GM Foods

Safety Assessment of Genetically Modified Foods

FOOD STANDARDS
Australia New Zealand
Te Mana Kounga Kai – Ahitereiria me Aotearoa

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About the Cover:
The cover illustration depicts the wide array of corn varieties developed through traditional breeding techniques. The background image shows magnified corn cells, photographed by Kelli Gowland.

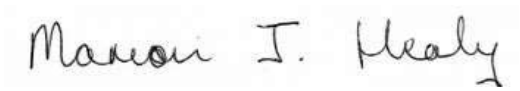
Contents

Foreword

In 2000, the then Australia New Zealand Food Authority (ANZFA) produced the booklet *GM foods and the consumer*. It was aimed at consumers who were interested in knowing more about the safety assessment of genetically modified (GM) foods. This booklet was a great success in addressing consumer concerns and explaining the ANZFA safety assessment process. In 2002, ANZFA became Food Standards Australia New Zealand (FSANZ), with a broader range of functions, although its role in the assessment and approval of GM foods remained unchanged.

In the four years since the publication of *GM foods and the consumer*, gene technology has developed rapidly and the safety assessments conducted by FSANZ have evolved to stay abreast of the best international methods for safety assessments. This booklet, GM foods, incorporates recent developments in safety assessment of *GM foods*, and follows a more user-friendly format.

I commend the *GM foods* to you. I am confident the safety assessment process for GM foods used by FSANZ is equal to the best in the world.



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Past and present staff of FSANZ involved in the preparation of *GM foods* (and the booklet on which it is based, *GM foods and the consumer*) include Dr Wendy Odgers, Dr Marion Healy, Ms Bronwyn Dixon, Dr Peter Abbott, Dr Dennis Bittisnich, Dr Paul Brent, Dr Nora Galway, Ms Lynda Graf, Dr Lisa Kelly, Ms Vanessa King and Dr Peter Thygesen.

GM foods was thoroughly reviewed by an external group of experts. FSANZ is especially grateful to these people who gave their time freely:

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FSANZ also wishes to thank the Office of the Gene Technology Regulator (OGTR) for providing information on the OGTR's processes for licensing genetically modified organisms and the New Zealand Food Safety Authority for providing information on the New Zealand system for developing maximum residue limits.

To these and others involved in the production of this booklet, FSANZ extends its appreciation for their significant contributions.

PART 1
An overview

1 Introduction

Most of the foods we eat today come from plants and animals that have been grown and bred by humans for countless generations, undergoing substantial genetic changes over several thousand years. Traditionally, plants or animals with the most desirable characteristics were chosen for food and for breeding the next generation. The desirable characteristics arose from naturally occurring variations in the genetic make-up of individual plants or animals. Thus, genetic modification, in this sense, occurs naturally and forms the fundamental basis of evolution and breeding.

Today's techniques of genetic modification provide new ways to identify particular characteristics and transfer them between living organisms. For example, it is now possible to make a copy of a particular gene from the cells of a plant, animal or microbe, and insert the copy into the cells of another organism to give it a desired characteristic (a process described in more detail in Section 3). Because the resulting plants or animals have had their genetic material altered in some way, they are commonly referred to as 'genetically modified' or 'GM' organisms. Consequently, foods derived from GM plants or animals are often called 'GM foods'. The term 'GM food' is also sometimes applied to foods that contain GM ingredients, and to food additives or processing aids produced using genetic modification.

The introduction of GM foods into our food supply has stimulated much discussion about the nature of these foods, their safety and their place in global food production. This publication explains the process that is used in Australia and New Zealand to assess the safety of GM foods:

Part 1 provides an overview of the safety assessment process. It looks at:

- how GM food is regulated in Australia and New Zealand (Section 2)
- the basics of gene technology (Section 3)
- the principles applied to the safety assessment of GM food, and what is required before a GM food can be approved for sale (Section 4)
- the GM foods that are available in Australia and New Zealand, and those that are available overseas (Section 5)
- how GM foods are likely to develop in the future (Section 6)
- answers to some frequently asked questions about GM foods (Section 7).

Part 2 looks in detail at the safety assessment of GM foods step by step, illustrated by a case study of a soybean modified to be tolerant to a herbicide (Sections 8–15).

In addition, there are a number of appendices, which provide further information about:

- Food Standards Australia New Zealand (FSANZ) (Appendix 1)
- the process for changing food standards (Appendix 2)
- labelling of GM foods (Appendix 3)
- the work of international organisations on the safety of GM foods (Appendix 4)
- technical or unfamiliar terms (Appendix 5)

- publications on aspects of GM foods covered in this publication (Appendix 6)
- contacts and publications on aspects not covered in this document, such as the environmental and ethical issues surrounding GM foods (Appendix 7).

As at June 2005, twenty-five GM foods have been approved for use in Australia and New Zealand. Most of these foods have come from plants that have been genetically modified to improve their growing characteristics; for example, to protect the crop from pests or to make it tolerant to herbicides. In the future, genetic modification may be used to provide more direct benefits to consumers; for example, by improving the flavour or nutritional properties of foods.

Gene technology may bring benefits. However, it may also bring new and unexpected risks. Government has to assess potential risks and ensure that any risks are properly managed. The role of FSANZ in relation to GM foods is to assess them to ensure they are safe for consumption, and thus to protect public health and safety in Australia and New Zealand.

2 Regulation of GM foods

2.1 General food safety

The level of risk that a community is prepared to accept in relation to food is influenced by the experience and knowledge that comes from the community's consumption of that food over many hundreds or even thousands of years. For example, we know that:

- rhubarb leaves, green potatoes and many types of mushrooms are unsafe because of their toxic components
- certain foods, such as cow's milk, eggs and nuts, can cause an allergic reaction in some people
- a diet with high levels of saturated fats and salt can lead to health problems in the long term
- a balanced and varied diet of nutritious foods is vital for good health.

We understand that we have to take care when preparing food, to prevent the growth of harmful bacteria. We also have developed methods to preserve foods so that they are safe to eat over longer periods of time, using techniques such as pasteurisation, sterilisation, pickling, salting, drying, chilling, freezing and canning.

Much of this knowledge about food safety was gained by our ancestors through trial and error. They learned how to manage the risks in their food through the food choices they made and the methods they used to prepare food. We have inherited this valuable knowledge as a part of our food culture, and most of the time we do not question whether commonly eaten foods are safe. Generally, we are satisfied that the benefits of these foods outweigh any potential risks.

Today, there is an increasing array of new foods and new food chemicals (for example, food additives) available that do not have a history of use in our society. These foods and food chemicals need to be carefully examined before they can be used in the food supply, to ensure they are safe for human consumption.

2.2 Regulating foods in Australia and New Zealand

New Zealand and each of the individual states and territories government of Australia have food laws designed to ensure a high degree of public health and safety protection. These laws, which require food to be safe and suitable, are interpreted and enforced by the respective governments. The history of food use is an important consideration when setting food regulations, and the regulations reflect the level of risk that the community generally accepts in relation to food.

Foods available for sale in Australia and New Zealand must also comply with fair-trading and trade practices laws and other laws, such as those protecting the environment or controlling the use of poisons.

2.3 The Australia New Zealand Food Standards Code

In Australia and New Zealand, food standards, or rules regulating food products, are set out in the *Australia New Zealand Food Standards Code*. All the standards in this code apply to Australian states and territories. However, parts of the code do not apply to New Zealand, which sets its own standards in the areas of food hygiene, processing requirements, maximum residue limits, primary production and processing.

FSANZ is responsible for developing, varying and reviewing the food standards that apply to both Australia and New Zealand, and those that apply to Australia only.

The *Australia New Zealand Food Standards Code*:

- prohibits the use of additives, processing aids and nutritive substances in food unless there is a specific permission for these substances following a safety assessment
- prohibits the use of novel foods, irradiated foods and foods produced using gene technology unless there is a specific permission for these foods following a safety assessment.
- specifies maximum limits for contaminants and natural toxicants in food
- establishes microbiological and processing requirements for food
- specifies the composition and labelling requirements for many commodities.

2.4 Food produced using gene technology (Standard 1.5.2)[1]

Standard 1.5.2 – *Food Produced Using Gene Technology*, of the *Australia New Zealand Food Standards Code* regulates food derived from GM plants, animals or microorganisms. Standard 1.5.2 does not apply to GM food additives or processing aids, which are already covered by other food standards.

Any GM foods (or ingredients derived from them) that are listed in Standard 1.5.2 have passed the safety assessment and approval process, and can therefore be sold in Australia and New Zealand, and used to make other foods.

Safety assessments of GM foods

Under Standard 1.5.2, GM foods must be assessed for safety, and only those found to be safe are approved for sale.

The safety assessment of GM foods is described in more detail in Section 4.

1. The Australian New Zealand Food Standards Code, including Standard 1.5.2 is available on the FSANZ website at http://www.foodstandards.gov.au/food standards code/

FSANZ is responsible for carrying out safety assessments of GM foods on behalf of the Australian Government, the state and territory governments of Australia, and the Government of New Zealand. In doing so, FSANZ takes a cautious approach because, even though most GM foods are derived from foods with a long-established history of safe human consumption (such as corn and soybean), the GM versions are new to the diet.

Labelling of GM foods

Standard 1.5.2 also contains provisions for the labelling of GM foods – these provisions have been in effect since December 2001. The safety of a GM food is assessed before it can be sold as food; therefore, the purpose of labelling is simply to provide information to consumers, allowing them to purchase or avoid GM foods depending on their own views and beliefs. The GM food labelling regulations, which are among the most stringent in the world, represent a balance between the needs of consumers and what governments can realistically enforce.

More information on the basics of DNA and gene technology is provided in Section 3.

Under Standard 1.5.2, if a food, food ingredient, additive or processing aid contains novel DNA or protein that has come from an approved GM food, it must be labelled with the words 'genetically modified'. Labelling regulations also cover GM foods that differ in composition to the conventional counterpart; in this case, the labelling must make clear to consumers the altered characteristics of the food.

More detailed information on the labelling of GM foods is provided in Appendix 3.

There are some exemptions to the labelling requirements for GM foods. Foods that do not need to be labelled as 'genetically modified' include highly refined foods that contain no DNA or protein (for example, oil made from GM soy beans), and foods in which GM ingredients are present accidentally and make up less than 1% of the final food.

2.5 Role of other agencies

In Australia and New Zealand, FSANZ is not the only government agency involved with the regulation of GM microorganisms, plants and animals and their products. As shown in Table 2.1, the responsibilities of other agencies cover broader issues than food safety, such as the environment, quarantine and the registration of agricultural chemicals. Where products require the approval of several agencies, the agencies coordinate with one another.

Table 2.1 Agency involvement with GM microorganisms plants and animals and their products

Activity	Government agency *Australia*	*New Zealand*
Safety of food (Standard 1.5.2)	• Food Standards Australia New Zealand	• Food Standards Australia New Zealand
Enforcement of Standard 1.5.2	• State and territory departments	• New Zealand Food Safety Authority
Environmental issues (including live releases of GMOs)	• Australian Government Department of the Environment and Heritage • Office of the Gene Technology Regulator	• Environmental Risk Management Authority • Ministry for the Environment
Broader public health matters	• Office of the Gene Technology Regulator	• Ministry of Health • New Zealand Food Safety Authority • Biosecurity New Zealand
Imports and exports	• Australian Quarantine and Inspection Service • Australian Government Department of the Environment and Heritage • Food Standards Australia New Zealand • Office of the Gene Technology Regulator	• New Zealand Food Safety Authority • Biosecurity New Zealand • Environmental Risk Management Authority
Insecticide or herbicide issues (such as registration of insect-protected crops, registration of herbicides used on herbicide-tolerant crops, setting of residue limits in foods)	• Australian Pesticides and Veterinary Medicines Authority • Australian Government Department of the Environment and Heritage • Food Standards Australia New Zealand	• New Zealand Food Safety Authority • Environmental Risk Management Authority • Ministry for the Environment • Ministry of Agriculture and Forestry
Other issues (e.g. medicines, biotechnology communications, ethics etc)	• Therapeutic Goods Administration • Department of Health and Ageing • Department of Agriculture, Fisheries and Forestry • Biotechnology Australia	• Environmental Risk Management Authority • Ministry of Research Science and Technology • Ministry for the Environment • Ministry of Agriculture and Forestry • Bioethics Council

The role of the Office of the Gene Technology Regulator

In Australia, responsibility for the regulation of gene technology rests with the Australian Government's Gene Technology Regulator and the agency supporting that position – the Office of the Gene Technology Regulator (OGTR).

The OGTR is located in the Australian Government Department of Health and Ageing, as part of the Therapeutic Goods Administration. It operates under the *Gene Technology Act 2000*, which came into force on 21 June 2001, and aims to:

> . . . protect the health and safety of people, and to protect the environment, by identifying risks posed by or as a result of gene technology, and by managing those risks through regulating certain dealings with GMOs.

The Regulator's responsibilities include setting requirements for the use of live genetically modified organisms (GMOs) in contained facilities such as research laboratories and in the environment (for example, field trials and commercial plantings of GM crops).

The Act places a prohibition on any dealing with a GMO unless that dealing is:

- licensed by the Regulator for contained use or intentional release into the environment;
- a Notifiable Low Risk Dealing;
- an exempt dealing; or
- on the Register of GMOs.

For dealings that do require a licence, the Regulator assesses such licence applications based on provisions in the Act, the associated *Gene Technology Regulations 2001* and corresponding state and territory legislation. A risk assessment and risk management plan for each licence application form the basis of the decision whether or not to issue a licence. In preparing the assessment and the plan, the Regulator identifies and assesses what risks the GMO might pose to human health and safety and to the environment, and considers the means available to manage those risks. The Gene Technology Tecchnical Advisory Committee assists the Regulator in this process by providing scientific and technical advice.

Two other committees have been set up to provide the Regulator with general advice on ethical issues and issues of concern to the community. These committees are:

- the Gene Technology Ethics Committee
- the Gene Technology Community Consultative Committee.

Where GMOs have been developed for intentional release into the environment, the Regulator also consults extensively with a wide range of expert groups and key stakeholders, including the public.

If the Regulator is satisfied that the risks can be managed, a licence is issued, with conditions that ensure the risk management plan is implemented effectively. The Regulator has extensive powers to monitor and enforce licence conditions.

The Regulator also liaises with other regulatory agencies, including FSANZ, the Australian Pesticides and Veterinary Medicines Authority (APVMA) and the Therapeutic Goods Administration (TGA), to coordinate the approval of GM products for use and sale.

Coordination between FSANZ and the OGTR

Both FSANZ and the OGTR play important roles in the protection of human health. Because of their overlapping interests, the two agencies benefit from working closely together. For example, consultation between OGTR and FSANZ allows FSANZ to be aware of any applications for release of GMOs into the environment and to identify any potential food safety issues. In turn, FSANZ notifies the OGTR of all GM food applications, as part of the FSANZ consultation process.

The cooperation between FSANZ and the OGTR is part of a wider cross-government coordination between FSANZ, OGTR, the Australian Government Department of Health and Ageing and the Australian Government Department of Agriculture Fisheries and Forestry. Representatives from these organisations share information and technical data on applications for field trials, commercial releases and food approvals for products of gene technology.

Further information on the role of the OGTR, including a list of the licences and licence conditions issued by the regulator, is available on the OGTR website (http://www.ogtr.gov.au).

3 The basics of gene technology

Gene technology is the use of specialised techniques to alter the genetic material of plants, animals or microorganisms to produce 'genetically modified organisms' or 'GMOs'. The technology allows certain characteristics of living organisms to be altered in a specific and directed way, usually by introducing new segments of genetic material (DNA – deoxyribonucleic acid) from another living organism.

3.1 DNA, genes and the genome

DNA is the molecule that carries the genetic blueprint for life. It is like a long string of beads. The 'beads' or 'building blocks' of DNA are called bases, and they come in four types that can link together in different sequences. The four bases (also called nucleotides) are adenine, cytosine, guanine and thymine. DNA is usually double stranded (see Figure 3.1a), with base pairing between adenine and thymine, and cytosine and guanine forming the 'rungs' between the phosphate backbones of the two DNA strands. The order of bases on each strand makes up the DNA sequence. The number of possible sequences is almost endless because an individual strand of DNA may contain millions of bases.

The DNA sequence in each cell contains the instructions needed for the cell to function – the ***genes***. A gene might contain the instructions for the cell to make a specific protein or it might have another role in the cell.

An organism's complete set of genes, which is called the '***genome***', contains between 50,000 and 100,000 genes. All the cells in an organism carry an identical and complete genome, which means that every cell contains at least one copy of every gene. The genome contains all the genes required for the organism to function. By switching different combinations of genes on or off, cells develop into different types – for example, heart, lung and skin cells in animals; or leaf, root and flower cells in plants. Thus, in any given cell type, only certain genes are active (switched on), although the entire genome is present in the cell.

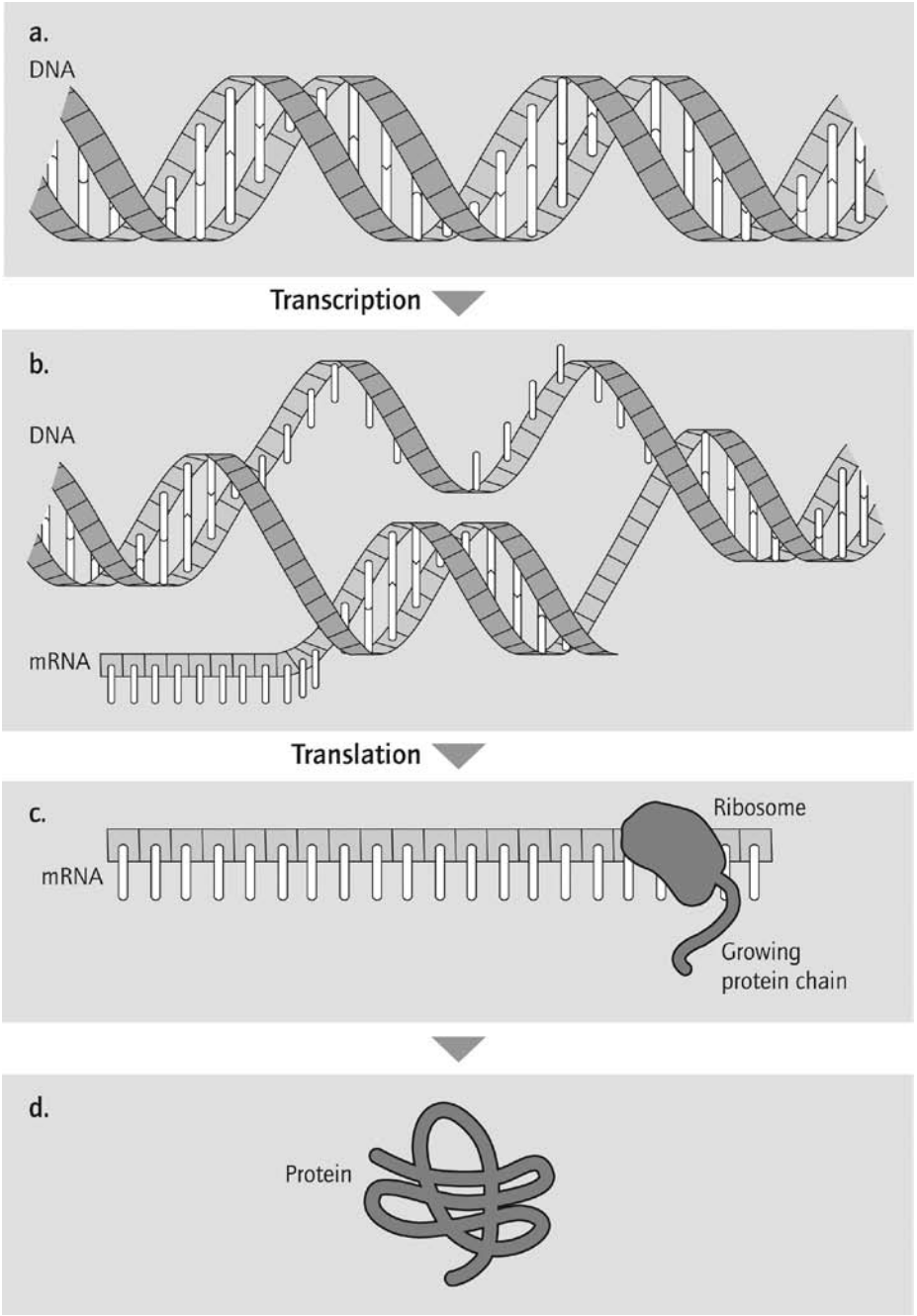
3.2 Making protein from DNA

Genes can contain the formula needed by the cell to produce proteins. Proteins are the most common of the complex molecules in your body. They are made up of long chains of amino acids and have a variety of roles in the cell. Types of proteins include structural proteins (for example, muscles) and enzymes that carry out many of the life processes in plants and animals, for example by converting sunlight and carbon dioxide into energy (photosynthesis).

The process by which proteins are made following the instructions of a gene is shown in Figure 3.1. The first step involves a messenger RNA (mRNA) copy of the gene being produced. It is called messenger RNA as it carries the gene sequence from the DNA to the ribosome. The ribosome is a large structure in the cell that acts like a factory for protein production. The ribosome reads the protein formula from the mRNA copy of the gene and produces the protein by adding amino acids, one at a time, into a the protein chain. When the ribosome finishes making the protein chain, it detaches from the protein and the mRNA. The protein chain will then fold up into its correct shape (3.1d) and form a functional protein.

Figure 3.1. Making protein from DNA

a. Bases of DNA forming a DNA sequence (gene). b. During transcription, DNA is copied into messenger RNA (mRNA) chains. c. During translation, mRNA moves to the ribosome, where the building blocks of proteins (amino acids) are added. d. This sequence of amino acids ultimately forms a protein.



3.3 How is genetic modification possible?

Genetic modification, involving the copying and transfer of genes from one organism to another, is possible because the genetic code is universal. That is, the DNA of all organisms is made up of the same building blocks (the bases that constitute DNA), and is decoded (transcribed and translated) in exactly the same way. So, once a DNA sequence that codes for a particular characteristic in one organism has been identified, it is possible to transfer a copy of that DNA sequence (or gene) into the cells of a different organism. Once the gene becomes incorporated into the genome of the recipient organism, the resulting organism is considered to be genetically modified. The new characteristics coded by that gene will be inherited by subsequent generations.

Box 3.1 describes a type of corn that has been genetically modified to be resistant to certain insect pests.

Box 3.1 Bt corn — an approved GM food

One of the first GM foods to be approved for sale in Australia and New Zealand was corn modified to be resistant to insect pests, referred to as 'Bt corn'. The name comes from the insect resistance system that has been incorporated into the GM corn plants, which is derived from *Bacillus thuringiensis* (Bt), a bacterium that is commonly found in the soil. The Bt bacterium naturally produces a number of crystal proteins that are toxic to certain insects. GM plants with Bt have been genetically modified to contain one or more of the genes from Bt that produce these crystal proteins. The modified plants produce one or more types of Bt crystal protein (in their leaves, stems, roots and other plant tissue), and susceptible insects that eat the plant are poisoned.

Most of the crystal proteins produced by Bt are toxic to particular groups of insects (either butterflies and moths, beetles or flies). The proteins are not toxic to any other insects or living organisms, and are harmless to humans.

Bt proteins derived directly from the soil bacterium have a long history of safe use as a natural insecticide. This insecticide is used in the organic food industry and in many developing countries. The bacterium has probably always been present (in trace amounts) in the human diet, because it is so widespread in soil, water and on the surfaces of plants.

Particular varieties of Bt corn have been through the FSANZ safety assessment process, and are approved for sale in Australia and New Zealand.

3.4 How are GMOs developed?

The steps involved in developing a genetically modified organism (GMO) are shown in Figure 3.2.

The first step is to identify a particular characteristic from any organism (for example, a plant, animal or microorganism) and work out which gene or genes in the organism are responsible for producing that characteristic. In the example in Figure 3.2, the desired characteristic and the gene that produces this characteristic has been identified in a microorganism (a bacterium). This is the gene of interest. Step 2 is to use the techniques of molecular biology to isolate and copy the required gene.

If the gene of interest was found in a bacterium it will have an 'on switch' (and other switches) that function only in bacterial cells. For a gene to function in a different type of cell (for example, in a plant

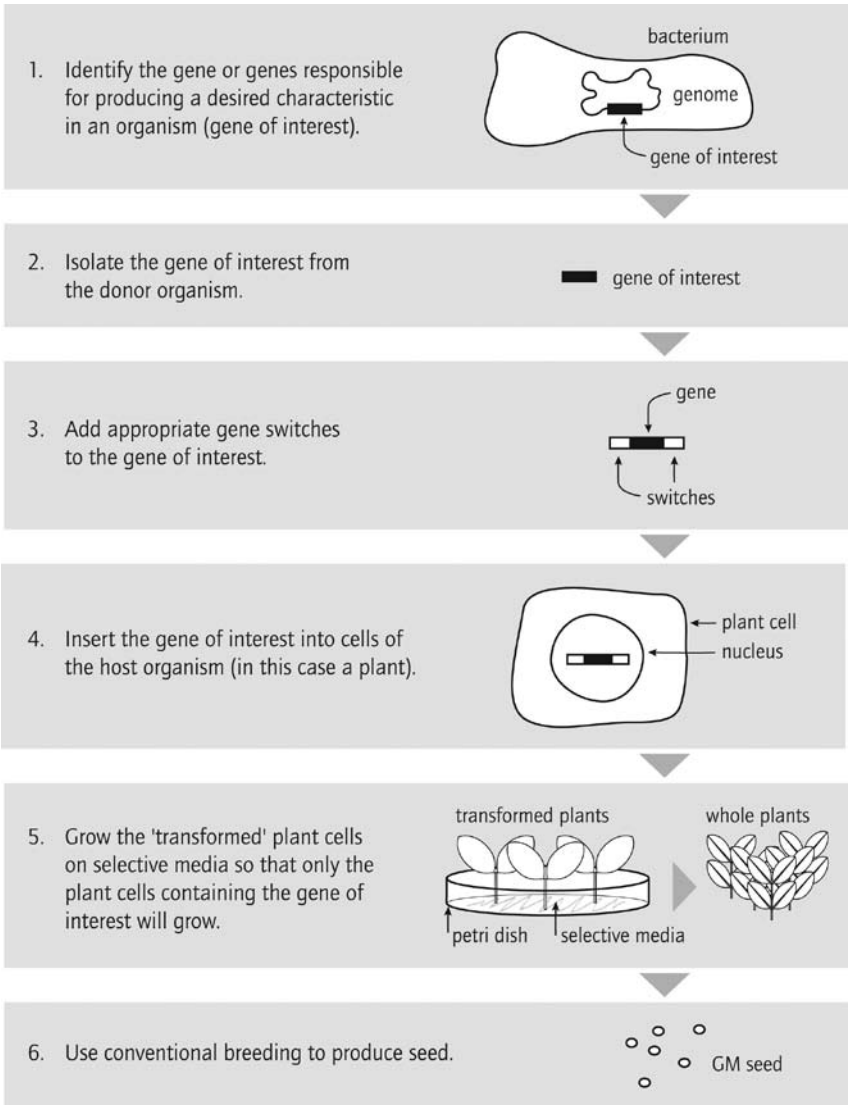
For more information on the methods used in genetic modification see Section 10.1.

cell), the bacterial switches need to be removed and different switches added to the gene to allow it to function in a plant cell. These switches may function in all plant cells or in specific plant tissues (for example, in root tissue only), so that the new trait will only be switched on in the roots. Thus, Step 3 in developing a GMO is to add appropriate gene switches to the gene of interest, to allow it to function in the cells of the recipient organism. In Figure 3.2, the recipient cell is a plant cell, and the gene switches therefore need to be able to function in plants.

In Step 4, the gene of interest, together with its gene switches, is inserted into the cells of the host organism, again using molecular biology techniques. Cells with the new gene inserted into their genome are referred to as 'transformed' cells. They contain all the usual genes of the recipient organism as well as the new gene or genes with which they have been transformed.

In the case of GM plants, Step 5 is to grow transformed cells into whole plants in the laboratory; this is done using selective nutrient-rich media. The plants are examined to ensure that they have the desired physical characteristic conferred by the new gene. In Step 6, the genetically modified plants are bred with conventional plants of the same variety to produce seed for further testing and possibly for future commercial use. The entire process from the initial gene selection to commercial production can take up to ten years or more.

Figure 3.2. Developing a genetically modified organism



3.5 Further information

More information on gene technology is available on the following websites:

http://www.biotechnology.gov.au
http://www.ogtr.gov.au
http://genetech.csiro.au
http://www.agresearch.co.nz/scied/search/index.htm

4 The safety assessment process

A GM food can only be sold legally in Australia or New Zealand if it has been assessed, found to be safe and approved by FSANZ. The producer of the GM food must apply to FSANZ for the food to be approved at the commodity level – that is, as a new primary product. Until food from a particular commodity has been approved, products containing food or ingredients derived from that commodity cannot be sold lawfully.

4.1 Principles used in the safety assessment process

FSANZ's process for assessing the safety of GM foods is based on concepts and principles developed by international organisations such as the World Health Organization (WHO), the Food and Agriculture Organization (FAO) of the United Nations, the Organisation for Economic Co-operation and Development (OECD) and the Codex Alimentarius Commission (see Appendix 4 for more information on these organisations and their role in food safety assessment). These concepts and principles are summarised in Box 4.1 and discussed in detail below.

Box 4.1 Principles used by FSANZ in assessing the safety of GM foods

Safety assessments for GM foods should:

- be based on the best current scientific knowledge
- be carried out on a case-by-case basis (because the safety concerns depend on the type of food and the nature of the genetic modification)
- fully consider the safety of each new component in a GM food (that is, any new DNA and protein) separately
- consider both the intended effects of the genetic modification (for example, the presence of a new protein) and the unintended effects (for example, changes to the levels of toxins or allergens)

Best current scientific knowledge

The safety assessment for a GM food should be based on the best current scientific knowledge, to ensure that the best possible assessment is made. To obtain this scientific knowledge, FSANZ seeks information from a variety of sources, including the applicant (that is, the organisation applying for approval for the GM food), published scientific literature, general technical information, independent scientists, other regulatory agencies, international bodies and the community. All scientific data provided by the applicant must have been generated according to international standards of good

See Section 15 for more detail about the scientific data used by FSANZ to assess the safety of GM foods.

laboratory practice, in laboratories that are independently audited (this allows FSANZ to be sure that the information provided is reliable). FSANZ can request further information from the applicant at any time. For example, if FSANZ finds that the information provided by the applicant is insufficient, or if new information comes to light that requires further consideration.

Case-by-case assessments

GM food obtained from a particular type of GM microorganism, plant or animal requires a separate safety assessment. GM foods cannot be assessed as a single class because the safety concerns will vary, depending on the type of food and the type of genetic modification. For example, if two types of soybean were modified to have different characteristics, or were modified in different ways to achieve the same characteristic, separate safety assessments would be needed for the different GM soybeans. Similarly, if the GM soybeans were modified further, they would require another safety assessment.

Once foods derived from a GM microorganism, plant or animal have been assessed as safe, they may be used as ingredients in other foods. For example, oil, flour and lecithin obtained from GM soybeans can be used in foods such as breads, pastries and snack foods if the GM soybeans have been assessed as safe. The various breads, pastries and snack foods containing the GM soybean do not need to be assessed individually.

So far, the applications made to FSANZ to approve GM foods have only concerned GM plants or microorganisms, not GM animals, although this may change in the future (see Section 6.2).

Full consideration of each new component

GM foods generally contain both new genetic material (that is, new DNA) and new proteins (coded for by the new DNA). They are 'new' in the sense that they may not have previously existed in the food being considered. FSANZ considers the safety of each of these new components in the GM food separately and fully.

Consideration of intended and unintended effects

See Sections 11 and 12 for more information about assessing the intended and unintended effects of the genetic modification.

The 'intended effects' of genetic modification are those that happen as a direct result of the presence of new genetic material and proteins, as described above. However, genetic modification may also have 'unintended effects'. For example, it may change the levels of toxins, allergenic components, nutrients or antinutrients[2] in a food. The safety assessment looks specifically at these characteristics, to ensure that there are no major differences between the GM food and its conventional equivalent. FSANZ assesses any significant differences between the GM food and the conventional food to see whether they could be harmful to health.

See Section 7.4 for more detail about genetic material from GM foods transferring to cells in the human gut.

Another potential unintended effect that FSANZ considers in a safety assessment is whether new genetic material in the GM food could affect human health, by moving from the GM food to bacterial cells in the human gut.

2. Antinutrients are substances that prevent nutritional components from being absorbed

4.2 Basis for approval of GM foods

FSANZ prepares a detailed report on the safety assessment of each new GM food, covering all the points outlined below. In general, a GM food is considered safe for human consumption if FSANZ is satisfied of the following:

All new genetic material has been examined in detail.

- Where did the new genetic material come from, what is its function, how was it put into the GM food and how is it arranged within the genetic material of the plant or animal?

The new genetic material stays the same and is passed on in a predictable way from generation to generation.

- Is the new genetic material stably integrated within the DNA of the GM organism?
- Is the novel trait expressed consistently over a number of generations?

All new proteins have been examined in detail.

- Where and when are the new proteins found in the plant or animal?
- Do they have the expected size, structure and biological activity?

The new proteins are unlikely to be toxic or allergenic.

- Do the new proteins come from living organisms that contain no major toxins or allergens?
- Are the new proteins dissimilar to known toxins and allergens?
- Do the new proteins lack other physical and biochemical characteristics typical of toxins and allergens?

The new proteins do not cause any detectable toxicity in animal studies.

- When the purified new proteins are given in large doses to rats or mice, are there any adverse effects?

The potential transfer of new genetic material to bacterial cells in the human digestive tract will not have a significant impact on human health.

- Are antibiotic resistance genes present? Is the corresponding antibiotic used in human or veterinary medicine?
- What would be the health impact if the new genes were to be transferred to bacteria in the human gut?

The composition of the food, including naturally occurring toxins, allergens and antinutrients, is not significantly altered compared to the non GM food.

- Is the composition of the food (for example, the proteins, fat, fibre, carbohydrate, amino acids, vitamins, minerals, moisture content and other biologically active molecules) substantially different from that of the conventional food?
- If so, does the difference found in the GM food affect the safety of the food, and will it make the food less nutritious or healthy?

Consultation with the public

FSANZ is committed to open and transparent processes and so engages with the public to keep them informed and seek their views. Each safety assessment for GM foods is made available on the FSANZ website (http://www.foodstandards.gov.au). FSANZ staff also provide information to the media and run educational activities, to stimulate informed debate.

The aim of consulting with the public on GM food safety assessments is to ensure that any legitimate issues are addressed before a final decision is made on whether or not to approve the GM food. If necessary, FSANZ also asks an external panel of independent experts to review the safety assessment report.

As discussed in Section 1, all foods carry benefits and risks. For this reason, no food, whether GM or not, can be guaranteed to be absolutely safe for all people. Thus, despite the extensive testing of GM foods, their absolute safety cannot be guaranteed. However, the safety assessment process used for GM foods is more thorough than that used for any other food. It is designed to ensure that GM foods provide all the benefits of conventional foods with no additional risks.

5 GM foods in the marketplace

5.1 GM foods available in Australia and New Zealand

GM foods from soybeans, canola, corn, potato, sugar beet and cotton are currently approved for sale in Australia and New Zealand. Table 5.1 lists the main GM crops, the traits that have been added through genetic modification and the potential food uses of these crops. So far, insect protection and herbicide tolerance are the characteristics most commonly introduced into crops.

As at June 2005, FSANZ has approved twenty-five GM foods, all of which come from the six crops listed in Table 5.1. Most of the GM foods available in Australia today come from GM crops grown and processed overseas. To date, the only GM food crops approved for growing on a commercial scale in Australia are certain varieties of GM cotton and two varieties of GM canola. The approval processes for allowing GM crops to be grown in Australia and New Zealand are separate from the processes used for approving GM food safety.

Table 5.1 GM foods currently approved for sale in Australia and New Zealand[3]

Crop	Trait	Examples of potential food uses
Soybean	• Herbicide tolerance • High oleic acid content	Soy foods include soy beverages, tofu, soy oil, soy flour and lecithin. Products containing soy may include breads, pastries, snack foods, baked products, fried products, edible oil products and special purpose foods
Canola (oilseed rape)	• Herbicide tolerance	Canola oil. Products made with canola oil may include fried foods, baked products and snack foods.
Corn	• Insect protection • Herbicide tolerance • Insect protection plus herbicide tolerance	Corn foods include kernels, oil, corn flour, sugar and syrup. Products containing corn may include snack foods, baked goods, fried foods, edible oil products, confectionery, special purpose foods and soft drinks
Potato	• Insect protection • Insect protection plus virus protection	Whole potatoes. Products containing potato may include snack foods, processed potato products and other processed foods.
Sugar beet	• Herbicide tolerance	Sugar beet is processed into sugar which may be used in processed foods.
Cotton	• Insect protection • Herbicide tolerance • Insect protection plus herbicide tolerance	Cottonseed oil and linters may be used in blended vegetable oils, fried foods, baked foods, snack foods, edible oil products and small goods casings.

5.2 GM foods available overseas

More GM foods have been approved overseas than in Australia and New Zealand. GM foods approved for sale in the United States of America (USA), Canada, Japan or the European Union, but which have not yet been assessed in Australia and New Zealand, include varieties of rockmelon, chicory, flax, papaya, radicchio, rice, squash and tomato. Currently, food produced from these GM crops is not permitted in Australia and New Zealand.

6 GM foods in the future

6.1 GM food crops in development

Development of new GM crops requires many years of research and development in the laboratory and in the field, to discover and understand new traits. At present, only a small number of food plants have been genetically modified, and most of the modifications have been for the benefit of growers (for example, herbicide tolerance and resistance to pests). In the future, a wider range of fruit, vegetable and cereal crops are likely to be genetically altered in various ways, some of which could be of benefit to consumers. For example, modifications could be used to create GM foods with increased vitamin and mineral content, or healthier fatty acid profiles. Other traits could provide environmental benefits such as crops that are more tolerant of drought.

3. All FSANZ's assessments of GM foods are available on the FSANZ website at http://www.foodstandards.gov.au/whatsinfood/gmfoods/gmcurrentapplication1030.cfm. These are also available as technical reports at http://www.foodstandards.gov.au/mediareleasespublications/technicalreportserie1338.cfm.

6.2 GM animals

Gene technology can be used to modify animals as well as plants. GM animals – often referred to as 'transgenic' animals – have had their genetic material modified in some way. Such animals might have been modified to contain one or more new genes from other organisms. Alternatively, one of their own genes could have been altered, perhaps by being duplicated or removed.

The types of animals that are being genetically modified include cows, sheep, goats, pigs, fish and insects. Animals are being modified to develop pharmaceutical and health-related products, as well as food and agricultural products. For example, GM fish have been developed that contain a gene for an antifreeze protein, allowing them to survive in very cold water. The gene for the antifreeze protein was taken from another species of fish that thrives in freezing water.

See Appendix 4 for more information on the international work on the safety of GM foods.

The regulatory system for GM animals and their products has been the subject of increasing recent attention and discussion among the media, policymakers, research scientists and the general public. Many countries are considering how food derived from GM animals might be regulated, and what type of scientific data might be required to assess its safety. International bodies, including the FAO, the WHO and Codex Alimentarius, have set up committees of experts to consider this issue.

In Australia and New Zealand, food from GM animals will be regulated, as for GM plants, under Standard 1.5.2 – *Food Produced Using Gene Technology* (see Section 2.4).

As of June 2005, no GM animals have been approved for food use anywhere in the world. FSANZ will continue to monitor this situation and to actively participate in the international debate on this issue.

7 Answers to frequently asked questions

7.1 What if I eat DNA in a GM food?

We eat DNA every day – it is a completely natural and harmless component of most of the foods that we eat. For example, DNA is present in every cell of foods such as fruit, vegetables, cereals and meat. Thus, whenever we eat those foods, we are eating the DNA that they contain. In the digestive system, the food, including the DNA, is broken down to its building block components, which can then be metabolised by the body.

In terms of its chemical structure, the introduced DNA in a genetically modified organism (GMO) is identical to any other DNA, regardless of which species the introduced DNA may have come from. GMOs simply contain new or modified genes that give them their particular distinguishing characteristics, in addition to the 50 000–100 000 genes that are naturally present.

The digestive system digests all DNA in exactly the same way. It cannot tell the difference between DNA from GMOs and any other DNA. If you eat DNA in a GM food or a conventional food, it will not change your own DNA or that of your children.

7.2 What about allergens in GM foods?

Most foods do not cause an allergy in most people, but for the 1 in 50 or so people who have a food allergy of some sort, certain proteins in food can cause an unusual immune reaction. The proteins that

provoke this reaction are known as allergens, and people with allergies generally react to just one or a few allergens in one or two specific foods.

Common examples of foods that cause allergies are cow's milk, eggs, fish, crustaceans, peanuts, tree nuts, soybeans, wheat and sesame seeds. Allergies to these foods cause over 90% of serious allergic reactions to foods. Although allergies to other foods occur, they tend to be far less common.

The severity of an allergic reaction will depend on the person and the nature of the allergy. For example, nuts tend to cause more severe allergic reactions than other allergens. In the worst cases, extremely small traces of an allergen can lead to severe reactions. The most severe form of allergic reaction, called anaphylactic shock, can be life threatening.

It is also possible to outgrow some allergies. For example, children with allergies to eggs or milk will normally be able to eat these foods as adults without having a reaction. Many other allergies are likely to stay for life.

If conventional food that contains allergens is genetically modified, the GM food may contain those allergens, just as the conventional food does. For example, soy naturally contains proteins that cause an allergic reaction in some people. Unless these specific proteins are removed, they will also be found in GM soy varieties.

In assessing the safety of a GM food, FSANZ checks to ensure that the levels of naturally occurring allergens in GM foods have not significantly increased above the natural range in the conventional food. FSANZ also checks to ensure that the new proteins in GM foods are not likely to be allergenic. It does this by asking the following questions:

- Do the new proteins come from living organisms that contain significant allergens?
- Is the sequence of amino acids (the building blocks that make up proteins) in the new proteins similar to that of any known allergens?
- Do the new proteins have any other physical or biochemical characteristics typical of allergens?

If the answer to one or more of these questions is 'yes', then further information is required for FSANZ to work out whether or not the new protein is allergenic.

If FSANZ had scientific evidence that a new protein in a GM food was allergenic, it is unlikely that the food containing that protein would be given approval for sale in Australia or New Zealand, even with appropriate labelling. This is because it would not be appropriate to increase the community's exposure to allergenic proteins in the food supply.

See Section 11.3 for more detail about the process of assessing the allergenicity of GM foods.

7.3 What about toxins in GM foods?

All substances — both natural and human-made — are toxic at some dose. However, substances classed as toxins are those that can be harmful to health at typical levels of exposure. A number of different toxins are found naturally in various foods, but the vast majority of these are present at concentrations well below the level that would harm the consumer.

Examples of toxic substances found in foods include:

- glycoalkaloids found in green potatoes
- fungal toxins that sometimes contaminate food
- glucosinolates in cabbage, cauliflower, broccoli, brussels sprouts and canola

- erucic acid in canola
- psoralens in celery
- cyanogenic glycosides in bitter almonds
- substances in poisonous species of fish and mushrooms.

Thus, toxic substances are naturally present in many conventional foods that are subsequently genetically modified. For example, both GM and conventional varieties of canola naturally contain erucic acid, and there is a limit on the amount of erucic acid that is allowed in foods derived from canola, such as canola oil. These limits apply whether the food is derived from conventional or GM canola.

Unless any toxins present in a conventional food are specifically removed, they will remain in the GM version of the food. FSANZ compares the levels of naturally occurring toxins in the conventional food with those in the GM food. If a safety assessment found that levels of naturally occurring toxins were higher in a GM food, FSANZ would need to assess how much of the food is normally eaten (that is, the dietary intake), to ensure that the levels of toxins consumed would not be harmful to health.

FSANZ also checks to ensure that the new proteins in GM foods are not likely to be toxic. It does this by asking the following questions:

- Do the new proteins come from a source that is known to contain significant toxins?
- Are the new proteins similar to known toxins?
- In animal studies, do the new proteins cause acute toxicity?

See Section 11.2 for more detail about the process of assessing the potential toxicity of novel proteins in GM foods.

If a safety assessment suggested a new protein in a GM food was a toxin and might result in adverse health effects at levels of expected dietary intake, the GM food would not be approved for sale in Australia or New Zealand.

7.4 Is there a concern with antibiotic resistance genes in GM foods?

There has been concern in the community about the consequences to human health and safety if genes present in GM foods were able to transfer to cells in the human digestive tract. Sometimes, genes that give bacteria resistance to a particular antibiotic have been used in the genetic modification process. A particular concern is the possibility that the genes conferring antibiotic resistance could transfer to disease-causing bacteria in the human digestive tract. If this were to happen, the concern is that it could result in infections that are resistant to treatment with antibiotics.

However, the antibiotic resistance genes currently present in GM foods code for resistance to antibiotics that are not widely used in human medicine, because resistance to them is already widespread.

In the future, as genetic modification techniques improve, antibiotic resistance genes will not be present in GM foods because they will either have been removed during development or have been replaced by other types of marker genes. Nevertheless, FSANZ considers this issue on a case-by-case basis in all safety assessments for GM foods, because the human health considerations depend on the nature of each particular genetic modification.

See Section 10.5 for more detail about the issue of antibiotic resistance genes in GM foods.

7.5 What about herbicide and pesticide residues in GM foods?

All foods sold in Australia and New Zealand must comply with relevant maximum residue limits, whether the foods have been genetically modified or not. This means that foods cannot be sold if they contain levels of chemical residues that are above the limit that has been set for that substance. Therefore, even if herbicide or pesticide uses change because crops have been modified to tolerate these chemicals, food sold in Australia and New Zealand will not contain unsafe levels of residues. In some cases, the level of herbicide and pesticide used on GM crops may actually be reduced.

Maximum residue limits are not included in the joint Australia and New Zealand food standard setting system because these are nationally specific and relevant to the agricultural environment. In Australia, FSANZ, the Australian Pesticides and Veterinary Medicines Authority and the Therapeutic Goods Administration together establish the Australian maximum residue limits (which are set out in the *Australia New Zealand Food Standards Code*), New Zealand's maximum residue limit food standards are set by the New Zealand Food Safety Authority. The standards of both countries take into account growing conditions, good agricultural practise and the pattern of consumption of the food that may contain residues. International standards for maximum residue limits set by the Codex Alimentarius Commission of the United Nations (see Appendix 4 for more information on this organisation) are also taken into account.

7.6 Will GM foods be safe in the long term?

The long-term safety of foods relies on an understanding of the nature and composition of the food, together with a history of safe use for that food or a related food. In this respect, assuring the safety of GM food is no different from assuring the safety of more traditional foods. It is important to remember that foods carry both benefits in the form of nutrients and, in some cases, risks in the form of antinutrients, toxins or allergens. A detailed understanding of the composition of a food can provide a better understanding of the nature and extent of any risks and thus a strong assurance of safety.

The long-term safety of substances added to food (food additives and processing aids) or substances used in food production (agricultural and veterinary chemicals) is generally assessed though long-term studies in animals fed high levels of these chemicals. However, such studies are not appropriate for examining the safety of whole foods, including GM foods, because of the experimental difficulties of feeding animals with high levels of whole foods, particularly when these foods are not part of the animal's normal diet.

As described in detail in Part 2 of this booklet, GM foods undergo a thorough safety assessment that is appropriate for whole foods. The safety assessment process is designed to ensure that GM foods provide all of the benefits of conventionally produced foods and that no additional health risks have been introduced as a result of the genetic modification.

In recent times, we have begun to understand more about the nature and composition of our food and to further investigate the important relationships between our diet and our health. Over the long-term, a balanced diet of nutritious foods is probably more important than the level of intake of any one food.

7.7 What about food from animals that have eaten GM stockfeed?

Many animal feeds are derived from the same GM food crops that are used for human consumption. Concerns are occasionally expressed that this practice may pose an indirect risk to humans, through consumption of the meat, milk and eggs derived from such animals.

Scientific evidence published so far, including the OECD document entitled *Considerations for the safety assessment of animal feedstuffs derived from genetically modified plants*[4], indicates that feeding GM plant material to livestock and poultry does not affect the nutritional value or safety of the meat, milk and eggs derived from those animals.

Fragments of plant DNA have been detected in animal tissues, including milk, but there is no basis to suppose that the new DNA poses a hazard.

Of more concern is the potential for a GM crop grown for stockfeed, which has not been assessed for safety for human consumption, to be inadvertently mixed with other crops destined for the human food supply. For this reason, Australia's Office of the Gene Technology Regulator has agreed not to approve any GM food crop for use as stockfeed unless it has also been approved by FSANZ for human consumption. This means that a GM food crop cannot be grown for stockfeed in Australia unless it has been approved for human consumption.

4. http://www.olis.oecd.org/olis/2003doc.nsf/LinkTo/env-jm-mono(2003)10

Part 2
A detailed look at the safety assessment of GM foods

8 Introduction to Part 2

When assessing the safety of a GM food, FSANZ looks carefully at the newly introduced genetic material, new proteins and the general characteristics of the particular food. The safety assessment covers five main areas:

- the history of use of the donor and recipient organisms
- the description of the genetic modification
- characterisation of the new proteins
- compositional analysis
- nutritional impact.

This section describes the safety assessment in detail, focusing on each of the areas outlined above. A case study (herbicide-tolerant soybeans) has been chosen to illustrate each step of the safety assessment process. Text relating to the case study appears in boxes, such as the one below.

Case study — herbicide-tolerant soybeans (Roundup Ready soy)

Background

Roundup is a herbicide used by farmers to kill weeds. The active ingredient in Roundup is the chemical glyphosate. This chemical works by blocking the function of one of the plant's enzymes (a type of protein), known as EPSPS (5-enolpyruvylshikimate-3-phosphate synthase). Plants need EPSPS enzymes to make certain amino acids, which are used to create proteins.

Glyphosate kills crops as well as weeds; therefore, the biotechnology company Monsanto looked at how soybean crops could be protected from the effects of this chemical. The company focused its research on a naturally occurring soil bacterium (*Agrobacterium*), because the EPSPS enzyme in this bacterium is tolerant to glyphosate, meaning that *Agrobacterium* is not killed by the herbicide.

Monsanto purified the bacterial gene coding for the EPSPS enzyme, and put it into soybean plants. These plants (known as Roundup Ready soy) produce two EPSPS enzymes: the soybean version already present in the plant, and the bacterial version added in the genetic modification. When the herbicide is applied, the soybean EPSPS enzyme is blocked and cannot function. However, the plant survives because the bacterial EPSPS enzyme that has been transferred into the plant remains active, allowing it to continue to make the necessary amino acids. Thus, the bacterial protein is able to function in the soybean in the same way that it does in the soil bacterium.

The application

Monsanto applied to FSANZ (at that time the Australia New Zealand Food Authority, ANZFA) to have Roundup Ready soy (line 40-3-2) included in the list of permitted foods under Standard 1.5.2 of the *Australia New Zealand Food Standards Code*. The application comprised about 3000 pages of information and experimental data. It included quality assurance certification showing that all the scientific experiments were carried out in independently audited laboratories, according to international standards of good laboratory practice.

All the information contained in the application is publicly available through the FSANZ public register, and many of the scientific studies have been published in scientific journals that are publicly available and peer-reviewed.

The assessment

FSANZ staff assessed the application and, where necessary, used relevant information from other sources, such as the published scientific literature, independent scientists, other agencies, international bodies and public submissions. Satisfied that Roundup Ready soy (line 40-3-2) was safe, FSANZ then approved the sale of foods derived from this GM food. The safety assessment for Roundup Ready soy formed part of the assessment report (previously called the full assessment) for this food and is available from FSANZ on request.

9 History of use

In the first part of a safety assessment, FSANZ looks at the history of use of the conventional food (the recipient or host organism). This includes identifying:

- the edible components of the food
- food products commonly containing these edible components
- processing requirements.

FSANZ also examines the organism that the new gene came from (referred to as the donor organism). If the donor organism is known to be toxic or allergenic to humans, it is unlikely that FSANZ could approve a GM food containing a gene from that organism. However, if there is scientific evidence that the specific protein produced by the new gene does not cause the toxicity or allergenicity found in the host organism, then the food could be approved, if it satisfies the other criteria examined in the safety assessment.

See Section 4 for more information about the safety assessment process for GM foods.

Case study — Roundup Ready soy

History of use of the host organism

In the case of Roundup Ready soy (line 40-3-2), the host organism is the soy (or soybean) plant.

The part of the soy plant that is consumed by humans is the seed — the soybean. Soybeans can be cooked and consumed whole or processed into many types of foods. Foods made from soy include soy beverages, tofu, soy oil, soy flour and lecithin. Products containing soy may

include breads, pastries, snack foods, baked products, fried products, edible oil products and special purpose foods such as infant formula.

Most of the Roundup Ready soy imported into Australia and New Zealand is processed into oil for human consumption, or into animal feed.

Since soy is used in a variety of products and has an established history of use, FSANZ judged that it was an acceptable host organism.

History of use of the donor organism

The donor organism for Roundup Ready soy (line 40-3-2), is the common soil bacterium *Agrobacterium* (species strain CP4), from which the EPSPS gene was derived. *Agrobacterium* is found everywhere in the environment, so it could be expected to be commonly encountered in foods harvested directly from soil, such as potatoes. As *Agrobacterium* has been ingested by humans over a long period of time, and there is no evidence that it causes toxicity or allergenicity in humans, FSANZ also determined that the donor organism was acceptable.

10 Description of the genetic modification

The next step is to consider information about the genetic modification. Aspects of the genetic modification that FSANZ considers are:

- the methods used to introduce any new genes (or to modify existing genes)
- the function and regulation of any new genes
- the characterisation of any new genes in the host organism (including the number of copies and the DNA sequence of any new genes)
- stability of any new genes
- effects of any new genes on human health.

Each of these aspects is discussed below.

10.1 Methods used in the genetic modification

Several methods can be used to put new genes into living organisms, depending on the species being modified. In plants, the two most common methods are *Agrobacterium*-mediated transformation (adapted from a process that already occurs in nature) and particle bombardment. FSANZ requires clear descriptions of the methods used to genetically modify each organism.

Case study — Roundup Ready soy

Methods used in the genetic modification

Roundup Ready soy was produced using particle bombardment. In this process, the plant cells are bombarded with microscopic particles of gold or tungsten coated with DNA that contains the new EPSPS gene from the donor organism (*Agrobacterium*). The aim is to get the new gene across the plant cell wall, so that it can be incorporated into the plant cell's genetic material.[5]

5. An animation explaining this process can be viewed at http://www.agriculture.purdue.edu/agbiotech/images/Genegun1.html

10.2 Function and regulation of the new genes

To understand how the new genes function in the plant, FSANZ looks at:

- the new genes and their products (that is the proteins coded for by the new genes)
- the genetic material that controls how, where and when the new genes are switched on
- the genetic material that targets any new proteins to specific parts of the cell.

Case study — Roundup Ready soy

Function and regulation of the new genes

Roundup Ready soy contains a single new gene, which codes for the EPSPS enzyme and comes from a strain of the common soil bacterium, *Agrobacterium*.

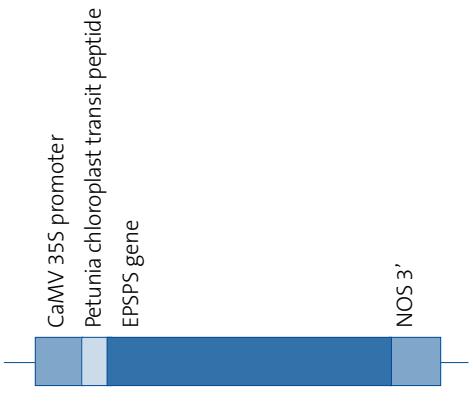
Cells control the activity of genes through 'regulatory' sequences; these are pieces of DNA that do not code for a protein, but instead regulate genes; for example, by switching them on or off. Usually, plant cells do not recognise the regulatory signals found in bacteria. Therefore, when bacterial genes are transferred into plants, the regulatory sequences must be replaced by sequences the plant recognises. Thus, because the EPSPS gene is from a bacterium, it can only work in a plant cell if its regulatory sequences are replaced by sequences that are recognised by a plant cell. The regulatory sequences in Roundup Ready soy (line 40-3-2) are shown in the Figure 10.1, below.

In front of the bacterial EPSPS gene in Roundup Ready soy is a regulatory sequence that tells the plant to turn the gene on. Known as the CaMV 35S promoter, this sequence comes from the cauliflower mosaic virus, a common virus that infects cauliflowers. At the other end of the EPSPS gene, another regulatory sequence tells the plant where the EPSPS gene ends. This sequence, known as NOS 3' , comes from a nopaline synthase gene found in bacteria. Although NOS 3' is from a bacterium, it is able to function in plants.

A further regulatory sequence comes from petunia. Referred to as the 'chloroplast transit peptide sequence', its function is to tell the plant cell to transport the bacterial EPSPS enzyme into the chloroplast of the cell. For the plant to be tolerant to Roundup herbicide, the EPSPS enzyme needs to function in the chloroplast, because this is where the amino acids that form the building blocks of proteins are produced. Once the EPSPS enzyme has been transported into the chloroplast, the chloroplast transit peptide sequence is removed, so that the EPSPS enzyme can function.

The entire DNA sequence of the new bacterial EPSPS gene and its flanking DNA were provided by the applicant and assessed by FSANZ.

Figure 10.1. EPSPS gene and regulatory elements



10.3 Characterisation of the new genes

FSANZ requires detailed information from the applicant on the arrangement of the new genetic material in the genome (the complete genetic make-up) of the host organism. This includes the results of standard molecular biological techniques that demonstrate how many complete or incomplete copies of the new genetic material are present. FSANZ also compares the DNA sequence of the new genetic material in the GM plant's genome with that of the original DNA to determine if there are any unexpected changes in the DNA sequence in the plant.

Newly introduced genetic material is normally inserted into a random location in the host genome. In complex life forms, such as plants and animals, the genes themselves usually make up only a small fraction of the total genome. Most of the genome is composed of repetitive DNA sequences that do not correspond to genes and whose function is yet to be determined. Therefore, it is likely that newly introduced genetic material will be inserted into this repetitive DNA, and will not have any measurable impact on other genes. There are several ways to test whether or not this has happened:

- Where new genetic material has been inserted into a segment of DNA coding for a gene, the gene in question is likely to be inactivated. If the gene has an important function, its inactivation is likely to cause some visible effect on the development, growth or reproduction of the plant (or animal).
- GM plant varieties that progress to the stage of commercialisation have been through many stages of selection. Any plants not found to develop, grow and reproduce normally are discarded. Foods derived from GM plants are also extensively tested in other ways (see case study below); thus, if an important gene has been inactivated by the genetic modification, it is likely that this would be detected.
- In some cases, the new genetic material does insert into a segment of DNA that encodes a gene, resulting in a hybrid gene[6]. Standard molecular biology techniques can be used to detect the presence of hybrid gene products (RNA or protein) in GM varieties. In such cases, the characteristics of the hybrid gene and its product would be very closely examined in the safety assessment process.

Case study — Roundup Ready soy

Characterisation of the new gene in the soybean plant

Standard molecular biology techniques were used to show that a single full copy of the bacterial EPSPS gene plus flanking DNA sequences was present in the genome of Roundup Ready soy (line 40-3-2). This gene was intact and of the correct size and sequence.

10.4 Stability of the genetic changes

The genetic changes in each GM plant must be stable. The new genetic material is considered to have become a stable part of the host genome if they remain the same over several generations of plants produced by conventional breeding. This means that the newly introduced traits should be shown to pass from one generation to the next in a normal predictable way, following the principles of inheritance.

6. This refers to a gene that consists of part of an original plant gene and part of the new DNA. A hybrid gene may or may not produce a gene product (protein), depending on whether the correct regulatory sequences are also present.

Molecular analyses of a number of generations are used to show that no changes have occurred in the arrangement of the new DNA. The applicant also needs to show that the amount of new gene product is constant (and thus the new trait, e.g. herbicide tolerance, remains stable) over subsequent generations.

Case study — Roundup Ready soy

Stability of the genetic changes

The new DNA in Roundup Ready soy (line 40-3-2) was examined in third and sixth generation plants, using standard molecular biology techniques. This showed that the new DNA was stably integrated into the soy genome. Also, the Roundup Ready trait was studied over more than seven generations and was shown to be passed from one generation to the next in a normal and predictable way, according to the laws of inheritance.

10.5 Effect of the new gene on human health

Some people are concerned that new genes, particularly antibiotic resistance genes, in GM foods might be able to transfer to disease-causing bacteria in the human digestive tract. Antibiotics are chemicals that either kill bacteria or prevent them from multiplying, and are therefore used to treat bacterial infections. Antibiotic resistance genes code for proteins that protect bacteria from the action of particular antibiotics. If bacteria acquire a particular antibiotic resistance gene, they will not be killed when treated with the corresponding antibiotic. Just as there are many different types of antibiotics working in different ways, there are also many different types of antibiotic resistance genes. Such genes occur naturally in some types of bacteria, and they are often found on small DNA molecules known as plasmids that can transfer naturally between bacteria in the environment.

If antibiotic resistance genes from GM foods were to transfer to bacteria in the human digestive system, this might diminish the effectiveness of the relevant antibiotics in the treatment of human disease.

Why are antibiotic resistance genes used in genetic modification?

Antibiotic resistance genes are used to mark the presence of other genes during the process of genetic modification. When a new gene is inserted into a plant cell it is often attached to a second gene — an antibiotic resistance gene — that allows scientists to easily determine which plant cells contain the new gene. The antibiotic resistance gene is attached to the gene which gives the desired trait (for example, a herbicide tolerance gene); thus, if the plant cells can grow in the presence of the relevant antibiotic, this indicates that the new gene will also be present in those cells. Therefore, antibiotic resistance genes are sometimes called 'marker' genes. The use of antibiotic resistance genes as markers in GM crops is likely to be phased out in the future because of concerns over their use and the growing availability of marker genes that do not rely on antibiotic resistance. Also, techniques are now available for removing marker genes before commercialisation; making the removal of antibiotic resistance a possibility.

Is transfer of new genes a concern for human health?

Whether new genetic material in GM foods could transfer to gut bacteria and impact on human

health has been considered in detail by the World Health Organization (WHO) and several European expert advisory panels, and in numerous scientific papers published in peer reviewed journals. There is general agreement that new genetic material in GM foods will effectively have no impact on human health, for the reasons outlined below:

- Humans have always consumed large amounts of DNA as a normal component of food, with no evidence of any adverse effect on human health.
- New DNA sequences in GM foods make up only a minute fraction of the total DNA in the food (generally less than 0.01%) and do not pose any special additional risks compared with the large amount of DNA naturally present in all foods.
- Current scientific knowledge has not revealed any DNA sequences from ingested foods that have been incorporated into human DNA.
- The transfer of antibiotic resistance from GM foods to bacteria in the human digestive tract is extremely unlikely, because of the many complex and improbable steps that would need to take place consecutively for this to occur.
- Even if there were cases of antibiotic resistance transferring from GM food to bacteria in the human digestive tract, this is unlikely to have any significant health impact because bacteria with resistance to the antibiotics in question are already widespread in nature.

Do GM foods available in Australia and New Zealand contain antibiotic resistance genes?

Some GM foods currently available in Australia and New Zealand contain genes coding for resistance to the antibiotics kanamycin/neomycin, spectinomycin/streptomycin and ampicillin. These genes are unlikely to have a significant impact on human health for the reasons outlined above.

Case study — Roundup Ready soy

Impact on human health from potential transfer of new genetic material to cells in the human digestive tract

This issue is most relevant to the potential transfer of antibiotic resistance from GM foods to gut bacteria. As Roundup Ready soy (line 40-3-2) contains no antibiotic resistance genes, this is not a concern in this case.

The only new gene in Roundup Ready soy that could potentially be transferred to cells in the human digestive tract is the bacterial EPSPS gene. No impact is expected on human health if this gene were to transfer to bacteria in the human gut, because the EPSPS enzyme in Roundup Ready soy would function in the same way as the EPSPS enzyme naturally present in the gut bacteria.

Finally, there is no evidence that DNA sequences from ingested foods have ever been taken up by human cells and incorporated into human DNA.

11 Characterisation of new proteins

11.1 Nature of the new protein

The safety assessment includes an examination of the nature and function of any new proteins in the GM food. Standard molecular and biochemical techniques are used to verify that the size of any new protein is as expected, and to quantify how much new protein is present in particular tissues.

The presence and level of new proteins in particular components of GM varieties used as food, or in food preparation, may present safety issues. FSANZ assesses this in the parts of GM plants that are actually eaten. It is possible that the new protein is:

- only expressed in non-edible parts of the plant
- inactivated, denatured or removed by heat or processing (that is cooking)
- only present at very low levels in the edible part of the plant.

This information is taken into consideration in determining if the new protein in the GM food is safe.

Case study — Roundup Ready soy

Nature of the new protein

The bacterial EPSPS enzyme in Roundup Ready soy (line 40-3-2) has a similar structure and function to the EPSPS enzyme naturally present in soybean plants and other plants that form part of the food supply. The bacterial and plant EPSPS enzymes have the same function, but differ in their tolerance to the herbicide Roundup, with the bacterial EPSPS being more tolerant of Roundup than the soybean enzyme.

Published scientific studies have shown that a single amino acid change in the EPSPS enzyme makes it tolerant to glyphosate. The amino acid sequence of the bacterial EPSPS enzyme is known — it is made up of 457 amino acids and has a total molecular weight of 47.6 kiloDaltons.

In the safety assessment, the level of the bacterial EPSPS enzyme in fresh or processed edible parts of soy was found to make up less than 0.1% of the total protein. The EPSPS enzyme was shown to have no activity in the edible parts of the soy, because the enzyme is inactivated by heat during processing of the food.

11.2 Potential toxicity of new proteins

This part of the assessment examines the potential toxicity of any new proteins in the GM food.

The applicant must supply data on whether there are any known toxins in the donor organism. Computer searches of publicly available databases of protein sequences are also used to check that the amino acid sequence of any new protein is not highly similar to known toxins.

The applicant must also supply data demonstrating that new proteins do not cause any detectable toxicity in animal studies. In these studies, the purified new protein is given to animals such as rats, mice and quails at high doses (100–1000 times more than a person would expect to eat in a normal

portion of GM food). The animals are usually observed for a period of time (usually 14 days) after being given the protein, to determine whether there are any obvious adverse effects caused by the new protein. The animals are then sacrificed and post-mortems are used to determine any changes in pathology compared to control animals.

Case study — Roundup Ready soy

Potential toxicity of new proteins

The bacterial EPSPS enzyme in Roundup Ready soy (line 40-3-2) has no significant similarity to any known toxin. This was tested by comparing the sequence of the bacterial EPSPS enzyme with 1935 known protein toxins found in publicly available databases. The sequences were compared using internationally accepted mathematical algorithms. No significant similarities in protein sequence were detected.

Standard molecular biology techniques were used to show that the bacterial EPSPS enzyme is broken down in a matter of seconds or minutes following digestion in simulated gastric and intestinal fluids. As the soy must be cooked before eating, the protein is likely to have been substantially degraded before it even reaches the human digestive system.

Toxic proteins usually act in an acute way (that is, they have an immediate, intense effect). The purified bacterial EPSPS enzyme was tested for acute toxicity in mice. There were no adverse effects on the mice at doses of up to 572 mg/kg — estimated to be at least 1300 times higher than the level expected to be consumed by humans.

Finally, there is no history of EPSPS proteins being toxic. The bacterial EPSPS enzyme in the soybean has a similar structure and function to the EPSPS enzyme naturally present in the soybean and other plants forming part of the human food supply.

On the basis of the evidence described above, the bacterial EPSPS enzyme in Roundup Ready soy is unlikely to be toxic.

11.3 Potential allergenicity of new proteins

In this part of the assessment, FSANZ looks at whether any new protein present in the GM food is likely to cause an allergic reaction in some people.

Which foods are likely to contain allergens?

Allergenic proteins can be found in a wide variety of foods and the prevalence of allergy to particular foods varies around the world. In Australia and New Zealand, the foods that are the most significant sources of allergens are milk, eggs, fish, crustaceans, wheat, peanuts, tree nuts, soybeans and sesame seeds. These foods are required to be declared on the label when present in processed food to allow allergic individuals to avoid them.

The number of proteins that are allergenic is very small compared to the thousands of proteins in the diet that are not allergenic. With the exception of nuts and seeds, plant foods are a poor source of protein in the diet because they contain low levels of proteins. The nutritional value of plants lies in high-energy carbohydrate, sugar, starch, oils, fats, vitamins and minerals. New proteins introduced

into plants — such as those conferring herbicide tolerance and insect protection are typically present in the edible parts of these plants at very low levels.

How are GM foods assessed for their potential to cause an allergic reaction?

Currently, there are no suitable animal models that can be used to test the allergenicity of food or new proteins in food. However, several methods have been developed to help to predict whether new proteins in GM foods are likely to be allergenic.

To assess the allergenic potential of new proteins, the applicant must provide information to FSANZ on:

- any significant allergens present in the organism that the new proteins came from
- any significant similarity with any known allergens
- any other physical features characteristic of allergens.

The similarity of new proteins to known allergens is detected by computer searches of protein-sequence databases. The amino acid sequence of the new protein is compared with those of allergenic proteins in the databases, to detect stretches (eight or more contiguous amino acids) of similarity.

Most allergens share several physical features — they are small, abundant and resistant to degradation by processing and cooking, and by acids and enzymes in the human digestive system. The applicant must supply information to allow FSANZ to evaluate whether the new proteins have any of these characteristics. Standard biochemical and molecular techniques, and simulated mammalian intestinal digestive mixtures can be used for this purpose. Proteins that are easily degraded or digested into segments shorter than eight amino acids in length are unlikely to be allergenic, because only proteins larger than this can stimulate the human immune system and cause an allergic reaction.

If the new protein is from a source known to contain allergens, or if it has significant sequence similarity to a known allergen, further testing on humans would be required to determine whether the protein is allergenic in people with the corresponding allergy.

If FSANZ had scientific evidence that any new protein in a GM food were allergenic, it is unlikely that the food would be permitted to be sold in Australia and New Zealand, even with appropriate labelling. This is because FSANZ considers it to be inappropriate to increase the community's level of exposure to allergenic proteins in the food supply. FSANZ would make such decisions on a case-by-case basis.

If the new protein is not from an allergenic source and it does not have significant sequence similarity to a known allergen, then other features of the new protein (size, abundance, resistance to processing, cooking or digestion) are used to assess potential allergenicity. If the new protein has other physical features characteristic of allergens, there may be increased potential for it to be allergenic and further data may be required. Once again, the decision on whether to permit such a food would be made on a case-by-case basis.

In summary, the potential allergenicity of new proteins present in food is assessed in a systematic way, using the best current techniques and up-to-date knowledge about allergens.

A brazil nut protein was introduced into soybeans to make them more nutritious. Because brazil nuts are known to cause severe allergy in some people, as part of the research the allergenicity of the modified soybeans was tested. Laboratory tests found the brazil nut protein in the soybeans to be allergenic to people with brazil nut allergy, and this was confirmed with skin tests. Therefore, the soybeans were never commercialised because of their potential allergenicity.

Case study — Roundup Ready soy

Potential allergenicity of new proteins

The bacterial EPSPS enzyme in Roundup Ready soy (line 40-3-2) has no significant similarity to any known allergen. This was tested by comparing the sequence of the bacterial EPSPS enzyme with 219 known protein allergens found in publicly available databases. The sequences were compared using internationally accepted mathematical algorithms. No significant similarities in protein sequence were detected.

The bacterial EPSPS enzyme was also found to lack many of the physical features that are characteristic of allergenic proteins — abundance and resistance to degradation by cooking, processing and digestion. The bacterial EPSPS enzyme comprises less that 0.1% of the total protein in edible parts of the soybean plant and is likely to be substantially degraded before it reaches the human digestive system, because it is inactivated by cooking. Furthermore, the enzyme is rapidly broken down in a matter of seconds or minutes in simulated gastric and intestinal fluids.

Finally, there is no history of EPSPS proteins being allergenic. The bacterial EPSPS enzyme in the soybean has a similar structure and function to the EPSPS enzyme that is naturally present in the soybean and in other plants that form part of the human food supply.

Based on the evidence described above, the bacterial EPSPS enzyme in Roundup Ready soy is unlikely to be allergenic.

12 Compositional analyses

If there is a long history of safe use for the conventional food, FSANZ compares the composition of the conventional food with the GM variety, to identify differences in levels of naturally occurring nutrients, antinutrients, toxins and allergens. The GM crop and the conventional variety from which the GM crop was produced are grown at different locations that represent areas where the GM crop might be grown in the future. The edible part (for example, the grain) is harvested and tested to determine its composition. The levels of nutrients and other components of the GM food are compared to the conventional food. In addition to this, levels of nutrients and other components of the GM food are compared to levels reported in the scientific literature for other varieties of the same food. Any significant differences between the GM and the conventional food are then assessed for potential adverse health effects.

Case study — Roundup Ready soy

Compositional analysis

The levels of nutrients and antinutrients in the Roundup Ready soy (line 40-3-2) were compared to the levels in the commercial soybean variety from which the Roundup Ready version was derived. Both soybean varieties were grown in nine field locations, and whole seeds and processed products of the resultant soybeans were analysed and compared. These field studies also compared soybeans that had been sprayed with the herbicide Roundup to those that had not been sprayed. The results were also compared to the levels reported in the scientific literature for other soybean varieties.

12.1 Nutrient analysis

Typical nutrient analyses are:

- proximate composition — this refers to the approximate levels of ash, moisture, protein, fat, fibre and carbohydrate
- amino acid analysis
- fatty acid analysis
- carbohydrate analysis
- vitamin and mineral analysis.

Other compounds present in particular foods may also be measured if they are likely to have a significant impact in the overall diet. For example, the assessment would consider isoflavones (phytoestrogens) in soybeans.

Case study — Roundup Ready soy

Nutrient analysis

No significant differences were found in the levels of nutrients between Roundup Ready soy and conventional soy, sprayed (with Roundup) or unsprayed. The following components were analysed:

- protein, fat, moisture, fibre and ash in whole soybeans, toasted meal, non-toasted meal, protein isolate and protein concentrate
- 18 amino acids, including those that the EPSPS enzymes help to synthesise
- fatty acids (palmitic, stearic, oleic, linoleic and linolenic) in whole soybeans and refined, bleached and deodorised soybean oil
- seed storage proteins.

The level of isoflavones (genistein, daidzein and coumestrol) was also analysed. No differences were found between Roundup Ready soy and conventional soy, sprayed (with Roundup) or unsprayed.

12.2 Levels of antinutrients

An antinutrient is a substance within a food that interferes with the uptake of nutrients from food. Antinutrients found in conventional foods include trypsin inhibitors and phytic acid, described below.

High levels of trypsin inhibitors are often found in raw cereals and legumes, especially soybean. Trypsin is an enzyme (a type of protein) produced in the gut, which digests proteins in foods. Trypsin inhibitors interfere with the action of trypsin, affecting the digestion of proteins in the gut and subsequent absorption of nutrients, resulting in malnutrition. They are easily inactivated by heat and so may not be of concern as long as foods containing them are heat treated (for example cooked) before being eaten.

Phytic acid is naturally present in plants such as soybeans and canola. It reduces the uptake of phosphorous, calcium, magnesium and zinc from food. However, phytic acid also appears to protect against some forms of cancer, so this beneficial effect needs to be weighed against the antinutritional effect.

FSANZ looks at the levels of any known naturally occurring antinutrients in the food, to check that the genetic modification has not significantly increased their levels above the natural range found in the conventional food.

Processing of the foods must also be taken into account, because this may inactivate any antinutrients in the unprocessed food.

Case study — Roundup Ready soy

Levels of antinutrients

The only significant antinutrients known to occur naturally in soybeans are soybean lectin, trypsin inhibitor and phytate. Soybean lectin and trypsin inhibitor are destroyed during the heat treatments or processing applied to all soy products before they are eaten. No differences were found in the levels of soybean lectin, trypsin inhibitor and phytate between Roundup Ready soy and conventional soy.

Two other components were also measured: raffinose and stachyose — while not strictly antinutrients, increased levels of these carbohydrates would be considered undesirable because they cause flatulence. No differences were found in the levels of raffinose or stachyose between Roundup Ready soy and conventional soy.

12.3 Levels of naturally occurring toxins

FSANZ also considers the level of any known naturally occurring toxins, to check that the genetic modification has not significantly increased levels above the natural range in the equivalent conventional food.

Case study — Roundup Ready soy

Levels of naturally occurring toxins

There are no known naturally occurring toxins in soybeans.

12.4 Levels of naturally occurring allergenic proteins

The levels of any known naturally occurring allergens in the food are checked to ensure that the genetic modification has not increased the levels above the natural range found in the equivalent conventional food.

Case study — Roundup Ready soy

Levels of naturally occurring allergenic proteins

Conventional soybeans naturally contain several proteins that cause allergies in some people. Laboratory studies looked at whether the level of these proteins had increased as an unintended effect of the genetic modification.

The studies analysed the immune reaction in people with soy allergies when Roundup Ready soy and conventional soy was added to their immune serum. The nature and size of the immune reactions were similar between Roundup Ready soy and several varieties of conventional soy, showing that Roundup Ready soy was not more allergenic than unmodified soy.

13 Nutritional impact

13.1 Ability of GM food to support typical growth and wellbeing

FSANZ must also establish that a GM food is nutritionally adequate and will support typical human growth and wellbeing. This is usually achieved by understanding the genetic modification and its consequences, and analysing the composition of the food. If the compositional analysis indicates significant differences in a number of important nutrients or other components, or if there is concern that the bioavailability of key nutrients may be compromised by the genetic changes to the food, then feeding studies in animals can determine whether the food is nutritionally adequate.

Case study — Roundup Ready soy

Ability to support typical growth and wellbeing

In the case of Roundup Ready soy the extent of the compositional and other data were considered sufficient to establish the nutritional adequacy of the food. However, several animal-feeding studies had been conducted and were evaluated by FSANZ.

These studies confirmed that there were no unexpected changes in palatability or wholesomeness of Roundup Ready Soy. In these studies, Roundup Ready soy and conventional soy were fed to groups of rats, chickens and dairy cows for 4–6 weeks. These animals commonly eat soybeans.

During the feeding studies with rats and chickens, regular observations were made for adverse signs and weekly measurements were taken of the amount of food consumed and body weight. At the end of the studies, the animals were sacrificed. Rat organs were collected, weighed and examined. Chicken breast muscles and abdominal fat pads were collected and weighed. During the feeding studies with dairy cows, feed consumption, milk production, milk composition and nitrogen balance were examined.

The studies showed that Roundup Ready soy was palatable and able to support typical growth and wellbeing in rats, chickens and dairy cows. They also confirmed the results of studies showing no acute toxicity when the bacterial EPSPS enzyme was given to mice at high doses.

Feeding studies with catfish and quail also gave results that were consistent with the studies on rats, chickens and dairy cows.

14 Other safety issues

FSANZ considers other relevant safety issues relating to a new GM food on a case-by-case basis. For example, in a nutritionally enhanced food, the nutritional impact of the changed nutrient profile on the human diet would be considered.

Case study — Roundup Ready soy

The level of glyphosate residue in Roundup Ready soy

All foods sold in Australia and New Zealand must comply with relevant maximum residue limits, whether the foods have been genetically modified or not.

The levels of glyphosate residues in Roundup Ready soy must comply with the maximum residue limits established for all soybeans in Australia and New Zealand. Therefore, Roundup Ready soy will not contain unsafe levels of glyphosate residues.

15 Summary of scientific data used by FSANZ to assess the safety of GM foods

Detailed scientific data for safety assessments are obtained from the following sources to ensure that assessments are based on the best current scientific knowledge:

- the applicant
- scientific literature
- general technical information
- independent scientists
- other regulatory agencies and international bodies
- the general community.

The information that FSANZ requires is shown in Table 15.1.

Table 15.1 Information required by FSANZ for the safety assessment of a GM food

Information required
The identity of host and donor organisms.
Any known pathogenicity in host or donor organisms.
The previous use of host and donor organisms in food production.
The new genetic material that has been introduced through genetic modification: • origin, nature, purpose, function • method of introduction into the host organism.
The new genetic material in the GM organism: • the DNA sequence of the novel genetic material and border regions with the plant's genome • number of complete or incomplete copies present • stability.
The new protein in the GM organism: • purpose, physical and biological characteristics • expression profile (which tissues the protein is found in and when the protein is present).
Potential adverse effects of the new protein, such as allergenicity and toxicity: • similarity of the new protein to known allergens or toxins • physical features that are characteristic of allergens • acute toxicity (animal studies).
Composition compared to conventional counterpart — levels of nutrients, antinutrients, natural allergens and toxins.
Impact on human health from potential transfer of new genetic material to cells in the human digestive tract.
End uses of the food, including any requirement for processing prior to consumption.
If required, ability of the food to promote typical growth and wellbeing (animal feeding studies).
Any other relevant information.

Appendix 1

Food Standards Australia New Zealand

Food Standards Australia New Zealand (FSANZ) is a statutory authority with legal responsibilities relating to food in Australia and New Zealand. These responsibilities are set out in the *Food Standards Australia New Zealand Act 1991* and the *Agreement between the government of Australia and the government of New Zealand concerning a joint food standards system*.

FSANZ's primary objectives in developing, varying and reviewing the code are to:

- protect public health and safety
- provide adequate information relating to food to enable consumers to make informed choices
- prevent misleading and deceptive conduct.

Among these objectives, the protection of public health and safety has the highest priority.

In setting food standards, FSANZ uses scientifically based risk assessment methods and the best available scientific information. FSANZ also seeks to promote consistency between domestic and international food standards, an efficient and internationally competitive food industry and fair trading in food.

FSANZ also has a range of other functions, including:

- coordinating national food surveillance and recall systems in Australia
- conducting research
- assessing policies about imported food
- developing codes of practice with industry.

Appendix 2
Changing the food standards

Wide ranging and numerous changes are now occurring in the area of food technology. It is important to make sure that the *Australia New Zealand Food Standards Code* is kept up to date with these changes, and with the increased scientific and clinical knowledge about foods. Food standards may need to be changed where:

- a new technology is applied to a food
- an existing technology will be used in a different way
- unusual foods that most people have not eaten before are to be introduced to the food supply.

Certain types of foods and certain chemical components found in some foods must go through a safety assessment process before entering the market. Food types that require a safety assessment include genetically modified (GM) foods, new foods and irradiated foods; chemicals requiring assessment include additives, processing aids and pesticide residues. Such foods or components of food are only permitted if they have been assessed by Food Standards Australia New Zealand (FSANZ), are considered to be safe, and have been considered by the Australia and New Zealand Food Regulation Ministerial Council (the ministerial council).

Any person or organisation may apply to have the *Australia New Zealand Food Standards Code* amended by way of an application. Also, FSANZ may, on its own initiative, raise a proposal to develop or vary food standards.

A2.1 The process for changing the *Australia New Zealand Food Standards Code*

The *Australia New Zealand Food Standards Code* can be changed through a variation to an existing standard or the creation of a new standard by way of an application or a proposal through the following steps:

1. An application is made to FSANZ or a proposal is developed by FSANZ to change the code.
2. The application or proposal is scoped by FSANZ and then accepted into the workplan.
3. If FSANZ decides to accept the application or proposal for further consideration, it approves the release of an initial assessment report to the community and other stakeholders and invites submissions before it proceeds any further with the assessment. If FSANZ rejects the application at this point, the reasons and appeal rights are made available to the applicant. Following an initial assessment of an application to make a new or vary a current food standard, FSANZ has 12 months to fully consider and finalise the application (no such time limit exists for a proposal).
4. Public submissions to the initial assessment report are sought through advertisements in national newspapers and through mailouts to stakeholders who have indicated an interest in the area addressed by the application or proposal. Generally, the initial assessment report will be open to public consultation for a six-week period, though this timeframe may vary.
5. Following the public consultation period, FSANZ makes a draft assessment of the application or proposal. This includes a safety assessment for any food requiring pre-market clearance,

such as GM foods and novel foods. Issues raised in public submissions are also addressed. A draft assessment report is prepared and, after approval by the FSANZ Board, it is released to the public and other stakeholders for further public consultation.

The FSANZ Board comprises:

- a chairperson
- the FSANZ Chief Executive Officer
- three members nominated by the New Zealand lead minister on the ministerial council
- a member nominated by consumer organisations
- a member nominated by the National Health and Medical Research Council
- three members nominated by organisations established for purposes relating to science or public health
- two members nominated by organisations established for purposes relating to the food industry.

Members must have expertise in particular areas, such as public health, consumer affairs or food science.

The information included in the draft assessment report includes the proposed draft standard, or variation to the standard, and accompanying explanatory notes.

As before, if FSANZ rejects the application, the reasons and appeal rights are made available to the applicant.

6. FSANZ prepares a final assessment report, taking into account any information received during the second round of public consultation, and the board approves or rejects the standard or standard variation.

7. Once the FSANZ Board approves a new standard or a variation to a food standard the ministerial council is notified.

   The Ministerial Council is made up of Australian Government, state and territory and New Zealand health ministers as lead ministers, and nominated ministers from other portfolios with an ancillary interest in the food supply and food regulatory system. The ministerial council may request that FSANZ review the standards or variations, accept the standards or variations, or after two reviews, amend or reject them.

8. If, when the ministerial council process is finalised, the standards or variations stand, they are gazetted and then automatically adopted by reference under the food laws of the Australian states and territories and New Zealand.

9. Copies of all initial, draft and final assessment reports are available on the FSANZ website (http://www.foodstandards.gov.au).

Appendix 3
Labelling GM foods

A3.1 General labelling requirements

Standard 1.5.2 — *Food produced using gene technology* — contains the provisions for the labelling of genetically modified (GM) foods and ingredients.

For the purposes of labelling, the standard defines GM food as follows:

'genetically modified food means food that is, or contains as an ingredient, including a processing aid, a food produced using gene technology which

a) contains novel DNA and/or novel protein

b) has altered characteristics;

but does not include

a) highly refined food, other than that with altered characteristics, where the effect of the refining process is to remove novel DNA and/or novel protein

b) a processing aid or food additive, except where novel DNA and/or novel protein from the processing aid or food additive remains present in the food to which it has been added

c) flavours present in the food in a concentration no more than 1 g/kg

d) a food, ingredient, or processing aid in which genetically modified food is unintentionally present in a quantity of no more than 10 g/kg per ingredient.'

Therefore, a product such as soy flour is required to be labelled if it is derived from GM soybeans. Conversely, a highly refined oil, such as GM soybean oil, is not required to be labelled because it contains no DNA (deoxyribonucleic acid) or protein, and is chemically identical to conventional soybean oil.

The statement 'genetically modified' must be used in conjunction with the name of the food or in association with the specific ingredient in the ingredient list. If the food is unpackaged, then the information that otherwise would have been on the package must be displayed on or in connection with the display of the food.

A3.2 Additional labelling and information requirements

There are additional labelling and information requirements for GM foods that have 'altered characteristics'; that is, any GM foods that differ from their conventional counterpart in relation to:

- composition or nutritional values
- antinutritional factors or natural toxicants
- factors known to cause allergic responses in particular sections of the population
- its intended use.

Additional labelling or other information requirements may be specified on a case-by-case basis for

any GM food with altered characteristics or where the GM food raises significant ethical, cultural and religious concerns with respect to genetic modification. FSANZ determines whether an additional labelling requirement is warranted through the process for standard development or variation.

The only GM food with altered characteristics approved for human consumption in Australia and New Zealand to date is a type of soybean genetically modified to contain higher levels of oleic acid than conventional soybeans. Food products derived from this type of soybean are required to be labelled as such.

A3.3 Exclusions from labelling

As indicated in Section 5.1, the labelling requirements do not apply to all food produced using gene technology. Types of food not subject to labelling requirements are primarily:

- highly processed food where the processing removes all DNA and/or protein
- minor ingredients, including processing aids and food additives (unless they contain novel DNA and/or novel protein).

Unintentional presence of GM foods in non-GM foods

The standard also allows a food in which an approved GM food is unintentionally present in a quantity of no more than 10 g/kg (1%) per ingredient to remain unlabelled (GM foods that are not listed in the standard are not permitted in any food either intentionally or unintentionally). This exclusion applies to circumstances where the manufacturer has actively sought to avoid GM ingredients but GM material is inadvertently present. As long as the presence is unintentional and is less than the permitted amount of 10 g/kg per ingredient, there is no requirement to label the product as containing an approved GM food, ingredient or processing aid.

For this provision to apply, the food manufacturer needs to be able to demonstrate that they have sought to source non-GM food for their product. Such measures include document verification, identity preservation systems[7] or batch testing. However, if testing shows a GM ingredient is present, labelling is required regardless of whether the level is below 1%. Further information on this is available on the FSANZ website.[8]

Foods prepared for immediate consumption

Food intended for immediate consumption that is prepared and sold from food premises and vending vehicles is exempt from GM food labelling requirements. Types of food premises captured by this exemption include restaurants, take away outlets, caterers and self-catering institutions. In this situation, if a consumer wants to know whether the ingredients used are from a GM source they can enquire at the point of sale.

7. Identity preservation is a system of procedures that is used commercially to maintain a segregrated supply chain. Normally applied from 'seed to supermarket', an identity preservation system includes fully documented evidence of compliance of ingredient supply with procedures designed to eliminate accidental mixing of GM foods with non-GM foods.
8. http://www.foodstandards.gov.au/assistanceforindustry/userguides/index.cfm

A3.5 Negative claims

Standard 1.5.2 is silent on the use of negative claims such as 'GM free' and 'non-GM'. Such claims are made voluntarily by food manufacturers and are subject to the provisions regarding false and misleading conduct under the Australian *Trade Practices Act 1974*, the New Zealand *Fair Trading Act 1986* and the fair trading and food acts in each Australian state and territory.

Review of GM food labelling

As Australia and New Zealand were among the first countries in the world to require GM food to be labelled, when the requirements were agreed (in 2000), the ministerial council requested that FSANZ conduct a review of these labelling requirements after three years.

FSANZ completed this review at the end of 2003 and found that Australia and New Zealand have one of the most comprehensive labelling regimes for GM food in the world. The review also found a high level of industry compliance with the labelling requirements.

The final report of the *Review of Labelling of Genetically Modified Food* is publicly available on the FSANZ website.[10]

10. http://www.foodstandards.gov.au/mediareleasespublications/publications/gmlabellingreviewrep2460.cfm

Appendix 4
International work on the safety of GM foods

Internationally, there are a number of organisations that are involved in developing methods to assess the safety of genetically modified (GM) foods. These include the World Health Organization (WHO) and the Food and Agriculture Organization (of the United Nations) (FAO), who have provided advice to the Codex Alimentarius Commission, and the Organisation for Economic Co-operation and Development (OECD).

A4.1 The Organisation for Economic Co-operation and Development

The OECD is an intergovernmental organisation made up of representatives from 30 industrialised countries in North America, Europe and the Pacific, as well as the European Commission. The role of the OECD is to discuss issues of mutual concern, coordinate and harmonise policies and work together to respond to international problems. More than 200 specialised committees made up of delegates from member countries carry out most of the work of the OECD.

The OECD has been working on the issues raised by biotechnology for more than 20 years. During this time, the need for effective policies on biotechnology has become an international priority. Member countries share information, discuss new policy approaches and jointly develop collaborative policies where appropriate. Other OECD activities include the development of policy options for science and technology infrastructure, the implications of intellectual property rights and licensing and considerations for human health and environmental safety.

The OECD also helps to foster international agreement about the safety of novel foods and feeds by developing consensus documents for the regulatory assessment of biotechnology products. These documents are intended to be mutually recognised among OECD member countries. They focus on the biology of organisms, introduced novel traits, nutrients, antinutrients or toxicants, information on the product's use as a food/feed and other relevant information. FSANZ staff members are involved in OECD expert committees and in the process of developing consensus documents.

Further information about the activities of the OECD in relation to biotechnology is available from the OECD website (http://www.oecd.org).

A4.2 WHO/FAO expert consultation on GM foods

WHO and FAO have convened a number of scientific expert consultations to provide advice to their member states on scientific and technical issues related to GM foods. The first of these consultations - *Strategies for Assessing the Safety of Foods Produced using Biotechnology* - was held in 1990, with subsequent consultations continuing to build on this body of work.

Several joint expert consultations on foods derived from biotechnology have been held since 2000, covering the principles of safety assessment of foods from GM plants, animals and microorganisms, and the assessment of GM foods for allergenicity. The most recent was the Expert Consultation on Transgenic Animals Including Fish, held in Rome, in 2003.

The scientific advice of the joint FAO/WHO expert consultations on foods derived from biotechnology serve as the scientific basis for the Codex Alimentarius Commission in their work on risk analysis and safety assessment guidelines for GM foods. Member states can also use the advice of the expert

consultations directly to develop their own processes for GM foods safety assessments.

Further information and the reports of the expert consultations are available on the web.[11]

A4.3 Codex Alimentarius Commission

Both WHO and FAO are jointly responsible for the global food standards body — the Codex Alimentarius Commission (Codex). The Codex work on the entry of GM foods into the global food market has been organised by the Ad Hoc Intergovernmental Task Force on Foods Derived from Biotechnology, which was convened in 2000 and met annually until 2003. The role of this task force was to develop standards, guidelines or other principles, as appropriate, for GM foods. The task force took into account existing scientific work and risk assessment carried out by other agencies including national authorities and international organisations (for example, WHO and FAO). It also considered other issues relevant to the health of consumers and the promotion of fair trade practices.

The work of the task force is summarised in three major documents that serve as international references on the safety assessment process. These three documents are:

- *Principles for the risk analysis of foods derived from modern biotechnology*
- *Guideline for the conduct of food safety assessment of foods derived from recombinant-DNA plants*
- *Guideline for the conduct of food safety assessment of foods produced using recombinant-DNA micro-organisms*

All three documents are available on the FAO website.

Despite these documents, future research on food derived from biotechnology is needed, and a new task force will be convened in 2005. It may discuss issues such as transgenic animals, cloned animals, plant expression of bioactive substances and the low-level presence of unauthorised GM food. The task force will report its conclusions by 2009.

A4.4 Work by other expert groups on the safety of GM foods

In addition to the international bodies mentioned above, a number of expert groups in different countries around the world have examined many of the issues raised by GM foods. One of these expert groups was the New Zealand Royal Commission, which was formed in 2000 to investigate and report on the strategic options available in New Zealand to address the issue of gene technology.

Information about the outcomes of the New Zealand Royal Commission is available on the website of the New Zealand Ministry for the Environment.[13]

Work by other expert groups includes *Genetically modified plants for food use and human health* (The Royal Society (UK), 2002), *Elements of Precaution: Recommendations for the Regulation of Food Biotechnology in Canada* (Royal Society of Canada's Expert Panel on the Future of Food Biotechnology, 2001) and *Safety of Genetically Engineered Foods: Approaches to Assessing Unintended Health Effects* (Institute of Medicine and National Research Council of the National Academy of Sciences, USA 2004).

11. http://www.who.int/foodsafety/biotech/consult/en/
12. http://www.fao.org/es/ESN/food/risk_biotech_taskforce_en.stm
13. http://www.mfe.govt.nz

A4.5 International harmonisation of regulations and information sharing

FSANZ considers international harmonisation and capacity building in the safety assessment of GM foods to be integral to the future development and regulation of this technology. A key component is the sharing of information about GM food safety assessments between agencies involved in the regulation of GM food. Better use of existing information and mechanisms for information exchange are vital as a first step towards international recognition of GM food assessments and adoption of broad regulatory principles of operation such as transparency, and public consultation and participation.

The data requirements for GM food safety assessments are similar among countries that have independent safety assessments. Often, regulators consult with one another and harmonise their data requirements. Most regulators have, for example, adopted elements of the earlier principles developed by the OECD as the basis of their guidelines, and recognise Codex as the appropriate body for setting international food standards.

Information sharing, capacity building and method harmonisation are being increasingly recognised by international organisations as essential for the future of GM food safety assessments and international regulation.

Appendix 5
Glossary

The glossary defines biological terms and acronyms that are not explained in Section 3 or the frequently asked questions in Section 7.

A

allergen – A substance, usually a protein, that causes an allergic reaction.

allergenicity – The capacity of an allergen to cause an allergic reaction.

amino acid – The building block components of proteins. Twenty different essential amino acids are used by all living organisms to make proteins.

antinutrient – A substance within a food that interferes with the uptake of nutrients from food.

ANZFRMC – Australia New Zealand Food Regulation Ministerial Council. This Ministerial Council is made up of the health ministers of the two national governments and eight Australian state and territory governments.

ANZFSC – Australia New Zealand Food Standards Council (now ANZFRMC).

AQIS – Australian Quarantine and Inspection Service.

B

bacterium (plural: bacteria) – A single-celled life form whose genetic material is not enclosed in a nucleus.

C

carbohydrate – Simple sugars and starches present in foods that provide the body with energy and nutrition.

Codex Alimentarius Commission – A commission set up by the Food and Agriculture Organization and the World Health Organization of the United Nations in 1962 to develop a code of food standards for all nations. (Codex Alimentarius means 'food code' in Latin.)

D

DNA – The acronym DNA stands for deoxyribonucleic acid. DNA is made up of four nucleotides (or 'bases'), adenine, guanine, cytosine and thymine on a phosphate backbone. DNA is usually double stranded with base pairing between strands occurring between adenine and thymine, and cytosine and guanine.

E

ERMA – Environmental Risk Management Authority (New Zealand). An authority that regulates and monitors the importation, development and use of new organisms under the *Hazardous Substances and New Organisms Act 1996*. Before ERMA was established, the Advisory Committee on Novel Genetic Techniques and the Interim Assessment Group carried out these functions. ERMA also receives input from Nga Kaihautu Tikanga Taiao – an advisory committee established to provide Maori perspectives into decision-making processes.

F

food additive – Substances added to foods to improve taste, appearance, texture, storage life or other qualities.

G

gene – A small section of a DNA strand that contains the instructions for the cell to carry out a function. For example, genes often code for proteins, that is, they contain the information for the cell to create a specific protein.

genetically modified organism (GMO) – A life form that has been genetically modified using techniques of modern gene technology.

genome – The total genetic material of a living organism.

H

herbicide – A substance that is able to kill certain types of plants when applied at specific doses.

herbicide tolerant – Plants with an increased ability to tolerate commercial applications of herbicide.

host – An organism that has been genetically modified is sometimes said to be the 'host' for genetic material provided by another organism.

I

insect protected – Plants that have an inbuilt capacity to protect themselves from damage by particular insect pests. An example of an insect protection system that has been incorporated into GM plants is Bt. GM plants with Bt contain one or more genes for crystal proteins from the common soil bacterium *Bacillus thuringiensis* (Bt) that are toxic to certain insect pests.

irradiated food – A food that has been subjected to a measured dose of radiation to reduce the level of bacterial contamination or to control quarantine pests.

K

kilodalton (kDa) –A kilodalton is a unit used to measure the mass of atoms as well as molecules, such as proteins. One kilodalton is equal to 1000 daltons. One dalton equals the atomic weight of a hydrogen atom (1.66 x 10-24 grams).

M

marker gene – A marker gene is a gene attached to the desired gene and used in genetic modification to allow researchers to identify those cells that have successfully taken up the new DNA. A marker gene usually either gives a selective advantage to the cell, e.g. antibiotic or herbicide resistance, or can lead to the production of visible compounds such as fluorescent proteins.

maximum residue limit (MRL) – The highest chemical residue concentrations that are legally permitted in food. They are always set at levels lower than (and normally very much lower than) those shown to cause adverse effects on human health and safety.

microorganism – A microscopic life form, usually single-celled, such as bacteria or yeast.

Ministerial Council – See ANZFRMC (Australia New Zealand Food Regulatory Ministerial Council).

molecular biology – The study of biology at the level of molecules, especially genetic material (DNA) and genes.

N

novel food – Non-traditional foods for which there is insufficient knowledge in the broad community to enable safe use in the form or context in which the food is presented (for example, fat replacers or exotic foods).

nutrient – A substance that provides nourishment and promotes growth, health and wellbeing.

O

OGTR – Office of the Gene Technology Regulator (Australia). An independent statutory office regulating all aspects of the development, production and use of genetically modified organisms (GMOs) where no other existing regulatory body has responsibility. It is located in the Australian Government Department of Health and Ageing as part of the Therapeutic Goods Administration.

P

pesticide – A substance that is able to kill certain types of pests when applied at specific doses.

plasmid – A plasmid is a small piece of DNA that can replicate itself within a bacterial cell. Plasmids are used in gene technology as a way to introduce new genes into other cells.

processing aid – A substance used to aid the processing of raw materials, foods or ingredients. Processing aids do not have any function in the final food.

promoter – A DNA sequence that enables a cell to turn a particular gene on.

R

ribosome – A structure within the cell where mRNA is translated into protein. Each cell contains many ribosomes.

RNA – RNA stands for ribonucleic acid. RNA is similar in structure to DNA but is generally single stranded. RNA in the cell has many functions, one of these is to act as a template for the synthesis of proteins. RNA that acts as a template for the synthesis of proteins is called messenger RNA or mRNA.

T

toxin – A substance that can cause adverse health effects under typical circumstances of exposure.

toxicity – The capacity of a toxin to cause a toxic reaction.

trait – A distinguishing feature or quality.

transcription – Transcription is the process of copying information from DNA in the cell to RNA. The RNA is then used to make proteins by a process called translation.

translation – Translation is the process where information contained on an RNA strand is decoded into an amino acid sequence to produce a protein.

V

virus – A microscopic particle containing genetic material that is only able to reproduce by infecting a living cell.

Appendix 6
Key references

Antinutrients in food

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GM animals

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Appendix 7
Contacts and further information

Australian Government departments and agencies

Australian Pesticides and Veterinary Medicines Authority (APVMA)	http://www.apvma.gov.au
Australian Quarantine and Inspection Service (AQIS)	http://www.aqis.gov.au
Biotechnology Australia	http://www.biotechnology.gov.au
Department of Agriculture, Fisheries and Forestry	http://www.daff.gov.au
Department of Health and Ageing	http://www.health.gov.au
Department of Industry, Tourism and Resources	http://www.industry.gov.au
Department of the Environment and Heritage	http://www.deh.gov.au/
Food Standards Australia New Zealand (FSANZ)	http://www.foodstandards.gov.au
Office of the Gene Technology Regulator (OGTR)	http://www.ogtr.gov.au
Therapeutic Goods Administration (TGA)	http://www.tga.gov.au

New Zealand Government departments and agencies

Environmental Risk Management Authority (ERMA)	http://www.ermanz.govt.nz
Food Standards Australia New Zealand (FSANZ)	http://www.foodstandards.govt.nz
Ministry of Agriculture and Forestry (MAF)	http://www.maf.govt.nz
Ministry for the Environment (MfE)	http://www.mfe.govt.nz
Ministry of Health (MoH)	http://www.moh.govt.nz
Ministry of Research Science and Technology (MoRST)	http://www.morst.govt.nz
New Zealand Food Safety Authority	http://www.nzfsa.govt.nz

Other organisations – Australia

Agrifood Awareness Australia	http://www.afaa.com.au
Australian Academy of Science	http://science.org.au
AusBiotech	http://www.ausbiotech.org/
Australian Conservation Foundation	http://www.acfonline.org.au
Australian Consumers Association	http://www.choice.com.au
Australian GeneEthics Network	http://www.geneethics.orgAustralian
Food and Grocery Council	http://www.afgc.org.au/
Organic Federation of Australia	http://www.ofa.org.au/

Other organisations – New Zealand

Bio-Grow New Zealand	http://www.bio-gro.co.nz
Consumers Institute of New Zealand	http://www.consumer.org.nz
Food and Grocery Council	http://www.gma.org.nz/
New Zealand Institute of Food Science and Technology	http://www.nzifst.org.nz

Biotechnology companies

Aventis	http://www.aventis.com
Dupont	http://www.dupont.com
Monsanto	http://www.monsanto.com
Novartis	http://www.novartis.com
PioneerHi-Bred International	http://www.pioneer.com/index.htmFor a
list of Australian biotechnology companies see: AusBioInfo	http://www.ausbioinfo.com

Further information

ABC Science	http://www.abc.net.au/science
CSIRO Gene Technology	http://genetech.csiro.au
Independent Biotechnology Advisory Council (IBAC)	http://www.ibac.org.nz
Nuffield Council on Bioethics	http://www.nuffieldbioethics.org/
OECD	http://www.oecd.org
The Royal Society of New Zealand	http://www.rsnz.govt.nz
For details on the work of the Nga Kaihautu Tikanga Taiao see:	http://www.ermanz.govt.nz/