05/02
10 October 2001

FINAL ASSESSMENT REPORT
(INQUIRY - SECTION 17)

APPLICATION A378

FOOD DERIVED FROM GLYPHOSATE-TOLERANT SUGARBEET LINE 77

TABLE OF CONTENTS

EXECUTIVE SUMMARY

Background

Monsanto Australia Ltd have made an application to ANZFA to vary Standard A18 of the *Food Standards Code* to include food derived from sugarbeet line 77 which has been genetically modified to tolerate applications of the herbicide glyphosate. The genetically modified sugarbeet line 77 (GTSB77) is marketed in the USA under the names Roundup® Ready Sugar Beet or Glyphosate-Tolerant Sugar Beet. Glyphosate-tolerant Sugar Beet is not grown in either Australia or New Zealand and the only imported foods derived from the crop are refined sugar and molasses.

Issues addressed during assessment

(i) Safety evaluation

Food from glyphosate-tolerant sugarbeet line 77 has been evaluated according to the safety assessment guidelines prepared by ANZFA. The assessment considered the following issues: (1) the nature of the genetic modification; (2) general safety issues such as novel protein expression and the potential for transfer of antibiotic resistance genes to microorganisms in the human digestive tract; (3) toxicological issues; and (4) nutritional issues.

On the basis of the available information, it is concluded that food from glyphosate-tolerant sugarbeet line 77 is not different to food from other commercial varieties in terms of its safety and nutritional adequacy. A detailed report on the safety of food from glyphosate-tolerant sugarbeet line 77 has been prepared.

(ii) Labelling information for consumers

Under the current Standard A18, which remains in effect until 7 December 2001, food derived from glyphosate-tolerant sugarbeet line 77 does not require labelling as it is regarded as substantially equivalent to food derived from non-genetically modified sugarbeet varieties.

When the amended Standard comes into effect on 7 December 2001, food products containing glyphosate-tolerant sugarbeet line 77 will require labelling if it can be shown that novel DNA and/or protein is present in the final food.

(iii) Public consultation

ANZFA undertook two rounds of public consultation in relation to this application and a total of 56 submissions were received overall – 45 submissions in the first round and 24 submissions in the second round. The majority of submissions were not supportive. Those opposing the application did so primarily on the basis that they perceive GM food to be unsafe. The food safety concerns raised in submissions have been addressed by the safety assessment report.

Conclusions

No potential public health and safety concerns have been identified in the assessment of glyphosate-tolerant sugarbeet line 77. Food derived from glyphosate-tolerant sugarbeet line, principally refined sugar and molasses, can be regarded as equivalent in terms of its safety and nutritional adequacy to food derived from conventional sugarbeet.

There are no public health and safety concerns associated with the gene introduced into glyphosate-tolerant sugarbeet line 77.

Food from glyphosate-tolerant sugarbeet line 77 is equivalent to that from other commercially available sugarbeet in terms of their safety and nutritional adequacy.

On 7 December 2001, food products containing food derived from glyphosate-tolerant sugarbeet line 77 will require labelling if it can be shown that novel DNA and/or protein is present in the final food.

The proposed amendment to the *Food Standards Code* is consistent with the section 10 objectives of the *Australia New Zealand Food Authority Act 1991* and the regulatory impact assessment.

Recommendation

On the basis of the assessment, which concludes that food derived from glyphosate-tolerant sugarbeet line 77 is as safe for human consumption as food derived from other commercial sugarbeet varieties, ANZFA recommends that Standard A18 in Volume 1 and Standard 1.5.2 in Volume 2 of the *Food Standards Code* be amended to give approval to the sale of such food in Australia and New Zealand.

1. BACKGROUND TO THE APPLICATION

Glyphosate-tolerant sugarbeet line 77 is referred to as Roundup® Ready sugarbeet and is tolerant to applications of the herbicide glyphosate through the transfer of the 5-enolpyruvylshikimate-3-phosphate synthase (CP4 EPSPS) gene. This gene encodes an enzyme that can function under applications of glyphosate unlike plant-derived forms, which are sensitive to glyphosate. The *uid*A gene is also present in the sugarbeet and encodes β–D-glucuronidase (GUS), which is a selectable marker that is used during plant transformation. A chimeric *gox* gene is transferred to the sugarbeet but does not result in a stable protein product in the plant.

Glyphosate-tolerant sugarbeet line 77 is not currently grown in either New Zealand or Australia. The two primary products from sugarbeet, pure sucrose and molasses are also not likely to be imported into Australia or New Zealand but may be present as ingredients in imported processed food products.

The main benefits of glyphosate-tolerant sugarbeet line 77 are agronomic in nature, and are therefore likely to accrue mainly to the primary producer. It is envisaged that production of these crops will reduce reliance on agricultural chemicals for weed control with potentially higher overall crop yields. More general benefits may flow to the community as a result of reduced primary production costs.

2. PUBLIC CONSULTATION

Upon receipt of the application, ANZFA completed an Initial Assessment (formerly the Preliminary Assessment), which was released for public comment on 3 November 1999. A total of 45 submissions were received in response to the information summary.

ANZFA then conducted an assessment of the Application, including a safety evaluation of the food, taking into account the comments received. A Full Assessment Report was released for public comment on 7 March 2001 resulting in a further 11 submissions being received. ANZFA has now completed a Final Assessment (Inquiry - section 17) of the Application taking into account the public comments. Attachment 5 contains a summary of all submissions received.

3. NOTIFICATION OF THE WORLD TRADE ORGANIZATION

During the ANZFA assessment process, comments are also sought internationally from other Members of the World Trade Organization (WTO). As Members of the WTO, Australia and New Zealand are signatories to the agreements on the Application of Sanitary and Phytosanitary Measures (SPS Agreement) and on Technical Barriers to Trade (TBT Agreements) (for further details on WTO, see Attachment 4). In some circumstances, Australia and New Zealand have an obligation to notify the WTO of changes to food standards to enable other member countries of the WTO to make comment.

As there is significant international interest in the safety of GM foods, the proposed amendments are considered to raise potential Technical Barrier to Trade or Sanitary/Phytosanitary matters and were therefore notified to the WTO.

4. ISSUES ADDRESSED DURING THE ASSESSMENT

4.1 Safety assessment

Food from glyphosate-tolerant sugarbeet line 77 has been evaluated according to the safety assessment guidelines prepared by ANZFA[1]. The assessment considered the following issues: (1) the nature of the genetic modification; (2) general safety issues such as novel protein expression and the potential for transfer of novel genetic material to cells in the human digestive tract; (3) toxicological issues; and (4) nutritional issues. On the basis of the available information, ANZFA concluded that food from glyphosate-tolerant sugarbeet line 77 is equivalent to food from other commercial sugarbeet varieties in terms of its safety and nutritional adequacy. The full safety assessment report can be found at Attachment 2 to this document.

4.2 Labelling of food derived from glyphosate-tolerant sugarbeet line 77

On 28 July 2000 the Australia New Zealand Food Standards Council agreed to a revised standard which requires labelling of food where novel DNA and/or protein is present in the final food and also where the food has altered characteristics. The revised standard (A18 in the Australian *Food Standards Code*, 1.5.2 in the Australia New Zealand Food Standards Code) was gazetted on 7 December 2000 and will come into effect 12 months from the date of gazettal.

Until the new labelling requirements take effect, the provisions in the original Standard A18 apply. Under these provisions, food from glyphosate-tolerant sugarbeet line 77 does not require labelling as it is regarded as substantially equivalent to food derived from non-genetically modified cotton varieties.

4.3 Issues arising from public submissions

General issues

Many of the submissions received in both the first and second rounds of public comment raised issues of a general nature relating to gene technology or issues that had already been addressed in the safety assessment report (see Attachment 2). A discussion of some of the more general issues raised can be found in Attachment 6.

However, in light of the rapid developments in this field, some general issues raised in the second round of public consultation have been addressed again taking into account more recent outcomes of intensive deliberations on gene technology issues, such as the publishing of the report of the New Zealand Royal Commission on Genetic Modification, the second OECD Conference on "New Biotechnology Food and Crops: Science, Safety and Society", and the deliberations of various Codex Alimentarius and OECD taskforces and FAO/WHO expert Consultations.

[1] ANZFA (1999) Guidelines for the safety assessment of foods to be included in Standard A18 – food produced using gene technology.

1. ANZFA's processes

Several criticisms of ANZFA's general processes for the risk assessment of GM foods were raised by submitters including: the Public Health Association of Australia (PHAA), the GeneEthics Network, the National Council of Women of Australia (NCWA), Consumer's Institute of New Zealand, GE Free New Zealand, Paul Elwell-Sutton, Sandra Jacobs, Brian Lister and Lorraine Leader, Claire Bleakely, Julian Yates, Oraina Jones, Leila Huebner and Dr Kate Clinch-Jones.

Response

The processes used by ANZFA for safety assessment and labelling of GM foods were subject to an independent assessment by the New Zealand Royal Commission on Genetic Modification. In its deliberations, the Royal Commission considered that both the New Zealand Environmental Risk Management Authority (ERMA) and ANZFA provided a robust regulatory environment and the authorities "carry out their functions conscientiously and soundly". The Commission also stated "We have confidence in the ANZFA safety assessment process. We consider it unlikely that foods that have satisfied the food standard will have harmful effects", and "The Commission was reassured that ANZFA carries out its functions with an appropriate degree of independence not only from political influence but also from the influence of commercial interests." In reaching this view, it should be noted that the Commission examined the criticisms levelled at ANZFA's processes and the detailed rebuttal of those criticisms supplied to the Commission by ANZFA, including issues such as adequacy of the toxicological studies, use of substantial equivalence, sources and independence of data, antibiotic resistance marker genes etc, that are similar to those raised by the PHAA in their present submission.

The Report can be accessed at http://www.gmcommission.govt.nz .

2. Substantial equivalence

Several submitters (PHAA, GeneEthics, Dr Kate Clinch-Jones, Consumer's Institute of New Zealand) raised concerns with the use of the concept of substantial equivalence

Response

On the issues of the appropriate use of the concept of substantial equivalence, ANZFA reiterates that it uses this tool as a starting point in the safety assessment process for GM foods as supported by international bodies such as Codex Alimentarius, OECD, FAO/WHO, other regulators such as the UK, the EU, Japan, Canada and the recent report of the Canadian Royal Society.

3. Antibiotic resistance marker genes

Several submitters (PHAA, GeneEthics Network, Dr Kate Clinch-Jones) raised some concerns about the use of antibiotic resistance marker genes (ARMGs) in the development of GM foods. In particular, the PHAA submission asserts that ANZFA is "remarkably out-of-step with scientific opinion…" and quotes the JETACAR Report as evidence of this.

Response

The JETACAR Report states (page 117 referring to a specific gene called *nptII*) that the use of antibiotic resistance genes in GM foods is unlikely to contribute in any significant way to the spread of antibiotic resistance in humans. The issue of the use of antibiotic resistance marker genes in GM foods was discussed at the recent Ministerial Council meeting held in Adelaide in late July 200. At that meeting, Professor John Turnidge, former Chair of JETACAR and now Chair of the NHMRC Expert Advisory Group on Antibiotic Resistance (EAGAR) appeared at the Council meeting to present his expert advice on the safety of the use of ARMGs in GM foods in support of ANZFA's views on this issue.

4. Source of data

Some submitters (PHAA, GeneEthics) raised concerns over the independence of the source of the data submitted to ANZFA

Response

It is a requirement of the ANZFA assessment process that raw data from experiments supporting the safety of a GM food are submitted to ANZFA for assessment. These data are assessed in detail by ANZFA scientists and then the assessment report undergoes a robust process of internal review by ANZFA's own scientific experts and external review by ANZFA's expert panel and senior health officials from State and Territory and New Zealand Health Departments. The quality and sources of the data supplied to ANZFA in support of applications for approval of GM foods was the subject of particularly intense scrutiny during ANZFA's evidence at the New Zealand Royal Commission on Genetic Modification. ANZFA submitted a full data package (15 volumes of raw data on Roundup Ready Soybeans) to the Commission for inspection. The Commission states that it looked closely at the quality of this data and came to the view that ANZFA did receive and assess raw data and that its processes were not wanting in this regard.

Furthermore, in relation to the issue of the independence, integrity and different sources of data submitted in support of applications for approval of GM foods, at the recent OECD Conference "New Biotechnology Food and Crops: Science, Safety and Society" held on 16-20 July 2001 in Bangkok, there was agreement by participants (as stated in the Conference Rapporteurs report) attending the Conference that "There is information for regulatory dossiers – where there is a high level of quality assurance and validation – and information in general scientific literature which is peer-reviewed but not necessarily subject to quality assurance procedures (e.g. Good Laboratory Practice). The frameworks and designs for work generating data are important determinants of quality."

5. Imported GM foods versus GM crops

Some submitters (GeneEthics Network, National Council of Women of Australia) have argued that approvals for GM foods for import is a tacit approval for the GM crop to be grown in Australia

Response

The regulatory framework for approval by ANZFA of safety of GM foods (imported foods and derived from GM crops grown in Australia) is separate from that of the Office of the Gene Technology Regulator (OGTR), which has responsibility for approving the environmental release of GM crops. ANZFA's responsibilities are to ensure the safety of the food supply and protect public health. Approval of GM food under Standard A18 of the Food Standards Code (Standard 1.5.2 of the joint Australia New Zealand Food Standards Code) is not, and would never be, a tacit approval for the environmental release of the crop in Australia since the environmental issues are completely separate and entirely different to food safety issues.

Specific issues

This section of the report will only address those issues raised in public submissions that are specific to the assessment of this application.

Issues raised in first round of public comment (see Attachment 5 for summary)

1. GeneEthics and the Genetic Engineering Action Group express the concern that growing a crop with a herbicide-resistant trait inevitably results in higher levels of usage of the herbicide, with concomitant concerns in relation to the potential toxicity of the herbicide in food and its effects on human health.

Response

This concern is raised frequently about plants genetically modified to be resistant to a herbicide and in this instance, glyphosate. However, as glyphosate is used commercially on conventional crops, this is not an issue that is peculiar to the transgenic sugarbeet in this application. In Australia, the National Registration Authority for Agricultural and Veterinary Chemicals (NRA) is responsible for assessing the toxicity of agricultural chemicals prior to their incorporation into farming practices, especially in the production of food crops. This is a rigorous process that entails investigation into the human and animal toxicity of the chemical, its effects on the environment and the potential effects of occupational exposure to the chemical. Consequently, a wide range of scientific data and technical information is taken into consideration when determining the maximum permissible amount of glyphosate residues in food, referred to as the Maximum Residue Limit (MRL).

The toxicity of glyphosate has been extensively studied in animal testing of a range of different species including rats, dogs, mice, rabbits, guinea pigs and monkeys. The testing of the toxicity of glyphosate also included long term studies in which animals were exposed to varying levels of the herbicide over periods of time in excess of 2 years. An assessment of this toxicological data has been undertaken by the Commonwealth Department of Health and Aged Care to support the establishment of acceptable daily intake levels. The results of the animal studies indicate that glyphosate exhibits a very low degree of toxicity.

Furthermore, in the agricultural environment, when applied to emerged weeds, glyphosate shows no residual activity. This is because it binds strongly to soil particles and is readily broken down by soil microorganisms.

Because of the rapid transportation from the leaves of treated plants to the roots, it is effective in destroying perennial weeds, which can survive other herbicides, which only affect the above-ground parts of the weed plant.

Issues raised in second round of public comment (see Attachment 5 for summary)

1. The PHAA have raised some issues in relation to Attachments 5 and 6 of the risk assessment reports.

Response

The PHAA states that previous comments made on previous applications "do not even get a mention in Attachment 5: Summary of Public Submissions and Attachment 6: General Issues Raised in Public Comments". Only the issues raised by submitters during the two rounds of public consultation are listed in Attachment 5 of the specific reports. Attachment 6 addresses the more general issues, which have been raised in relation to GM foods. This includes the issues raised by PHAA.

2. The PHAA raised concerns regarding the lack of detail in reporting of the parameters investigated in the acute toxicity tests on CP4 EPSPS, GUS and Protein 34550

Response

Acute toxicity studies in experimental animals are required by ANZFA for investigation of the safety of the newly expressed protein. The few proteins in nature, which exert toxic activity, (e.g. diphtheria toxin, certain snake venoms etc) do so within a short time period.

It should be noted that acute toxicity studies or short-term feeding studies are not meant to substitute for long-term toxicity tests. ANZFA takes the view, based on all the supporting evidence including comprehensive data on the molecular characterisation, and the compositional, toxicological and nutritional analysis, that long-term studies on the novel proteins are not necessary (see Attachment 6).

ANZFA requires that, as with all methods of analysis, acute oral toxicity studies are conducted according to international guidelines (e.g. OECD, FIFRA, EPA). The studies supplied by the applicant in support of application A378 – Food derived from glyphosate-tolerant sugarbeet line 77 have been consistent with such guidelines. For instance, the OECD Guidelines for Testing of Chemicals ("Acute Oral Toxicity") are based on international documents including: the *Principles and Methods for Evaluating the Toxicology of Chemicals*. WHO Publication: Environmental Health Criteria 6; the *Principles and Procedures for Evaluating the Toxicity of Household Substances*. National Academy of Sciences; and *A European Community Study on an Intercomparison Exercise on the Determination of Single Dose Oral LD50 in Rats*. Commission of the European Communities.

The OECD guideline for acute oral toxicity testing requires that animals should be carefully examined at least once a day. Animals that die during the test are necropsied as are those animals that survived and have been sacrificed at the end of the test.

In terms of examination after death, the guidelines recommend that necropsy of all animals should be carried out and all gross pathological change be recorded. Gross pathology is the first step in examination of organs and refers to clear and obvious changes, abnormalities or lesions visible upon inspection.

In addition, protein toxicity is dependent on integrity of the three dimensional structure. Consequently, in addition to acute toxicity testing, susceptibility of the protein to heat and other processing conditions that the food may undergo, and its digestibility in the gastrointestinal tract are required. These tests can provide additional re-assurance that the proteins will have no adverse effects in humans when consumed as part of a food.

As science advances, should developments in the technology result in modifications that provide significantly different nutrient combinations or other novel food characteristics not previously encountered in the food supply, such foods may require additional considerations to permit comprehensive assessment. The guidelines for the safety assessment of GM foods provide this flexibility of approach.

3. The National Council of Women of Australia assert that ANZFA are approving GM sugarbeet as a food on the basis of previous approval by the US FDA and when it is not approved for growing in Australia.

Response

In all cases ANZFA undertakes its own assessment of the safety of foods produced using gene technology. In addition to internal peer review by the ANZFA scientific specialists, the safety assessments also undergo peer review by an independent panel of external experts who are considered leaders in this field. ANZFA has never relied on approvals given by the US FDA as a basis for approval of GM foods in Australia.

It should be again noted that the application is for approval of a GM food that at this time is imported only. The approval of the food has no connection with approval for growing in Australia and New Zealand.

4. Dr Kate Clinch-Jones raised safety concerns on feeding GM sugarbeet by-products (animal feeds) to animals

Response

GM Sugarbeet is not approved to be grown in Australia. Thus, there is little likelihood of any portion of GM sugarbeet plants being fed to animals. Since the bulk of the food derived from glyphosate-tolerant sugarbeet line 77 (GTSB77) will be in the form of imported food products such as refined sugar and molasses, it is extremely unlikely that such products will be used as animal feed.

The issue of the regulation of GM feeds is the responsibility of the Office of the Gene Technology Regulator (OGTR).

Many animal feeds are derived from the same GM foods that are used for human consumption and 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.

The human health consequences, if any, of the feeding of GM foods to animals should be assessed on a case-by-case basis, taking into account any potential hazards identified for the novel proteins present in the food and changes to the composition of the food combined with a consideration of the animal feeding practices used for the particular food/feed in question. If hazards are identified in an assessment of a GM food, then consideration should also be given to potential human exposure to that hazard through the use of the GM food as a feed for animals.

Information available from the Federation of Animal Science Societies (FASS – a professional organization made up of approximately 10,000 scientists in academia, government and industry which exists to serve society through the improvement of all aspects of food animal production) indicates that no DNA and/or protein can be detected in animals (products such as meat muscle, whole milk, poultry and eggs), fed a variety of GM commodities. In addition, nutrients in meat, milk and eggs from livestock fed GM feeds are the same as those from livestock fed conventional feeds. Because components of feeds are broken into smaller components during digestion by the animal, plant proteins have not been detected in milk, meat or eggs. Peer reviewed journal articles (e.g. "The fate of forage plant DNA in farm animals: a collaborative case study investigating cattle and chicken fed recombinant plant material" Einspauier et al., Eur Food Res Technol 212:129-134, 2001) have recently investigated the fate of ingested recombinant DNA plant material in cattle and chickens being fed conventional maize or recombinant Bt maize. The results clearly showed no recombinant DNA Bt maize in cattle or poultry.

5. Dr Kate Clinch-Jones raised the findings of Arpad Pusztai.

Response

The publicised and controversial research projects carried out by Dr Arpad Pusztai and Dr Stanley Owen into the toxic effect of inserting lectin genes into potatoes have been examined by the British Royal Society who have rebutted the work of Pusztai as being seriously flawed. Within the scientific community there is general agreement that the results of Dr Pusztai's experiments are inconclusive insofar as there were flaws in the process, and the project was incomplete.

5. Some submitters (GeneEthics Network, Dr Kate Clinch-Jones) have used the example of L-tryptophan to demonstrate an unintentional effect of gene technology

Response

This issue has been previously addressed and the consensus of opinion by experts on this issue is that the fermentation process used to produce the L-tryptophan in this case resulted in a toxin that caused the deaths, not the GM bacteria used in the process.

4.4 Risk management

Under Standard 1.5.2, a GM food must undergo a safety assessment in accordance with ANZFA's safety assessment guidelines.

On the basis of the conclusions of the safety assessment, together with a consideration of the public submissions, it is recommended that Table 1 to Clause 2 of Standard 1.5.2 be amended to include food from glyphosate-tolerant sugarbeet line 77. The recommended variation to Standard 1.5.2 is provided in Attachment 1.

In relation to the concerns raised in the public submissions with regard to gene technology and GM food, ANZFA has prepared a public discussion paper on the safety assessment process for GM food[2]. This is widely available and may assist in addressing some of the concerns raised by the public. Other government and industry bodies are also addressing the broader concerns in relation to gene technology.

4.5 Regulatory impact assessment

The benefits and costs associated with the proposed amendment to Standard 1.5.2 have been analysed in a Regulatory Impact Assessment (see Attachment 3). The benefits of the proposed amendment to approve food from glyphosate-tolerant sugarbeet line 77 primarily accrue to the food industry and government, with potentially a small benefit to the consumer.

5. CONCLUSIONS

- There are no public health and safety concerns associated with the genetic modifications used to produce glyphosate-tolerant sugarbeet line 77.

- Food from glyphosate-tolerant sugarbeet line 77 is not different to that from other commercially available sugarbeet in terms of their safety and nutritional adequacy.

- On 7 December 2001, food products containing food from glyphosate-tolerant sugarbeet line 77 will require labelling if it is shown that novel DNA and/or protein is present in the final food.

- The proposed amendment to the *Food Standards Code* is consistent with the section 10 objectives of the *Australia New Zealand Food Authority Act* 1991 and the Regulatory Impact Assessment.

6. RECOMMENDATION

On the basis of this assessment, ANZFA recommends that Standard A18 in Volume 1 and Standard 1.5.2 in Volume 2 of the *Food Standards Code* be amended to give approval to the sale of such food in Australia and New Zealand. The proposed amendment to Standard A18 in Volume 1 (Standard 1.5.2 in Volume 2) is provided in Attachment 1 to this report.

[2] ANZFA (2000) GM foods and the consumer: ANZFA's safety assessment process for genetically modified foods. ANZFA Occasional Paper Series No.1

FOOD STANDARDS SETTING IN AUSTRALIA AND NEW ZEALAND

The Governments of Australia and New Zealand entered an Agreement in December 1995 establishing a system for the development of joint food standards. On 24 November 2000, Health Ministers in the Australia New Zealand Food Standards Council (ANZFSC) agreed to adopt the new *Australian New Zealand Food Standards Code*. The new Code was gazetted on 20 December 2000 in both Australia and New Zealand as an alternate to existing food regulations until December 2002 when it will become the sole food code for both countries. It aims to reduce the prescription of existing food regulations in both countries and lead to greater industry innovation, competition and trade.

Until the joint *Australia New Zealand Food Standards Code* is finalised the following arrangements for the two countries apply:

- **Food imported into New Zealand other than from Australia** must comply with either Volume 1 (known as Australian *Food Standards Code)* or Volume 2 (known as the joint *Australia New Zealand Food Standards Code)* of the Australian *Food Standards Code*, as gazetted in New Zealand, or the New Zealand *Food Regulations 1984,* but not a combination thereof. However, in all cases maximum residue limits for agricultural and veterinary chemicals must comply solely with those limits specified in the New Zealand *(Maximum Residue Limits of Agricultural Compounds) Mandatory Food Standard 1999.*

- **Food imported into Australia other than from New Zealand** must comply solely with Volume 1 (known as Australian *Food Standards Code)* or Volume 2 (known as the joint *Australia New Zealand Food Standards Code)* of the Australian *Food Standards Code*, but not a combination of the two.

- **Food imported into New Zealand from Australia** must comply with either Volume 1 (known as Australian *Food Standards Code)* or Volume 2 (known as *Australia New Zealand Food Standards Code)* of the Australian *Food Standards Code* as gazetted in New Zealand, but not a combination thereof. Certain foods listed in Standard T1 in Volume 1 may be manufactured in Australia to equivalent provisions in the New Zealand *Food Regulations 1984.*

- **Food imported into Australia from New Zealand** must comply with Volume 1 (known as Australian *Food Standards Code)* or Volume 2 (known as *Australia New Zealand Food Standards Code)* of the Australian *Food Standards Code*, but not a combination of the two. However, under the provisions of the Trans-Tasman Mutual Recognition Arrangement, food may **also** be imported into Australia from New Zealand provided it complies with the New Zealand *Food Regulations 1984.*

- **Food manufactured in Australia and sold in Australia** must comply with Volume 1 (known as Australian *Food Standards Code)* or Volume 2 (known as *Australia New Zealand Food Standards Code)* of the Australian *Food Standards Code* but not a combination of the two. Certain foods listed in Standard T1 in Volume 1 may be manufactured in Australia to equivalent provisions in the New Zealand *Food Regulations 1984.*

In addition to the above, all food sold in New Zealand must comply with the New Zealand *Fair Trading Act 1986* and all food sold in Australia must comply with the Australian *Trade Practices Act 1974,* and the respective Australian State and Territory *Fair Trading Acts.*

Any person or organisation may apply to ANZFA to have the *Food Standards Code* amended. In addition, ANZFA may develop proposals to amend the Australian *Food Standards Code* or to develop joint Australia New Zealand food standards. ANZFA can provide advice on the requirements for applications to amend the *Food Standards Code*.

FURTHER INFORMATION

Submissions: No submissions on this matter are sought as the Authority has completed its assessment and the matter is now with the Australia New Zealand Food Standards Council for consideration.

Further information on this and other matters should be addressed to the Standards Liaison Officer at the Australia New Zealand Food Authority at one of the following addresses:

PO Box 7186
Canberra BC ACT 2610
AUSTRALIA
Tel (02) 6271 2258
email: slo@anzfa.gov.au

PO Box 10559
The Terrace WELLINGTON 6036
NEW ZEALAND
Tel (04) 4739942
email: anzfa.nz@anzfa.gov.au

Copies of assessment reports or other information papers are available on the website at www.anzfa.gov.au then <Food Standards> then < Recent Standards Development>. Further information should be addressed to the Authority's Information Officer at the above address, or e-mail info@anzfa.gov.au.

ATTACHMENTS

1. Draft variation to Volume 1 and Volume 2 of the *Food Standards Code*
2. Safety assessment report
3. Regulatory impact assessment
4. World Trade Organization agreements
5. Summary of public submissions
6. General issues raised in public submission (Attachment 6)
7. Statement of Reasons

ATTACHMENT 1

DRAFT VARIATION TO THE *FOOD STANDARDS CODE*

APPLICATION A378

FOOD DERIVED FROM GLYPHOSATE-TOLERANT SUGARBEET LINE 77

To commence: on gazettal

[1] *Standard A18 of Volume 1 and Standard 1.5.2 of Volume 2 are varied by inserting in Column 1 of the Table to clause 2 -*

Food derived from glyphosate-tolerant sugarbeet line 77.

ATTACHMENT 2

SAFETY ASSESSMENT REPORT

APPLICATION A378

FOOD DERIVED FROM GLYPHOSATE-TOLERANT SUGARBEET LINE 77 (GTSB77)

SUMMARY AND CONCLUSIONS

Food derived from glyphosate-tolerant sugarbeet line 77 has been assessed by ANZFA to evaluate its safety for human consumption. The modified sugarbeet under consideration is known commercially as Roundup Ready® sugarbeet and is tolerant to applications of the herbicide glyphosate. This report describes the scientific assessment of the application. A number of criteria are used in this assessment including a characterisation of the transferred genes, the modifications at the DNA, protein and whole food levels, compositional analyses, and the potential allergenicity and toxicity of the newly expressed proteins. This enables the intended as well as any significant unintended changes to be identified, characterised and evaluated for their safety.

Nature of the genetic modification

Glyphosate-tolerant sugarbeet line 77 was generated by the transfer of three new genes: the *cp4-epsps* gene, the *uidA* gene and a modified *gox* gene. Two of the transferred genes - the *cp4 epsps* and *gox* genes confer tolerance to the herbicide glyphosate. Both genes are bacterially-derived and have distinct modes of action. The *cp4 epsps* gene encodes a 5–enolpyruvyl shikimate–3–phosphate synthase enzyme that is not sensitive to applications of glyphosate. The *gox* gene encodes the glyphosate oxidoreductase enzyme that can degrade the herbicide however it was truncated during transformation and 69% of the gene is fused to sugarbeet DNA resulting in a chimeric gene. Although mRNA transcripts from this chimeric gox sequence are present in the sugarbeet, no novel protein is translated and the sugarbeet does not have GOX enzyme activity.

The *uid*A gene encodes β–D-glucuronidase (GUS), which serves as a marker for plant transformation.

Glyphosate-tolerant sugarbeet was generated using *Agrobacterium*-mediated transformation.

Single copies of the *cp4 epsps*, *uid*A and the chimeric *gox* gene were stably integrated at one insertion site in sugarbeet over multiple generations. They were also inherited in a Mendelian manner, and always segregated together.

General safety issues

Sugarbeet has a long history of use as a source of sugar production and accounts for approximately one third of world sugar production. The major food products are pure sucrose and molasses. Sugarbeet pulp may be used as food fibre. By-products from sugarbeet (tops, leaves and post-processing trash) are used as cattle feed.

Two new proteins are present in glyphosate-tolerant sugarbeet line 77, namely the CP4 EPSPS and GUS proteins. These proteins were detected in very low levels in root tissue of sugar beet line77 (58ppm and 0.5ppm for CP4 EPSPS and GUS respectively). They were also present at higher levels in leaf and stem tissue (237ppm and 3ppm for CP4-EPSPS and GUS respectively). Neither protein was detected in the principal food fractions produced from sugar beet, refined sugar and molasses. The novel proteins were also detected at very low levels in sugar pulp, which may be used as a source of dietary fibre. However the proteins are not expected to be present due to the extensive refining that pulp undergoes if it is processed into refined dietary fibre. Thus exposure to the novel proteins is likely to be extremely low.

Glyphosate-tolerant sugar beet line 77 contains no antibiotic resistance genes and therefore poses no risk to the development of antibiotic resistant pathogenic bacteria through the horizontal transfer of antibiotic resistance genes. The transfer of novel genetic material from glyphosate-tolerant sugar beet line 77 to human cells via the digestive tract was assessed, but was considered to be extremely unlikely to occur, and unlikely to pose any special additional risks compared with the large amount of DNA naturally present in all foods.

Toxicological issues

The presence of naturally occurring toxins and allergens in glyphosate-tolerant sugar beet line 77 was investigated. Saponins are the only known toxicants found in sugar beet and are actively eliminated in sugar processing. However, the levels of saponins were evaluated in glyphosate-tolerant sugar beet line 77. In most field trials, no differences between saponin levels in glyphosate-tolerant sugar beet line 77 and control sugarbeets were observed. In one trial, small but significant decreases in saponin levels were evident when glyphosate-tolerant sugar beet line 77 was treated with glyphosate. However, as the difference was not consistent across all field trials and the differences was a decrease in this toxicant, which is regarded as beneficial, it is concluded that no health and safety concerns are raised.

The potential toxicity and allergenicity of the CP4 EPSPS and GUS proteins as well as the potential protein product from the chimeric *gox* gene were assessed. These proteins did not possess characteristics of known toxins and results from acute oral toxicity testing in mice did not indicate any toxic effects.

The potential for the novel proteins to be allergenic was investigated using a number of criteria, including amino acid sequence homology with known allergens, history of use and common physicochemical properties of allergens, including the sensitivity to digestion by digestive enzymes. The novel proteins were found to be rapidly digested in conditions that mimic human digestion. Additionally, they show no amino acid similarity to known allergens and are not detectable in products refined from the glyphosate-tolerant sugarbeet.

Nutritional issues

Detailed compositional analyses conducted over multiple years and geographic regions (USA and Europe) were carried out to establish the nutritional adequacy of glyphosate-tolerant sugar beet line 77. The effect of glyphosate use on the composition of sugarbeet was also examined. Analyses included crude ash, crude fibre, crude protein, carbohydrate and dry matter in both tops and roots (both raw and processed into brei powder used in sugar production).

Additional quality components were measured in roots including, variously, invert sugar (glucose + fructose) content, polarisation (% sucrose), sodium, potassium and amino nitrogen.

No biologically meaningful differences in any compositional and quality parameters relevant to food were identified between non-transgenic, control sugar beet and sugarbeet line 77, both untreated or treated with glyphosate at recommended agronomic application rates.

It is concluded that glyphosate-tolerant sugar beet is equivalent to other commercially available sugarbeet with respect to composition and nutritional quality. No nutritional risks are posed by consuming food derived from glyphosate-tolerant sugarbeet line 77.

Conclusion

On the basis of the data submitted in the present application, glyphosate-tolerant sugar beet line 77 is equivalent to other commercially available sugarbeet in terms of its safety and nutritional adequacy.

1. BACKGROUND

Monsanto Australia Ltd have made an application to ANZFA to vary Standard A18 of the *Food Standards Code* to include food derived from sugarbeet which has been genetically modified to tolerate applications of the herbicide glyphosate. The genetically modified sugarbeet is marketed in the USA under the names Roundup® Ready Sugar Beet or Glyphosate-Tolerant Sugar Beet.

Sugarbeet has been grown for sugar production since the late eighteenth century when 'white Silesian beet' was identified as a source of sugar in Europe. Napoleon encouraged the use and breeding of sugarbeet to provide an alternative to cane sugar, which required shipment from the West Indies. Sugarbeet currently accounts for approximately 1/3rd of world sugar production with some 35% being produced in the EU, 20% in Russia and 10% in the USA (Macrae *et al.* 1993). Sugar in Australia is entirely produced from sugar cane.

Sugarbeet is processed into two major food products - pure sucrose and molasses. Sugarbeet pulp is a by-product of processing which has occasionally been purified and sold as food fibre. Waste products from both pre-processing (leaves and tops) and post-processing (trash) are used as cattle feed.

Weed competition in commercial sugarbeet fields constitutes a significant crop production problem. Glyphosate is the active ingredient of the herbicide Roundup® which is used widely as a non-selective pre-emergent weed control agent in primary crops including sugarbeet. Glyphosate acts by specifically binding and blocking the activity of the enzyme 5-enolpyruvylshikimate-3-phosphate synthase (EPSPS) that is essential for the biosynthesis of aromatic amino acids in all plants, bacteria and fungi (Steinrucken and Amrhein, 1980). Biochemical studies of the EPSPS enzyme have shown that natural variation in glyphosate-enzyme binding affinity exists across a variety of organisms, particularly across bacterial species (Schulz *et al*. 1985). Tolerance to glyphosate in plants can therefore be achieved by introducing a bacterial version of the *epsps* gene that encodes for a version of the EPSPS protein with a reduced binding affinity for glyphosate, thus allowing plant aromatic amino acid synthesis to function normally in the presence of the herbicide.

The glyphosate-tolerant sugarbeet in this application – referred to as glyphosate-tolerant sugar beet line 77 – was developed through the introduction of the *cp4-epsps* gene derived from the soil bacterium *Agrobacterium sp.*CP4 (Padgette *et al.*, 1996). The *cp4-epsps* gene has been transferred into a number of other crop plants, including soybean, canola, corn, and cotton, to establish glyphosate tolerance. These plants are also the subjects of applications to ANZFA to vary Standard A18 (ANZFA 1999a).

Glyphosate-tolerant sugarbeet line 77 was approved for environmental release by the US Department of Agriculture (USDA)/Animal and Plant Health Inspection Service (APHIS) in 1998 (US Federal Register 64(5) Jan. 1999). Food and feed use of glyphosate-tolerant sugar beet GTSB77 was also notified to the US Food and Drug Administration (FDA) in 1998.

Glyphosate-tolerant sugarbeet line 77 has not been submitted for environmental release approval in either Australia or New Zealand.

While refined sugar derived from sugarbeet line 77 is not specifically imported into Australia and New Zealand, it may occur as an element within ingredients used in locally-produced processed foods or as an ingredient within imported processed foods.

2. DESCRIPTION OF THE GENETIC MODIFICATION

2.1 Methods used in the genetic modification

Monsanto have submitted the following report:

Kolacz, K.H. and G.F. Barry 1996. Roundup® Ready Sugar Beet: Plant Transformation Vector. Monsanto Technical Report MSL-14678. Monsanto Company, St Louis, USA.

Glyphosate-tolerant sugar beet line 77 was produced by *Agrobacterium*-mediated transformation of the proprietary cytoplasmic male sterile sugarbeet line A1012 with plasmid PV-BVGT03 (see Figure 1). The *Agrobacterium*-mediated DNA transformation system is the basis of natural plasmid-induced crown-gall formation in many plants and is well understood (Zambryski, 1992). The genes of interest were inserted into the plasmid between DNA sequences known as the Left and Right Borders (LB and RB). These border sequences were isolated from the Ti plasmid of *Agrobacterium* and normally delimit the DNA sequence (T-DNA) transferred into the plant.

Plasmid PV-BVGT03 contained four gene cassettes each consisting of the gene of interest plus specific controlling sequences within the Left and Right Borders. The primary genes of interest in each of the cassettes were:

1. the *cp4-epsps* gene from *Agrobacterium sp*. strain CP4. This gene encodes for glyphosate-insensitive form of 5-enolpyruvylshikimate-3-phosphate synthase (CP4-EPSPS) which maintains aromatic amino acid synthesis in the presence of glyphosate;
2. the *uidA* gene from the common bacterium *Escherichia coli.* This gene encodes for β-D-glucuronidase (GUS) which serves as a visible marker during the plant transformation process;
3. a modified *gox* gene from the soil bacterium *Ochromobactrum anthropii* strain LBAA [previously *Achromobacter sp*]. This gene encodes for glyphosate oxidoreductase which metabolises glyphosate to an inactive form; and

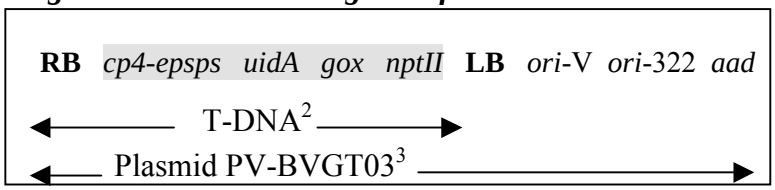
4. the *nptII* gene coded by the bacterial transposon Tn5. This gene encodes for neomycin phosphotransferase II that enables selection of transformed plant tissues in the presence of the antibiotic kanamycin.

Genes outside the Left and Right Border segments are generally not transferred during the transformation. Three genetic elements are located outside the border sequences in plasmid PV-BVGT03:

1. the vegetative origin of replication (ori-V) that permits plasmid replication in *Agrobacterium* (Rodgers *et al*, 1987).
2. the bacterial origin of replication (*ori-322*) that permits plasmid replication in *Escherichia coli* (Sutcliffe, 1979), and;
3. *aad* – derived from bacterial transposon Tn7 and encodes aminoglycoside adenyltransferase (AAD) which confers resistance to the antibiotics spectinomycin and streptomycin. This gene was included in the construct as a marker to allow for selection of bacteria containing plasmid PV-BVGT03 prior to transformation of the plant cells.

The gene arrangement is shown in Figure 1.

Figure 1: Schematic diagram of PV-BVGT03[1]



[1]See text or Table 1 for abbreviations.
[2]The shaded region denotes the T-DNA – genes within the LB and RB which are usually transferred via the *Agrobacterium* transformation system.
[3]Genes contained in the entire plasmid. Genes outside the LB and RB are normally not transferred.

2.2 Function and regulation of the novel genes

Monsanto have submitted the following reports:

Mannerlof, M., Tuvesson, S., Steen, P. and P. Tenning. 1997. Transgenic sugar beet tolerance to glyphosate. Euphytica 94: 83-91.

Mannerlof, M. and J. Gielsen. 1996. Molecular analysis of Roundup Ready sugar beet line T9100152 (Note: this line is the same as GTSB77). Novartis Seeds, Technical Report.

Each of the genes of interest, intended for transfer from plasmid PV-BVGT03 to sugar beet requires regulatory sequences that promote and terminate gene transcription into messenger RNA (mRNA) and translation into a protein product targeted to the appropriate cellular compartment. A promoter sequence is the leading control element of a gene that dictates when, where and to what extent, the gene is transcribed into mRNA. A terminator is a DNA sequence that defines the terminal end of a gene by stopping the transcription of mRNA. These sequences can be unique in each organism and thus regulatory elements derived from plants are often used in gene constructs to enable the functioning of novel genes derived from other organisms.

The regulatory and coding regions for each novel gene cassette to be transferred from plasmid PV-BVGT03 are summarised in Table 1 below.

Table 1: Description of gene cassettes for transfer from plasmid PV-BVGT03.

Cassette	Genetic Elements	Source	Function
EPSPS	Modified 35S promoter (35S)	figwort mosaic virus	Promoter of high level constitutive gene expression in plant tissues
	Chloroplast Transit Peptide (CTP2)	*Arabidopsis thaliana* *epsps* gene	Directs the EPSPS protein into the chloroplast where it is active
	CP4-EPSPS coding region (*cp4-epsps*)	*Agrobacterium* sp. Strain CP4	Coding sequence for 5-enolpyruvylshikimate-3-phosphate synthase (CP4-EPSPS) which maintains aromatic amino acid synthesis through its insensitivity to glyphosate
	Pea E9 3' terminator (E9-3')	*Pisum sativum* *rbcS* gene	Contains signal sequences for termination of transcription and directs polyadenylation
GUS	Modified cauliflower mosaic virus 35S promoter (CaMV)	cauliflower mosaic virus	Promoter for high level constitutive gene expression in plant tissues
	UidA coding region (*uidA*)	Protein coding sequence of the enzyme β-glucuronidase (*uidA* gene) from *Escherichia coli*	Colourimetric marker enzyme used for selection of transformed plant lines
	Pea E9 3' terminator (E9-3')	*Pisum sativum* *rbcS* gene	Contains signal sequences for termination of transcription and directs polyadenylation
GOX	Modified 35S promoter (35S)	figwort mosaic virus	Promoter for high level constitutive gene expression in plant tissues
	Chloroplast Transit Peptide (CTP1)	Chloroplast transit peptide sequence from small subunit 1A of Ribulose bisphosphate carboxylase from *Arabidopsis thaliana*	Directs the GOX protein into the chloroplast which is the site of action
	Gox coding region (*gox*)	Synthetic glyphosate oxidoreductase gene based on sequence from the bacterium *Ochromobactrum anthropii* strain LBAA	Metabolises glyphosate to amino-methyl phosphonic acid (AMPA) and glyoxylate which are not active on EPSPS
	NOS 3' terminator	From nopaline synthase gene from *Agrobacterium* sp.	Contains signal sequences for termination of transcription and directs polyadenylation
NPTII	Modified Cauliflower mosaic virus 35s promoter (CaMV)	cauliflower mosaic virus	Promoter for high level constitutive gene expression in plant tissues
	NptII coding region (*nptII*)	Neomycin phosphotransferase II gene from bacterial transposon Tn5	Confers resistance to aminoglycoside antibiotics used as a plant selectable marker following transformation
	NOS 3' terminator	From nopaline synthase gene from *Agrobacterium* sp.	Contains signal sequences for termination of transcription and directs polyadenylation

2.2.1 The *cp4 epsps* gene cassette

EPSPS is an essential enzyme involved in the biosynthesis of aromatic amino acids via the shikimate metabolic pathway. This metabolic pathway is present in all plants, bacteria and fungi (Haslam, 1993). Plant variants of the EPSPS enzyme are inhibited by the herbicide glyphosate, however, bacterial variants of the EPSPS enzyme are, in general, not inhibited due to reduced binding affinity to the herbicide (Schültz *et al*, 1985). One such low binding-affinity variant is the *cp4-epsps* gene derived from the common soil bacterium *Agrobacterium.* The *cp4-epsps* gene was intended to be transferred to sugar beet to confer tolerance to glyphosate.

In the EPSPS cassette the *cp4-epsps* coding sequence from *Agrobacterium* was fused between a modified version of the 35S promoter from a figwort mosaic virus (P-CMoVb), which promotes constitutive expression of the gene in plant tissues, and the 3' end of the pea rbcS E9 gene (E9 3'), which terminates transcription and contains sequences that will direct the polyadenylation of the mRNA. The bacterial *cp4 epsps* gene was modified to create a synthetic gene, which allows for higher expression in plants. Bacterial genes have several features that reduce their ability to function efficiently in plants. These features include potential polyadenylation sites that are often rich with A+T nucleotides, a higher G+C nucleotide content than that often found in plant genes and codons that are not frequently used in plants. Some of these features can affect expression or stability of the RNA. These changes to the DNA sequence do not affect the functional activity of the expressed proteins.

The bacterial EPSPS enzyme was targeted to the chloroplast, the active site of the enzyme in higher plants (della Ciopa *et al*, 1986), by the chloroplast transit peptide sequence (CTP2) derived from the *Arabidopsis thaliana epsps* gene. This sequence was fused between the 35S promoter and the *cp4-epsps* coding region.

2.2.2 The GUS gene cassette

The *uidA* gene from the common bacterium *Escherichia coli* (*E. coli*) codes for the enzyme β-glucuronidase (GUS), an acid hydrolase that cleaves β-glucuronides (Jefferson *et al.,* 1987). The *uidA* gene was intended for introduction into sugarbeet line 77 to act as a visible marker in plant transformation. When present, GUS is capable of hydrolysing the chemical p-nitrophenyl-β-D-glucuronide into a colour-forming compound that enables visual scoring of transgenic events. GUS activity also occurs naturally in vertebrates and has been detected in a number of plant species including sugar beet where it can be differentiated from the *uidA* derived GUS due to a different pH activity optimum (Hu *et al.* 1990; Wozniak and Owens 1994).

In the GUS gene cassette the *uidA* coding sequence was fused between an enhanced 35S promoter derived from cauliflower mosaic virus (which promotes high-level constitutive gene expression in plant tissues), and the 3' non-translated region of the *rbcS* E9 gene from pea which directs polyadenylation.

2.2.3 The GOX gene cassette

The *gox* gene from the commonly found soil bacterium *Ochromobactrum anthropii* strain LBAA [formerly *Achromobacter sp*] codes for the enzyme glyphosate oxidoreductase (GOX) which, degrades glyphosate to aminomethylphosphonic acid (AMPA) and glyoxylate thus effectively inactivating the herbicide (Pipke and Amrhein, 1988; Barry *et al*, 1992).

AMPA is the principal metabolite of glyphosate and is readily degraded by several microorganisms. Glyoxylate is commonly found in plant cells and is broken down by the glyoxylic acid pathway for lipid metabolism.

The *gox* gene was intended for transfer to sugar beet to augment its resistance to glyphosate. In the GOX gene cassette the *gox* coding region was fused, between a modified 35S promoter sequence from a figwort mosaic virus (which promotes constitutive expression in plants) and a terminator sequence derived from the 3' non-translated region of the nopaline synthase gene from *Agrobacterium*. The GOX protein was targeted to the chloroplast, the site of action of glyphosate, by a chloroplast transit peptide (CTP1) sequence fused between the 35S promoter and the *gox* coding region. The CTP1 sequence was derived from the *Arabidopsis thaliana rubisco* gene (Timko *et al*, 1988).

2.2.4 The NPTII gene cassette

The *nptII* gene originates from the Tn5 bacterial transposon and is widely used as a selectable marker in the regeneration of transgenic plants (Kärenlampi 1996). The gene functions as a dominant selectable marker in the initial laboratory stages of plant cell selection following transformation (Horsch *et al* 1984, DeBlock *et al* 1984). It codes for the enzyme neomycin phosphotransferase II (NPTII) that confers resistance to the aminoglycoside antibiotics, neomycin, kanamycin, and geneticin (G418). The *nptII* gene was intended for transfer along with the *gox*, *cp4 epsps* and *uidA* genes, enabling those plant cells successfully transformed to grow in the presence of kanamycin.

In the *nptII* gene cassette the coding region of the *nptII* gene was fused between the 35S promoter sequence from cauliflower mosaic virus (which drives constitutive expression of the gene in plant tissues) and a terminator sequence derived from the 3' nontranslated region of the nopaline synthase gene from *Agrobacterium*.

2.3 Characterisation of the genes transferred to the plant

Molecular analysis of glyphosate-tolerant sugarbeet line 77 was used to detect the presence of transferred DNA sequences and to determine the copy number and stability of the inserted DNA.

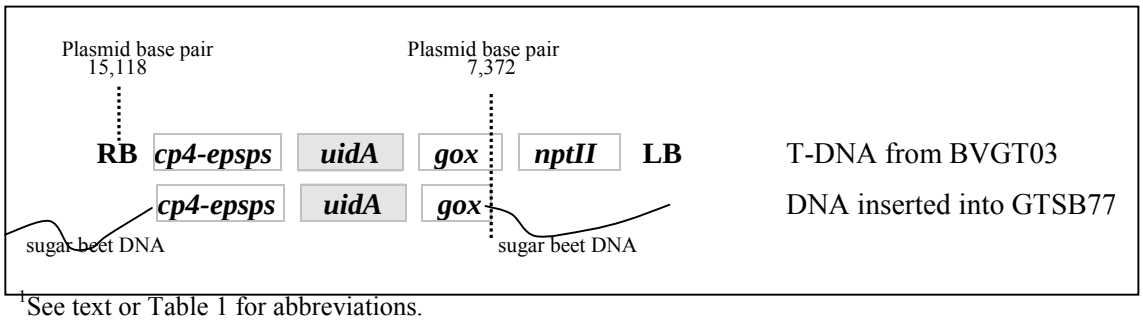
Using DNA hybridisation probes specific to each gene cassette, Southern blot analysis revealed that a single insertion event occurred with complete copies of the *cp4-epsps* and *uidA* genes and a partial copy of the *gox* gene being transferred from the T-DNA of plasmid PV-BVGT03. The analysis also demonstrated that the following genetic elements from PV-BVGT03 had not been transferred into glyphosate-tolerant sugarbeet line 77:

- the *nptII* gene;
- the bacterial origins of replication *ori-322* and *ori-V;* and
- the *aad* gene.

A genomic library of sugarbeet line 77 was made to characterise the border sequences of the insertion event with the sugar beet genome. Nucleotide sequencing revealed (Fig. 2) that the integrated DNA commenced 25bp downstream of the right border prior to the figwort mosaic virus promoter sequence of the *cp4-epsps* gene cassette and terminated 897 base pairs downstream of the *gox* gene start codon (at base pair 7372 of the T-DNA) within the coding region of the *gox* gene.

The upstream regulatory elements of the *gox* gene, the constitutive promoter 35S and the *A. thaliana* SSU1A gene chloroplast transit peptide (CTP1), were found to be intact. Sequencing downstream of the truncated *gox* gene into the sugarbeet genomic DNA revealed that 897bp of the *gox* gene had been transferred (representing 69% of the complete *gox* coding sequence). Two translational stop codons were identified in the sugar beet genome 130 base pairs and 234 base pairs downstream of the fusion junction in frame with the *gox* gene reading frame. A transcription termination signal was also identified within the sugar beet genomic DNA 650 base pairs downstream of the junction point.

Figure 2: Schematic diagram of the T-DNA from PV-BVGT03 and the DNA inserted into sugar beet GTSB77[1]



[1]See text or Table 1 for abbreviations.

The *nptII* gene and its associated genetic elements were not transferred into sugar beet line 77.

As the truncated-*gox* gene had the potential to be transcribed and translated into one or more chimeric GOX-like proteins, expression analysis of these putative proteins was undertaken (see Section 3 – General Safety Issues below).

2.4 Stability of the genetic changes

The stability of the inserted DNA was demonstrated using Southern blot analysis of tissues from the R_2, R_3 and R_4 generations of sugarbeet line 77. The right junction region was probed using an internal fragment of the *cp4-epsps* gene and the left border region was probed using an internal fragment of the *gox* gene. Segregation analysis based on this molecular analysis showed that a single dominant insertion event had occurred that segregated as a single locus according to Mendelian principles. The analysis further showed that the chimeric *gox* gene was stably maintained through generations.

Phenotypic segregation analysis was also undertaken of the glyphosate-tolerant trait and GUS activity in these generations and confirmed an inheritance pattern consistent with the stable transfer of a single dominant locus for these genes. These phenotypes were also shown to be stable over multiple generations in successive cropping years.

2.5 Conclusions regarding the genetic modification

The data supports the conclusion that an *Agrobacterium*-mediated transformation system was successful in transferring as one insertion event, a single complete copy of the *cp4 epsps* and *uidA* gene cassettes and a truncated version of the *gox* gene cassette from plasmid PV-BVGT03 into glyphosate-tolerant sugarbeet line 77.

All three transferred elements were demonstrated to be stably integrated over several generations. No other genetic elements, including the *nptII* gene cassette, were shown to be transferred from the plasmid in this transformation event. As the gox gene cassette truncation ran into the sugar beet genome, the possibility that novel GOX-like chimeric proteins may be expressed was further analysed (see Section 3.2 – Nature of expressed novel proteins).

3. GENERAL SAFETY ISSUES

Monsanto have submitted the following reports:

Anderson, J.S. 1995. Adaptation of an indirect ELISA to quantitate of CP4-EPSPS in Roundup Ready™ beet leaf and root tissue. Monsanto Technical Report MSL-14332. Monsanto Company, St. Louis USA 63198.

Geis, M.T. 1995. Adaptation of a direct ELISA to detect and quantitated β-glucuronidase (GUS) in Roundup ™ sugar beets. Monsanto Technical Report MSL-14252. . Monsanto Company, USA 63198.

Harrison, L.A., Bailey, M.R., Lleimbruber, R.M., Smith C.E., Nida, D.L., Taylor, M.L., Gustafson, M., Heeren, B. and S.R. Padgette. 1993. Characterisation of microbially-expressed protein: CP4 EPSPS. Monsanto Technical Report MSL-12901. Monsanto Company, USA 63198.

Hontis, A.M. 1997. Protein expression analysis of roots and tops from glyphosate-tolerant beet (RR beet). 1996 European field trials. Monsanto Technical Report MLL-30570. Monsanto Company, USA 63198.

Lee, T.C. and J.D. Astwood. 2000. Determination of CP4-EPSPS, GUS and Protein 34550 in sugar beet pulp, molasses and sugar. Monsanto Technical Report MSL-16285. Monsanto Company, USA 63198.

Nickson, T.E., Mhadeo, D. and G. Go. 1997. Characterization of Protein 34550 produced in *Escherichia coli* containing pMON34550. Monsanto Technical Report MSL-14944. Monsanto Company, USA 63198.

Silvanovich, A., Lee, J.L., Mikols, C.L., and J.D. Astwood. 2000. Characterization of products derived from the *34550* transcriptional unit in Roundup Ready® sugar beet line #77. Monsanto Technical Report MSL 16253. Monsanto Company, USA 63198.

Taylor, M.L., M.T. Geis, P.T., Weston, P. and T.E. Nickson. 1996. Assessment of equivalence of CP4-EPSPS and GUS proteins produced in *Escherichia coli* and Roundup Ready™ sugar beet. Monsanto Technical Report MSL 14560. Monsanto Company, USA 63198.

Glyphosate-tolerant sugarbeet line 77 was approved for environmental release in the USA in 1998 (USDA/APHIS 1998). Foods derived from sugarbeet line 77 were approved for use in human food and animal feed in the USA in 1998. While refined sugar derived from sugar beet GTSB77 is not specifically imported into Australia and New Zealand, it may occur as an element within ingredients used in locally produced processed foods or as an ingredient within imported processed foods.

Glyphosate-tolerant sugarbeet line 77 has been evaluated against the safety assessment guidelines developed by ANZFA. The majority of data presented has been derived from whole sugar beet plants. Refined sugar components and, rarely, refined dietary fibre are the only human food products derived from sugarbeet line 77. The safety assessment issues relate to Group B foods – food ingredients – as indicated in the guidelines for safety assessment of food produced using gene technology (ANZFA 1999b).

3.1 History of the use of sugar and sugar beet as a food source

Sugar, as the simple carbohydrate sucrose, has multiple uses and functions in food preparation and production. These range from:

- use as a sweetener in, for example, beverages, confectionary and ice cream;
- use as the energy source for yeasts used to leaven bread;
- use as a preservative agent in jams and jellies.

Aside from water, carbohydrates are the single largest energy component in common diets with most being derived from fruit, vegetables and cereal products. Approximately 12% of an individual's daily energy intake is derived from sugar, added in either raw (such as molasses) or refined (such as crystalline sugar) forms to various foods or food components (Silliman and Coulston, 1991). Sugar use patterns in the Australian domestic market in 1990 are shown in Table 2.

Table 2: Sugar use patterns in the Australian domestic market*

Beverages	
non-alcoholic	**30%**
alcoholic	**7%**
Retail (table sugar etc)	**20%**
Confectionary	**11%**
Other (incl. Wholesale)	**11%**
Bakery products	**8%**
Preserved foods	**8%**
Dairy foods	**5%**

*** from Food Australia, 1995.**

Sugar produced in Australia and New Zealand is derived entirely from sugar cane with 3-4 million tonnes being produced annually depending on season and markets. Approximately 20% (600-800,000 tonnes) is used domestically and the remainder exported to markets principally in Sth East Asia and Nth America. Approximately 10,000 tonnes of sugar is imported annually accounting for 1.5% of domestic sugar use. Imported sugars are mainly from sugar cane sourced from Sth. East Asia and are chiefly in the form of refined specialty products.

Sugarbeet root has been used as a source of sugar since ancient times being initially cultivated in southern Europe and North Africa, although production was limited. The prominence of sugarbeet rose, however, when a practical method for extracting sugar was invented in Germany in the mid 18th century. Sugarbeet production in France, Austria, Hungary and Russia grew rapidly thereafter and was boosted in other European countries during the reign of Napoleon who ordered mass plantings following the closure of European ports to ships bearing sugarcane from tropical regions. Sugarbeet was brought to the United States in the middle of the 19th century where it now accounts for approximately half of the sugar produced (one third of sugar consumed in the USA is imported).

Sugarbeet is currently grown in many climates, from temperate (California, Spain and Italy) to cold climates (Dakota, Finland and Russia) and accounts for approximately 40% of world refined sugar production.

In general, sugarbeet in the USA and Europe is converted directly to white refined sugar, through a process involving shredding of the beetroot, diffusion of soluble sugars into water, clarification, concentration (by boiling), crystallisation and centrifugation. Crystalline sugar is further refined from molasses by-products. Some intermediate raw sugar is produced in eastern European areas due to limited processing facilities. Sugarbeet root pulp is another by-product that, in recent years, has been purified and sold as food fibre used, for example, in breakfast cereals etc. (CADMOS, 1997).

Sugar and sugar products derived from glyphosate-tolerant sugarbeet line 77 would be consumed in Australia and New Zealand only as an ingredient within processed foods originating from the USA where it is permitted for use in agriculture and food. Known uses of purified beet sugar include soft drinks, chocolates and confectionery, yoghurts and other milk-based foods, pastries and biscuits, syrups, jams and preserved fruits, wines, breakfast foods, ice-creams and sorbets, liquors and spirits, concentrated and powdered milk, sweets and burnt sugar (used to dye and aromatise).

Some products made from molasses derived from glyphosate-tolerant sugarbeet line 77 could be used as raw materials by the food industry. These products are handled as bulk materials and are made from various sources thus the use of beet in their production cannot be established because of high purity of these products. The products include e*thanol, citric acid (acidulant and preservative), glutamic acid* (taste enhancer), *and lactic acid* (acidulant).

The main use of sugarbeet pulp is in animal feedstuffs. Other products, representing a very small percentage of the total use, are processed from pulp. The food components which could be extracted from pulp include: *L-arabinose* (hemicellulose monomer) and *araban gel* used as a fat substitute, *pectins* (polymer of D-glutamic acid) used for specific food applications (emulsion stabilisation), and *fibre products* used as texturing agents and as a source of fibrin by the bakery and breakfast cereal industry.

As with purified sugar products, citric acid, lactic acid, glutamic acid and pectins are food additives and/or flavourings. All products from these processes are highly purified and thus do not contain viable genetically modified organisms or functional recombinant DNA.

The nutrition and health aspects of sugar consumption have been extensively researched over the last 20 years and other than the contribution to dental caries, there is no conclusive evidence that demonstrates that sugar is a hazard to the general public when consumed at the levels and in the manner currently practised. As a consequence sugar has GRAS (Generally Recognised as Safe) status.

3.2 Nature of the novel proteins

On the basis of the inserted gene cassettes two novel proteins were expected to be expressed in glyphosate-tolerant sugarbeet line 77: CP4-EPSPS and GUS. As a truncated version of the *gox* gene had also been transferred, a possibility also existed that chimeric GOX-like proteins may also be expressed.

3.2.1 CP4-EPSPS Protein

CP4-EPSPS is an essential enzyme in the biosynthesis of the aromatic amino acids via the shikimate metabolic pathway. This metabolic pathway is present in all plants, bacteria and fungi. The EPSPS enzyme of plants is inhibited by glyphosate (Steinrucken and Amrhein 1980), however bacterial EPSPSs, such as CP4-EPSPS, have reduced affinity for glyphosate. The CP4-EPSPS protein is 47.6 kD in size and consists of a single polypeptide of 455 amino acids.

Plant EPSPSs are localised in the chloroplast. In sugarbeet line 77, the CP4-EPSPS gene has been fused to the *Arabidopsis thaliana* EPSPS chloroplast transit peptide (CTP) that targets the protein to the chloroplast. *In vitro* chloroplast uptake assays have shown that the *A. thaliana* EPSPS CTP delivers CP4-EPSPS to the chloroplast where it is subsequently cleaved from the pre–protein, yielding mature CP4-EPSPS with no CTP amino acids retained (della Ciopa *et al*, 1986). The chloroplast transit peptides are rapidly degraded after cleavage *in vivo* by cellular proteases. Thus, only mature CP4-EPSPS without any additional CTP residues at the amino terminus is predicted to be expressed in sugarbeet line 77.

CP4-EPSPS has previously been introduced in soybeans, potato, canola, corn and cotton (Padgette *et al* 1996b). Products of these transgenic commodities are variously permitted for sale in the EU, USA, Canada and Japan and are the subject of other applications with ANZFA.

3.2.2 GUS protein

The *uidA* gene inserted into sugarbeet line 77 is derived from *E. coli* and encodes a single β-glucuronidase protein, designated GUS, with an experimentally determined molecular weight of 68.2kD. GUS catalyses the hydrolysis of a wide range of glycosides including synthetic p-nitrophenyl-β-D-glucuronide. Hydrolysis of this chromogenic compound produces a blue colour that has proved a versatile visual marker in a range of plant transformation systems (Jefferson *et al.* 1987). GUS is naturally present in a wide range of microbes, animals and plants including sugar beet (Wozniak and Owens, 1994). The *E. coli* variant of GUS expressed in sugarbeet line 77 was distinguishable from endogenous sugarbeet GUS due to differential pH specificity for the chromogenic substrate.

3.2.3 Chimeric GOX-like proteins

The *gox* gene intended for insertion into sugarbeet line 77 is derived from the bacterium *Ochrobactrum anthropii* and encodes a single protein of 431 amino acids with a molecular mass of 46.1 kD. The glyphosate oxidoreductase (GOX) protein breaks glyphosate down to aminomethylphosphonic acid (AMPA) and glyoxylate.

Molecular analysis of the insertion event showed that a truncated version of the *gox* gene was inserted into sugarbeet line 77. The truncation incorporated 897 bp of the *gox* gene cassette (representing 69% of the complete *gox* coding sequence). The truncation event also had the effect of excluding the incorporation of the *nptII* gene cassette, which was intended for transfer. Sequencing into the sugarbeet genome identified two translational stop codons in the sugarbeet genome 130 base pairs and 234 base pairs downstream of the fusion junction in frame with the *gox* translational frame. A transcription termination signal was also identified within the sugar beet genome 650 base pairs downstream of the junction point.

Because the sequence data revealed the possibility for a functional gene a thorough investigation of *gox*-like expression products was undertaken.

Northern blot analysis of RNA recovered from sugarbeet line 77 tissue showed that two transcripts of differing abundance hybridised to random primed DNA probe. The high abundance transcript displayed a molecular weight of approx. 1.5-1.7 kb. The lower abundance transcript had a molecular size of approx. 2.0 kb. The different transcripts were concluded to represent transcription of the chimeric *gox* fusion gene through to the two alternative transcription termination sites. Both transcripts however were concluded to be of sufficient length to code for GOX-like proteins and further studies to identify the expression of these proteins were undertaken (see below).

3.3 Expression of the novel proteins in the plant

As the expression of all three genes; *cp4-epsps*, *uidA*, and chimeric *gox*, are under the control of constitutive promoters it is expected that respectively expressed proteins would be found in all tissues of sugar beet line 77.

Expression levels of CP4-EPSP, GUS and putative GOX-like proteins were measured using either ELISA or Western blotting. ELISA is a highly sensitive technique that can detect the presence of a protein generally to a sensitivity of 10-100 pg.

ELISAs for CP4-EPSPS and GUS protein were conducted using antibodies raised to each protein expressed in *E. coli* cultures into which the *cp4-epsps* and *uidA* genes were cloned. The *E. coli*-derived proteins were determined to be equivalent to the plant-expressed forms through a number of analyses (see 4.2 - Potential toxicity of newly expressed protein(s)). Analyses were performed on early and mature leaf tissue (referred to as top) and processed root (referred to as brei), from segregating populations of sugarbeet line 77 in separate field trials. Segregating plants not expressing the glyphosate-tolerant phenotype were used as controls. Trials were conducted in six different geographic sites in Europe in 1995 and 1996, and in five different geographic sites in the USA in 1996. Results are presented in Table 3.

The results outlined in Table 3 show that expression of CP4-EPSPS and GUS proteins are generally at low levels in sugarbeet with highest expression occurring in young leaves and mature tops and the lowest in brei. The level of CP4-EPSPS protein is near two orders of magnitude higher than the level of GUS in nearly all tissues. Expression levels for both proteins in mature tops and brei from glyphosate-tolerant sugarbeet line 77 plants treated with glyphosate levels representative of commercial conditions were comparable to levels in untreated GTSB77 plants. Similar results were obtained in studies run over two successive years in a range of geographical locations. These data indicate that expression of *cp4-epsps* and *uidA* genes is consistent over generations and reflects that both genes are stably inherited. They also indicate that spraying with glyphosate does not influence the expression of these two genes.

Table 3. Summary of expression levels of CP4-EPSPS and GUS in sugar beet GTSB77*

Tissue Type	CP4-EPSPS protein[1] (ng/mg tissue fresh wt)			GUS protein[1] (ng/mg tissue fresh wt)		
	EU 1995[2]	EU 1996[3]	US 1996[4]	EU 1995[2]	EU 1996[3]	US 1996[4]
Early Leaf						
Mean	145	n.a.	n.a.	2	n.a.	n.a.
Range	130 - 179			0.8 - 3.6		
Top Untreated						
Mean	285	190	172	3.0	3.4	2.78
Range	249 - 370	134 - 273	126 - 193	2.4 - 3.6	2.4 - 3.6	2.35 - 3.35
Treated						
Mean	n.a.	n.a.	151	n.a.	n.a.	2.69
Range			130 - 167			2.29 - 3.18
Brei						
Untreated						
Mean	54	63	47	0.6	0.5	0.39
Range	46 - 64	50 - 76	32 - 60	0.4 - 0.8	0.08 - 0.6	0.28 - 0.55
Treated						
Mean	n.a.	n.a.	50	n.a.	n.a.	0.48
Range			32 - 60			0.41- 0.64

n.a. not available

* Treated values represent plants sprayed with glyphosate at the recommended agronomic rate: 3 applications at 0.75 lb (active equivalent) per acre.

[1] No expression products were detected in untransformed negative control plants for either protein.

2 Mean and range were calculated using n=6 with one sample being provided from 6 different geographic sites.

[3] Mean and range were calculated using n=12 with two samples being provided from 6 different geographic sites.

[4] Mean and range were calculated using n=10 with two samples being provided from 5 different geographic sites.

The level of GOX-like proteins potentially expressed in sugarbeet line 77 tissue was analysed by Western blot analysis using antibodies raised to protein expressed in *E. coli* cultures into which the chimeric *gox*-fusion gene had been cloned. Cloning was undertaken using a PCR-based strategy to amplify the *gox*-fusion sequence from sugar beet line 77. The *gox*-fusion cloned into *E. coli* included the CTP1 sequence, the truncated *gox* sequence and 130bp of fused sugar beet genomic DNA ending at an identified translational stop codon. The plasmid transformation vector containing the *gox*-fusion sequence was named pMON34550.

Protein extracted from refractile bodies in cultures of *E. coli* transformed with pMON34550 were purified and run on SDS-PAGE against GOX protein standards (from a transgenic sugar beet line expressing GOX). A protein – designated Protein 34550 – ran concurrent with the GOX standard at approximately 46kD. Amino acid sequencing of Protein 34550 indicated it was composed of the 89 amino acids of the CTP1 sequence, 299 amino acids from the N-terminus of the GOX protein, and 43 amino acids encoded by sugar beet genomic DNA.

Western blots using antibodies raised and affinity purified to Protein 34550 were undertaken on plant tissue extracts from three different sugarbeet line 77 varietal lines grown at three different locations in the USA.

Tissues analysed included seeds, whole plants (at the two leaf stage and at three months of age), and extracts from leaves and roots from plants at the four, six and eight leaf stage. For all samples, no Protein 34550 was shown to be present at a limit of detection in plant tissue of 180ppb.

Further, analysis of mRNA transcripts from the truncated *gox* gene in sugarbeet line 77 tissues showed that the mRNA transcribed contain a C-terminal coding region and a 3' untranslated region that is rich in AU nucleotide sequence. Such AU motifs are associated with mRNA degradation (Di Noia *et al.,* 2000). Translation from such transcripts may be inhibited or the translation products are highly unstable polypeptides, which results in their rapid degradation and thus a lack of detectable Protein 34550 in sugarbeet line 77 tissues.

To confirm that Protein 34550 does not exhibit GOX-like activity an ancillary study was undertaken by monitoring the production of glyoxylate, the breakdown product of glyphosate associated with GOX activity. No detectable GOX-like activity could be demonstrated for Protein 34550 purified from *E. coli*. A similar study confirmed that sugarbeet line 77 does not display GOX activity.

3.4 Dietary intake of expressed proteins

Sugar beet is generally converted directly to refined white sugar (which is composed almost entirely of sucrose) through extensive purification processes described previously. Sugar beet pulp is a by-product that, in recent years, has been purified and sold in limited amounts as food fibre for breakfast cereals etc. (Macrae *et al*. 1993).

Analysis of highly refined sugar liquor and crystalline sugar from sugarbeet shows that total protein within derivative food products range from 0.004 to 1.2 μg per g (Potter *et al.* 1990). This compares with an average figure of 56 mg total protein per g of brei. On this basis sugar refining reduces protein content in refined sugar by a minimum factor of 1.7×10^5.

Using Western blot methodology no immunoreactive protein bands were detected for CP4-EPSPS, GUS or Protein 34550 in either sugar or molasses samples derived from sugarbeet line 77 that had been treated with agronomically recommended levels of glyphosate or left untreated. The limits of detection were 2ppb, 4ppb and 100 ppb for each protein, respectively, in these processed components. These results indicate that consumers would not be exposed to any of the three novel proteins from consuming sugar or molasses derived from sugarbeet line 77.

In the case of pulp derived from the same sources of sugarbeet line 77, CP4-EPSPS was detected in a range of 11.5 - 71.8ppm across five samples analysed (mean approximately 50ppm). Levels of GUS ranged from 0.3 – 1.2ppm (mean approximately 1ppm). No Protein 34550 was detected in any pulp sample. Limits of detection were the same as those described above for sugar and molasses.

Human consumption of CP4-EPSPS and GUS proteins through consumption of dietary fibre of fibre components derived from sugar beet line 77 are considered to be negligible as:

- sugar beet pulp is used on a limited scale to produce dietary fibre or fibre components,
- dietary fibre additives are refined to accentuate only soluble carbohydrate fractions, and
- dietary fibre additives are used at concentrations of 1% v/v in the final food (Southgate, 1986).

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

The human health considerations in this regard depend on the nature of the novel genes and must be assessed on a case-by-case basis.

In 1991, the World Health Organization (WHO) issued a report of a Joint FAO[3]/WHO Expert Consultation which looked at strategies for assessing the safety of foods produced by biotechnology (WHO 1991). It was concluded by that consultation that as DNA from all living organisms is structurally similar, the presence of transferred DNA in food products, in itself poses no health risk to consumers.

The major concern in relation to the transfer of novel genetic material to gut microorganisms is with antibiotic resistance genes. It is generally accepted that there are no safety concerns with regard to the presence in the food of antibiotic resistance gene DNA *per se* (WHO 1993). There are concerns, however, that there could be horizontal gene transfer of the antibiotic resistance gene from ingested food to gut microorganisms and that if the microorganisms are able to express the transferred resistance gene this could lead to an increase, in the gastrointestinal tract, of microorganisms resistant to a specific antibiotic. This, in turn, might lead to an increased potential for the transfer of the antibiotic resistance gene to pathogenic microorganisms, thus compromising the therapeutic use of such antibiotics. There are further concerns that, if the antibiotic resistance gene is expressed in the plant, the expressed protein, when ingested, could inactivate oral doses of the antibiotic to which it confers resistance.

While the T-DNA intended for transfer from plasmid PV-BVGT03 contained the antibiotic resistance gene *nptII* (Table 1), Southern blot and sequencing analysis showed this gene was not integrated into sugar beet GTSB77 as a consequence of the *gox* gene truncation event which occurred at the Left Border of the T-DNA.

As discussed above, it is extremely unlikely that novel genetic material will transfer from GM foods to bacteria in the human digestive tract because of the number of complex and unlikely steps that would need to take place consecutively.

It is equally unlikely that novel genetic material will transfer from GM foods to human cells via the digestive tract. In considering the potential impact on human health, it is important to note that humans have always consumed large amounts of DNA as a normal component of food and there is no evidence that this consumption has had any adverse effect on human health. Furthermore, current scientific knowledge has not revealed any DNA sequences from ingested foods that have been incorporated into human DNA. Novel DNA sequences in GM foods comprise only a minute fraction of the total DNA in the food (generally less than 0.01%) and are therefore unlikely to pose any special additional risks compared with the large amount of DNA naturally present in all foods.

Given the information above, the horizontal gene transfer of any genetic material from the glyphosate tolerant sugarbeet line 77 is not considered to pose any risk to public health and safety, including the development of antibiotic resistant pathogenic bacteria.

[3] Food and Agriculture Organization.

3.6 Conclusions

The *cp4 epsps* gene and CP4-EPSPS protein have been sourced from the common soil bacterium *Agrobacterium tumefaciens* and have been well characterised. *cp4 epsps* is considered similar to plant *epsps* genes which are consumed in the normal diet.

The GUS gene and protein have been sourced from the common bacterium *E. coli,* which is commensal in many animals, including humans, and are also well characterised.

The GOX gene and protein has been sourced from a common soil bacterium *Ochrobactrum anthropii,* which has no history of food-borne pathogenicity. The chimeric truncated GOX gene found in sugarbeet line 77 was cloned into *E. coli* and a protein – Protein 34550 - was expressed which has no known history of consumption in food.

From Western and ELISA analyses both CP4-EPSPS and GUS are expressed at very low levels in the tops and brei of glyphosate-tolerant sugarbeet line 77. In contrast, Protein 34550 was not detected in any tissue of sugarbeet line 77 tested.

The products intended for human consumption from sugarbeet line 77 include refined and semi refined sugars, and potentially, refined dietary fibre to a limited extent. No CP4-EPSPS, GUS or Protein 34550 were detected in sugar and molasses derived from sugarbeet line 77. CP4-EPSPS and GUS were found at very low levels in the case of beet pulp (average of 50 ppm and 1 ppm respectively) and their levels are expected to be negligible in refined dietary fibre derived from sugar beet pulp. No Protein 34550 was found in beet pulp (limit of detection 100ppb).

The risk of transfer of the novel genetic material to cells of the human digestive tract is considered negligible. Additionally, there is no risk of horizontal transfer of antibiotic resistance genes to gut bacteria as no such genes were transferred into glyphosate-tolerant sugarbeet line 77

4. TOXICOLOGICAL ISSUES

Monsanto Australia Limited submitted the following related reports with their application:

Astwood, J.A. 1995. CP4-EPSPS synthase shares no significant sequence similarity with proteins associated with allergy and coeliac disease. Monsanto Technical Report MSL-14174 Monsanto Company, St. Louis, USA, 63198.

Astwood, J.A. 1996. β-D-glucuronidase (GUS) shares no significant sequence similarity with protein associated with allergy or coeliac disease. Monsanto Technical Report MSL-14632 Monsanto Company, St. Louis, USA, 63198.

Astwood, J.A. 1996. β-D-glucuronidase (GUS) shares no significant sequence similarity with protein toxins found in the public domain databases. Monsanto Technical Report MSL-14633. Monsanto Company, St. Louis, USA, 63198.

Astwood, J.D. 1997. Protein 34550 has no significant sequence similarity to known allergens and toxins. Monsanto Technical Report MSL-14988. Monsanto Company, St. Louis ,USA, 63198.

Harrison, L.A., Bailey, M.R., Nida, D.L., Taylor, M.L., Holden, L.R. and S.R. Padgette. 1993. Preparation and confirmation of doses for an acute mouse feeding study with CP4-EPSPS. Monsanto Technical Report MSL-12900. Monsanto Company, St. Louis, USA, 63198.

Harrison, L.A., Biest, N.A., Leimburger, R. and S.R. Padgette. 1996. Equivalence of plant- and microbially-expressed proteins: β-D-glucuronidase from glyphosate-tolerant soybean and *E. coli*. Monsanto Technical Report MSL-12881. Monsanto Company, St. Louis, USA, 63198.

Harrison, L.A., Biest, N.A., Leimburger, R. and S.R. Padgette. 1996. Preparation, characterisation and confirmation of doses for an acute mouse feeding study with β-D-glucuronidase. Monsanto Technical Report MSL-12979. Monsanto Company, St. Louis, USA, 63198.

Leach, J.N. and J.D. Astwood. 1997. Assessment of the digestibility and fate of purified Protein 34550 *in vitro* using mammalian digestive fate models. Monsanto Technical Report MSL-14973. Monsanto Company, St. Louis, USA, 63198.

Lee, T.C. and G. Go. 1997. Preparation and confirmation of doses for an acute mouse toxicity study (EHL-96210) with Protein 34550. Monsanto Technical Report MSL-14982. Monsanto Company, St. Louis, USA, 63198.

Mitsky, T.A., 1993. Comparative alignment of CP4-EPSPS to known allergenic and toxic proteins using the FASTa algorithm. Monsanto Technical Report MSL-12820. Monsanto Company, St. Louis, USA, 63198.

Naylor, M.W. 1992. Acute oral toxicity study of β-D-glucuronidase (GUS) protein in albino mice. Monsanto Technical Report MSL-12485. Monsanto Company, St. Louis, USA, 63198.

Naylor, M.W. and F. Ruecker. 1997. Acute oral toxicity study of Protein 34550 in albino mice. Monsanto Technical Report MSL-15042. Monsanto Company, St. Louis ,USA, 63198.

Ream, J.E., Bailey, M.R., Leach, J.N. and N. Biset. 1993. Assessment of the *in vitro* digestive fate of CP4-EPSPS synthase. Monsanto Technical Report MSL-12949. Monsanto Company, St. Louis, USA, 63198.
Ream, J.E. 1996. Assessment of the in vitro digestive fate of β-glucuronidase. Monsanto Technical Report MSL-14607. Monsanto Company, St. Louis, USA, 63198.

Taylor, M.L., Go, G., Mahadeo, D.A. Rochester, D.E. and T.E. Nickson. 1997. Assessment of equivalence of Protein 34550 expressed in Roundup Ready® sugar beet (Line #77) and *E. coli*. Monsanto Technical Report MSL-14870. Monsanto Company, St. Louis, USA, 63198.

4.1 Levels of naturally-occurring toxins

Sugarbeet varieties naturally contain low levels of toxic saponins which, as their name implies, are a group compounds with properties resembling soap and detergents. Saponins are a complex and chemically diverse group incorporating both triterpenes and steroids linked to one or more sugar groups. Saponins are found naturally, and in significant amounts, in commonly used food and forage plants such as clover, alfalfa, soybeans, chickpeas, eggplant silver beet and spinach (Oakenfull and Sidhu, 1989) and are characterised by having a bitter and astringent taste. Saponins have been generally well characterised with the predominant sapogenic form in sugar beet being oleanolic acid. Due to their surface-active properties saponins have been implicated in foaming and turbidity problems during sugar production from sugar beet and efforts are made to limit saponin levels through processing.

The wide range of chemical and physical properties of saponins is matched by the extent and range of their physiological and pharmacological properties. In general they have been shown to interact with biological membranes, due to their detergent qualities, and to both inhibit and stimulate enzymes and metabolic activity (Oakenfull and Sidhu, 1989). Whilst there has been a tendency to treat saponins exclusively as antinutritional or toxic constituents, more recent work has shown several beneficial dietary effects of saponins, including an enhancement of nutrient absorption in digestion and an ability to lower blood cholesterol levels (Oakenfull and Sidhu, 1989).

Levels of saponin were analysed in the roots and tops of non-transgenic control and GTSB77 sugar beet plants, both untreated and treated with glyphosate at agronomically recommended rates, in European field trials conducted in 1995, 1996 and 1997 and in European and US field trials conducted in 1996. The results of the saponin analysis are presented for root tissue (Table 4), as this is the only tissue used in food production.

Table 4. Mean values and ranges of saponin levels in roots for control and sugarbeet line 77 (GTSB77) (both untreated and treated with Roundup) from all field trials*.

Trial/Year	Control		GTSB77 - untreated		GTSB77 – treated[1]		Literature Range[2]
	Mean	Range	Mean	Range	Mean	Range	
EU 1995	151	72-233	137	60-261	134	91-197	75-965
EU 1996	529	304-999	484	293-846	365[3]	215-609	
USA 1996	215	111-304	208	128-260	180	116-255	
EU 1997	446	290-720	422	305-689	338[3]	217-496	

* Values are given on a mg/kg fresh weight basis. Values are means of samples analysed from 6 (Europe 1995, Europe and USA; 1996) or 8 (Europe 1997) sites. Analysis determined according to published methods.
[1] Treated with three applications 0.75lb active equivalents per acre Roundup.
[2] Reference Lüdecke *et al.*,1958.
[3] Significantly less than control at the 5% significance level.

Two-sided pooled-variance statistical *t*-tests were undertaken in the European trials to determine whether significant differences occur in saponin level between conditions and treatment. No statistical differences, at the 5% level of significance, were observed for saponin levels between untreated sugarbeet line 77 (GTSB77) and the non-transgenic control in trials covering multiple growth seasons and geographic regions. No significant difference was found for saponin levels between glyphosate-treated GTSB77 and control sugar beet except for the 1996 and 1997 European field trials were saponin level was reduced in treated GTSB77. These differences are, however, not biologically or nutritionally significant as they were inconsistent across seasons and sites (suggesting that it is not an influence of the genetic modification *per se*). Furthermore, all mean saponin values are within the range established for conventional sugar beet in the literature. On this basis, saponin level in the root of sugar beet GTSB77, both untreated and treated with glyphosate at recommended agronomic application rates, is similar in terms of saponin levels to commercially available sugar beet.

It is concluded that saponin levels in sugarbeet line 77, both treated and untreated with glyphosate, are not considered to pose a risk to human health since:

- saponins are, in general, at very low levels in sugar beet tissues;
- sugar beet processing aims to eliminate saponins and other extraneous material from refined sugar products; and
- saponin levels in both glyphosate-treated and untreated line 77 do not differ significantly across seasons and sites, and fall within the range described for traditional sugar beet varieties in the literature.

4.2 Potential toxicity of newly expressed protein(s)

The potential toxicity and dietary exposure of the CP4-EPSPS and GUS proteins, and Protein 34550 were assessed through four different approaches;

1. potential human exposure;
2. homology to known protein toxins;
3. digestive fate in simulated gastric and intestinal fluids; and
4. acute mouse toxicity studies.

The toxicity of the CP4-EPSPS protein expressed in sugarbeet line 77 has also been addressed by ANZFA in other safety assessments of foods assessed under Standard A18 (see A338 Roundup Ready soybeans, A355 Roundup Ready cotton, A362 Roundup Ready corn and A363 Roundup Ready canola). The safety of the GUS protein and Protein 34550 have not been addressed in other applications. Certain aspects of the toxicity data have been published in the scientific literature as cited in the text.

The *cp4-epsps, uidA* and *chimeric-gox* genes were cloned into *E. coli* in order to obtain sufficient amounts of each respective protein to assess its safety. CP4-EPSPS and GUS proteins derived from *E. coli* were shown to be equivalent for safety assessment purposes to the respective plant expressed proteins on the basis that:

- comparative Western blot analysis demonstrated similar immunoreactivity and equivalent molecular weights (the latter also shown by SDS-PAGE analysis);
- positive correlation occurred between quantity and immunological dose-response in ELISA assays;
- comparative functional enzyme assays demonstrated correlative activities (in the case of CP4-EPSP and GUS); and
- homology of the N-terminal sequence of amino acids through 15 positions; and
- there are no differences in glycosylation patterns.

As no Protein 34550 was identified in sugarbeet line 77 tissue, no equivalence of the *E. coli* cloned Protein 34550 could be established. PCR analysis using primers specific to the *truncated-gox* gene did, however, show that the sizes of the genes in both sugarbeet line 77 and *E. coli* are equivalent at approximately 1273 bp.

4.2.1 Potential human exposure

Protein levels in sugar products produced from sugar beet

The high temperatures and precipitation methods used in the production of sugar from sugar beets are known to reduce protein levels significantly with the highest level of protein detected in refined sugar being 1.2 µg per g (Potter, *et al.,* 1990). Since CP4-EPSPS and GUS proteins are expressed at low levels in the sugar beet root (CP4-EPSPS ranging between 32-76 µg per g fresh weight and GUS ranging between 0.08-0.8 µg per g fresh weight), the level of these proteins in refined sugar is extremely low or absent (i.e. less than 2 ppb and 4 ppb respectively, as discussed in Section 3.4).

It is concluded that little if any CP4-EPSPS or GUS protein would be consumed as a consequence eating food containing sugar derived from sugarbeet line 77.

History of human exposure to CP4-EPSPS

The CP4-EPSPS protein has a specific catalytic function in the aromatic acid shikimate pathway of plants, bacteria and fungi. This pathway is not present in mammals. The CP4-EPSPS protein shows high amino acid sequence homology to the other EPSPS enzymes found in common food crops (for example, soybean and tomato) that have a long history of safe human consumption, or that are present in fungal and microbial food sources such as Baker's yeast (*Saccharomyces cerevisiae*) or *Bacillus subtilis*. Thus, CP4-EPSPS is a member of a family of closely related proteins from plants and microbes that are commonly found in human foods.

History of human exposure to GUS

The *uidA* gene was originally isolated from *E. coli* which is a commensal bacterium found in the gut microflora of many animals including humans (Jefferson *et al.*, 1986). The GUS protein is an acid hydrolase that catalyses the cleavage of certain β-glucuronides and has been used extensively as a visible marker in evaluating putative genetic transformation events (Jefferson *et al.*, 1987). Apart from its expression in animals, GUS activity has also been detected in a number of plant tissues including sugarbeet (Wozniak and Owens, 1994). The GUS protein is thus a common component of bacteria native to humans and animals regularly associated with a range of foods and feeds.

History of human exposure to the chimeric *gox* gene product; Protein 34550

The native *gox* gene is derived from *Ochromobactrum anthropii* strain LBAA [formerly *Achromobacter sp*], a commonly found bacterium in soil and is likely to occur on food plants. Southern and PCR analysis identified that a truncated chimeric version of the *gox* gene was present in sugarbeet line 77. When cloned into *E. coli* the truncated chimeric *gox* gene expressed a new protein which was labelled Protein 34550. Protein 34550 is composed of the 89 amino acids of the CTP1 genetic element, 299 amino acids of the N-terminus of the GOX protein and 43 amino acids encoded by sugar beet DNA. Protein 34550 has no GOX enzymatic activity. If Protein 34550 were expressed in sugarbeet line 77 it would represent a novel protein not previously found in the human diet.

Western and ELISA analysis for the presence of Protein 34550 in sugar beet line 77 revealed that it is not expressed in either leaves, roots or in derivative food components (refined sugar, molasses and dietary fibre). While no evidence of the presence of Protein 34550 was found in sugarbeet line 77, toxicity studies of the protein were still carried out.

4.2.2 Sequence similarity to known protein toxins

Patterns of amino acid sequence or shared regions between proteins may provide insight into the biological significance of a protein including its toxicity and allergenicity. When compared to the amino acid sequences of protein toxins in the PIR, EMBL, SwissProt and GenBank databases, the amino acid sequence of the CP4-EPSPS and GUS proteins, and Protein 34550, showed no significant similarities to any of the 1,935 protein toxins, or toxin-associated proteins, listed in these databases.

4.2.3 Digestive fate of novel proteins in simulated gastric and intestinal fluids

Most proteins are readily degraded upon exposure to gastric and intestinal fluids in the digestive tract with 50% of solid food emptying from the human stomach in 2 hr (Sleisenger and Fordtran, 1989). The rate of degradation of novel proteins in simulated gastric (SGF) and intestinal fluids (SIF) thus enables a prediction of their fate in digestion.

The degradation of C4 EPSPS, GUS and Protein 34550 were followed, either through Western blot or enzyme activity assays, in both SGF and SIF at 37^{o}C. CP4-EPSPS protein was shown to have a half-life of 15sec in SGF and 10min in SIF. No detectable GUS protein was present after 15sec exposure to SGF and over 50% had been degraded in SIF after 60 to 120min. Over 90% of GUS activity had dissipated after 4h in SIF. Protein 34550 was degraded within 15 seconds exposure to SGF and within 60 seconds exposure to SIF, moreover no intermediate stable protein fragments larger that 2kD were generated by digestion of Protein 34550 in either SGF or SIF.

On the basis of these data all three novel proteins were demonstrated to be readily digestible.

4.2.4 Acute oral toxicity of novel proteins mice

To directly assess the potential toxicity of the CP4-EPSPS, GUS and 34550 proteins acute gavage tests were undertaken in mice using purified forms of each protein. The dosage of administration, treatment-related findings, and the safety factors relative to the highest potential human consumption are shown in Table 5. Note, the safety factors were calculated on the basis of the level which humans would be exposed if each protein were expressed in soybean, corn, tomato and potato assuming no loss of protein due to processing.

Table 5. Acute gavage studies of CP4-EPSPS, GUS and Protein 34550 toxicity in mice and exposure safety factor.

Protein	Max. dosage (mg/kg body wt)	Significant treatment-related effects[4]	Human exposure safety factor[5]
CP4-EPSPS[1]	572	None	1,300
GUS[2]	100	None	>1,000
34550[3]	20	None	10^{10}- 10^{11}

[1] Administered as a single dose by gavage to groups of 10 mice per sex at dosages of 49, 154 and 572 mg/kg (Harrison *et al.,* 1996).
[2] Administered as a single dose by gavage to groups of 10 mice per sex at dosages of 1, 10 and 100 mg/kg.
[3] Administered as a single dose by gavage to groups of 10 mice per sex at dosages of 0.2, 2 and 20 mg/kg.
[4] In-life observations included body weights, food consumption and signs of toxicity. Post-mortem observations included internal and external examinations, kidney weights and kidney histopathology. No statistical differences were observed outside those expected by chance alone at $p \leq 0.05$.
[5] Based on the potential exposure to humans if the protein were expressed in soybean, corn, tomato and potato assuming no loss due to processing.

Despite the level of all three proteins being well in excess of the likely human dietary exposure factor, no mortality or morbidity resulted and there were no significant differences in terminal body weights between the treated and control groups. Upon necropsy, body cavities were opened and organs examined *in situ* and removed. No pathological findings attributable to the treatment with any protein were observed.

4.3 Levels of naturally occurring allergenic proteins

Allergic reactions to foods arise from an immune reaction to a particular protein that may be present in the food in very small amounts. Some common foods are known to elicit an allergic response in susceptible individuals. Foods such as cow's milk, soybeans and tree nuts are some of the better-known sources of food allergies.

Very rare instances in the literature describe allergic response to beet sugar taken orally and to beet sugar solutions administered by injection (Randolf and Rollins, 1950; Richter *et al.*, 1976). One report (Richter *et al.*, 1976) pointed to certain polysaccharide components as the potential allergen. However, the identity of the immunogenic substances in sugar beet sugar has not been positively established. The instances of sugar beet sugar induced allergic responses are very rare and as refined sugar is generally recognised as safe, further investigation of putative naturally occurring allergens is not considered necessary.

4.4 Potential allergenicity of novel proteins

Although there are no predictive assays available to assess the allergic potential of proteins, a number of characteristics are common among many of the allergens that have been characterised. Known allergens tend to be:

- glycosylated proteins with a molecular weight of 10–70 kD,
- heat stable,
- resistant to proteolytic digestion and the acidic conditions of the stomach, and
- expressed as major proteins in commonly consumed foods.

The CP4-EPSPS, GUS and 34550 proteins were evaluated for potential allergenicity against well-accepted criteria for allergens (Taylor, 1992a; Taylor *et al.*, 1987; 1992b). These were whether:

- the source organism(s) has a history of allergenicity;
- the proteins are stable to digestion;
- the proteins are stable to food processing;
- the proteins are similar in amino acid sequence to known protein allergens; and
- the proteins are a principal component of the food.

4.4.1 Allergenicity of source organisms

The CP4-EPSPS protein was obtained from the naturally occurring soil-borne plant-symbiotic bacterium *Agrobacterium sp.* strain CP4. The *gox* coding region was obtained from the common soil bacterium *Ochrobactrum anthropi.* This coding region is responsible for the production of protein 34550. The *uidA* gene was obtained from *E. coli,* a bacteria prevalent in the gastrointestinal tract of animals including humans. None of these source organisms are known to be allergenic to humans.

4.4.2 Stability of protein to digestion

As reported above in Section 4.2.3, the CP4-EPSPS, GUS and 34550 proteins are degraded rapidly after exposure to simulated gastric fluid. Such rapid digestion would severely limit the amount of protein absorbed via the intestine and thus restrict any potential immunological response.

4.4.3 Stability of the protein to food processing

The levels of CP4-EPSPS and GUS proteins in sugarbeet line 77 are extremely low in the root (0.005% and 0.00006% respectively) and Protein 34550 was undetectable at a limit of detection of 100ppb. None of these proteins were detectable in molasses and refined sugar components derived from sugarbeet line 77 at limits of detection ranging from 2 – 100ppb. CP4-EPSPS and GUS were detected at levels of 50ppm and 1ppm respectively in sugarbeet pulp. Beet pulp is used to a limited degree in the manufacture of refined soluble food fibre that could potentially be used as an additive at less than 1% in some specific foods (breakfast cereals etc.). While no direct analysis of these proteins was undertaken in soluble fibre derivatives, it is expected that they would be at negligible concentrations due to the processing steps involved.

4.4.4 Sequence similarity to known protein allergens

Amino acid sequence similarity with known allergens is a useful indicator of the allergenic potential of novel proteins. The amino acid sequence of the CP4-EPSPS, GUS and 34550 proteins were compared to the amino acid sequences of 219 known allergens present in public domain databases (eg GenBank, EMBL, Swissprot, PIR). Sequence similarity was defined as a sequence identity of greater than seven contiguous amino acids. No biologically significant similarity was found between any of the novel proteins with any of allergens listed in these databases.

4.4.5 Level of novel protein in the final food

Allergenic proteins in known allergenic foods (such as milk, soybeans and peanuts) exist as major proteins (Metcalfe *et al.*, 1996). There is very limited potential for the novel proteins from sugarbeet line 77 to act as allergens in final food products as:

- none of the novel proteins could be detected in either sugar or molasses derived from sugarbeet line 77, and
- dietary fibre refined from pulp derived from sugarbeet line 77 would contain extremely low levels of CP4-EPSPS and GUS as these are expressed in the crude pulp at very low levels (50ppm and 1ppm respectively). Protein 34550 was not detected in pulp samples.

4.5 Conclusions regarding toxicological issues

There is no evidence to indicate that there is any potential for the CP4-EPSPS, GUS or Protein 34550 to be either toxic or allergenic to humans. Proteins from the EPSPS or GUS family of proteins are naturally present in our food supply or expressed in human intestinal microflora. Although the truncated GOX protein (Protein 34550) is not present in foods normally, it does not possess any of the characteristics common to many allergens or toxins or any significant sequence similarity to any known allergens or toxins. Furthermore:

- none of the proteins are detectable in the principal food components sugar and molasses, and

- Protein 34550 was absent and CP4-EPS PS and GUS are detectable at very low levels in sugar beet pulp (50ppm and 1ppm respectively) - dietary fibre derived from pulp is highly refined and used at very low levels in food products (<1%v/v)
- none of the three proteins were detected in refined sugar or molasses derived from sugarbeet line 77,
- all three proteins are rapidly digested in conditions that mimic human digestion,
- none of the proteins had toxic effects on mice given acute doses of the equivalent bacterially produced proteins,

From these data it can be concluded that the food products derived from sugarbeet line 77 should pose no greater risk as a source of toxins or allergens than food products derived from conventional sugar beets.

5. NUTRITIONAL ISSUES

Monsanto have submitted the following reports:

Andersen, A., Dideriksen, T.B., Knudsen, D. and E. Smed. 1996. Compositional analysis of beet with Roundup Ready gene from 1995 field trials. Danisco Technical Report RR SB 01. Holeby, Denmark.

Andersen, A., Dideriksen, T.B., Knudsen, D. and E. Smed. 1997. Compositional analysis of beet with Roundup Ready gene from 1996 field trials. Danisco Technical Report RR SB 02. Holeby, Denmark.

Mueth, M. 1996. Compositional analysis of Roundup Ready™ sugar beet (line #77) from 1996 field trials. Monsanto Company/CEREGEN;Environmental Sciences. Study No. 96-01-49-01. Monsanto Company, St. Louis ,USA, 63198.

Nickson, T.E. and M.T. Gies. 1996. Analysis of roots, leaves and tops from glyphosate-tolerant sugar beet from the 1995 field trial. Monsanto Technical Report MSL-14561. Monsanto Company, St. Louis, USA, 63198.

Taylor, M.L., Mueth, M.G. and T.E. Nickson. 1997. Analytical and compositional analyses of Roundup Ready™ sugar beet (line #77) from 1996 US field trials. Monsanto Technical Report MSL-15048. Monsanto Company, St. Louis ,USA, 63198.

5.1 Compositional analysis

In order to determine the equivalence of sugarbeet line 77 to conventional sugar beet, a broad range of compositional analyses were undertaken on samples of sugarbeet line 77 root and top tissue obtained from five trials in the USA in 1996 and 20 trials across Europe in 1995 (6 trials), 1996 (6 trials) and 1997 (8 trials). As root tissue is the only component of sugar beet used in food production, only compositional and quality data for this tissue is presented. Roots were processed into brei – shredded roots used in the first step of sugar processing.

The analyses included proximate values for:

- crude ash;
- crude fibre;
- crude protein;
- carbohydrate;
- dry matter
- crude fats were also determined in tops.

Additional quality components were measured included:

- invert sugar (glucose + fructose) content;
- sodium;
- amino nitrogen.
- polarisation (% sucrose);
- potassium;

Data on saponins, the principal toxicant in sugar beet root, were considered previously under Section 4 - Toxicological Issues.

The effect of applications of glyphosate on the level of these components was also assessed in all trials. Glyphosate was applied at the suggested agronomic concentration of 0.75 lb (active equivalents) per acre.

Analyses in the USA were conducted by Monsanto Co. in St. Louis, MO and at the Research Centre of American Crystal Sugar Co. in Moorehead, MN. Samples in the European trials were analysed by DANISCO Seeds in Holeby, Denmark and the DANISCO Sugar Development Centre in Nakskov, Denmark.

5.1.1 Proximate and quality component analysis

Mean values and ranges of proximate constituents and quality components for root/brei tissue from all field trials, both untreated and treated with glyphosate, are summarised in Table 6.

Table 6: Mean values and ranges for the proximate and quality component analyses of sugar beet GTSB77 roots/brei from various field trials*.

	Control		GTSB77 – untreated		GTSB77 – treated[2]		Literature Range[3]
ROOTS/BREI	Mean	Range	Mean	Range	Mean	Range	
Crude Ash							
1995 Europe	3.4	2.7-4.9	3.4	2.7-5.1	3.0	2.3-4.0	1.1-17.7
1996 Europe	2.5	2.0-3.2	2.5	2.1-3.4	2.7	2.3-3.2	
1996 USA	5.5	4.6-6.3	6.6	4.8-9.0	8.8	4.9-15.6	
1997 Europe	2.7	2.0-3.8	2.7	2.0-4.0	2.8	2.0-4.4	
Crude Fibre							
1995 Europe	4.1	3.5-5.2	4.0	3.1-5.3	3.6	3.0-4.8	2.9-7.4
1996 Europe	4.2	3.9-4.6	4.2	3.9-4.6	4.2	3.6-4.8	
1996 USA	4.1	2.8-5.0	4.0	3.3-4.7	4.1	3.3-4.8	
1997 Europe	4.2	3.7-4.7	4.2	3.5-5.1	4.1	3.7-4.9	
Crude Protein							
1995 Europe	6.2	4.8-8.2	6.3	4.9-7.9	5.3	3.4-7.0	1.2-12.4
1996 Europe	4.3	3.0-5.4	4.3	3.0-5.2	4.8	3.1-5.9	
1996 USA	6.3	3.4-9.5	5.6	2.4-8.0	5.8	3.9-8.0	
1997 Europe	5.0	3.1-6.9	4.9	3.0-6.6	4.8	3.2-6.6	
Dry Matter							
1995 Europe	20.5	14.1-23.5	20.5	13.6-23.1	21.3	14.5-23.8	19.8-23.0
1996 Europe	23.9	19.2-26.4	23.9	19.5-26.2	23.5	18.9-26.0	
1996 USA	19.4	17.8-22.6	21.1	19.4-22.6	21.0	19.1-22.8	
1997 Europe	22.7	20.9-24.9	22.4	20.2-24.4	22.5	21.3-24.6	

Invert Sugar							
1995 Europe	1.7	0.3-3.7	1.8	0.4-4.24	1.0	0.3-1.9	0.3-2.7
1996 Europe	0.4	0.3-0.5	0.4	0.3-0.5	0.4	0.3-0.6	
1996 USA	n/d	n/d	n/d	n/d	n/d	n/d	
1997 Europe	0.6	0.3-1.7	0.7	0.3-2.6	0.5	0.3-1.0	
Amino Nitrogen							
1995 Europe	2.8	2.0-4.0	2.9	2.0-3.9	2.5	0.6-4.2	0.9-5.1
1996 Europe	1.6	0.7-2.8	1.6	0.8-2.5	2.0	0.7-2.8	
1996 USA	5.6	2.7-7.6	5.7	3.4-7.2	5.9	4.3-7.7	
1997 Europe	2.6	1.0-4.3	2.5	0.8-3.8	2.5	0.9-4.0	
Carbohydrate							
1995 Europe	86.3	81.7-88.9	86.3	81.7-88.7	88.2	86.6-90.0	67.3-91.0
1996 Europe	89.0	87.1-91.1	89.0	87.6-90.9	88.3	86.5-91.1	
1996 USA	84.1	80.3-87.2	84.1	79.0-88.1	82.0	74.0-86.0	
1997 Europe	88.1	84.9-91.0	88.2	85.1-91.1	88.3	85.2-91.1	
Polarisation							
1995 Europe	14.4	8.4-17.4	14.5	7.9-17.2	15.6	9.9-18.2	10.8-20.7
1996 Europe	17.3	13.8-19.4	17.3	14.1-19.4	16.8	13.1-18.9	
1996 USA	14.8	12.9-17.1	14.6	12.7-16.2	14.7	13.4-15.9	
1997 Europe	16.6	14.7-18.9	16.2	14.3-18.5	16.4	14.7-18.7	
Sodium							
1995 Europe	1.7	0.5-3.1	1.8	0.4-3.5	1.1	0.4-2.2	0.4-5.5
1996 Europe	0.5	0.3-0.8	0.5	0.2-0.8	0.5	0.3-1.2	
1996 USA	1.5	1.0-2.3	1.5	1.3-1.9	1.6	0.8-2.2	
1997 Europe	0.7	0.3-1.6	0.9	0.4-2.2	0.8	0.3-0.6	
Potassium							
1995 Europe	5.3	4.6-5.9	5.3	4.2-6.0	5.2	3.4-6.6	4.2-10.2
1996 Europe	4.9	4.1-6.0	5.0	4.0-6.4	5.2	3.8-5.9	
1996 USA	8.2	6.8-11.7	8.0	6.7-11.5	8.4	6.2-12.5	
1997 Europe	4.6	3.8-6.2	4.7	3.9-6.3	4.7	3.3-6.3	

*All units in g/100g dry weight except dry matter and polarisation (g/100g fresh weight). Sodium, Potassium, invert sugar (glucose+fructose) and Amino Nitrogen expressed as mmol/100g fresh weight. Analyses performed according to published methods.
[1] Samples taken from single plots at six (Europe '95&'96), five (USA '96) or eight (Europe '97) geographically different field trials. Non-expressing isogenic lines grown adjacent to trial plots acted as controls. Analyses undertaken according to standard published methods.
[2] Treated with three applications of 0.75lb active equivalents per acre glyphosate as recommended for agronomic purposes.
[3] See references Marlander *et al.,* 1996; Smed *et al.,* 1996; Augustinussen and Smed, 1979, and DLG, 1991.

Two-sided pooled-variance *t*-tests (and in some cases parametric and non-parametric statistical analyses) of proximate and quality values were undertaken for the European trials comparing values of non-transgenic control sugar beet (which was isogenic to the sugarbeet line 77 background) to sugarbeet line 77 both untreated or treated with glyphosate at recommended agronomic levels (three applications of 0.75lb active equivalents per acre glyphosate). No statistical analysis was performed on the US trial.

In the European trials no statistically significant differences were found for any value at the 5% level of significance between untreated sugarbeet line 77 and its non-transgenic control within any trial year. Only two significant differences were found in glyphosate-treated GTSB77 compared to non-transgenic control plants; crude fibre in 1995 trials (-13.2%), and protein in 1996 trials (+12.0%). As no broadly consistent differences occur in compositional or quality parameters for glyphosate-treated sugarbeet line 77 compared to the non-transgenic control these values are most probably outliers.

Given that these data show no consistent effect, and that the component types affected are not significant to food products derived from sugar beet, it is concluded that applications of glyphosate to sugarbeet line 77 pose no human health and safety issue with respect to proximate or quality components.

None of the mean values for either non-transgenic control sugarbeet or sugarbeet line 77 either untreated or treated with glyphosate falls outside the literature range except for higher amino nitrogen levels in the 1996 US trial. These outliers occurred for both the non-transgenic control and sugarbeet line 77 (both untreated and treated with glyphosate). As both the isogenic control line and the transgenic line were affected, this anomaly may reflect a differential agronomic practice being applied in the US trial. Given that this outlier occurs for only one characteristics (amino nitrogen) which is not significant to the food products derived from sugarbeet, this finding is not considered significant to the human health and safety of sugar or ancillary food products derived from sugarbeet line 77 under different conditions.

On the basis of the data provided it is concluded that sugarbeet line 77, both untreated or treated with glyphosate at recommended agronomic application rates, is equivalent to conventional sugarbeet with respect to composition and quality values relevant to the human health and safety of final food derivatives.

5.2 Ability to support typical growth and well-being

In assessing the safety of a genetically modified food, a key factor is the need to establish that the food is nutritionally adequate and will support typical growth and well-being. In most cases, this can be achieved through an understanding of the genetic modification and its consequences together with an extensive compositional analysis of the food. Where, on the basis of available data, there is still concern or doubt in this regard, carefully designed feeding studies in animals may provide further re-assurance that the food is nutritionally adequate. Such studies may be considered necessary where the compositional analysis indicates significant differences in a number of important components or nutrients or where there is concern that the bioavailability of key nutrients may be compromised by the nature of the genetic changes to the food.

In the case of glyphosate-tolerant sugarbeet line 77, no significant differences regarding nutritional and toxicological parameters were evident and no feeding studies were thus undertaken.

Another important factor in the assessment of sugarbeet line 77 to support growth and well-being is that the principal human food derivative is highly refined sugar composed of 96-99% sucrose and 0.6-1.2% other sugars such as glucose and fructose. Refined sugar from any source has a history of safe use and is generally recognised as safe for human consumption.

5.3 Conclusions of Nutritional Analysis

On the basis of the compositional data submitted in the present application sugarbeet line 77 is equivalent to other commercially available sugar beet in terms of its composition and nutritional adequacy.

Acknowledgement

ANZFA gratefully acknowledges the expert opinion of Professor Jimmy Botella, University of Queensland, Department of Botany, for peer review of the risk assessment.

REFERENCES

Augustinussen E. and E. Smed. 1979. Influence of temperature, sugar loss and chemical transformation during storage of sugar beet. Tidsskrift for Planteavl. **82**: 549-563.

Australia New Zealand Food Authority (ANZFA). 1999a. Full Assessment Reports for applications to amend Standard A18 are available on ANZFA web site at www.anzfa.gov.au.

Australia New Zealand Food Authority (ANZFA). 1999b. Guidelines for the safety assessment of foods to be included in Standard A18 – Food Produced Using Gene Technology - available on ANZFA web site at www.anzfa.gov.au.

Barry G., et al. 1992. Inhibitors of amino acid biosynthesis: strategies for imparting glyphosate tolerance to crop plants. In *Biosynthesis and Molecular Regulation of Amino Acids in Plants*. Singh (Ed). American Society of Plant Physiologists.

CAD*m*OS (sa). 1997. Uses of sugar-beet products in food and feed in the EU.

DeBlock, M., Herrera-Estrella, L., Van Montague, M., Schell, J. and Zambryski, P. (1984). Expression of foreign genes in regenerated plants and their progeny. EMBO J. **3**: 1681-1689.

della Ciopa et al, 1986. Translocation of the precursor of 5-enolpyruvylshikimate-3-phosphate synthase into chloroplasts of higher plants in vitro. Proc. Natl. Acad. Sci. USA **83**: 6873-6877.

Di Noia, J. M., D'Orso I., Sanchez, D. O. and A. C. Frasch. 2000. AU-rich elements in the 3'-untranslated region on a new mucin-type gene family of *Trypanosoma cruzi* confers mRNA instability and modulates translation efficiency. J. Biol. Chem. **275**: 10218-10227.

DLG (Deutscher Landwirtschafts-Gesellschaft). 1991 DLG Futterwerttabelle 6. Auflage, p. 24 & 44.

Food Australia. 1995. C. Prattley (ed.) Agri Food Media. Burwood, Vic., Australia

Harrison, L.A., Bailey, M.R., Naylor, M.W., Ream, J.E., Hammond, B.G., Nida, D.L., Burnette, B.L., Nickson, T.E., Mitsky, T.A., Taylor, M.L., Fuchs, R.L., and Padgette, S.R. 1996 The expressed protein in glyphosate-tolerant soybean, 5-enolpyruvylshikimate-3-phosphate synthase from *Agrobacterium* sp. strain CP4, is rapidly digested *in vitro* and is not toxic to acutely gavaged mice. J Nutr **126**: 728-740.

Haslam, E. 1993. Shimikic Acid: Metabolism and Metabolites. Haslam (Ed). John Wiley and Sons, Inc. Chichester, UK.

Horsch, R.B., Fraley, R.T., Rogers, S.G., Sanders, P.R., Lloyd, A. and Hoffmann, N. (1984). Inheritance of functional foreign genes in plants. Science **223**: 496-498.

Hu, C.Y., P.P. Chee, R.H. Chesney, J.H. Zhou, P.D. Miller and W.T. O'Brien. 1990. Intrinsic GUS-like activities in seed plants. Plant Cell Rep. **9**: 1-5.

Jefferson, R. A., S. M. Burgess and D. Hirsh. 1986. ß-D-glucuronidase from *Escherichia coli* as a gene-fusion marker. Proc. Natl. Acad. Sci. USA **83**: 8447-8451.

Jefferson, R. A., T. A. Kavanagh, and M. W. Bevan. 1987. GUS Fusions: ß-D-glucuronidase as a sensitive and versatile gene fusion marker in higher plants. EMBO J. **6**(13): 3901-3907.

Kärenlampi, S. (1996). Health effects of marker genes in genetically engineered food plants. Nordic Council of Ministers, Copenhagen, Denmark, 66 pp.

Lüdecke, H., and I. Feyerabend. 1958. Beiträge zum Saponingehalt der Zuckerrübe. Zucker, **17**: 389-393.

Macrae, R., R.K. Robinson and M.J. Sadler (eds.). 1993. Encyclopedia of Food Science, food technology and nutrition. Academic Press Ltd. London, San Diego.

Märländer, B., H. Glattkowski and K. Buchholz. 1996. Entwicklung einer Formel zur Bewertung des Technischen Qualität der Zuckerrüben in Deutschland. IIRB 59th Congress, Brussels. p. 343-352.

Metcalfe, D.D., Astwood, J.D., Townsend, R., Sampson, H.A., Taylor, S.L. and Fuchs, R.L., 1996. Assessment of the allergenic potential of foods derived from genetically engineered crop plants. Crit. Rev. Food Sci. Nutr. **36**(S): S165-S186.

Oakenfull, D and G.S. Sidhu. 1989. Saponins. In *Toxicants of Plant Origin*. Vol. II Glycosides. CRC Press, Boca Raton, FL, p. 97-141.

Padgette, S. R., D. B. Re, D. B., Barry, G. F., Eichholtz D. A., Delannay X., Fuchs R. L., Kishore G. M., and R. T. Fraley. 1996. New Weed Control Opportunities: Development of Soybeans with a Roundup Ready™ Gene. In *Herbicide Resistant Crops*. Edited by S. O. Duke. C.R.C Press Inc. p. 53-84.

Pipke, R. and N. Amrhein. 1988. Degradation of the phosphonate herbicide glyphosate by *Arthrobacter atrocyaneus* ATCC 13752. Appl. Environ. Microbiol. **54**: 1293-1296.

Potter, R.L., J.D. Bacheller, L.M. Chassy, and R. L. Mansell. 1990. Isolation of Proteins from Commercial Beet Sugar Preparations. J. Agric. Food Chem. **38**: 1498-1502.

Randolph, T. G. and J. P. Rollins. 1950. Beet sensitivity: allergic reactions from ingestion of beet sugar (sucrose) and monosodium glutamate of beet origin. J. Lab. Clin. Med. **36**: 407.

Richter, A. W., Granath, K. and G. Ostling. Anaphalactoid reactions in connection with infusion of invert sugar solutions are due to macromolecular contaminants. Int. Arch. Allergy Appl. Immunol. **50**: 606.

Rodgers, S.G., H. Klee, R. Horsch and R.T. Fraley. 1987. Improved vectors for plant transformation: Expression cassette vectors and new selectable markers. Meth. Enzymol. **153**: 253-277.

Schulz, A., Kruper A. and N. Amrhein. 1985. Differential sensitivity of bacterial 5-enopyruvylshikimate-3-phosphate synthases to the herbicide glyphosate. FEMS Microbiol. Lett. **28**: 297-301.

Silliman, K. and A. M. Coulston. 1991. In *Sugars and Sweeteners.* N. Kretchmer and C. Hollenbeck (eds.) CRC Press, Boca Raton, FL, USA. p. 17-27.

Sleisenger, M.H. and J.S. Fordtran. 1989. Gastrointestinal Disease, Vol. 1. In *Pathophysiology Diagnosis Management*. W. B. Saunders Company, Philadelphia. p. 675-689.

Smed, E., A.W. Huijbregts, D. Hadjiantoniou and G. Vallini. 1996. Influence of Agronomic Factors on Nonconventional Parameters of the Internal Quality of Sugar Beet. IIRB 59th Congress, Brussels. p. 385-389.

Southgate, D. A. T. 1986 In *CRC Handbook of dietary finer in human nutrition.* G. A. Spiller (ed). p.27. CRC Press, Boca Raton, FL, USA.

Steinrucken, H. and N. Amrhein. 1980. The herbicide glyphosate is a potent inhibitor of 5-enolpyruvylshikimic acid-3-phosphate synthase. Biochem. Biophys. Res. Comm. **94**: 1207-1212.

Sutcliffe, J.G. 1979. Complete nucleotide sequence of the *Escherichia coli* plasmid pBR322. Cold Spring Harbor Symposium **43**: 77-90.

Taylor, S.L., R.F. Lemanske Jr., R.K. Bush, and W.W. Busse. 1987. Food allergens: structure and immunologic properties. Ann. Allergy **59**: 93-99.

Taylor, S.L. 1992a. Chemistry and detection of food allergens. Food Technology **46**: 146-152.

Taylor, S.L., J.A. Nordlee, and R.K. Bush. 1992b. Food Allergies. In *Food Safety Assessment, ACS Symposium Series* 484. eds. J.W. Finley, S.F. Robinson, and D.J. Armstrong, American Chemical Society, Washington DC, USA.

Timko, M.P., L. Herdies, E. de Alameida, A.R. Cashmore, J. Leemans and E. Krebbers. 1988. Genetic engineering of nuclear-encoded components of the photosynthetic apparatus of Arabidopsis. In *The impact of chemistry on biotechnology – a multidisciplinary discussion*. M. Phillips, S.P. Shoemaker, R. Middlekauff and R.M. Ottenbrite (Eds). ACS Books, Washington DC. p. 279-295

WHO (1991). Strategies for assessing the safety of foods produced by biotechnology. Report of a joint FAO/WHO Consultation. World Health Organization, Geneva, 59 pp.

WHO (1993). Health aspects of marker genes in genetically modified plants. Report of a WHO Workshop. World Health Organization, Geneva, 32 pp.

Wozniak, C.A. and L.D. Owens. 1994. Native ß-glucuronidase activity in sugarbeet (*Beta vulgaris*). Physiol. Plant. **90**: 763-771.

Zambryski P. 1992. Chronicles from the Agrobacterium-plant cell DNA transfer story. Annu. Rev. Plant. Physiol. Plant Mol. Biol. **43**: 465-490.

ATTACHMENT 3

REGULATORY IMPACT ASSESSMENT

The Authority is required, in the course of developing regulations suitable for adoption in Australia and New Zealand, to consider the impact of various options (including non-regulatory options) on all sectors of the community, including consumers, the food industry and governments in both countries. The regulatory impact assessment will identify and evaluate, though not be limited to, the costs and benefits of the regulation, and its health, economic and social impacts.

- *Identification of affected parties*

1. Governments in Australia and New Zealand

2. Consumers in Australia and New Zealand

3. Manufacturers, producers and importers of food products

- *Options*

Option 1–To prohibit the sale of food produced using gene technology

GOVERNMENT Commonwealth, New Zealand Health Departments, State/Territory Health Departments	**Benefits** • no benefits were identified.	**Costs** • the governments of Australia and New Zealand may be challenged under the WTO to justify the need for more stringent restrictions than apply internationally. • a prohibition on food produced using gene technology in Australia and New Zealand could result in retaliatory trade measures from other countries. • there may be technical problems for AQIS in enforcing such a prohibition at the import barrier.
INDUSTRY Manufacturers, producers and importers of food products	**Benefits** • Some companies may benefit from being able to exploit niche markets for non-GM products overseas.	**Costs** • food manufacturers and producers will be unable to use the processed food fractions from foods produced using gene technology thus requiring the switch to non-GM ingredients and the reformulation of many processed food products. The cost to manufacturers of going non-GM has been estimated to be $A 207m in Australia and $NZ 37m in New Zealand[4]. This is equivalent to 0.51% of turnover in Australia and 0.19% in New Zealand.

[4] Report on the costs of labelling genetically modified foods (2000)

CONSUMERS	**Benefits** • no benefits were identified, however as some consumers perceive GM food to be unsafe, they may perceive prohibition of GM food to provide a public health and safety benefit.	**Costs** • could lead to decreased availability of certain food products. • increased costs to consumers because manufacturers and producers may have to source non-GM ingredients.

Option 2– to permit the sale of food produced using gene technology

GOVERNMENT Commonwealth, New Zealand Health Departments, State/Territory Health Departments	**Benefits** • increased innovation and competitiveness in the food industry will benefit the economy.	**Costs** • minor costs associated with amending the *Food Standards Code.*
INDUSTRY Manufacturers, producers and importers of food products	**Benefits** • food producers and manufacturers will be able to capitalise on the latest technology. • food importers will continue to be able to import manufactured products from overseas markets including the USA and Canada where there is no restriction on the use of food produced using gene technology.	**Costs** • there may be some discrimination against Australian and New Zealand food products in overseas markets that have a preference for non-GM foods (e.g., Japan and the European Union).
CONSUMERS	**Benefits** • consumers may have access to a greater range of food products.	**Costs** • those consumers who wish to avoid GM food may experience restricted choice in food products. • those consumers who wish to avoid GM food may have to pay more for non-GM food.

- *Conclusion of the regulatory impact assessment*

Consideration of the regulatory impact for foods produced using gene technology concludes that the benefits of permitting foods produced using gene technology primarily accrue to the government and the food industry, with potentially a small benefit to consumers. These benefits are considered to outweigh the costs to government, consumers and industry, provided the safety assessment does not identify any public health and safety concerns.

ATTACHMENT 4

WORLD TRADE ORGANISATION AGREEMENTS

With the completion of the Uruguay Round of trade negotiations, the World Trade Organization (WTO) was created on 1 January 1995 to provide a forum for facilitating international trade.

The WTO does not engage in any standard-setting activities but is concerned with ensuring that standards and procedures for assessment of and conformity with standards do not create unnecessary obstacles to international trade.

Two agreements, which comprise part of the WTO treaty are particularly important for trade in food. They are the;

- Agreement on the Application of Sanitary and Phytosanitary Measures (SPS); and
- Agreement on Technical Barriers to Trade (TBT).

These agreements strongly encourage the use, where appropriate, of international standards, guidelines and recommendations, such as those established by Codex (in relation to composition, labelling, food additives, veterinary drug and pesticide residues, contaminants, methods of analysis and sampling) and the code and guidelines on hygienic practice.

Both Australia and New Zealand are members of the World Trade Organization (WTO) and signatories to the agreements on the Application of Sanitary and Phytosanitary Measures (SPS agreement) and on Technical Barriers to Trade (TBT agreement). Within Australia, the Council of Australian Governments (COAG) has put in place a Memorandum of Understanding binding all States and Territories to the agreements.

The WTO agreements are predicated on a set of underlying principles that standards and other regulatory measures should be:

- based on sound scientific principles;
- developed using consistent risk assessment practices;
- transparent;
- no more trade-restrictive than necessary to achieve a legitimate objective;
- recognise the equivalence of similar measures in other countries; and
- not used as arbitrary barriers to trade.

As members of the WTO both Australia and New Zealand have an obligation to notify the WTO of changes to food standards to enable other member countries of the WTO to make comment. Notification is required in the case of any new or changed standards which may have a significant trade effect and which depart from the relevant international standard (or where no international standard exists). Matters raised in this proposal may be notified to the WTO as either SPS notifications or TBT notifications, or both.

SPS Notifications

These are primarily health related, and refer to any sanitary and phytosanitary measure applied:

- to protect animal or plant life from risks arising from the entry, establishment or spread of pests, diseases or disease carrying organisms;

- to protect human or animal life or health from risks arising from additives, contaminants, toxins or disease-carrying organisms in foods, beverages or foodstuffs;

- to protect human life or health from risks arising from diseases carried by animals, plants or products thereof, or from the entry, establishment or spread of pests; and

- to prevent or limit other damage from the entry, establishment or spread of pests.

The Agreement on the Application of Sanitary or Phytosanitary Measures relates to any sanitary or phytosanitary measure applied to protect animal, plant or human life or health which may directly or indirectly affect international trade. Whether the SPS measure is in the form of a law or mandatory regulation, an advisory guideline, a code of practice or a requirement, it is the purpose of the measure that is important - not its regulatory status. Each WTO member country is entitled to apply SPS measures that are more stringent than the international standards in order to protect the health of its population. In the interests of transparency, each instance of such non-alignment, which could result in an impediment to trade must be identified and justified and the documentation of that justification must be readily available

Each member country is also required to apply its methods of risk assessment and management consistently so arrangements under the SPS Agreement do not generate what may really be technical barriers to trade

Under the SPS Agreement, an exporting country can have resort to the WTO's dispute settlement procedures with respect to such a non-alignment. These arrangements mean there is potential for a code of practice to introduce an SPS measure that may bring about non-alignment with international requirements. Such non-alignment would need to be justified scientifically on the grounds that it is necessary to protect human, animal or plant life or health.

TBT Notifications

A technical barrier to trade arises when a mandatory requirement in a country's food regulatory system does not align with the international standard and it is more trade restrictive than is necessary to fulfil a legitimate objective. However, it can be acceptable for a country to have a more stringent requirement than that set internationally for reasons including:

- Maintaining national security;
- Preventing deceptive practices; and
- Protecting human health or safety.

Instances of non-alignment with international standards, which could result in trade barriers must be identified and, if questioned, justified. Voluntary codes of practice are not expected to generate technical barriers to trade except where compliance with a code of practice or some aspect of a code of practice is expected. Consequently, it is possible for a voluntary code of practice to be viewed by the WTO as mandatory and subject to all the notification and other provisions applying to mandatory regulations.

The Agreement on Technical Barrier to Trade relates to requirements covering product characteristics or their related processes and production methods. TBT covers measures that are not SPS, such as requirements relating to terminology, symbols, packaging, marking, labelling, food composition and processing methods.

ATTACHMENT 5

SUMMARY OF PUBLIC SUBMISSIONS

A: First round submissions

1. National Genetic Awareness Alliance (Australia)

- Believes that the patenting of life-forms and living processes represents a violation of human rights, threat to food security, impediment to medical research and a threat to animal welfare
- Believes that current GM techniques are inherently hazardous, and have been shown recently to offer no benefits
  - Lower yields with high pesticide input
  - Intensification of the corporate monopoly on food
  - Spread of antibiotic resistance marker genes and promoter sequences
  - Possible increase of allergenicity due to spread of transgenic pollen
- Urges governments to use precautionary principle and carry out research into sustainable agricultural methods
- Calls for suspension of trials and sale of GM products and public inquiry.

2. Pola Lekstan and Anna Clements (Australia)

- Are concerned that approval without long-term testing may pose a health threat, that more GM food means less choice for those wanting to avoid it, that Bt may affect non-target organisms, and that herbicide resistance may lead to overuse of chemicals.

3. Arnold Ward (Australia)

- Questions the system of MRL setting in light of the levels of high glyphosate residues in Roundup Ready soybeans and of other chemicals (including the Bt toxin) in GM crops
- Is concerned about detrimental effect of Bt on non-target (beneficial) organisms and on humans, and believes that genetic engineering is imprecise with uncertainties in outcomes
- Believes that the concept of substantial equivalence is inadequate and should not be used to avoid more rigorous testing, and that commercial factors are overriding need for basic research. Also believes that ANZFA's arguments defend the needs of biotechnology companies and food processing industry, and that since ANZFA does no testing itself, the results can't be trusted.

4. Australian GeneEthics Network

- Believes that the data provided is insufficient to make an assessment, and clock should be stopped on the applications. Concerns include:
  - Direct health effects of pesticide residues
  - Possibility of transfer of antibiotic resistance marker genes leading to resistant bacteria
  - The possibility that transfer of other traits e.g. herbicide tolerance to bacteria, could lead to horizontal spread of unfavourable traits
  - Insertion of viral DNA could create new and virulent viruses

- The possibility that approval could lead to the growing of GMOs in Australia – ecological concerns including effects of, and increases in resistance to, Bt-toxins and the encouragement of increased herbicide use resulting from herbicide-tolerant crops
- The threat to GE-free status export markets

- Believes that the term 'substantial equivalence' is not useful– compositional data alone does not establish equivalence

5. Public and Environmental Health Service (Australia)

- Believes that the data provided should cover both the intentional and unintentional effects of the genetic modification. The unintended consequences of random insertion of new genetic material into the host genome could include loss or change of function of gene or controlling element, disregulation or amended regulation of the gene or controlling element, or production of a novel hybrid protein which could occur in an unregulated manner. They should also cover any compositional changes e.g. nutrients, antinutritional factors, natural toxicants, and define when a change would be considered 'significant'
- Potential effect of introduced proteins on metabolic pathways should be addressed e.g. over-expression or inhibition of enzymes
- Data should include details of whether introduced proteins are detectable in whole commodities, processed products and highly processed derivatives
- Data should include details of toxicity and allergenicity tests to prove that food is safe, as well as address issues of specificity and potency of proteins. It should also address the ability to support typical growth and well-being
- Data for herbicide-tolerant plants should be derived from studies performed on plants treated with herbicide. They should address the human toxicity of the herbicide and whether residues of the herbicide degradation process are present, toxic and/or subject to an MRL.

6. David Grundy (Australia)

- Considers that the expression of Bt toxins and other chemicals in plant tissues removes the choice of washing chemicals off fruit and vegetables. Believes that Roundup Ready crops have glyphosate or glufosinate molecules genetically attached
- Believes that GM crops should not be used for feed given to animals bound for human consumption, that products encouraging antibiotic resistance should not be used, and that labelling should be mandatory for all products containing GM ingredients

7. Leesa Daniels (Australia) Member of the Genetic Engineering Action Group

- Believes that:
  - Scientific research although limited, has brought concerns to light
  - Substantial equivalence is a subjective principal
  - Comprehensive and mandatory labelling must be urgently implemented
  - The cauliflower mosaic virus (CaMV) promoter could enhance the capability to transfer genes horizontally and has the potential for activating dormant or new viruses
  - Antibiotic marker genes could lead to increase in antibiotic resistance
  - Several of the transformations encourage the use of pesticides, all of which have shown to be harmful.

8. Australian Food and Grocery Council

- Fully endorses the policy of minimum affective regulation, supports these applications, and considers that food manufacturers should make their own choice with regard to use of GM crops or products derived from them
- Believes that since the growth of GM crops has been approved overseas, they would support their growth in Australia if approved through the GTAC/GMAC/OGTR process
- Considers it unfortunate that ANZFA has not negotiated "equivalence" agreements for products already approved overseas to enable approval without having to carry out its own safety assessment. In the absence of such an agreement it supports the ANZFA safety assessment process.
- Believes that an appropriate information and labelling scheme would enable consumers to make an informed choice.

9. New Zealand Ministry of Health

- Referred preliminary report to New Zealand Health Research Council, who stated concern that all safety aspects should be carefully considered in the ANZFA process.

10. Nestle Australia Ltd.

- Supports the continued approval of glufosinate ammonium-tolerant canola, and believes that manufacturers would be disadvantaged were approval not to be granted.

11. Consumers' Association of South Australia Inc. & National Council of Women of Australia (CASA supports submission of NCWA)

- Believe that current testing procedure is inadequate and that human trials are the only adequate method, as with testing of new drugs. Also that physiological and neurological effects as well as the toxicological and allergenic effects should be looked at, and that an independent body should be responsible for testing
- Do not support the use of antibiotic markers, since they believe they may pose a threat to efficacy of antibiotics in humans
- State that new research has shown that GM soybeans may be a less potent source of phytoestrogens than conventional soybeans confirming the inadequacy of the term 'substantial equivalence'
- Raise the point that although these crops have been approved elsewhere, this situation may change with consumer pressure
- Do not accept that it is impossible to source food to ascertain whether or not it contains GM ingredients. Believe that if McCain and Sanitarium can do it, then others should also be able to
- State general concern about the risk that MRLs will be raised as a result of herbicide-tolerant crops being developed, and feel that the calculations used are flawed and are not based on safety criteria
- Believe that the use of GM crops in animal feed should also be regulated.
- State concern over possible increase in glyphosate use (it is apparently confirmed in one reference that herbicide use increases with herbicide resistant crops), referring to studies that link the chemical to Hodgkin's lymphoma, and the possibility that Europe may ban it due to adverse effects on beneficial insects**.** They are particularly concerned that glyphosate is not looked at by the same regulatory body as that looking at GM foods

A379, A388

- State concern over the persistence and toxicity of bromoxynil, and consider that these have not been adequately assessed by the US FDA. They understand that the breakdown product of bromoxynil (DBHA) may be more potent than bromoxynil itself, and believe that a safety assessment needs to be done on this too. This is apparently the main residue, and they believe that this may appear in cotton oil and linters.

A372, A375, A380, A381, A386

- With respect to glufosinate ammonium, state concern about toxicity, neurotoxicity, teratogenicity and residues in food, soil and water. They believe that Monsanto is likely to apply for an increase in the MRL, and that such increases are likely to constitute a health hazard

A380, A382, A383, A384, A385, A386

- Raise issues of adverse effects of Bt toxins on non-target insects and think that it needs more study.

A387

- Believe that raising the amount of a nutrient in a food may have unknown drawbacks e.g. affecting the efficacy of other nutrients.

12. Health Department of Western Australia

- Highlights various health and environmental concerns:
  - the use of antibiotic resistance genes as markers may transfer resistance to animals via gut bacteria
  - the possibility that microbial gene sequences may contain fragments of other virulent genes, and also that ingesting Bt toxins may be harmful to humans
  - the possibility that insects may be more prone to developing resistance to Bt, since Bt toxins have been found to be released into the soil
- Believes that both safety data and gene sequences should be available for public scrutiny.

13. Meat New Zealand

A379

- Concerned at how labelling regulations will apply to sausage casings that may contain cotton linters even if they are not to be eaten, i.e. are effectively a processing aid. Think that labelling should only be used to advise the sausage manufacturer not consumers.

14. BRI Australia

- Supports the approval of all 13 applications provided ANZFA is satisfied with their safety.

15. Food Technology Association of Victoria Inc.

- Supports the approval of all 13 applications provided ANZFA is satisfied with their safety.

16. Diane Davie (Australia)

- Believes all 13 applications should be rejected, since they have not undergone human safety testing here or overseas, and have not been assessed on their ethical merits
- Believes that risks include:
  - Bacterial and viral vectors which could affect human physiology
  - Herbicide and insect-resistance genes, which could increase allergies and antibiotic resistance
  - Environmental risks
- Also believes that ANZFA must heed the concerns of consumers opposed to GM foods.

17. Martin Hurley, David Hook, Ian Smillie, Margaret Dawson, Tee Rodgers-Hayden, David Lovell-Smith (Natural Law Party), Barbara Brown, Ngaire Mason, Robert Anderson (member, Physicians and Scientists for Responsible Genetics), Louise Carroll, Gilbert Urquart, Caroline Allinson-Dunn, Megan Lewis, Peter Barnes, James Harlow, Gabrielle Dewan, Scott Young, Virginia Murray, Stephanie Chambers, Kay Dyson, Peter Fenwick, Joanne Xerri, Paul True, Josh Gill, James & Peysha Charlwood, Mitta Hirsch, Alan Florence, Nicole Paul, Lawrence Clarke, David Snowman, Reg Paling, Mark and Johanna Blows, David and Bev Seymour, Richard and Sharon Moreham (see also below), Stuart Drury and Helen Murphy (All Australia), Brennan Henderson (New Zealand) – Generic e-mail objection

- Believe that most Australians and New Zealanders do not want GM foods, there are no benefits, and deferral would not be disadvantageous. Approval should be delayed until they are proven safe.
- Feel that there is insufficient time to assess these applications thoroughly, and there are so many products under development that there is a high overall risk of a major disaster
- Believe that GM foods encourage pesticide use, and applications have made for commercial purposes only, and also that here could be commercial benefit to Australia and New Zealand in remaining GM-free.

18. Richard and Sharon Moreham (see also above)

- In addition to the points above, also think that it is unfortunate that the NZ government agreed to joint approval of food, as the Australian public are less educated about the issues surrounding GM foods
- Think that approval would only prove that ANZFA serves the interests of large multinational companies rather than those of the public.

19. Vicky Solah (Australia)

- Is for GM foods if the safety evaluation is carry out using approved, validated methods by an independent body, if the results are made available to consumers, and if all GM food is labelled
- Is concerned that transformation may lead to disruption of another gene, and that more research is needed before it is clear whether the process is safe
- With regard to herbicide tolerant crops, is concerned that consumers may not be aware of the need to wash products that have been sprayed, and that this therefore impacts on food safety. Also concerned about environmental impact of these chemicals, and of the possibility of resistance necessitating higher pesticide use in the future.

20. Dr Rosemary Keighley (Australia)

- Will not purchase foods unless they are certified GM-free. Believes that Australian producers who do not actually use GM products, but who fail to label them as such, will suffer.

21. Nicola Roil (Australia)

- Believes that GM foods pose health threats and may contaminate non-modified crops

22. Ian and Fran Fergusson (Australia)

- Believe there has been inadequate testing, and are concerned about possible side-effects.

23. Lyndal Vincent (Australia)

- Urges delay of approval until proven safe by extensive testing. Considers that genetic material is being released without knowing what the effects are, and cannot be recalled.
- Believes that there is no benefit to the consumer, and that national economic interests are best served by maintaining a GM-free market.

24. Fay Andary (Australia)

- Does not want any of the 13 products covered by the applications to be approved for inclusion in the food supply.

25. John and Francesca Irving (Australia)

- Thinks that no GE foods should be approved for inclusion in the food chain.

26. Diana Killen (Australia)

- Believes that there is no proven benefit to consumers and in many instances nutritional value is actually lower in GM crops, and it is therefore irresponsible to push through approval without thorough assessment of their long-term safety for public health.
- Suggests that research has highlighted adverse allergic reactions and a lowered immune response in some individuals, and that there are health implications with crops designed to be grown with greater concentrations of pesticides
- Thinks that labelling is essential for consumers to discriminate in purchasing, and that Australia has a unique opportunity in supply of organic and GM-free food.

27. Sheila Annesley (Australia)

- Does not want any of the 13 foods included in the food supply.

28. David and Edwina Ross (Australia)

- State concern for the future food supplies and well-being of their grandchildren.

29. Beth Schurr (Australia)

- Wishes to protest against the threat of GM foods, the possible future detrimental effects and the further endangering of the planet.

30. Beth Eager (Australia)

- As a parent is concerned that neither the long-term effects on health nor the environment are being considered.

31. Bruce Pont and Ljiljiana Kuzic-Pont (Australia)

- Believe that safety has not been, and cannot be satisfactorily determined, and that any party associated with GM foods could be legally liable should adverse health effects be seen. Thalidomide, smoking, 'Agent Orange' and asbestos all show that such things can affect subsequent generations
- Believe that an increase in use of pesticides will result from pesticide-tolerant crops, and that the emphasis should be on organic and/or safe agriculture
- Believe that GM-food is a retrograde step, contrary to nature and has the potential to destroy the human race.

32. Chitta Mylvaganum (Australia)

- Wishes to know what tests were done to assess negative effects on human and environmental health, how thorough they were, what the outcomes were, are the results publicly available, and what further avenues of inquiry are open to the public
- Requests the prevention of the import or release of any products until tests are carried out by unbiased scientists in order to prove the lack of health or environmental effects.

33. John Stevens (Australia)

- Would be concerned if approval were granted before sufficient research had been completed on potential impacts on human health and gene pools of nearby crops. Once grown, spread via pollen would be impossible to stop, and labelling would not prevent exposure by this route
- Considers that utmost caution should be exercised and import approval denied indefinitely.

34. Tim Carr (Convenor of the Emergency Committee against GE Foods)(Australia)

- Believes that GM-foods are produced using a radical and unpredictable new technology so should be subject to more rigorous testing
- States that it is unknown how the introduced gene will interact with and influence genetic expression in the host genome, and could change the chemical nature of the food
- Considers that health risks could result from the increased use of pesticides, and also that ANZFA should consider wider environmental, ethical and socio-economic issues.

35. Jan Kingsbury (Australia)

- Believes that GM-foods could result in loss of economic advantage for Australia and New Zealand since they are known internationally for pure and safe products
- Believes that foods are being complicated and pushed by big internationals, and organic farmers are being contaminated by cross-pollination.

36. Teresa Sackett (Australia)

- Believes that:
  - The KPMG report on labelling was prepared in a ridiculously short time and provided limited analysis
  - The proposal of 'no label' for foods which 'may contain' or in which there is 'no evidence' of GM material is inadequate
  - Inadequate testing procedures should not be used to declare a product is GM-free just because material can't be detected. In fact testing methods have been developed that can be used to work out the GM content

- Government and industry seem to be favouring the introduction of GM foods. This will result in the increased use of chemicals and the destruction of soil life
- Organic farming pay high costs for producing healthy plants, while conventional farmers have little restriction on pollution of air, soil and water. Salinity problems, the death of the Great Barrier Reef, rivers and streams has resulted from ignorance in farming and broader community. Such problems will increase with GM foods.
- The implication that the public will not understand the issues is wrong. Everyone needs to be fully informed.

- Asks the question of whether workers in the food industry are to be better informed, and also why no 'verification documents' are to be required by retailers? Believes that certification schemes should be on a par with those for Kosher foods and organics.

37. John and Sandy Price (Australia)

- Approval of GM foods and seeds should not be allowed, as it is an affront to the sovereignty of Australia and the dignity of the Australian people. The results of the experiment cannot be reversed.

38. John Scott (New Zealand)

- Encloses article from The Irish Times, which describes the restrictions that have been placed by the US EPA on the cultivation of GM corn. These appear to have resulted from fears that Bt crops may be harmful to Monarch butterflies and that resistance may develop to Bt.

39. R A Randell (New Zealand)

- Believes that all GM products should be placed under a moratorium until the Royal Commission of Inquiry has considered the issue, and until all scientific, philosophical, ethical and moral issues have been looked at.

40. National Council of Women of New Zealand

- Believes that:
  - approval of all 13 applications should be rejected, and that none should be approved for planting.
  - Independently-funded body should be responsible for safety assessments
  - If it is possible to segregate high-oleic soybeans, then RoundUp Ready soybeans should be segregated too
  - Consumers should be made aware of the extent of GM ingredients in their food
  - GM foods, additives or processing aids already on the market must be labelled comprehensively and without extra cost to the consumer – suggest 'GM unknown' rather than 'may contain'
- Appreciates that rejection may contravene the WTO agreement, but consider that the primary role of ANZFA is the assurance of health and safety.

41. Safe Food Campaign (New Zealand)

- Believes that approval should be rejected, and a moratorium be put in place until after the Royal Commission of Inquiry, for various reasons:
  - Possible effects on non-target insects
  - Spread of GM pollen may cause contamination of non-GM (especially organic) crops, and may result in the spread of herbicide-tolerance genes and an increase in resistance development. Cross-pollination is considered a particular risk for canola (A372 & A388). Bt resistance development is noted as being a particular risk for A382, A383 & A384
  - Lack of long-term testing means health risks are not known
  - Use of broad-spectrum pesticides affects wild flowers and non-target insects.

42. Jocelyn Logan, Caroline Phillips (New Zealand)

- Oppose all 13 applications for the following reasons:
  - Testing has not been long-term or independent, precautionary principle should apply. Approval can happen later if GM is proven safe.
  - No clear public benefit, and lack of opportunity for informed choice (immoral and undemocratic). Labelling regulations also unsatisfactory in this respect.
  - Environmental concerns (increase in pesticides, threat to organic farming, Bt resistance).

43. Robert Anderson (member of Physicians and Scientists for Responsible Genetics – New Zealand)

- Considers that the GM issue should be reconsidered in the light of the release of internal FDA documents made available for a recent lawsuit aimed at amending their policy. Attached document (presentation given by Steven Druker, Alliance for Bio-integrity) suggests that:
  - Scientist's warnings have been ignored
  - FDA policy may be illegal, violating the Food, Drugs and Cosmetic Act – Mr Druker believes that the term generally-regarded-as-safe (GRAS) cannot apply to foreign DNA.

44. Stephen Blackheath (New Zealand)

- Argues that ANZFA's approach to safety assessments is scientifically unsound:
  - Antibiotic resistance marker genes have been cited as being potentially dangerous by groups other than ANZFA e.g. the Royal Society
  - Unanticipated toxins and allergens are a concern, and it is suggested that the ANZFA process does not adequately consider these possibilities
  - Doesn't address the question of whether risks exist that are unique to the GM process
  - It relies on data from the manufacturers themselves, with little sway given to evidence from public submissions. Companies have vested interests the results and cannot be trusted (also gives evidence of Monsanto's past dishonesty)
- Believes that ANZFA is subject to undue influence through the directors, and is biased towards being pro-GM
- Suggests that RoundUp Ready soybeans are not substantially equivalent as the stems have been found to be more brittle than traditional lines, and may be lower in phytoestrogen content

- Also cites the lawsuit being brought by the Alliance for Bio-integrity, and the internal FDA documents that suggest concern from FDA scientists, as evidence of the FDA ignoring important evidence.

45. Claire Bleakley (New Zealand)

- Believes that approval should be rejected for various reasons:
  - They may be against Maori views
  - Further long-term trials are needed and should be carried out by ANZFA themselves - certain trials have apparently shown effects on immune system, allergies and rare syndromes
  - Health concerns of pesticide overuse
  - The possibility of horizontal gene transfer with respect to antibiotic resistance transfer
  - Lack of labelling and the use of the unsatisfactory 'substantial equivalence' concept, which makes hazard difficult to assess
  - There is no substantial gain to consumers

SUMMARY OF SECOND ROUND PUBLIC SUBMISSIONS

The draft Risk Analysis Reports (formerly referred to as the Full Assessment Report) for A372, A375, A378 and A379 were released for a 6-week period of public comment on 1 March 2001. At the end of the public comment period (20 April 2000) a total of 23 submissions had been received. These are summarized below.

1. Australian Food and Grocery Council (AFGC)

- Supports the approval of the four applications:
  A372: Oil derived from - glufosinate ammonium tolerant canola lines - Topas 19/2 And T45 and Oil derived from glufosinate-ammonium tolerant and pollination-controlled lines Ms1, Ms8, Rf1, Rf2 And Rf3;
  A375: Food derived from glufosinate ammonium tolerant corn line T35;
  A378: Food derived from glyphosate-tolerant sugarbeet line GTSB77; and
  A379: Oil and linters from bromoxynil-tolerant cotton transformation events 10211 and 10222.
- Submits that as ANZFA has concluded that foods encompassed by the four applications do not raise any public health and safety concerns, that there should be no reason for retaining the generic prohibition on their use merely because they are GM foods.
- Supports the application of the revised labelling requirements of Standard A18 to the products encompassed by these four GM applications.

2. Bentleigh-Bayside Gene Alert, Campaign for Safe Food

- Opposes all four of the GM food applications because of overwhelming concerns about the risks to health and the environment, particularly in the use of herbicides.
- Supports independent testing and questions the role and validity of overseas approvals of GM commodities in the Australian process.
- Contends that the safety assessments were questionable and scientifically unsound because of apparent inadequacies in the toxicity testing and in the conclusions drawn from the animal feeding studies.
- Considers that the assessment should include possible changes to the food product as it is metabolised by livestock that are bred for human consumption.

- Advises that the precautionary principle should be adopted in relation to the use of antibiotic resistance marker genes.

3. New Zealand Ministry of Health

- Supports the conclusions of the ANZFA Draft Risk Analysis Reports for all four applications, that the foods are safe for human consumption.
- Considers that the most important data are the molecular characterisation of the inserted DNA and compositional analyses, requiring presentation of as much raw data as possible, and that brief summaries of other issues are all that is required, especially where the same proteins have been previously assessed.

4. Anne FitzSimon (NZ)

- Opposes the approval of all four applications primarily for ethical reasons and concerns about safety.
- Demands detailed labelling of GM foods to enable consumer choice.

5. Nelson GE Awareness Group (Susie Lees)

- Do not support the approval of the four GM applications because they consider that GM foods pose unique public and environmental health risks.
- Submits that there has been no independent scientific testing of the products.
- Suggests complete removal of these foods from the market until safety testing and long term feeding studies of at least 12-18 years duration have been completed.
- Considers that the new labelling provisions do not capture all foods produced using gene technology.
- A372 – expresses grave concerns associated with the use of the *barnase*/*barstar* gene system (uses the term 'terminator technology'), and claims that whole canola seeds are used in certain bakery products.
- Opposes the use of antibiotic resistance genes in all of the applications.

6. Kate Clinch-Jones

- Opposes all of the applications on the basis that the respective Draft Risk Analysis Reports do not address the potential public health and safety issues associated with the genetic modifications.
- Claims that the safety assessments are not comprehensive, and lack adequate scientific evidence and peer review.
- Opposes the use of the herbicides glyphosate and glufosinate-ammonium because of concerns relating to potential toxicity in humans and the environment.
- Criticises the regulatory impact statement for each GM application. Contends that benefits of prohibiting the sale of GM foods include the protection of the integrity of the food chain, avoiding irreversible environmental damage, upholding the precautionary principle and meeting consumer demands.
- Disagrees with government obligations in relation to the WTO.
- Disagrees with ANZFA's assessment and discussion of the possibility for horizontal gene-transfer and refers to supporting scientific articles.
- Expresses concerns about food products derived from stock animals that consume GM crops.
- States that because of the confidentiality of some of the information, potential hazards may not be identified by independent reviewers.
- Suggests that ANZFA seek advice about antibiotic resistance genes from microbiology and infectious disease specialists.

- Supports full proteome analysis on all GM foods.
- Recommends that an expert team of advisors be established to design scientifically sound feeding studies that also consider ethical issues.

7. Food Technology Association of Victoria Inc.

- Supports approval of the four applications (A372, A375, A378 and A379) provided ANZFA is satisfied with their safety and that the foods will be appropriately labelled for the benefit of consumers.

8. Adrian Elliot (Aus)

- Supports the approval of the GM food applications and regards these as trailblazers.
- Claims that the new GM foods will assist in keeping Australian industry in step with developments made by the rest of the world.
- Considers that both industry and consumers benefit from the development of new varieties and new technology.
- Comments that the public would benefit from a national education campaign to provide greater awareness of the food supply and to promote public understanding of the technology, the safety and regulation of the products arising from this technology.

9. Aventis CropScience

- Suggests minor amendments and corrections to the Draft Risk Analysis Reports for each of the applications, which will be addressed in the respective Final Risk Analysis Reports.

10. GeneEthics Network (Arlene Buchan and Bob Phelps)

- Opposes all four of the applications because of perceived adverse effects on the environment and public health.
- Opposes the use of the herbicides glyphosate, glufosinate ammonium and bromoxynil because of concerns about toxicity.
- States that ANZFA's regulatory impact assessment fails to acknowledge that primary production could be negatively affected by GM crops. ANZFA should consider the economic effects of its decisions.
- Considers that ANZFA's safety assessment process is too narrowly focussed and fails to consider environmental and animal health issues.
- Disagrees that ANZFA's assessments adopt a cautious approach.
- Considers that the safety assessment reports lack sufficient information to demonstrate food safety, and do not adequately consider the possibility of trace amounts of unintentional or unanticipated products.
- Expresses outrage that there is no post-market surveillance system in place to monitor any effects of crop release or GM food consumption.
- States that the new labelling regime is too lax and contravenes the rights of consumers to know whether foodstuffs have been genetically modified.

11. Public Health Association of Australia Inc (PHAA)

- Asserts that ANZFA does not respond to all issues raised in their previous submissions.
- Expresses concerns on the use by ANZFA of the concept of substantial equivalence.
- Raises concerns on the use of antibiotic resistance marker genes during GM crop development.

- Claims that ANZFA does not require data in support of applications that is generated by independent laboratories other than the applicant.
- Raises concerns regarding the lack of detail in reporting of the parameters investigated in the acute toxicity tests on CP$ EPSPS, GUS and Protein 34550.

A375

- Raised concerns about the enzyme specificity of the PAT gene.
- Raised concerns about the adequacy of the toxicity studies.
- Commented on small compositional differences between GM and non-GM varieties of corn.
- Asserted that that there were no spray data submitted with the application.
- Commented on the adequacy of the feeding study submitted with the application.

A372

- Comments on the toxicity of glufosinate-ammonium.
- Expresses concerns relating to the use of the *barnase* gene in canola.
- Considers that the compositional analyses were insufficient to comprehensively assess the canola.
- Contends that nutritional studies would be useful.
- Considers that animal feeding studies using every line under assessment should be submitted.
- Objects to the commercial-in-confidence aspects of the application.

A378

- Raised concerns about the adequacy of the toxicity studies.

A379

- Raised concern about the adequacy of the toxicity studies.
- Raised concerns about ANZFA's assessment of the toxicity of bromoxynil and its break down products.
- Commented on the compositional differences between the GM versus control lines.

12. Consumers' Institute

- Provides comments on the GM applications as a group, not as individual foods, stating that the regulatory process should take into consideration new scientific information or data as, or when, it becomes available and react accordingly.
- Favours ongoing monitoring of any long term effects
- States that consumers are primarily concerned with the apparent lack of independent verification of testing carried out by developers of the products, as well as the failure to do long term testing and animal testing of the products.
- Expresses a lack of confidence in the assessment process and in the principle of 'substantial equivalence' because of concerns that unexpected changes may not be identified.
- Considers that the system of regulation applying to new medicines, which require random controlled trials, is rigorous and the same has not been applied to GM foods.

13. Claire Bleakley (NZ)

- States that the foods covered by applications A372, A375, A378, A379, A385 and A386 should not be allowed on the market until the New Zealand Royal Commission has reported and labelling of GM foods is in place.
- Expresses concerns about the safety of GM foods in general.
- Considers that the previous decisions do not reflect a "high degree of consumer confidence" in the regulations as per the ANZFA Act.
- Considers that not enough information is provided to consumers.
- States that long term studies are required to show that the genetic constructs do not cause harm to the environment.

14. National Council of Women of Australia Inc

- Does not support the approval of any of the four applications due to concerns that GM foods have not been tested either adequately or appropriately.
- Provided comment on individual applications, which will be addressed within the specific issues section of the Final Risk Assessment Report.
- Raised concerns about the environmental impact as well as toxicity, neurotoxicity and teratogenicity of glufosinate ammonium and provided information about overdoses of glufosinate ammonium.
- Is concerned that GM applications for herbicide tolerant crops will result in the increasing use of herbicides.
- Considers that any health risk is not acceptable as the technology is not needed to feed the world or wanted by consumers.
- States that no further GM applications should be accepted until the Office of the Gene Technology Regulator has addressed the environmental, social and ethical issues, as ANZFA has no community consultative or ethics group to consider these issues.
- Considers that the benefits of the technology accrue to the applicant.
- Considers that ANZFA is not responding to objections raised previously and is repeating previous responses, leading to little desirable outcome from a community and public interest perspective.
- Believes that ANZFA is dismissing public opinion given that the majority of submissions are against approval of GM applications.
- States that the labelling laws are inadequate.

15. Consumers' Association of South Australia Inc

- Supports the submissions made by the National Council of Women.

16. Food Branch, South Australian Department of Human Services

- A372 – considers that data on tocopherol levels would enhance the compositional analyses; questions whether the proposed approval should refer to the hybrid lines rather than to the Ms and Rf parental lines.
- A375 – compositional analyses should relate to the line for which the proposed approval is sought; Vitamin A and carotene analyses were not provided for line T25.
- A378 – questions details in the drafting of the proposed variation to the *FSC*.

17. GE Free New Zealand (RAGE)

- Opposes all four of the applications, A372, A375, A378 and A379.
- Provides a list of health and medical concerns that are claimed to be attributable to gene technology.
- Expresses grave fears about the possible health consequences of GM foods in general.
- Application specific concerns include:
  A379 – the use of the CaMV 35S promoter and the presence of antibiotic resistance genes
  A372 – the use of antibiotic resistance genes.

18. Sandra Jacobs (NZ)

- Opposes all four of the applications, A372, A375, A378 and A379 due to the lack of long term independent testing.
- Considers that GE foods are polluting other crops, particularly GE canola containing the *barnase* gene.

19. Brian Lister and Lorraine Leader (NZ)

- Opposes all four of the applications, A372, A375, A378 and A379 due to the lack of long term independent testing.
- Considers that the safety of GE foods cannot be guaranteed.

20. Paul Elwell-Sutton (NZ)

- Opposes application A372, because of a lack of confidence in the independence of the laboratories that generated the assessment data.
- Expresses concerns about the possible presence of novel substances or proteins in the canola meal that may enter the food supply.
- Considers that the labelling provisions are not adequate to ensure that consumers will be able to know about GE foods in products.
- Considers that ANZFA has not addressed the issue of the possible transfer of antibiotic resistance marker genes to gut microorganisms of stock, as animals are fed on canola meal and stubble.
- ANZFA's reports do not address the precautionary principle.
- Considers that GE food could have effects on the ageing process in animals, including humans, which ANZFA failed to consider in the assessment.
- Expresses concern that food approval will lead to planting of GE canola in New Zealand that will then lead to inevitable contamination of other crops.
- ANZFA has not adequately considered consumers in the assessment process.
- Opposes the remaining GM applications A375, A378 and A379 for the same reasons.

21. Julian Yates (NZ)

- Opposes all four of the applications, A372, A375, A378 and A379 due to the lack of long term independent testing.

22. Oraina Jones (NZ)

- Opposes all four of the applications, A372, A375, A378 and A379 due to philosophical and ethical concerns relating to the environment and health.

23. Leila Huebner (NZ)

- Opposes application A372, because of concerns about the use of the *barnase* gene both from an environmental perspective (effect on neighbouring canola crops) and from a human and animal health perspective (barnase toxicity to cells).

24 Queensland Sugar

- Submit that the scientific evidence presented in the draft assessment report demonstrates that the introduced gene in GTSB77 does not increase public health or safety risks.
- Produced evidence demonstrating the degradation of cellular DNA during the standard purification steps of the sugar manufacturing process from conventional and transgenic beets.

ATTACHMENT 6

GENERAL ISSUES RAISED IN PUBLIC SUBMISSIONS

The majority of submissions received in response to the section 14 Gazette Notice, express general views against the use of gene technology and assert that food produced using this technology is unsafe for human consumption. A number of general issues were raised in these submissions that are addressed below.

1. *The safety of genetically modified foods for human consumption*

A majority of submitters raised the issue of public health and safety in relation to food produced using gene technology. In particular, it was stated that there has been inadequate testing of genetically modified foods, that there is limited knowledge concerning the risks associated with the technology and that there may be potential long–term risks associated with the consumption of such foods.

- *Evaluation*

It is a reasonable expectation of the community that foods offered for sale are safe and wholesome. In this context, *safe* means that there is a reasonable certainty of no harm. As with other aspects of human activity, the absolute safety of food consumption cannot be guaranteed. Conventionally produced foods, while having a long history of safe use, are associated with human disease and carry a level of risk which must be balanced against the health benefits of a nutritious and varied diet.

Because the use of gene technology in food production is relatively new, and a long history of safe use of these foods has yet to be established, it is appropriate that a cautious approach is taken to the introduction of these foods onto the market. The purpose of the pre–market assessment of a food produced using gene technology under Standard A18/Standard 1.5.2 is to establish that the new food is at least as safe as the existing food. The comprehensive nature of the scientific safety assessment, undertaken on a case-by-case basis, for each new modification is reflective of this cautious approach.

The safety assessment focuses on the new gene product(s), including intentional and unintentional effects of the genetic modification, its properties including potential allergenicity, toxicity, compositional differences in the food and it's history of use as a food or food product.

Foods produced using gene technology are assessed in part by a comparison with commonly consumed foods that are already regarded as safe. This concept has been adopted by both the World Health Organization (WHO)/Food and Agriculture Organization (FAO) and the Organisation for Economic Cooperation and Development (OECD). ANZFA has developed detailed procedures for the safety assessment of foods produced using gene technology that are constantly under review to ensure that the process reflects both recent scientific and regulatory developments and are consistent with protocols developed internationally.

2. *The need for long-term feeding studies*

A number of submissions were concerned about the lack of long-term toxicity studies on genetically modified foods.

- *Evaluation*

Animal studies are a major element in the safety assessment of many compounds, including pesticides, pharmaceuticals, industrial chemicals and food additives. In most cases, the test substance is well characterised, of known purity and of no nutritional value, and human exposure is generally low. It is therefore relatively straightforward to feed such compounds to laboratory animals at a range of doses (some several orders of magnitude above expected human exposure levels) in order to identify any potential adverse effects. Establishing a dose-response relationship is a pivotal step in toxicological testing. By determining the level of exposure at which no adverse effects occur, a safe level of exposure for humans can be established which includes appropriate safety factors.

By contrast, foods are complex mixtures of compounds characterised by wide variations in composition and nutritional value. Due to their bulk, they can usually be fed to animals only at low multiples of the amounts that might be present in the human diet. Therefore, in most cases, it is not possible to conduct dose-response experiments for foods in the same way that these experiments are conducted for chemicals. In addition, a key factor to be considered in conducting animal feeding studies is the need to maintain the nutritional value and balance of the diet. A diet that consists entirely of a single food is poorly balanced and will compromise the interpretation of the study, since the effects observed will confound and usually override any other small adverse effect which may be related to a component or components of the food being tested. Identifying any potentially adverse effects and relating these to an individual component or characteristic of a food can, therefore, be extremely difficult. Another consideration in determining the need for animal studies is whether it is appropriate from an ethical standpoint to subject experimental animals to such a study if it is unlikely to produce meaningful information.

If there is a need to examine the safety of a newly expressed protein in a genetically modified food, it is more appropriate to examine the safety of this protein alone in an animal study rather than when it is part of a whole food. For newly expressed proteins in genetically modified foods, the acute toxicity is normally examined in experimental animals. In some cases, studies up to 14 days have also been performed. These can provide additional reassurance that the proteins will have no adverse effects in humans when consumed as part of a food.

While animal experiments using a single new protein can provide more meaningful information than experiments on the whole food, additional reassurance regarding the safety of newly expressed protein can be obtained by examining the digestibility of the new protein in laboratory conducted *in vitro* assays using conditions which simulate the human gastric system.

3. *Substantial equivalence*

A number of submitters express concern regarding the use of the concept of substantial equivalence as part of the assessment process. Some reject the premise of substantial equivalence on the grounds that differences at the DNA level make foods substantially different.

- *Evaluation*

Substantial equivalence embodies the concept that, as part of the safety assessment of a genetically modified food, a comparison can be made in relation to the characteristics and properties between the new food and traditionally produced food. This can include physical characteristics and compositional factors, as well as an examination of the levels of naturally occurring allergens, toxins and anti-nutrients.

This allows the safety assessment to focus on any significant differences between the genetically modified food and its conventionally produced counterpart. Genotypic differences (i.e. differences at the DNA level) are not normally considered in a determination of substantial equivalence, if that difference does not significantly change the characteristics for composition of the new food relative to the conventional food. This is partly because differences at the DNA level occur with every breeding event and often arise also as a result of certain environmental factors.

The concept of substantial equivalence allows for an evaluation of the important constituents of a new food in a systematic manner while recognizing that there is general acceptance that normally consumed food produced by conventional methods is regarded by the community as safe. It is important to note that, although a genetically modified food may be found to be different in composition to the traditional food, this in itself does not necessarily mean that the food is unsafe or nutritionally inadequate. Each food needs to be evaluated on an individual basis with regard to the significance of any changes in relation to its composition or to its properties.

The concept of *substantial equivalence* was first espoused by a 1991 Joint Consultation of the Food and Agricultural Organisation (FAO) and the World Health Organisation (WHO) where it was noted that the '*comparison of a final product with one having an acceptable standard of safety provides an important element of safety assessment*'. Since this time, the concept has been integrated into safety assessment procedures used by regulatory authorities worldwide. It has thus been in use for approximately ten years and has been an integral part of the safety assessment of some 40 products.

Although the concept of *substantial equivalence* has attracted criticism, it remains as the most appropriate mechanism for assessing the nutritional and food safety implications of foods produced using gene technology. It is generally agreed also that continual review of the concept, in response to the criticism, provides a useful stimulus to ensure that safety assessment procedures are kept at the forefront of scientific knowledge (Nick Tomlinson, Food Standards Agency, United Kingdom: Joint FAO/WHO Expert Consultation on Foods Derived from Biotechnology, Geneva, 2000).

4. *The nutritional value of food produced using gene technology*

A small number of submitters express concern that the genetic alteration of food decreases its nutritional value.

- *Evaluation*

The assessment of food produced using gene technology by ANZFA entails an exhaustive evaluation of analytical data on any intentional or unintentional compositional changes to the food. This assessment encompasses the major constituents of the food (fat, protein, carbohydrate, fibre, ash and moisture) as well as the key nutrients (amino acids, vitamins, fatty acids). There is no evidence to suggest that genetic modification *per se* reduces the nutritional value of food.

In the future, genetic modification may be used intentionally to improve the nutritional value of food. In this regard, GM foods may be able to assist in addressing the general nutritional needs of the community and also specific dietary needs of sub-populations.

5. *Potential toxins and allergens*

Some submitters express concerns about the risks of the introduction of new toxins or allergens.

- *Evaluation*

This issue is considered in detail as part of the safety assessment conducted on each new genetic modification applied to a food or commodity crop. New toxins or allergens may be introduced into food by either gene technology or by traditional breeding techniques, or by altered production processes. It is also possible to use these techniques to develop foods specifically where such compounds are significantly reduced or eliminated. One advantage of gene technology, in comparison with these other methods, is that any transferred genes are well characterised and defined, thus the possibility of developing a food with a new toxic or allergenic compound is likely to be reduced.

6. *Antibiotic resistance*

Some submitters raise concerns about an increase in antibiotic resistance resulting from the use of gene technology. Some consider that it would be reassuring if independent biomedical advice were available to inform the public that the use of antibiotic resistance markers does not pose a risk to the future use of antibiotics in the management of human disease.

- *Evaluation*

The human health considerations in relation to the potential for the development of antibiotic resistance depend on the nature of the novel genes and must be assessed on a case-by case basis. This issue arises because of the use of antibiotic resistance marker genes in the generation of genetically modified plants. In some circumstances, antibiotic resistance genes are linked to the gene of interest, to enable the initial selection of the engineered cells in the laboratory.

Those cells that contain the antibiotic resistance marker gene, and hence the gene of interest, will be able to grow in the presence of the antibiotic. Those cells that failed the transformation process are eliminated during the selection procedure.

Concern has arisen that ingestion of food containing copies of antibiotic resistance genes could facilitate the transfer of the gene to bacteria inhabiting the gut of animals and humans. It is argued that these genes may then be transferred to disease causing bacteria and that this would compromise the therapeutic use of these antibiotics.

In 1993, the World Health Organisation Food Safety Unit considered this issue at a Workshop on the health aspects of marker genes in genetically modified plants. It was concluded at that Workshop that the potential for such gene transfers is effectively zero, given the complexity of the steps required. Since this time, several separate expert panels (Report to the Nordic Council, Copenhagen 1996; Advisory Committee on Novel Foods and Processes, UK 1994, 1996; The Royal Society, UK 1998) and numerous scientific papers published in peer reviewed journals have also considered the available evidence on this issue. It is generally agreed that the presence and subsequent transfer of an intact functional gene from transgenic food to micro-organisms in the human intestine is an extremely unlikely event. Furthermore, if this were to occur, bacteria would not normally retain the resistance genes unless there was an environment for positive selection. The majority of these genes provide for resistance to antibiotics whose use is confined to the laboratory and are not considered to be of major therapeutic use in humans.

Antibiotic resistant bacteria are naturally occurring, ubiquitous and normally inhabit the gut of animals and humans. There is a general consensus that the transfer of antibiotic resistance genes is much more likely to arise from this source and from associated medical practices, rather than from ingested genetically modified food. Even so, at the recent OECD Conference (GM Food Safety: Facts, Uncertainties, and Assessment) held in Edinburgh on 28 February – 1 March 2000, there was general consensus that the continued use of antibiotic marker genes in GM food crops is unnecessary given the existence of adequate alternatives, and should be phased out.

7. Transfer of novel genes

Some submitters have expressed concern that the transfer of any novel gene may be a health concern.

- *Evaluation*

It is extremely unlikely that novel genetic material will transfer from GM foods to bacteria in the human digestive tract because of the number of complex and unlikely steps that would need to take place consecutively. It is equally unlikely that novel genetic material will transfer from GM foods to human cells via the digestive tract. In considering the potential impact on human health, it is important to note that humans have always consumed large amounts of DNA as a normal component of food and there is no evidence that this consumption has had any adverse effect on human health. Furthermore, current scientific knowledge has not revealed any DNA sequences from ingested foods that have been incorporated into human DNA.

Novel DNA sequences in GM foods comprise only a minute fraction of the total DNA in the food (generally less than 0.01%) and are therefore unlikely to pose any special additional risks compared with the large amount of DNA naturally present in all foods.

8. *Viral recombination*

Some submitters express concern about the long-term effects of transferring viral sequences to plants.

- *Evaluation*

This is an issue that is commonly raised because some of the genes that are transferred to plants use a plant virus promoter. Promoters are controlling DNA sequences which act like a switch and enable the transferred genes to be expressed (i.e. to give rise to a protein product) in a plant cell. The routine use of these viral promoters is often confused with research which has shown that plant virus genes, which have been transferred into plants to render them virus–resistant, may recombine with related plant viruses that subsequently infect the plant, creating new viral variants. This research demonstrates that there may be a greater risk to the environment if viral genes are transferred to plants because it may lead to the generation of new plant virus variants capable of infecting a broader range of plants. This is a matter that will be addressed by the Genetic Manipulation Advisory Committee (GMAC) on a case–by–case basis when it assesses such plants.

However, the presence of plant viruses, plant virus genes or plant virus segments in food is not considered to pose any greater risk to human health as plant viruses are ubiquitous in nature and are commonly found in food eaten by animals and humans. Plant viruses are also biologically incapable of naturally infecting human or animal cells.

9. *Labelling of foods produced using gene technology*

A majority of submissions focus on this issue. Specifically, the submissions call for comprehensive labelling of foods produced using gene technology, regardless of whether they are substantially equivalent to conventional foods. The submitters base their demands for full labelling on the presumption that all foods produced using gene technology are unsafe, even where no novel genes are present, and on consumer "right to know" arguments. It is stated that full labelling is the only means of identification of foods produced using gene technology available to consumers.

- *Evaluation*

In response to consumer sentiment on this issue, on 28 July 2000, Health Ministers (from New Zealand, the Commonwealth, States and Territories of Australia) agreed to new labelling rules for genetically modified foods. Amendments to the Standard were subsequently confirmed by the Ministerial Council on 24 November 2000 and finally gazetted on 7 December 2000. The amended Standard A18 (Volume 1) is now also known as Standard 1.5.2 in the *Australia New Zealand Food Standards Code* (Volume 2). To allow adequate time for compliance to the new provisions of the Standard, it will come into effect on 7 December 2001, twelve months after the date of gazettal.

The new Standard requires the labelling of food and food ingredients where novel DNA and/or protein is present in the final food and where the food has altered characteristics.

Exempt from these requirements are:

- highly refined food, where the effect of the refining process is to remove novel genetic material and/or protein;
- processing aids and food additives, except where novel genetic material and/or protein is present in the final food;
- flavours which are present in a concentration less than or equal to 0.1 per cent in the final food; and
- food prepared at point of sale (e.g. restaurants, takeaway food outlets).

In addition, the new Standard allows for a maximum of 1 per cent of unintended presence of genetically modified product, as ascertained by laboratory testing, before labelling would be required. The comprehensive provisions of the new Standard represent the culmination of extensive consultation between Government, consumers and the food industry to ensure practical and relevant information is available to all in relation to the sale of genetically modified foods.

A User Guide has been prepared by the Authority under direction of the Ministerial Council, to assist with compliance with the amended labelling provisions of the Standard. A copy of the guide is available on the ANZFA website (www.anzfa.gov.au).

10. The need for post marketing surveillance of genetically modified foods

A number of submitters have commented on the need for post-market surveillance of genetically modified food consumption.

- *Evaluation*

Surveillance of potential adverse or beneficial effects of GM foods is seen by many as a logical follow-up to the initial scientific risk assessment. Nevertheless, it is recognised that there are limitations to the application of epidemiology studies, particularly in relation to food components. A key requirement for post-market surveillance systems is that a clear hypothesis be identified for testing. Establishing a system for the surveillance of potential health effects of exposure to novel foods requires monitoring of the consumption patterns of novel foods in the population, and health effects in both “exposed” and “non-exposed” individuals/populations, so that risk estimates can be derived. For any such monitoring system to be useful, there needs to be a range of exposures, otherwise, any variation in health outcome would be unexplainable by that exposure. Variations in exposure could be apparent over time (temporal trends), space (geographical trends) or both.

Availability of robust data on consumption of the foods in question is vital in order to establish a surveillance system. The other side of the equation is the need for access to data on population health outcomes. Such a system could also be used to identify potential positive health outcomes, such as improved nutritional status or lower cholesterol levels. The availability of linked basic data (e.g. date of birth, sex, geographical location), and the ability to correlate with demographic data, could potentially offer the means of establishing links with food consumption.

The possibility of setting up a post-market health surveillance system for novel foods, including GM foods, has been examined by the UK's Advisory Committee on Novel Foods and Processes (ACNFP). Recognising the many difficulties involved in developing such a system, an initial feasibility study to look at the available data and its usefulness has been proposed. Work is currently being commissioned; when completed in 18 months, it will be subject to peer review. If such a feasibility study suggests that post-market surveillance is practical, methods and details concerning data collection will be determined in the UK, but common strategies might be able to be harmonised internationally in order to minimise the use of resources while maximising the reliability of the final results. This is an area that ANZFA will be monitoring closely, along with international regulatory bodies such as the OECD Taskforce for the Safety of Novel Foods and Feeds.

11. *Public consultation and information about gene technology*

A number of submitters were concerned that the public has not been properly consulted or informed by government or ANZFA on the introduction of foods produced using gene technology. Some submitters urged to undertake wider consultation with all affected parties including growers, the food industry and consumers before these food commodities are introduced, and to ensure that adequate consultation is undertaken as part of its assessment process.

- *Evaluation*

The issue of gene technology and its use in food has been under consideration in Australia since 1992. The Agreement between the Governments of Australia and New Zealand for a joint food standard setting system, however, did not occur until 1995, and the New Zealand community therefore had not been consulted on this matter by the Authority until after that time. Consequently, the proposed standard (the current Standard A18) underwent only one round of public comment in New Zealand at which time significant objections were raised by the New Zealand community to the use of gene technology in food production. Many New Zealand consumers, both in these submissions, and in previous submissions to the Authority, have expressed the view that there has been insufficient consultation and a consistent lack of information about gene technology.

Although Standard A18 came into force in May 1999, the public have a continuous and ongoing opportunity to provide comment in relation to applications under the standard. ANZFA's statutory process for all applications to amend the *Food Standards Code* normally involves two rounds of public comment. Furthermore, all the documentation (except for commercial in confidence information) relating to these applications is available in the public domain, including the safety assessment reports. There is ample evidence that the provision of such information by ANZFA has already significantly stimulated public debate on this matter.

In addition, other government departments including the Environmental Risk Management Authority (ERMA) are potential sources of information about gene technology available to consumers in New Zealand. ERMA is a statutory authority set up by the New Zealand Government to administer the *Hazardous Substances and New Organisms (HSNO) Act 1996*, and has responsibility for assessing the risks to the environment from genetically modified organisms. This body has been assessing applications for the approval of genetically modified organisms since July 1998 and this has involved a number of public meetings.

In response to the concerns raised in public submissions with regard to gene technology and GM foods, ANZFA has prepared a public discussion paper on the safety assessment process for GM foods[5], available at no charge on request. Since completion, this document has been widely distributed and may assist in addressing some of the concerns raised by the public. Other government and industry bodies are also addressing the broader concerns in relation to gene technology.

12. *Maori beliefs and values*

Some New Zealand submitters stated that Maori people find genetic engineering in conflict with their beliefs and values and that, out of respect to Maori, no genetically modified foods should be allowed into New Zealand until a wider discussion, both within Maori and non–Maori, is held.

- *Evaluation*

This issue was also raised during consideration of the proposal for the establishment of Standard A18. At that time, it was stated that the likely implications for Maori regarding genetically modified organisms surround the issues of the rights of Maori to the genetic material from flora and fauna indigenous to New Zealand and the release into the environment of genetically modified organisms. The *HSNO Act 1996* requires that these matters be considered by ERMA.

13. *Environmental concerns and the broader regulatory framework*

A number of submitters have raised concerns that genetically modified crops may pose a risk to the environment.

- *Evaluation*

These issues are considered as part of the comprehensive assessment processes of the Office of the Gene Technology Regulator (OGTR) in Australia, and the Environmental Risk Management Authority (ERMA) in New Zealand. Since June 2001, OGTR regulates all GMOs and any 'gap' products (i.e. products for which no other regulator has responsibility).

The Australia New Zealand Food Authority (ANZFA) does not have the mandate to assess matters relating to environmental risks resulting from the release of foods produced using gene technology into the environment. However, links exist between ANZFA and these other regulatory agencies in both Australia and New Zealand, and a large degree of information sharing occurs.

In Australia, the current regulatory system includes a number of other agencies with a legal remit to cover some aspects of GM products (such as imports, food, agricultural and veterinary chemicals):

- the Australia New Zealand Food Authority (ANZFA)
- the Therapeutic Goods Administration (TGA)

[5] Gm foods and the consumer – ANZFA Occasional Paper Series No.1, Australia New Zealand Food Authority, June 2000.

- the National Registration Authority for Agricultural and Veterinary Chemicals (NRA)
- the National Industrial Chemicals Notification and Assessment Scheme (NICNAS)
- the Australian Quarantine and Inspection Service (AQIS).

All GM foods continue to be assessed and regulated by ANZFA under the direction of Commonwealth, State and Territories Health Ministers and the New Zealand Health Minister, sitting as the Australia New Zealand Food Standards Council (ANZFSC). However, an interface between ANZFA and OGTR has been established through amendments to the ANZFA Act arising from the Gene Technology Bill 2000. These amendments to the ANZFA Act require the Authority to advise OGTR of recommendations to ANZFSC regarding the standard for foods produced using gene technology (Standard A18/1.5.2).

Similarly, in New Zealand various other government departments and agencies play their role in the regulatory process:

- the Ministry of Agriculture and Fisheries (MAF)
- the Ministry of Health (MoH)
- the Ministry of Research, Science and Technology (MoRST)

14. Maximum residue levels of agriculture/veterinary chemicals

A number of submitters have raised concerns that residues of agricultural and veterinary chemicals in genetically modified (e.g. herbicide tolerant) crops may pose a health risk.

- *Response*

Residues of these chemicals can only legally be present if the chemical has been registered for use in Australia and/or New Zealand, and it has been demonstrated that the residue at specified levels does not lead to adverse health impacts. The concentration of a chemical residue that may be present in a food is regulated through maximum residue limits (MRLs). The MRL is the highest residue concentration that is legally permitted in the food. Food products have to meet the MRL, whether or not they are derived from genetically modified organisms. The MRL does not indicate the chemical residue level that is always present in a food, but it does indicate the highest residue level that could result from the registered conditions of use.

It is important to note that MRLs are not direct public health and safety limits but rather, are primarily indicators of appropriate chemical usage. MRLs are always set at levels lower than, and normally very much lower than, the health and safety limits. The MRL is determined following a comprehensive evaluation of scientific studies on chemistry, metabolism, analytical methods and residue levels. In Australia, the National Registration Authority (NRA) applies to ANZFA to amend the MRLs in the Food Standards Code and the application is considered by ANZFA through its legislated decision making processes. In New Zealand MRLs are set by the Ministry of Health, generally following a request from, and in collaboration with, the Ministry of Agriculture and Forestry. Only following demonstration that the use of agricultural and veterinary chemicals will not result in unsafe residues will the MRL enter into food law, through its inclusion in either the Food Standards Code in Australia, or the New Zealand Mandatory Food Standard 1999 (Maximum Residue Limits of Agricultural Compounds).

ATTACHMENT 7

STATEMENT OF REASONS

APPLICATION A378 - FOR RECOMMENDING A VARIATION TO STANDARDS A18 AND 1.5.2 - FOOD PRODUCED USING GENE TECHNOLOGY OF THE *FOOD STANDARDS CODE* FOR THE APPROVAL OF FOOD DERIVED FROM GLYPHOSATE-TOLERANT SUGARBEET LINE 77

The Australia New Zealand Food Authority (ANZFA) has before it an Application received on 30 April 1999 from Aventis CropScience Pty Ltd and the Stoneville Pedigreed Seed Company to amend Standard A18 (Volume 1) and Standard 1.5.2 (Volume 2) of the *Food Standards Code* for the approval of food derived from glyphosate-tolerant sugarbeet line 77.

ANZFA recommends the adoption of the draft variation for the following reasons:

There are no public health and safety concerns associated with the gene introduced into food derived from glyphosate-tolerant sugarbeet line 77.

Food derived from glyphosate-tolerant sugarbeet line 77 is equivalent to that from other commercially available sugarbeet in terms of safety and nutritional adequacy.

On 7 December 2001, food products containing food derived from glyphosate-tolerant sugarbeet will require labelling if it can be shown that novel DNA and/or protein is present in the final food.

The proposed amendment to the *Food Standards Code* is consistent with the section 10 objectives of the *Australia New Zealand Food Authority Act 1991* and the regulatory impact assessment.

The commencement date of the draft variation be the date of gazettal.

REGULATION IMPACT

ANZFA has undertaken a regulation impact assessment process, which also fulfils the requirement in New Zealand for an assessment of compliance costs. This process concluded that the amendment to the Code is necessary, cost effective and of benefit to both producers and consumers.

WORLD TRADE ORGANIZATION (WTO) NOTIFICATION

Australia and New Zealand are members of the WTO and are bound as parties to WTO agreements. In Australia, an agreement developed by the Council of Australian Governments (COAG) requires States and Territories to be bound as parties to those WTO agreements to which the Commonwealth is a signatory. Under the agreement between the Governments of Australia and New Zealand on Uniform Food Standards, ANZFA is required to ensure that food standards are consistent with the obligations of both countries as members of the WTO.

In certain circumstances Australia and New Zealand have an obligation to notify the WTO of changes to food standards to enable other member countries of the WTO to make comment. Notification is required in the case of any new or changed standards which may have a significant trade effect and which depart from the relevant international standard (or where no international standard exists).

This matter was notified to the WTO because there is significant international interest in the safety of GM foods and the proposed amendments are considered to raise potential Technical Barrier to Trade or Sanitary/Phytosanitary matters.