out introns in eukaryotic pre-mRNAs resulting in one gene producing several different mRNAs and protein products.

Alu family
A dispersed intermediately repetitive DNA sequence found in the human genome in about three hundred thousand copies. The sequence is about 300 bp long. The name Alu comes from the restriction endonuclease AluI that cleaves it.

Ames test
A widely used test to detect possible chemical carcinogens; based on mutagenicity in the bacterium *Salmonella*.

Amino acids
Building blocks of proteins. There are twenty common amino acids: alanine, arginine, asparagine, aspartic acid, cysteine, glutamic acid, glutamine, glycine, histidine, isoleucine, leucine, lysine, methionine, phenylalanine, proline, serine, threonine, tryptophan, tyrosine, and valine.

Amplification
The process of increasing the number of copies of a particular gene or chromosomal sequence. This can also include amplification of the signal to improve detection as an alternative to amplification of the sequence.

Anaerobic
Growing in the absence of oxygen.

Aneuploidy
The condition of a cell or of an organism that has additions or deletions of a small number of whole chromosomes from the expected balanced diploid number of chromosomes.

Annealing
Spontaneous alignment of two complementary single polynucleotide (RNA, or DNA, or RNA and DNA) strands to form a double helix.

Anti-oncogene
A gene that prevents malignant (cancerous) growth and whose absence, by mutation, results in malignancy (e.g. retinoblastoma).

Antibiotic
Chemical substance formed as a metabolic byproduct in bacteria or fungi and used to treat bacterial infections. Antibiotics can be produced naturally, using microorganisms, or synthetically.

Antibody
Protein produced by humans and higher animals in response to the presence of a specific antigen.

Anticodon
Triplet of nucleotide cases (codon) in transfer RNA that pairs with (is complementary to) a triplet in messenger RNA. For example, if the codon is UCG, the anticodon might be AGC.

Antigen
A substance to which an antibody will bind specifically.

Antigenic determinant
See Hapten.

Antihemophilic factors
A family of whole-blood proteins that initiate blood clotting, such as Factor VIII and kidney plasminogen activator.

Antisense RNA
RNA produced by copying and reversing a portion of an RNA-encoding DNA, usually including a protein-specifying region, and placing it next to a transcription-control sequence. This cassette can be delivered to the target cell, resulting in genetic transformation and production of RNA that is complementary to the RNA that is produced from the original, not-reversed, DNA segment. This complementary, or antisense, RNA is able to bind to the complementary sequences of the target RNA, resulting in inhibition of expression of the target gene.

Antiserum
Blood serum containing specific antibodies against an antigen. Antisera are used to confer passive immunity to many diseases and as analytical and preparative reagents for antigens.

Assay
Technique for measuring a biological response.

Attenuated
Weakened; with reference to vaccines, made from pathogenic organisms that have been treated so as to render them avirulent.

Autoimmune disease
A disease in which the body produces antibodies against its own tissues.

Autoimmunity
A condition in which the body mounts an immune response against one of its own organs or tissues.

Autosome
Any chromosome other than a sex chromosome.

Avirulent
Unable to cause disease.

Bacillus subtilis
A bacterium commonly used as a host in recombinant DNA experiments. Important because of its ability to secrete proteins.

Bactericide
An agent that kills bacteria. Also called biocide or germicide.

Bacteriophage
Virus that reproduces in and kills bacteria. Also called phage.

Bacterium
Any of a large group of microscopic, single-cell organisms with a very simple cell structure. Some manufacture their own food from inorganic precursors alone, some live as parasites on other organisms, and some live on decaying matter.

Base
On the DNA molecule, one of the four chemical units that, according to their order, represent the different amino acids. The four bases are: adenine (A), cytosine(C), guanine (G), and thymine(T). In RNA, uracil (U) substitutes for thymine.

Base pair
Two nucleotide bases on different strands of a nucleic acid molecule that bond together. The bases generally pair in only two combinations; adenine with thymine (DNA) or uracil (RNA), and guanine with cytosine.

Batch processing
Growth in a closed system with a specific amount of nutrient medium. In bioprocessing, defined amounts of nutrient material and living matter are placed in a bioreactor and removed when the process is completed. *Cf.* Continuous processing.

Bioassay
Determination of the effectiveness of a compound by measuring its effect on animals, tissues, or organisms, usually in comparison with a standard preparation.

Biocatalyst
In bioprocessing, an enzyme that activates or speeds up a biochemical reaction.

Biochemical
The product of a chemical reaction in a living organism.

Biochip
Electronic device that uses biologically derived or related organic molecules to form a semiconductor.

Biocide
An agent capable of killing almost any type of cell.

Bioconversion
Chemical restructuring of raw materials by using a biocatalyst.

Biodegradable
Capable of being broken down by the action of microorganisms under conditions generally found in the environment.

Biological oxygen demand (BOD)
The amount of oxygen used for growth by organisms in water that contains organic matter, in the process of degrading that matter.

Biologic response modulator
A substance that alters the growth or functioning of a cell. Includes hormones and compounds that affect the nervous and immune systems.

Biomass
The totality of biological matter in a given area. As commonly used in biotechnology, refers to the use of cellulose, a renewable resource, for the production of chemicals that can be used to generate energy or as alternative feedstocks for the chemical industry to reduce dependence on non-renewable fossil fuels.

Bioprocess
A process in which living cells, or components thereof, are used to produce a desired end product.

Bioreactor
Vessel used for bioprocessing.

Biosynthesis
Production of a chemical by a living organism.

Biotechnology
Biotechnology may be defined as the use of living organisms or their sub-cellular components to develop useful products, processes or services.

B lymphocytes (B-cells)
A class of lymphocytes, released from the bone marrow and which produce antibodies.

Bovine somatotropin (also called bovine growth hormone)
A hormone secreted by the bovine pituitary gland. It has been used to increase milk production by improving the feed efficiency in dairy cattle.

Callus
A cluster of undifferentiated plant cells that can, for some species, be induced to form the whole plant.

Carcinogen
Cancer-causing agent.

Catalyst
An agent (such as an enzyme or a metallic complex) that facilitates a reaction but is not itself changed at completion of the reaction.

Cell
The smallest structural unit of living organisms that is able to grow and reproduce independently.

Cell culture
Growth of a collection of cells, usually of just one genotype, under laboratory conditions.

Cell fusion
See Fusion.

Cell line
Cells which grow and replicate continuously in cell culture outside the living organism.

Cell-mediated immunity
Acquired immunity in which T lymphocytes play a predominant role. Development of the thymus in early life is critical to the proper development and functioning of cell-mediated immunity.

Chemostat
Growth chamber that keeps a bacterial or other cell culture at a specific volume and rate of growth by continually adding fresh nutrient medium while removing spent culture.

Chimera
An individual (animal, plant, or lower multicellular organism) composed of cells of more than one genotype. Chimeras are produced, for example, by grafting an embryonic part of one species onto an embryo of either the same or a different species.

Chromosomes
Threadlike components in the cell that contain DNA and proteins. Genes are carried on the chromosomes.

Cistron
A length of chromosomal DNA representing the smallest functional unit of heredity, essentially identical to a gene.

Clone
A group of genes, cells, or organisms derived from a common ancestor. Because there is no combining of genetic material (as in sexual reproduction), the members of the clone are genetically identical or nearly identical to the parent.

Codon
A sequence of three nucleotide bases that in the process of protein synthesis specifies an amino acid or provides a signal to stop or start protein synthesis (translation).

Coenzyme
An organic compound that is necessary for the functioning of an enzyme. Coenzymes are smaller than the enzymes themselves and may be tightly or loosely attached to the enzyme protein molecule.

Cofactor
A nonprotein substance required for certain enzymes to function. Cofactors can be coenzymes or metallic ions.

Colony-stimulating factors
A group of lymphokines which induce the maturation and proliferation of white blood cells from the primitive cell types present in bone marrow.

Complementarity
The relationship of the nucleotide bases on two different strands of DNA or RNA. When the bases are paired properly (adenine with thymine [DNA] or uracil [RNA] and guanine with cytosine), the strands are said to be "complementary."

Complementary DNA (cDNA)
DNA synthesised from an RNA template rather than from a DNA template. This type of DNA is used for cloning or as a DNA probe for locating specific genes in DNA hybridisation studies.

Conjugation
Sexual reproduction of bacterial cells in which there is a one-way exchange of genetic material between the cells in contact.

Continuous processing
A method of bioprocessing in which new materials are added and products removed continuously at a rate that maintains the volume at a specific level and usually maintain the composition of the mixture as well. *Cf.* Batch processing and chemostat.

Crossing over
Exchange of genes between two paired chromosomes.

Culture
As a noun, cultivation of living organism in prepared medium; as a verb, to grow in prepared medium.

Culture medium
Any nutrient system for the artificial cultivation of bacteria or other cells; usually a complex mixture of organic and inorganic materials.

Cyto
A prefix referring to cell or cell plasm.

Cytogenetics
Study of the cell and its heredity-related components, especially the study of chromosomes as they occur in their "condensed" state, when not replicating.

Cytokines
Intercellular signals, usually protein or glycoprotein, involved in the regulation of cellular proliferation and function.

Cytoplasm
Cellular material that is within the cell membrane and surround the nucleus.

Cytotoxic
Able to cause cell death. A cytotoxic substance is usually more subtle in its action than is a biocide.

Defensin
A natural defense protein isolated from cattle. It may prove effective against shipping fever, a viral disease that attacks cattle during transport, causing an estimated 250 million US dollars in losses each year.

Deoxyribonucleic acid (DNA)
The molecule that carries the genetic information for most living systems. The DNA molecule consists of four bases (adenine, cytosine, guanine, and thymine) and a sugar-phosphate backbone, arranged in two connected strands to form a double helix. *See also* Complementary DNA; Double helix; Recombinant DNA; Base pair.

Diagnostic
A product used for the diagnosis of disease or medical condition. Both monoclonal antibodies and DNA probes are useful diagnostic products.

Differentiation
The process of biochemical and structural changes by which cells become specialised in form and function as the organism develops.

Diploid
A cell with two complete sets of chromosomes. *Cf.* Haploid.

DNA
See Deoxyribonucleic acid.

DNA probe
A molecule (usually a nucleic acid) that has been labelled with a radioactive isotope, dye, or enzyme and is used to locate a particular nucleotide sequence or gene on a DNA or RNA molecule.

Double helix
A term often used to describe the configuration of the DNA molecule. The helix consists of two spiraling strands of nucleotides (a sugar, phosphate, and base), joined crosswise by specific pairing of the bases. *See also* Deoxyribonucleic acid; Base; Base pair.

Downstream processing
The stages of processing that take place after the fermentation or bioconversion stage, includes separation, purification, and packaging of the product.

Drug Delivery
The process by which a formulated drug is administered to the patient. Traditional routes have been orally or by intravenous perfusion. New methods that are being developed are through the skin by application of a transdermal patch or across the nasal membrane by administration of a specially formulated aerosol spray.

Electrophoresis
A technique for separating different types of molecules in a gel (or liquid), ion-conducting medium, based on their differential movement in an applied electrical field.

Endonuclease
An enzyme that breaks nucleic acids at specific interior bonding sites; thus producing nucleic acid fragments of various lengths. *Cf.* Exonuclease.

Enzyme
A protein catalyst that facilitates specific chemical or metabolic reactions necessary for cell growth and reproduction. *Cf.* Catalyst.

Epitope
A site on the surface of a macromolecule capable of being recognised by an antibody. An epitope may consist of just a few amino-acid residues in a protein or a few sugar residues in a polysaccharide. A synonym is “immunological determinant.”

Erythropoietin (EPO)
A protein that boosts production of red blood cells. It is clinically useful in treating certain types of anemias.

Escherichia coli (E. coli)
A bacterium that inhabits the intestinal tract of most vertebrates. Much of the work using recombinant DNA techniques has been carried out with this organism because it has been genetically very well characterised.

Eukaryote
A cell or organism containing a true nucleus, with a well-defined membrane surrounding the nucleus. All organisms **except** bacteria, archebacteria, viruses, and blue-green algae are eukaryotic. *Cf.* Prokaryote.

Exon
In eukaryotic cells, the part of the gene that is transcribed into messenger RNA and encodes a protein. *See also* Intron; Splicing.

Exonuclease
An enzyme that breaks down nucleic acids only at the ends of polynucleotide chains, thus releasing one nucleotide at a time, in sequential order. *Cf.* Endonuclease.

Expression
In genetics, manifestation of a characteristic that is specified by a gene. With hereditary diseases, for example, a person can carry the gene for the disease but not actually have the disease. In this case, the gene is present but not expressed. In molecular biology and industrial biotechnology, the term is often used to mean the production of a protein by a gene that has been inserted into a new host organism.

Expressed sequence tags (ESTs)
A unique DNA sequence derived from a cDNA library (therefore from a sequence which has been transcribed in some tissue or at some stage of development). The EST can be mapped, by a combination of genetic mapping procedures, to a unique locus in the genome and serves to identify that gene locus.

Factor VIII
A large, complex protein that aids in blood clotting and is used to treat hemophilia. *See also* Antihemophilic factors.

Feedstock
The raw material used in chemical or biological processes.

Fermentation
An anaerobic process of growing microorganisms for the production of various chemical or pharmaceutical compounds. Microbes are normally incubated under specific conditions in the presence of nutrients in large tanks called fermentors.

Frameshift
Insertion or deletion of one or more nucleotide bases such that incorrect triplets of bases are read as codons.

Fusion
Joining of the membrane of two cells, thus creating a new, fused cell that contains at least some of the nuclear material from both parent cells. Used in making hybridomas.

Fusion protein
A protein with a polypeptide chain derived from two or more proteins. A fusion protein is expressed from a gene prepared by recombinant DNA methods from the portions of genes encoding two or more proteins.

Gene
A segment of chromosome that encodes the necessary regulatory and sequence information to direct the synthesis of a protein or RNA product. *See also* Operator; Regulatory g.; Structural g.; Suppressor g.

"Gene machine"
A computer controlled, solid-state chemistry device for synthesising oligodeoxyribonucleotides by combining chemically-activated precursors of deoxyribonucleotides (bases) sequentially in the proper order.

Gene mapping
Determination of the relative locations of genes on a chromosome.

Gene sequencing
Determination of the sequence of nucleotide bases in a strand of DNA.

Gene therapy
The replacement of a defective gene in an organism suffering from a genetic disease. Recombinant DNA techniques are used to isolate the functioning gene and insert it into cells. Over three hundred single gene genetic disorders have been identified in humans. A significant percentage of these may be amenable to gene therapy.

Genetic code
The mechanism by which genetic information is stored in living organisms. The code uses sets of three nucleotide bases (codons) to make the amino aids that, in turn, constitute proteins.

Genetic engineering
A technology used to alter the genetic material of living cells in order to make them capable of producing new substances or performing new functions.

Genetic map
A linear designation of sites within a chromosome or genome, based upon the various frequencies of recombination between genetic markers. *See* linkage map.

Genetic screening
The use of a specific biological test to screen for inherited diseases or medical conditions. Testing can be conducted prenatally to check for metabolic defects and congenital disorders in the developing foetus as well as post-natally to screen for carriers of heritage diseases.

Genome
The total hereditary material of a cell, comprising the entire chromosomal set found in each nucleus of a given species.

Genotype
Genetic make-up of an individual or group. *Cf.* Phenotype.

Germ cell
Reproductive cell (sperm or egg). Also called gamete or sex cell.

Germicide
See Bactericide.

Germplasm
The total genetic variability, represented by germ cells or seeds, available within a particular population of organisms.

Gene pool
The total genetic information contained within a given population.

Growth hormone (also called somatotropin)
A protein produced by the pituitary gland that is involved in cell growth.
Human growth hormone is clinically used to treat dwarfism. Various animal growth hormones can be used to improved milk production as well as producing a leaner variety of meat.

Haploid
A cell with half the usual number of chromosomes, or only one chromosome set. Sex cells are haploid. *Cf.* Diploid.

Hapten
A small molecule which, when chemically coupled to a protein, acts as an immunogen and stimulates the formation of antibodies not only against the two-molecule complex but also against the hapten alone.

Hemagglutination
Clumping (agglutination) of red blood cells, for example by antibody molecules or virus particles.

Hereditary
Capable of being transferred as genetic information from parent cells to progeny.

Histocompatibility
Immunologic similarity of tissues such that grafting can be done without tissue rejection.

Histocompatibility antigen
An antigen that causes the rejection of grafted material from an animal different in genotype from that of the host animal.

Homologous
Corresponding or alike in structure, position, or origin.

Hormone
A chemical that acts as a messenger or stimulatory signal, relaying instructions to stop or start certain physiological activities. Hormones are synthesised in one type of cell and then released to direct the function of other cell types.

Host
A cell or organism used for growth of a virus, plasmid, or other form of foreign DNA, or for the production of cloned substances.

Host-vector system
Combination of DNA-receiving cells (host) and DNA-transporting substance (vector) used for introducing foreign DNA into a cell.

Humoral immunity
Immunity resulting from circulating antibodies in plasma protein.

Hybridisation
Production of offspring, or hybrids, from genetically dissimilar parents. The process can be used to produce hybrid plants (by cross-breeding two different varieties) or hybridomas (hybrid cells formed by fusing two unlike cells, used in producing monoclonal antibodies). The term is also used to refer to the binding of complementary strands of DNA or RNA.

Hybridoma
The cell produced by fusing two cells of different origin. In monoclonal antibody technology, hybridomas are formed by fusing an immortal cell (one that divides continuously) and an antibody-producing cell. *See also* Monoclonal antibody; Myeloma.

Immune serum
Blood serum containing antibodies.

Immune system
The aggregation of cells, biological substances (such as antibodies), and cellular activities that work together to provide resistance to disease.

Immunity
Nonsusceptibility to a disease or to the toxic effects of antigenic material. *See also* Active i., Cell-mediated i.; Humoral i.; Natural active i.; Natural passive.; Passive i.

Immunoassay
Technique for identifying substances based on the use of antibodies.

Immunodiagnostics
The use of specific antibodies to measure a substance. This tool is useful in diagnosing infectious diseases and the presence of foreign substances in a variety of human and animal fluids (blood, urine, etc.) It is currently being investigated as a way of locating tumor cells in the body.

Immunofluorescence
Technique for identifying antigenic material that uses antibody labelled with fluorescent material. Specific binding of the antibody and antigen can be seen under a microscope by applying ultraviolet light rays and noting the visible light that is produced.

Immunogen
Any substance that can elicit an immune response, especially specific antibody production. An immunogen that reacts with the elicited antibody may be called an antigen.

Immunoglobulin
General name for proteins that function as antibodies. These proteins differ somewhat in structure, and are grouped into five categories on the basis of these differences: immunoglobulin G (IgG) IgM, IgA, IgD and IgE.

Immunology
Study of all phenomena related the body's response to antigenic challenge (i.e. immunity, sensitivity, and allergy).

Immunomodulators
A diverse class of proteins that boost the immune system. Many are cell growth factors that accelerate the production of specific cells that are important in mounting an immune response in the body. These proteins are being investigated for use in possible cures for cancer.

Immunotoxins
Specific monoclonal antibodies that have a protein toxin molecule attached. The monoclonal antibody is targeted against a tumor cell and the toxin is designed to kill that cell when the antibody binds to it. Immunotoxins have also been termed "magic bullets."

Inducer
A molecule or substance that increases the rate of enzyme synthesis, usually by blocking the action of the corresponding repressor.

Interferon
A class of lymphokine proteins important in the immune response. The are three major types of interferon: alpha (leukocyte), beta (fibroblast), and gamma (immune). Interferons inhibit viral infections and may have anticancer properties.

Interleukin
A type of lymphokine whose role in the immune system is being extensively studied. Two types of interleukin have been identified. Interleukin 1 (IL-1), derived from macrophages, is produced during inflammation and amplifies the production of other lymphokines, notably interleukin 2 (IL-2). IL-2 regulates the maturation and replication of T lymphocytes.

Intron
In eukaryotic cells, a sequence of DNA that is contained in the gene but does not encode for protein. The presence of introns divides the coding region of the gene into segments called exons. *See also* Exon; Splicing.

In vitro
Literally, "in glass." Performed in a test tube or other laboratory apparatus.

In vivo
In the living organism.

Isoenzyme (isozyme)
One of the several forms that a given enzyme can take. The forms may differ in certain physical properties, but function similarly as biocatalysts.

Isogenic
Of the same genotype.

Kidney plasminogen activator
A precursor to the enzyme urokinase that has bloodclotting properties.

Leukocyte
A colourless cell in the blood, lymph, and tissues that is an important component of the body's immune system; also called white blood cell.

Library
A set of cloned DNA fragments.

Ligase
An enzyme used to join DNA or RNA segments together. They are called DNA ligase of RNA ligase, respectively.

Linkage
The tendency for certain genes to be inherited together due to their physical proximity on the chromosome.

Linkage group
A group of gene loci known to be linked; a chromosome. There are as many linkage groups as there are homologous pairs of chromosomes. *See* synteny.

Linkage map
An abstract map of chromosomal loci, based on recombinant frequencies.

Linker
A fragment of DNA with a restriction site that can be used to join DNA strands.

Lipoproteins
A class of serum proteins that transport lipids and cholesterol in the blood stream. Abnormalities in lipoprotein metabolism have been implicated in certain heart diseases.

Locus (Plural loci)
The position of a gene, DNA marker or genetic marker on a chromosome. *See* gene locus.

Lymphocyte
A type of leukocyte found in lymphatic tissue in the blood, lymph nodes, and organs. Lymphocytes are continuously made in the bone marrow and mature into antibody-forming cells. *See also* B lymphocytes; T lymphocytes.

Lymphokine
A class of soluble proteins produced by white blood cells that play a role, as yet not fully understood, in the immune response. *See also* Interferon; Interleukin.

Lymphoma
Form of cancer that affects the lymph tissue.

Lysis
Breaking apart of cells.

Lysozyme
An enzyme present in, for example, tears, saliva, egg whites and some plant tissues that destroys the cells of certain bacteria.

Macrophage
A type of white blood cell produced in blood vessels and loose connective tissues that can ingest dead tissue and cells and is involved in producing interleukin 1. When exposed to the lymphokine "macrophage-activating factor," macrophages also kill tumor cells. *See also* Phagocyte.

Macrophage-activating factor
An agent that stimulates macrophages to attack and ingest cancer cells.

Marker
Any genetic element (locus, allele, DNA sequence or chromosome feature) which can be readily detected by phenotype, cytological or molecular techniques, and used to follow a chromosome or chromosomal segment during genetic analysis. *See* centromere marker; chromosome marker; DNA marker; genetic marker; inside marker; outside marker.

Medium
A liquid or solid (gel) substance containing nutrients needed for cell growth.

Meiosis
Process of cell reproduction whereby the daughter cells have half the chromosome number of the parent cells. Sex cells are formed by meiosis. *Cf.* Mitosis.

Messenger RNA (mRNA)
Nucleic acid that carries instructions to a ribosome for the synthesis of a particular protein.

Metabolism
All biochemical activities carried out by an organism to maintain life.

Microbial herbicides/pesticides
Microorganisms that are toxic to specific plant/insects. Because of their narrow host range and limited toxicity, these microorganisms may be preferable to their chemical counterparts for certain pest control applications.

Microbiology
Study of living organisms and viruses, which can be seen only under a microscope.

Microorganism
Any organism that can be seen only with the aid of a microscope. Also called microbe.

Mitosis
Process of cell reproduction whereby the daughter cells are identical in chromosome number to the parent cells. *Cf.* Meiosis.

Molecular genetics
Study of how genes function to control cellular activities.

Monoclonal antibody
Highly specific purified antibody that is derived from only one clone of cells and recognises only one antigen. *See also* Hybridoma; Myeloma.

mRNA
Messenger RNA.

Multigenic
Of hereditary characteristics, one that is specified by several genes.

Mutagen
A substance that induces mutations.

Mutant
A cell that manifest new characteristics due to a change in its DNA.

Mutation
A change in the genetic material of a cell.

Muton
The smallest element of a chromosome whose alteration can result in a mutation or a mutant organism.

Myeloma
A type of tumor cell that is used monoclonal antibody technology to form hybridomas.

Natural active immunity
Immunity that is established after the occurrence of a disease.

Natural killer (NK) cell
A type of leukocyte that attacks cancerous or virus-infected cells without previous exposure to the antigen. NK cell activity is stimulated by interferon.

Natural passive immunity
Immunity conferred by the mother on the foetus or newborn.

Nitrogen fixation
A biological process (usually associated with plants) whereby certain bacteria convert nitrogen in the air to ammonia, thus forming a nutrient essential for growth.

Nuclease
An enzyme that, by cleaving chemical bonds, breaks down nucleic acids into their constituent nucleotides. *See also* Exonuclease.

Nucleic acid
Large molecules, generally found in the cell's nucleus and/or cytoplasm, that are made up of nucleotide bases. The two kinds of nucleic acid are DNA and RNA.

Nucleotide base
See Base.

Nucleotides
The building blocks of nucleic acids. Each nucleotide is composed of sugar, phosphate, and one of four nitrogen bases. If the sugar is ribose, the nucleotide is termed a "ribonucleotide," whereas deoxyribonucleotides have deoxyribose as the sugar component. The sequence of the nucleotides within the nucleic acid determines, for example, the amino acid sequence of an encoded protein.

Nucleus
The structure within eukaryotic cells that contains chromosomal DNA.

Oligodeoxyribonucleotide
A molecule consisting of a small number (about two to a few tens) of nucleotides linked sugar to phosphate in a linear chain.

Oncogene
Any of a family of cellular DNA sequences which possess the potential to become malignant by undergoing alteration. There are 4 groups of viral and non-viral onc genes: protein kinases, GTPases, nuclear proteins, and growth factors.

Oncogenic
Cancer causing.

Oncology
Study of tumors.

Open reading frame
A nucleotide sequence beginning with a start (AUG) codon, continuing in register with amino acid-encoding codons, and ending with a stop codon.

Operator
A region of the chromosome, adjacent to the sequences encoding the gene product, where a repressor protein binds to prevent transcription.

Operon
Sequence of genes responsible for synthesising the enzymes needed for biosynthesis of a molecule. An operon is controlled by an operator gene and a repressor gene.

Opsonin
An antibody that renders bacteria and other antigenic material susceptible to destruction by phagocytes.

Organic compound
A compound containing carbon.

Passive immunity
Immunity acquired from receiving preformed antibodies.

Pathogen
Disease-causing organism.

Peptide
Two or more amino acids joined by a linkage called a peptide bond.

Phage
See Bacteriophage.

Phagocyte
A type of white blood cell that can ingest invading microorganisms and other foreign material. *See also* Macrophage.

Phenotype
Observable characteristics, resulting from interaction between an organism's genetic make-up and the environment. *Cf.* Genotype

Photosynthesis
Conversion by plants of light energy into chemical energy, which is then used to support the plants' biological processes.

Plasma
The fluid (noncellular) fraction of blood.

Plasmapheresis
A technique used to separate useful factors from blood.

Plasmid
A small circular form of DNA that carries certain genes and is capable of replicating independently in a host cell.

Pleiotropic
Genes or mutations that result in the production of multiple effects at the phenotypic level. It is the consequence of the fact that biochemical pathways starting from different genes intersect in many places, inhibiting, deflecting, and variously modifying each other. Introduced genes may also insert into sites that effect phenotypic changes other than the one desired.

Polyclonal
Derived from different types of cells.

Polymer
A long molecule of repeated subunits.

Polymerase
General term for enzymes that carry out the synthesis of nucleic acids.

Polymerase chain reaction (PCR)
A technique used for enzymatic in vitro amplification of specific DNA sequences without utilising conventional procedures of molecular cloning. It allows the amplification of a DNA region situated between two convergent primers and utilises oligonucleotide primers that hybridise to opposite strands. Primer extension proceeds inward across the region between the two primers. The product of DNA synthesis of one primer serves as a template for the other primer; repeated cycles of DNA denaturation, annealing of primers, and extension result in an exponential increase in the number of copies of the region bounded by the primers.

Polypeptide
Long chain of amino acids joined by peptide bonds.

Probe
See DNA probe.

Prokaryote
A cellular organism (e.g., bacterium, blue-green algae) whose DNA is not enclosed within a nuclear membrane. *Cf.* Eukaryote.

Promoter
A DNA sequence that is located near or even partially within encoding nucleotide sequences and which controls gene expression. Promoters are required for binding of RNA polymerase to initiate transcription.

Prophage
Phage nucleic acid that is incorporated into the host's chromosome but does not cause cell lysis.

Protein
A molecule composed of amino acids. There are many types of proteins, most carrying out functions essential for cell growth.

Protein A
A protein produced by the bacterium *Staphylococcus aureus* that specifically binds antibodies. It is useful in the purification of monoclonal antibodies.

Protoplast
The cellular material that remains after the cell wall has been removed.

Pure culture
In vitro growth of only one type of microorganism.

Radioimmunoassay
A technique for quantifying a substance by measuring the reactivity of radioactively labelled forms of the substance with antibodies.

Reagent
Substance used in a chemical reaction, often for analytical purposes.

Recombinant DNA (rDNA)
The DNA formed by combining segments of DNA from two or more different sources or different regions of a genome.

Regeneration
Laboratory technique for forming a new plant from a clump of plant cells.

Regulatory gene
A gene that acts to control the protein-synthesising activity of other genes.

Replication
Reproduction or duplication, as of an exact copy of a strand of DNA.

Replicon
A segment of DNA (e.g., chromosome or plasmid) that can replicate independently.

Repressor
A protein that binds to an operator adjacent to a structural gene, inhibiting transcription of the gene.

Restriction enzyme
An enzyme that recognises a specific DNA nucleotide sequence, usually symmetrical, and cuts the DNA within or near the recognised sequence. This may create a gap into which new genes can be inserted.

Reticuloendothelial system
The system of macrophages, which serves as an important defense system against disease.

Retrovirus
An animal virus that contains the enzyme reverse transcriptase. This enzyme converts the viral RNA into DNA, which can combine with the DNA of the host cell and produce more viral particles.

Rheology
Study of the flow of matter such as fermentation liquids.

Rhizobium
A class of microorganisms that converts atmospheric nitrogen into a form that plants can utilise for growth. Species of this microorganism grow symbiotically on the roots of certain legumes such as peas, beans, and alfalfa.

RIA (Radioimmunoassay)
A diagnostic test using antibodies to detect trace amounts of substances. Such tests are useful in biomedical research to study how drugs interact with their receptors.

Ribonucleic acid (RNA)
A molecule similar to DNA that functions primarily to decode the instructions for protein synthesis that are carried by genes. *See also* Messenger RNA; Transfer RNA.

Ribosome
A cellular component, containing protein and RNA, that is involved in protein synthesis.

Ribozyme
Any of the RNA molecules possessing catalytic activity and acting as biological catalysts.

RNA
Ribonucleic acid.

Scale-up
Transition from small-scale production to production of large industrial quantities.

Selective medium
Nutrient material constituted such that it will support the growth of specific organisms while inhibiting the growth of others.

Sequence tagged site (STS)
Short (200 to 500 base pairs) DNA sequence that has a single occurrence in the human genome and whose location and base sequence are known. Detectable by polymerase chain reaction, STSs are useful for localising and orienting the mapping and sequence data reported from many different laboratories and serve as landmarks on the developing physical map of the human genome. Expressed sequence tags (ESTs) are STSs derived from cDNAs.

Serology
Study of blood serum and reaction between the antibodies and antigens therein.

Signal sequence
The N-terminal sequence of a secreted protein, which is required for transport through the cell membrane.

Single-cell protein
Cells or protein extracts from microorganisms, grown in large quantities for use as protein supplements. Single cell protein is expected to have a nutritionally favourable balance of amino acids.

Site-specific recombination
A crossover event, such as the integration of phage lambda, that requires homology of only a very short region and uses an enzyme specific for that recombination. Recombination occurring between two specific sequences that need not be homologous; mediated by a specific recombination system.

snRNP
Small nuclear ribonucleoprotein (RNA plus protein) particle. Component of the spliceosome, the intron-removing apparatus in eukaryotic nuclei.

Somatic cells
Cells other than sex or germ cells.

Splicing
The removal of introns and joining of exons to form a continuous coding sequence in RNA.

Strain
A pure-breeding lineage, usually of haploid organisms, bacteria, or viruses.

Stringent response
A translational control mechanism of prokaryotes that represses tRNA and rRNA synthesis during amino acid starvation.

Structural gene
A gene that codes for a protein, such as an enzyme.

Substrate
Material acted on by an enzyme.

Suppressor gene
A gene that can reverse the effect of a mutation in other genes.

Synteny
All loci on one chromosome are said to be syntenic (literally on the same ribbon). Loci may appear to be unlinked by conventional genetic tests for linkage but still be syntenic.

Synteny test
A test that determines whether two loci belong to the same linkage group (i.e. are syntenic) by observing concordance (occurrence of markers together) in hybrid cell lines.

Template
A molecule that serves as the pattern for synthesising another molecule.

Therapeutics
Compounds that are used to treat specific diseases or medical conditions.

Thymus
A lymphoid organ in the lower neck, the proper functioning of which in early life is necessary for development of the immune system.

Tissue culture
In vitro growth in nutrient medium of cells isolated from tissue.

Tissue plasminogen activator (tPA)
A protein produced in small amounts in the body that aids in dissolving blood clots.

T lymphocytes (T-cells)
White blood cells that produced in the bone marrow but mature in the thymus. They are important in the body's defense against certain bacteria and fungi, help B lymphocytes make antibodies, and help in the recognition and rejection of foreign tissues. T lymphocytes may also be important in the body's defense against cancers.

Toxin
A poisonous substance produced by certain microorganisms.

Transcription
Synthesis of messenger (or any other) RNA on a DNA template.

Transduction
Transfer of genetic material from one cell to another by means of a virus or phage vector.

Transfection
Infection of a cell with nucleic acid from a virus, resulting in replication of the complete virus.

Transfer RNA (tRNA)
RNA molecules that carry amino acids to sites on ribosomes where proteins are synthesised.

Transformation
Change in the genetic structure of an organism by the incorporation of foreign DNA.

Transgenic organism
An organism formed by the insertion of foreign genetic material into the germ line cells of organisms. Recombinant DNA techniques are commonly used to produce transgenic organisms.

Translation
Process by which the information on a messenger RNA molecule is used to direct the synthesis of a protein.

Transposon
A segment of DNA that can move around and be inserted at several sites in the genome of a cell possibly altering expression. The first to be described was the Ac/Ds system in maize shown by McClintock to cause unstable mutations.

tRNA
See transfer RNA.

Tumor necrosis factor
A cytokine with many actions including the destruction of some types of tumor cells without affecting healthy cells. However, hopes for their usefulness in cancer therapy have been dampened by toxic effects of the treatment. They are now being engineered for selective toxicity for cancer cells.

Tumor suppressor gene
Any of a category of genes that can suppress transformation or tumorigenicity (probably ordinarily involved in normal control of cell growth and division).

Vaccine
A preparation that contains an antigen consisting of whole disease-causing organisms (killed or weakened), or parts of such organisms, and is used to confer immunity against the disease that the organism causes. Vaccine preparation can be natural, synthetic, or derived by recombinant DNA technology.

Vector
The agent (e.g., plasmid or virus) used to carry new DNA into a cell.

Virion
An elementary viral particle consisting of genetic material and a protein covering.

Virology
Study of viruses.

Virulence
Ability to infect or cause disease.

Virus
A submicroscopic organism that contains genetic information but cannot reproduce itself. To replicate, it must invade another cell and use parts of that cell's reproductive machinery.

White blood cells
See Leukocytes.

Wild type
The form of an organism that occurs most frequently in nature.

Yeast
A general term for single-celled fungi that reproduce by budding. Some yeasts can ferment carbohydrates (starches and sugars), and thus are important in brewing and baking.

Annex 2 Bibliography of Suggested Reading

National References

- Environmental Protection Agency, "Regulation of Genetically Modified Organisms (GMOs) in Ireland by the EPA".
- Food Safety Authority of Ireland, "Food Safety and Genetically Modified Foods".
- Interdepartmental Committee Report on Modern Biotechnology, Department of Enterprise, Trade and Employment, October 2000.
- Irish Bioindustry Association Position Paper on "The Biotechnology Industry – A Unique Opportunity for Ireland to be a World Leader".
- National Consultation Debate on Genetically Modified Organisms and the Environment, Report of the Chairing Panel, Department of the Environment and Local Government, October 1999.
- Technology Foresight Ireland Reports, Forfás, April 1999.

International References

- EMBO (European Molecular Biology Organisation) Statement on Genetically Modified Organisms (GMOs) and the Public.
- Ernst & Young's Seventh Annual European Life Sciences Report 2000.
- European Federation of Biotechnology, "Ethical Aspects of Agricultural Biotechnology".
- European Federation of Biotechnology, "Public Opinion about Biotechnology: a survey of surveys".
- Nuffield Council on Bioethics, "Genetically modified crops: the ethical and social issues".
- Office of Science and Technology, UK "Genetically Modified Foods: Facts, Worries, Policies and Public Confidence", a note by Sir Robert May.
- Organisation for Economic Co-operation and Development (OECD), "Industrial Sustainability through Biotechnology".
- Organisation for Economic Co-operation and Development, "Modern Biotechnology and the OECD".
- The Royal Society Statement on "Genetically Modified Plants for Food Use".

Annex 3 Biotechnology Task Force Membership

Prof. Emer Colleran, NUI, Galway *(Chairperson)*

Dr. Jimmy Burke, Teagasc

Dr. Michael Comer, Private Consultant

Dr. Mark Lawler, St. James Hospital

Prof. David McConnell, TCD

Mr. Ronan O'Caoimh, Trinity Biotech

Prof. Peter Whittaker, NUI, Maynooth

Irish Council for Science, Technology and Innovation (ICSTI)

Dr Edward Walsh, Chairman
President Emeritus
University of Limerick
Foundation

Mr Brian Sweeney,
Deputy Chairman
Chairman
Siemens Group Ltd

Dr Leonora Bishop
Managing Director
Plateomic Ltd

Dr Alva Devoy
Senior Investment Analyst
KBC Asset Management Ltd

Ms Anne Downey
Senior Vice President
QSET

Professor Ted Farrell
Department of Environmental Resource Management
National University of Ireland, Dublin

Mr Denis Hayes
General Manager of Technical Operations
European Frozen Division, H.J. Heinz Ireland Ltd

Dr Peter Heffernan
Chief Executive Officer
Marine Institute

Ms Sharon Kennedy
Chief Executive Officer
Eirco Web

Mr Pádraig Kirk
STEPS, Project Manager
Institution of Engineers of Ireland

Dr Anita R Maguire
Department of Chemistry
National University of Ireland, Cork

Professor David McConnell
Genetics Department
Trinity College

Mr Seamus McManus
Former Chairman
Irish Science Teachers' Association

Dr David Melody
Vice President for R&D
Loctite (Ireland) Ltd

Dr Pat Morgan
Dean, Faculty of Science
National University of Ireland, Galway

Ms Anne Murphy
Department of Mathematics
Dublin Institute of Technology

Mr Annrai O'Toole
Chief Executive Officer
Cape Clear Software

Dr Ena Prosser
Director of Strategic Technology Analysis
Corporate Office of Technology, Elan Corporation

Dr Don Thornhill
Chairman
Higher Education Authority

Mr John Travers
Chief Executive Officer
Forfás

Mr Brian Trench
School of Communications
Dublin City University

Dr Fionnuala Walsh
Business Leader for Science and Technology
Eli Lilly SA

Ms Josephine Lynch
Secretary to Council
Forfás

ICSTI Statements

State Expenditure Priorities for 1998	September 1997
£250 Million Scientific and Technological Education (Investment) Fund	January 1998
A Partnership Approach to Research Funding – The Need for a National Science and Engineering Research Fund	May 1998
Science in Primary Schools	September 1998
Science, Technology and Innovation Culture	November 1998
Innovation in Enterprises in Ireland	November 1998
Mechanisms for Prioritisation of State Expenditures on Science and Technology	November 1998
State Expenditure Priorities for 1999	January 1999
Investing in Research, Technology and Innovation (RTI) in the Period 2000 to 2006	March 1999
Technology Foresight Report	April 1999
Science in Second Level Schools	November 1999
Benchmarking School Science, Technology and Mathematics Education in Ireland Against International Good Practice	February 2000
Public Research and Technology Services for Innovation in Enterprises	December 2000
Commercialisation of Publicly Funded Research	April 2001

The Irish Council for Science, Technology and Innovation (ICSTI)
The Secretariat is provided by Forfás, the national policy and advisory board for enterprise, trade, science, technology and innovation.

The ICSTI Secretariat
Wilton Park House, Wilton Place, Dublin 2, Ireland

Tel: +353 1 607 3186 Fax: +353 1 607 3260
Email: icsti@forfas.ie Web: www.forfas.ie/st/sti.htm