05/02
10 October 2001

FINAL ASSESSMENT REPORT
(Inquiry - Section 17)

APPLICATION A375

FOOD DERIVED FROM GLUFOSINATE AMMONIUM-TOLERANT CORN LINE T25

TABLE OF CONTENTS

EXECUTIVE SUMMARY

BACKGROUND

ANZFA received an Application from Aventis on 27 April 1999 to amend the Australian *Food Standards Code* to include food produced from glufosinate ammonium tolerant corn line T25. The modified corn under consideration is known commercially as Liberty Link® corn and is tolerant to applications of the herbicide glufosinate ammonium. Corn line T25 is not commercially grown in Australia or New Zealand.

ISSUES ADDRESSED DURING ASSESSMENT

(i) Safety Evaluation

Food from glufosinate ammonium tolerant corn line T25 corn has been evaluated according to the safety assessment guidelines prepared by ANZFA. The assessment considered the following issues: i) the nature of the genetic modification; ii) general safety issues such as novel protein expression and the potential for transfer of antibiotic resistance genes to micro-organisms in the human digestive tract; iii) toxicological issues; and iv) nutritional issues.

On the basis of the data submitted in the present application, it is concluded that food derived from glufosinate ammonium tolerant corn line T25 is as safe and wholesome as food from other commercially available corn varieties. A detailed food safety report on these foods has been prepared.

(ii) Labelling information for consumers

Under the current Standard A18, which remains in effect until 7 December 2001, food derived from glufosinate ammonium tolerant corn line T25 does not require labelling as it is regarded as substantially equivalent to food derived from non-genetically modified corn varieties.

When the amended Standard comes into effect on 7 December 2001, food products made from glufosinate ammonium tolerant corn line T25 will require labelling if it can be shown that novel DNA and/or protein is present in the final food.

(iii) Public Submissions

ANZFA undertook two rounds of public consultation in relation to this application and a total of 56 submissions were received overall – 45submissions in the first round and 16 in the second round. The majority of these submissions were not supportive, as most submitters perceive GM food to be unsafe. The food safety concerns raised in submissions have been addressed by the safety assessment report.

CONCLUSIONS

On the basis of the data submitted with the application and evidence obtained from the scientific literature, it is concluded that:

- the introduced gene in glufosinate ammonium tolerant corn line T25 is not considered to produce any increased public health and safety risk;
- food derived from glufosinate ammonium tolerant corn line T25 are as safe and wholesome as that produced from other commercial varieties of corn.
- on 7 December 2001, food or food ingredients derived from glufosinate ammonium tolerant corn line T25 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.

1. BACKGROUND TO THE APPLICATION

A genetically modified corn plant that is tolerant to applications of the herbicide glufosinate ammonium has been developed. This corn line (T25) now contains the *pat* gene which encodes an enzyme that permits detoxification of the broad-spectrum herbicide phosphinothricin, the active ingredient of glufosinate ammonium. It is known commercially as Liberty Link® corn. A second non-functional gene was also transferred to corn line T25. A truncated form of the *bla* gene is present in corn line T25 and has had the 3' end of the gene removed thereby rendering it non-functional in the plant.

Glufosinate ammonium-tolerant corn line T25 is not currently grown in either New Zealand or Australia. However, domestic production of corn-derived food products in both countries is supplemented by a small amount of imported corn-based products, including high-fructose corn syrup, which is not currently manufactured in either Australia or New Zealand. Corn ingredients include flour, syrup, oil, starch, meal or whole kernels and cobs. Corn-based processed products include snap frozen vegetable packs, corn chips, corn oil, breads, flours, popcorn, pastries, crackers, meat substitutes, milk substitutes and confectionary. There are also many industrial uses of corn products.

The main benefits of glufosinate ammonium tolerant corn line T25 are agronomic in nature, and are therefore likely to accrue mainly to the primary producer. It is envisaged that production of these crops 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

ANZFA completed an Initial Assessment (formerly referred to as the Preliminary Assessment Report) upon receipt of the application and called for public comment on 3 November 1999. A total of 45 submissions were subsequently received. Attachment 5 contains a summary of the submissions.

ANZFA conducted an assessment of the application, including a safety evaluation of the food, taking into account comments received. A Draft Assessment Report (formerly termed a Full Assessment Report) was released for public comment on 7 March 2001. ANZFA received a further 23 submissions. The assessment of the application has now taken into account the public comments from the second round of consultation. This document is the Final Assessment Report, containing ANZFA's recommendation.

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 these foods, the proposed amendments are considered to raise potential Technical Barrier to Trade and Sanitary/Phytosanitary matters and were therefore notified to the WTO under both agreements.

4. ISSUES ADDRESSED DURING ASSESSMENT

4.1. Safety assessment

Glufosinate ammonium tolerant corn line T25 has been evaluated according to safety assessment guidelines prepared by ANZFA[1]. The assessment involved an extensive analysis of 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 glufosinate ammonium tolerant corn line T25 does not raise any public health and safety concerns and is as safe and wholesome as other commercially available corn varieties. The full safety assessment report can be found at Attachment 2.

4.2. Labelling of food produced from glufosinate ammonium tolerant corn line T25

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 derived from glufosinate ammonium-tolerant corn line T25 does not require labelling as it is regarded as substantially equivalent to food derived from non-genetically modified corn varieties.

4.3. Issues arising from public submissions

General issues

The majority of submissions received in both rounds of consultation 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 general issues can be found at 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 (2001) Information for Applicants. Amending A18/1.5.2 – 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.

6. *Compositional studies*

The PHAA commented that some of the components of the genetically modified plant line under assessment were statistically different to the control line and that therefore the GM line is not comparable to the control line.

Response

Statistical differences observed in the compositional analyses were assessed by ANZFA in terms of their relevance in a biological system. In order to determine if the differences have biological significance, ANZFA compares these values to published ranges for each component. Many of the significant differences observed have been small differences, they are usually within the range that would be expected for other commercially available varieties and they do not indicate a trend, as they do not occur consistently. Additionally, many of the differences can be explained by differences between locations or seasons. Therefore ANZFA reached the conclusion that the line was comparable to other commercially available lines.

The use of published ranges and historical control data in safety assessment studies is standard procedure in the interpretation of biological and analytical components of variation. Although the most appropriate control group for interpretative purposes is always the concurrent control, there are instances in which the use of historical control information can aid an investigator in the overall evaluation of safety data. Studies (Carokostas and Banerjee (1990): Interpreting rodent clinical laboratory data in safety assessment studies: biological and analytical components of variation, Fundamental and Applied Toxicology.) suggest that statistically significant laboratory findings that are not biologically or toxicologically important will be present in many safety assessment studies with a standard design. Overreliance on the result of standard prepackaged statistical analyses for determining the presence of toxicologically significant findings can lead to misinterpretation of laboratory data. It is well recognized that sound judgement must be applied to laboratory findings using appropriate statistical analyses as a tool for pattern recognition.

Specific issues

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

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

(i) Toxicity of glufosinate ammonium breakdown products

The South Australia Public and Environmental Health Service raised the point that the ANZFA safety assessment should address the issue of whether residues of the herbicide degradation process are present, toxic and/or subject to an MRL. The Consumers' Association of South Australia Inc. & National Council of Women of Australia raised similar concerns.

Response

There is currently no MRL for either glufosinate ammonium or its metabolites in corn in Australia. Therefore, no glufosinate ammonium residues (or metabolites) are permitted on any foods in Australia. New Zealand also does not have an MRL for glufosinate ammonium, however a level of 0.1 ppm is allowed under default clause 6b of the regulation 257 (2A). A Codex MRL of 0.1 ppm also exists. There is no evidence to suggest that the metabolites MPP and MPA are any more toxic than glufosinate, and sub-chronic and developmental studies in the US concluded that they were of similar or lower toxicity compared to the parent compound.[2] The chemical is permitted for use on glufosinate ammonium tolerant corn line T25 corn in the USA and the US regulatory assessment concluded that a single tolerance limit of 0.2 ppm was suitable for field corn. The consumption of food produced from corn line T25 is therefore not considered to pose a risk to human health.

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

(i) New data

Aventis CropScience submitted an additional data package containing DNA sequence data of the insert and flanking plant regions.

Response

The new data provided by Aventis CropScience confirms previous data regarding the nature of the inserted DNA (size, orientation of genes, number of copies) that was transferred to the plant. It enables a close examination of the border regions and supports the previous data that indicated that there would be no unexpected gene products. The safety assessment report has been amended to incorporate the additional data. This new information is provides further support for ANZFA's previous assessment and thus the conclusions of the safety assessment remain the same.

(ii) Enzyme specificity of the PAT protein

The Public Health Association of Australia and the National Council of Women of Australia raised concerns about the enzyme specificity of the PAT protein and the potential for it to acetylate or deacetylate other proteins in human and farm animals.

[2] US Federal Register, Volume 65 (98), May 19 2000.

Response

The PAT enzyme is highly specific for its substrate, phosphinothricin – the active ingredient in glufosinate ammonium (Wehrmann et al, 1996). The PAT enzyme whether encoded by the *pat* or *bar* gene is highly specific for phosphinothricin and does not acetylate other L-amino acids, nor does it acetylate the D-isomer of phosphinothricin.

The high specificity of the PAT enzyme for L-phosphinothricin is widely accepted and has been detailed in a consensus document by the OECD (*Consensus Document on General Information Concerning the Genes and their Enzymes that Confer Tolerance to Phosphinothricin Herbicide, OECD 1999*).

(iii) Acute oral toxicity study of the PAT protein

The Public Health Association of Australia were concerned that measurements other than gross pathology had not been done on animals subjected to acute oral toxicity testing of the PAT protein. The National Council of Women noted that "gross pathology" is not explained.

Response

ANZFA requires that, as with all methods of analysis, acute oral toxicity studies are conducted according to international guidelines. The studies supplied by the applicant have been consistent with such guidelines and have reported appropriately as detailed below.

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 guidelines require that animals should be carefully examined at least once a day for a minimum of 14 days. Animals that die during the test are necropsied as are those animals that survived and have been sacrificed at the end of the test. The recommended cageside observations should include changes in the skin and fur, eyes and mucous membranes and also respiratory, circulatory, autonomic and central nervous system and somatomotor activity and behaviour pattern. The guidelines advise that particular attention should be directed to observation of tremors, convulsions, salivation, diarrhoea, lethargy, sleep and coma. Time of death should be recorded as precisely as possible. Individual weights of animals should be determined shortly before the test substance is administered, weekly thereafter and at death; changes in weight should be calculated and recorded when survival exceeds one day.

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. Microscopic examination of organs showing evidence of gross pathology in animals surviving 24 or more hours should also be considered because it may yield useful information.

(iv) Compositional studies

The Public Health Association of Australia and the National Council of Women of Australia commented that some of the components of the genetically modified corn were statistically different to the control corn line and that therefore the GM line is not comparable to the control corn line.

Response

Statistical differences observed in the compositional analyses were assessed by ANZFA in terms of their relevance in a biological system. In order to determine if the differences have biological significance, ANZFA compares these values to published ranges for each component. Many of the significant differences observed have been small differences, they are usually within the range that would be expected for other corn varieties and they do not indicate a trend, as they do not occur consistently. Additionally, many of the differences can be explained by differences between locations or seasons. Therefore ANZFA reached the conclusion that the corn line was comparable to other commercially available corn lines.

(v) Compositional data for sprayed GM corn

The Public Health Association of Australia commented that data for the genetically modified corn line that had been sprayed with herbicide was not given in the safety assessment report.

Response

This data was presented in the Draft Risk Analysis Report and can be found in Table 6.

(vi) Animal feeding studies

The Public Health Association of Australia commented that the feeding study of whole corn fed to chickens provides information more about the ability of chickens to grow on such feed as opposed to providing information about the risk to human health.

Response

The PHAA is correct in that these studies are designed to show that the chickens fed corn line T25 grow and develop as they would if fed other unmodified commercial varieties of corn. These types of experiments are not designed to directly assess risk to human health but are presented as additional support of the wholesomeness of the test corn line.

(vii) Hybrid analysis of corn line T25

The Food Branch within the South Australian Department of Human Services commented that the compositional analyses have been done on hybrids of line T25 and not line T25 itself.

Response

Commercial corn breeding involves the continuous development of hybrid lines. For example, pure lines (i.e. inbred lines known to have specific traits) are crossed with other lines known to contain other desirable traits. After a series of crosses, the result is the development of a line that has both the vigour associated with a hybrid as well as the desired trait/s.

More than 90% of current corn acreage in the United States is now hybrid corn. The number of hybrid combinations that can be made from a small number of inbred lines and their subsequent crossings (i.e. both single crosses and double crosses) is enormous.

The drafting for corn line T25 reflects traditional breeding practices that require the continuous production of hybrid lines and therefore refers to the original transformant. Subsequent inbred lines and hybrids derived from that line through traditional breeding are therefore approved in this process, as they are not new modifications but crosses with the genetically modified line.

(vii) Vitamin analysis of corn line T25

The Food Branch within the South Australian Department of Human Services noted that vitamin analyses were not done on corn line T25.

Response

Processed corn products are not substantial sources of vitamins in the diet as compared to fresh fruit and vegetables. Most of the corn derived from corn line T25 enter the food chain after processing and are thus not going to be significant sources of vitamin A or carotene in the diet. Additionally, as the consumption of fresh corn in Australia and New Zealand is not as great as other vegetables, an analysis of vitamin A and carotene was not considered essential the assessment of this application.

4. Risk Management

Under Standard A18 (Standard 1.5.2 in the Australia New Zealand Food Standards Code), a GM food must undergo a safety assessment in accordance with ANZFA's safety assessment guidelines.

On the basis of the conclusions from the safety assessment report, together with a consideration of the public submissions, it is proposed that the Table to clause 2 of Standard A18 be amended to include food from glufosinate ammonium tolerant corn line T25. The proposed amendment is provided in Attachment 1.

A public discussion paper on the safety assessment process for GM food[3] 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.

5. Regulatory Impact Assessment

The benefits and costs associated with the proposed amendment to Standard A18 to approve food from glufosinate ammonium tolerant corn line T25 have been analysed in a draft Regulatory Impact Statement (Attachment 3). The benefits of the proposed Standard A18 amendment primarily accrue to the food industry and government, with potentially a small benefit to the consumer.

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

CONCLUSIONS

ANZFA has conducted a comprehensive assessment of the application according to its *Guidelines for the safety assessment of foods to be included in Standard A18 – food produced using gene technology*. These guidelines are based on internationally accepted principles for establishing the safety of foods derived from genetically modified organisms.

It is concluded that:

- the introduced gene in glufosinate ammonium tolerant corn line T25 is not considered to produce any increased public health and safety risk;
- on the basis of the data provided in the application, food derived from glufosinate ammonium tolerant corn line T25 is equivalent to food derived from other commercial varieties of corn in terms of its safety and nutritional adequacy.

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 the Australian *Food Standards Code*
2. Safety assessment report
3. Regulatory impact assessment
4. World Trade Organization Agreements
5. Summary of public comments
6. General issues raised in public comments

ATTACHMENT 1

DRAFT VARIATION TO THE *FOOD STANDARDS CODE*

APPLICATION A375

FOOD DERIVED FROM GLUFOSINATE AMMONIUM TOLERANT CORN LINE T25

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 glufosinate ammonium-tolerant corn line T25.

ATTACHMENT 2

SAFETY ASSESSMENT REPORT

APPLICATION A375

FOOD DERIVED FROM GLUFOSINATE AMMONIUM-TOLERANT CORN LINE T25

SUMMARY AND CONCLUSIONS

Nature of the genetic modification

Tolerance to the herbicide glufosinate ammonium was conferred to an inbred corn line, B73, through traditional crossing with the tissue culture line He/89 which, had been transformed to contain the *pat* gene. Herbicide-tolerant corn line T25 was developed and is known commercially as Liberty Link corn. The *pat* gene is derived from the bacterium *Streptomyces viridochromogenes* strain Tu494. This gene is responsible for the production of the enzyme phosphinothricin acetyl transferase (PAT), which confers resistance to glufosinate ammonium herbicides by acetylating phosphinothricin, the active moiety of the herbicide.

A truncated ampicillin resistance gene (*bla*) is also present in corn line T25. This gene is non-functional in the plant.

The transferred novel genetic material is stably integrated at a single site and maintained in the corn over multiple generations.

General safety issues

Corn is a staple food for a significant proportion of the world's population. Corn-based products are routinely used in a wide range of foods and have a long history of safe use. Products derived from corn line T25 may include highly processed corn products such as flour, breakfast cereals, high fructose corn syrup and other starch products.

Glufosinate ammonium resistant corn line T25 produces one new protein — PAT. Expression of the PAT enzyme in corn kernels is low, with the highest level detected being in inbred T25 corn lines. In kernels of hybrid T25 corn lines, PAT could not be detected. Thus exposure to the novel protein is expected to be extremely low. Higher levels of the PAT protein were detected in other plant tissues that are not a normal part of the human diet such as leaves, whole plant and silage.

One of the important issues to consider in relation to genetically modified foods is the impact on human health from potential transfer of novel genetic material to cells in the human digestive tract. Much of the concern in this regard is with the presence of antibiotic resistance genes in genetically modified foods. Corn line T25 however, only contains a non-functional truncated copy of the ampicillin resistance (*bla*) gene, therefore the issue of transfer of an antibiotic resistance gene does not need to be addressed in this application. Transfer of the *pat* gene from corn line T25 to human cells via the digestive tract was considered to be unlikely. The amount of novel genetic material in corn line T25 is minute

compared to the total amount of DNA present and is therefore unlikely to pose any special additional risks compared with the large amount of DNA naturally present in all foods.

Toxicological issues

Corn contains no naturally occurring toxins or allergens and has a long history of safe use.

The potential toxicity and allergenicity of the PAT protein has already been assessed by ANZFA in other genetically modified food applications and is not considered likely to cause an allergic or toxic reaction.

In summary, in acute toxicity studies of the PAT protein in mice, there were no signs of toxicity at a dose of approximately 2.6 g/kg bodyweight. The newly expressed protein is also readily degradable in conditions that mimic human digestion and has no similarity with any known allergens. Thus, the evidence does not indicate that there is any potential for the novel protein to be toxic or allergenic. Additionally, the PAT protein is present at very low levels in kernels, therefore dietary exposure to PAT would be extremely low.

Nutritional issues

Detailed compositional analyses were undertaken to establish the nutritional adequacy of corn line T25, and to compare it to non-modified control lines. No consistent differences in corn components or nutrients were observed in genetically modified corn line T25 compared to controls, or in glufosinate ammonium -treated plants compared to untreated controls. Although some statistically significant differences were observed, these were small and did not have any biological significance or raise any safety concerns. All reported values fell within the range cited in the published literature.

An animal feeding study, using chickens was provided as additional supporting data to the application. The results of this study confirm the results of the compositional studies and demonstrate that corn line T25 is able to support typical growth and wellbeing.

Overall, these results demonstrate that corn line T25 is compositionally similar to non-modified corn hybrids, and support the conclusion that unintended secondary effects are unlikely to have occurred as a result of the genetic modification.

Conclusion

No potential public health and safety concerns have been identified in the assessment of glufosinate ammonium tolerant corn line T25. On the basis of the data provided in the present application, herbicide-tolerant corn line T25 is equivalent to other commercially available corn in terms of its safety and nutritional adequacy.

1. BACKGROUND

Aventis Pty. Ltd. have made an application to ANZFA to amend the Australian *Food Standards Code*, to include food derived from corn which has been genetically modified to be tolerant to the herbicide glufosinate ammonium. The corn is marketed as Liberty Link® corn.

Tolerance in T25 corn to the herbicide glufosinate ammonium is achieved through the

expression of the *pat* gene, which produces the phosphinothricin acetyl transferase (PAT) enzyme that chemically modifies the herbicide, thus rendering it inactive. Glufosinate ammonium tolerant corn line T25 can be grown under application of this herbicide.

Maize varieties are generally classified into flint, pop, dent and flour lines based on the hardness of the kernel. Flint varieties are preferred by dry millers for flour, grits and meal based products such as cereals and dent varieties are preferred by wet millers for starch and starch based products such as high fructose corn syrup. Corn oil may be produced from the germ of all varieties. Fermentation of cereal grains is also used for beverage and alcohol production.

A wide variety of food products are derived from the genetically modified corn including highly processed corn-based food ingredients such as high-fructose corn syrup, which is not currently manufactured in either Australia or New Zealand. Corn ingredients include flour, syrup, oil, starch, meal or whole kernels and cobs. Corn-based processed products include snap frozen vegetable packs, corn chips, corn oil, breads, flours, popcorn, pastries, crackers, meat substitutes, milk substitutes, breakfast cereals, and confectionary. There are also many industrial uses of corn products.

Food derived from glufosinate ammonium tolerant corn line T25 are most likely to be imported as processed food products, containing whole, part or constituents of corn and as corn derivatives.

2. DESCRIPTION OF THE GENETIC MODIFICATION

2.1 Methods used in the genetic modification

Corn line T25 was developed from a parental tissue culture line, He/89, which was transformed with a plasmid containing the *pat* gene and the *bla* gene. The *pat* gene confers glufosinate ammonium tolerance and the *bla* gene confers resistance to the antibiotic ampicillin. The *bla* gene has been truncated during transformation and is non-functional in the plant. The transformed plant cells were produced by direct DNA uptake by protoplast cultures with additional DNA. The full details of the method of transformation and the proprietary plasmid used in the transformation have been provided to ANZFA for assessment, however, at the request of the applicant, this information has been accepted as confidential commercial information under the ANZFA Act 1991.

2.2 Function and regulation of the novel genes

The pat *gene*

The *pat* gene is derived from the soil microorganism *Streptomyces viridochromogenes* strain Tu494. It codes for the enzyme phosphinothricin acetyl transferase (PAT), which modifies and inactivates the herbicide glufosinate ammonium. (Strauch *et al*, 1988)

The *pat* gene is often used as a selectable marker to distinguish genetically modified plant cells from unmodified cells. In this application, the *pat* gene has been transferred to corn to confer tolerance to glufosinate ammonium herbicides. The *pat* gene is under the control of the cauliflower mosaic virus (35S CaMV) promoter (Odell *et al*, 1985) and termination signal (Pietrzak *et al*, 1986). The CaMV 35S promoter drives constitutive expression of the *pat*

gene throughout the plant. The bacterial *pat* gene contains a high G:C content that is not typical of plant genes. To optimise expression in plants, a synthetic gene that has a lower G:C content has been transferred to corn and has approximately 70% DNA sequence similarity with the native gene. However, the amino acid sequence of the PAT protein has not been altered (Wohlleben *et al*, 1988; Strauch *et al*, 1988).

The bla *gene*

The *bla* gene is derived from *Escherichia coli* and encodes β-lactamase, which confers resistance to some β-lactam antibiotics, including the moderate-spectrum penicillin, ampicillin.

The *bla* gene is under the control of bacterial regulatory sequences and was used as a selectable marker to distinguish transformed bacterial cells from non-transformed cells. The transformed plant contains a truncated form of the *bla* gene, i.e. it is missing 25% of its 5' sequence. This shortened form of the gene is not functional in the modified corn.

2.3 Characterisation of the novel genes in the plant

Aventis submitted the following study regarding characterisation of the novel genes in corn line T25.

Klonus D (1998). Genomic characterization of maize transformant T25. Performing laboratory: Hoescht Schering Aventis GmbH, Department D-65926, Frankfurt am Main, Federal Republic of Germany. Report No. PSR98/029.

Southern blot experiments of the original T25 transformant and a third generation of back-crossing with line B73, confirmed the presence of the *pat* and *bla* genes in the genetically modified corn line. The transformation process resulted in a single copy of the *pat* and *bla* genes being integrated into T25 corn, as confirmed by full sequenced analysis of the DNA insert. During the transformation of the corn cells, the *bla* gene was disrupted (25% of the gene sequence was truncated) and is consequently not functional in the plant. This is supported by polymerase chain reaction (PCR) analysis and also that no β–lactamase activity was detected by HPLC-radio-monitoring as discussed in Section 3.3.

2.4 Stability of genetic changes

Aventis submitted the following study regarding the stability of genetic changes in T25 corn.

Klonus D (1998). Genomic characterization of maize transformant T25. Performing laboratory: Hoescht Schering Aventis GmbH, Department D-65926, Frankfurt am Main, Federal Republic of Germany. Report No. PSR98/029.

To determine the stability of the transgenic locus over multiple generations, T25 corn backcrossed with the parental line B73 was analysed by Southern blotting. Two generations of corn were tested; the original transformant and the third generation of back-crossing with B73. The inbred line B73 and non-transgenic regenerate plants of line HE89 were used as controls. The DNA fragments hybridising with a *pat* probe on Southern blots were identical in the original transformant and subsequent back-crossed generations, indicating stability of the DNA introduced into the corn.

Plants screened for phenotypic stability, i.e. tolerance to the herbicide glufosinate ammonium, demonstrated inheritance patterns consistent with a single insertion site that was stable over multiple generations.

2.5 Conclusions regarding the nature of the genetic modification

A single copy of the *pat* and truncated *bla* genes are transferred to corn resulting in the development of herbicide tolerant (glufosinate ammonium) corn line T25. Segregation analyses indicate that the transferred DNA is integrated into the corn genome as a single and stable insert.

3. GENERAL SAFETY ISSUES

3.1 History of use

Corn has been cultivated for centuries and is used as a basic food item by people throughout the world. A large part of corn production is used for human food products, and a wide variety of food products are derived from corn kernels. Sweet corn varieties are grown for human consumption. Grain and by-products from processing of corn are also used as animal feedstuffs.

Dry milling is a mechanical process in which the endosperm is separated from the other components of the kernels and fractionated into coarse particles (grits). The process is used to produce meal and flour for use in cereals, snack foods and bakery products, or for use in brewing (Alexander 1987). Food products derived from dry milling include flakes and grits. Corn flakes are produced by a process that involves high temperatures and pressures, grits are prepared by boiling.

The wet-milling process is designed to physically separate the major component parts of the kernel: starch, protein, oil and fibre. Wet milling produces primarily starch (typically 99.5% pure) (May 1987). In this process grain is steeped in slightly acidic water for 24–48 hours before being milled. Oil is produced from wet-milled corn by solvent extraction and heat (Rogers 1990).

Food derived from glufosinate ammonium tolerant corn line T25 will most likely be imported as processed food products, containing whole, part or constituents of corn and as corn derivatives.

3.2 Nature of novel protein

Only one new protein is expressed in corn line T25: phosphinothricin acetyltransferase (PAT). This protein, encoded by the *pat* gene, allows plants to detoxify the broad-spectrum herbicide phosphinothricin (the active moiety of glufosinate ammonium herbicide). The PAT protein has a very narrow substrate specificity for phosphinothricin and demethyl-phosphinothricin, both of which are not found in humans. Acetyl transferases are a class of enzymes common to all bacterial, plant and animal cells and play a major role in both the synthesis and oxidation of fats. Although the PAT protein may not normally be consumed, *Streptomyces* is a common soil bacterium which may be found on and around plant produce.

In plants, the enzyme glutamine synthetase, plays a central role in the uptake of nitrogen by catalysing the incorporation of ammonia into glutamine. The herbicide glufosinate ammonium inhibits this enzyme in plants, leading to an accumulation of ammonia in the tissues, which kills the plant. The PAT protein catalyses the acetylation of phosphinothricin, thus eliminating its herbicidal activity (Strauch *et al*, 1988). Acetylation of phosphinothricin produces N-acetyl-glufosinate (NAG) and two further metabolites, 3-methylphosphinico-propionic acid (MPP) and 3-methylphosphinicoacetic acid (MPA).

The level of expression of the PAT protein in corn line T25 is sufficiently high for the corn to be marketed as herbicide tolerant. Biapholos, an antibiotic produced by *S. viridochromogenes* is the natural substrate for the PAT protein. No additional substrates, apart from phosphinothricin, have been reported.

3.3 Expression of novel protein in the plant

PAT protein

The level of expression and activity of the PAT protein has been determined, in order to establish potential dietary exposure to this protein. Studies to confirm that the *bla* gene is non-functional were also done. Aventis submitted the following studies on this topic:

Van Wert S and Forster V (1996). Composition, nutrition and/or amount of phosphinothricin acetyltransferase in whole and processed fractions of glufosinate resistant corn: transformation events T14 and T25 and nontransgenic counterparts. Performing laboratory: Aventis USA Company, Wilmington DE, United States. Report No. BK-95B-01.

Klonus D. 1999. Expression of the phosphinothricin acetyltransferase in glufosinate tolerant T25 corn. Hoechst Schering Aventis GmbH, Germany. Report PSR99/005

Schulz 1993. Beta-lactamase activity in Ignite (Glufosinate ammonium based herbicide) resistant corn.

Klonus D. 1999. Polymerase chain reaction analysis (PCR) of the glufosinate tolerant maize line T25.

Field trials of glufosinate ammonium tolerant corn line T25 were conducted in 1994 at two locations in the USA (Indiana and Puerto Rico). Genetically modified hybrid and isogenic or near isogenic control corn lines (i.e. same genetic makeup except for the novel gene) were grown at the Indiana site using a randomised block design. A genetically modified inbred and their respective near isogenic control lines were grown in Puerto Rico. An independent laboratory, Woodson-Tenent Laboratories, Illinois, undertook duplicate analyses of at least three representative samples per site for each genetic background. PAT protein levels were analysed in several plant tissues including the mature kernel, forage (tasseling to silking), silage (late milk to early dough) and fodder (dry plant at harvest).

A double-antibody enzyme-linked immunosorbent assay (ELISA) was used to quantify the PAT protein from T25 hybrids and their isogenic controls. The ELISA detects both intact and denatured PAT, therefore the results are likely to overestimate the level of active protein. The limit of detection of the assay is approximately 1 ng PAT/mg protein.

No PAT protein was detected in any control plants or in kernels of T25 hybrid plants grown in Indiana (Table 1). Grain from inbred T25 corn grown in Puerto Rico contained 4.02 ng PAT/mg protein (± 0.62 ng/mg protein), representing a maximum of 0.00046% of the crude protein in the kernel. The highest level of protein was found in the silage, containing 119.24

ng PAT/mg protein representing a maximum of 0.00132% total protein. It is significant that most commercial corn lines are hybrids rather than inbred lines and these results indicate that PAT protein levels are virtually non-detectable in hybrid lines.

Table 1: Level of PAT protein in corn tissues from hybrid and inbred T25 corn[1]

		Mean levels ± standard deviation (ng/mg protein)[2]			
Indiana		**kernel**	**silage**	**forage**	**fodder**
Hybrid T25	T25-1	nd	14.82 ± 0.86	-	-
	T25-2	nd	12.51 ± 1.38	-	-
	T25-2[3]	nd	14.81 ± 1.30	-	-
Control	*T25*	nd	nd	-	-
Puerto Rico					
Inbred T25	T25-3	4.02 ± 0.62	119.24 ± 13.36	62.70 ± 40.07	79.91 ± 5.23
Control	*T25*	nd	nd	nd	nd

[1]Values are expressed as ng PAT/mg protein. At least three samples were analysed in duplicate.
[2]nd = not detected; '-' = analysis not done. Limit of detection is approximately 1 ng PAT/mg protein.
[3]Plants were treated with glufosinate ammonium at the V8 stage (i.e. 69 days prior to harvest of silage, 115 days prior to harvest of fodder and grain).

PAT activity

The level of PAT activity was measured in kernels, leaves, roots, stem and pollen of greenhouse grown flowering T25 corn plants. The enzyme was detectable in kernels, leaves, roots and stems but not in pollen. The highest activity was found in stems (62.54 µMol N-acetyl-glufosinate produced/minute/mg protein extract). The activity in kernels was significantly lower (less than 60 times lower), ranging from 0.192 - 1.29 µMol N-acetyl-glufosinate produced/ minute/ mg protein extract.

In most processed corn products, i.e. those produced from dry- and wet-milling corn fractions (including flakes and grits), it is unlikely that the enzyme is active, given that the corn is processed using temperatures up to 105°C (220°F) and this is sufficiently high to denature proteins and thus inactivate the enzyme.

β-lactamase

The glufosinate ammonium tolerant corn line T25 contains a single truncated copy of the bacterial *bla* gene. The gene was disrupted during transformation of the corn cells and is missing 25% of the gene sequence. Northern analyses were used to verify that the *bla* gene is neither transcribed to produce a stable transcript nor translated into an active protein with a β-lactamase function. β-lactamase activity in the genetically modified corn was assessed by HPLC-radio-monitoring. The standard assay contained 4.25 pmol of radio-labelled penicillin and β-lactamase activity could be detected in 1:500 dilutions of a bacterial culture fluid with a protein concentration as low as 6.6 µg/ml. No β-lactamase activity was detected in protein extracts of young growing leaves from wildtype and transgenic corn plants, at protein concentrations of 500–1000 fold higher than and incubation times of up to 12 times longer than the bacterial system. It can be concluded that the partial *bla* gene from the plasmid vector does not produce an active β-lactamase in the herbicide-tolerant corn line T25.

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

The potential human health impact of transfer of novel genetic material to cells of the human digestive tract depends 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[4]/WHO Consultation , which looked at strategies for assessing the safety of foods produced by biotechnology (WHO 1991). The consultation concluded 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. Antibiotic resistance genes can be present in some transgenic plants as a result of their use as marker genes to select transformed cells. 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). However, concerns have been expressed that there could be horizontal gene transfer of antibiotic resistance genes from ingested food to microorganisms present in the human digestive tract and that this could compromise the therapeutic use of antibiotics. However, no functional antibiotic resistance gene was transferred to corn line T25, as indicated by a range of analyses including PCR, enzyme assay and northern analysis. Therefore, as the disrupted *bla* gene is not functional and there is no functional gene product, it is not considered to pose any safety risk.

It is equally unlikely that novel genetic material from genetically modified food would transfer 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 genetically modified 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.

DNA digestibility study

Schneider, R., 1993. Fate of introduced DNA in gut: Degradation of phosphinothricin acetyl transferase gene from transgenic rape HCN 92 (Brassica napus) in stomach fluids from pig, chicken and cow. Hoechst AG Agricultural Division, Frankfurt am Main, Germany. Study No. BR 93/06

A study was conducted to determine whether the introduced *pat* gene is sensitive to degradation by mammalian and avian digestive processes. Although the study was conducted on canola that was genetically modified for tolerance to glufosinate ammonium, the outcomes are also relevant to the fate of the *pat* gene inserted into corn. The study used plant leaf material from transgenic rape line (*B. napus*) incubated in the digestive stomach fluids extracted from pig, chicken and cow. This genetically modified canola is also under

[4] Food and Agriculture Organization.

assessment by ANZFA (Application A372 - Liberty Link canola). Samples were tested in pH step gradients of the digestive fluids over a range of time points up to 1 hour.

The study also aimed to determine whether the novel gene in the plant material could transfer to competent *E. coli* bacteria in a laboratory situation, using the kanamycin resistance gene (*npt*II) as a marker for transformation. By extrapolation, this experiment attempts to determine whether novel DNA in plant material that has been subjected to degradative conditions can transfer to *E. coli* present in the gut. The *E. coli* strain was converted from a disabled laboratory strain to a competent living strain for the purpose. A PCR assay system was used to detect the presence of the *pat* gene in the various phases of the experiments.

The PCR analysis of DNA fragments remaining after digestion indicated that the *pat* gene was readily degraded in any of the digestive fluids tested. Detection was pH dependent, being most efficient at low Ph, which mimics physiological conditions. The degradation was less complete at higher pH, which is well above the normal acidic environment of the human stomach.

Some antibiotic resistant bacteria were recovered at the beginning of the experiment using the proprietary plasmid as the DNA source. However, no colonies were recovered after the plasmid was incubated for 60 minutes in the various stomach fluid preparations. More significantly, when the transgenic plant material was used as the DNA source, no transformed colonies could be recovered either initially or after 1 hour incubation in the stomach fluids from any of the test animal species.

This experiment demonstrates that DNA consumed in plant (canola) material is efficiently degraded by normal digestive fluids from a number of different animal species, in conditions which closely resemble the physiological environment in humans. These results confirm that it is highly unlikely that introduced DNA present in the canola plants, including the antibiotic resistance gene, *nptII,* could transfer to intestinal bacteria.

3.5 Conclusions regarding general safety issues

Although the PAT protein would not normally be present in the food supply, it is sourced from a common soil bacterium and is not considered to pose a health and safety risk. Additionally, the class of enzymes PAT belongs to is very commonly found in all bacterial, plant and animal cells and has a major metabolic role.

The *pat* gene is expressed at low levels in corn line T25. It is expressed at the highest levels in the plant silage tissue and is much lower in the kernel where it represents less than 0.0005% total protein. The level of DNA and protein in highly processed corn based products are expected to be very low and in some cases, negligible. It is also likely that the proteins will be degraded and/or removed during processing steps.

No functional antibiotic resistance genes were transferred to corn line T25. The novel genetic material in corn line T25 comprises only a minute fraction of the total DNA present in the corn and is therefore unlikely to pose any additional risks. Additionally, DNA digestibility studies in genetically modified canola (containing the *pat* gene), demonstrated that novel DNA was readily digested in conditions that mimic the human digestive system.

4. TOXICOLOGICAL ISSUES

4.1 Levels of naturally occurring toxins

There are no naturally occurring toxins known to occur at biologically significant levels in corn (Wright, 1987).

4.2 Potential toxicity of novel protein

Phosphinothricin, the substrate for PAT, is not present in humans. The acute oral toxicity of the PAT protein has been evaluated previously as part of applications A385 – Insect protected herbicide-tolerant Bt-176 corn, A386 – Insect-protected herbicide-tolerant Bt-11 corn and A380 DBT-418 corn. The following studies on the acute toxicity and physical and chemical characteristics of the PAT protein have been previously assessed.

An exemption from requirement to establish a maximum permissible level for residues of PAT and the genetic material necessary for its production was granted by the United States Environmental Protection Agency in April 1997 (US EPA 1997).

Reports submitted by Novartis:

Kuhn JO (1995). Phosphinothricin acetyltransferase (Sample PAT-0195) Acute oral toxicity study in mice. Performing Laboratory: Stillmeadow Inc, Sugar Land, Texas. Sponsor: Ciba-Geigy Corporation, Research Triangle Park, NC

Kuhn JO (1995). Phosphinothricin acetyltransferase (Sample PAT-0195) Acute oral toxicity study in mice. Performing Laboratory: Stillmeadow Inc, Sugar Land, Texas. Sponsor: Ciba-Geigy Corporation, Research Triangle Park, NC

(i) Similarity with known toxins

The PAT protein has been evaluated in Applications A385 Bt-176 corn and A386 Bt-11 corn. A comparison of the amino acid sequence of the PAT protein to the sequences of known toxins present in public databases (EMBL, Swissprot), demonstrated that it does not share any significant similarity with any known protein toxins. Additionally, no reports were found of toxicity associated with acetyl transferases as a class and the donor organism has no known pathogenic potential.

(ii) Equivalence of the plant PAT protein to the bacterially produced protein

The PAT protein was purified from plants by a combination of precipitation with ammonium sulphate and size-exclusion/ion-exchange chromatography. After purification, the protein extracted from the glufosinate ammonium tolerant canola migrated as a single band on a sodium dodecyl sulfate (SDS)-polyacrylamide gel, with a molecular mass of around 22 kDa. The kinetics and substrate specificity of the protein were characterised and PAT was found to be highly specific for the substrate L-phosphinothricin, with a very low affinity for related compounds and amino acids. High temperatures and extremes of pH were found to inactivate PAT. These properties of the PAT protein extracted from T25 corn were found to be indistinguishable from the protein extracted from *E. coli.*

(iii) Acute oral toxicity in mice – bacterially produced PAT

The scientific basis for using an acute test is that known protein toxins generally act via acute mechanisms (Jones and Maryanski 1991). Hsd:S-D ICR albino mice (source: Harlan Sprague Dawley Inc, Texas) were housed individually in controlled conditions with free access to food and water, except for the 16 hours before dosing when food was withheld. Groups (5/sex) of mice were given a single oral dose (gavage) of PAT protein (PAT-0195, purity 51% phosphinothricin acetyltransferase, expressed by the *bar* gene in *E. coli*) in carboxymethyl cellulose; heat inactivated PAT (PAT-0195C, 52% purity) in carboxymethyl cellulose; or carboxymethyl cellulose to a total dose of PAT protein of approximately 2600 mg/kg bw (i.e. 51-52% of 5050 mg/kg bw, given that this was the purity of the protein).

Mice were observed for clinical signs at least 3 times on the day of dosing and once daily after this for a 14-day observation period. Bodyweight was determined predosing (day 0) and on days 7 and 14. At the end of the study, mice were killed for post-mortem examination of gross pathology.

One male receiving the test substance died during the study. The only notable clinical signs were decreased activity, piloerection and ptosis (drooping eyelid) on days 6–8 in the male that died.

One male receiving the reference substance showed slight piloerection on the day of dosing. However, as no other clinical signs were observed in animals of any group, these signs are not considered to be treatment related. Bodyweight gain was unaffected by treatment, except in the male that died. There were no abnormal findings on post-mortem of animals surviving until the end of the study. The results do not indicate any potential toxicity from the PAT protein.

4.3 Levels of naturally occurring allergenic proteins

Corn does not contain any known naturally occurring allergenic proteins (Wright, 1987).

4.4 Potential allergenicity of novel protein

Although there are no simple 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. For instance, amino acid sequence similarity with known allergens may be a useful gauge of allergenic potential. A string of 8-12 consecutive amino acid residues in common with known allergens could be an indicator for allergenicity given that many T-cell epitopes of allergenic proteins are that length (Taylor and Lehrer, 1996). In terms of the chemical and physical nature of proteins, known allergens tend to be glycosylated proteins with a molecular weight of 10–70 KDa (Lehrer *et al*, 1996). Allergens also tend to be heat stable as well as resistant to peptic and tryptic digestion and the acidic conditions of the stomach. Consequently, many allergenic factors tend to be resistant to proteolytic digestion (Taylor and Lehrer, 1996). The PAT protein is evaluated for potential allergenicity against these criteria: molecular size, amino acid sequence similarity to known allergens, and how easily the protein is degraded by heat, acid and gastric enzymes (Lehrer and Reese 1998, Jones and Maryanski 1991).

The applicant submitted one study relevant to the possible immunological effects of the transformed corn, showing the effect of simulated gastric conditions on enzyme activity. Since potential allergenicity is often related to the presence of large, undigested protein molecules, it is also important to look at the digestibility of a novel protein. The *in vitro* digestibility of the PAT protein has previously been evaluated by ANZFA in applications A385 – Insect protected herbicide-tolerant Bt-176 corn and A386 – Insect-protected herbicide-tolerant Bt-11 corn. As the PAT protein in Bt-176 and Bt-11 and T25 corn are identical, this study is also relevant to this application.

Study submitted by Aventis:

Schulz A (1993) L-phosphinothricin N-acetyltransferase, biochemical chacterization. Performing laboratory: Biologische Forschung C, Biochemie der Pflanzen, Hoechst Aktiengessellschaft, Frankfurt. Report No. 93.01.

Van Wert S and V Forster. 1996. Composition, nutrition and/or amount of phosphinothricin acetyl transferase in whole and processed fractions of glufosinate resistant corn: Transformation events T14 and T25 and non-transgenic counterparts. Performing Laboratory: Xenos, Woodson-Tenent, Texas A&M, Agrevo.

Study by Novartis (A386):

Privalle L (1994). *In vitro* digestibility and inactivation of the *bar* marker gene product phosphinothricin acetyltransferase (PAT) under simulated mammalian gastric conditions. Ciba Seeds. Agricultural Biotechnology Research Unit, Ciba-Geigy Corporation, Research Triangle Park, NC, USA.

(i) Effect of simulated gastric conditions on activity of the PAT protein

The digestive lability of the PAT protein was assessed for stability in simulated gastric juices. Enzyme samples were incubated at 37°C in stomach fluid from beagle dogs, for up to 15 minutes. Over the course of the incubation samples were removed, diluted in buffer, adjusted to pH 8 and assayed immediately for enzyme activity. The original pH of the stomach fluid was 1.1, experiments were repeated with stomach fluid adjusted to pH 4, to determine the effect that pH modulating medications (taken for stomach disorders) might have on digestion of the protein.

Purified PAT in stomach fluid of pH 1.1 was rapidly inactivated, losing all activity within one minute. At pH 4, inactivation was slower, taking up to 10 minutes. Crude PAT was again inactivated rapidly by gastric juice at pH 1.1, at the higher pH inactivation of the crude protein was slower than that of the purified enzyme. This study supports the conclusion that any PAT protein consumed in foods derived from corn line T25 will be readily denatured upon entering an acidic environment, such as the human gut.

(ii) Digestibility of PAT protein

The PAT protein used in this trial was obtained from an *E. coli* expression system and was purified following fermentation. Simulated gastric fluid (SGF) contained NaCl (2 mg/mL), HCl and pepsin (3.2 mg/mL), the pH was 1.0 to 1.2, and the activity of the fluid was determined before use. Samples were taken at zero and two minutes. The presence of PAT in the fluid following incubation was determined by SDS-PAGE analysis. PAT enzymic activity was also determined at the pH optimum for the enzyme, at gastric pH and following serial incubation with a gastric solution containing 0.0032 mg/mL pepsin.

In the presence of SGF containing a standard concentration of pepsin, the PAT protein was completely degraded at time zero. After 2 minutes of incubation with 0.1 or 0.01 times the standard pepsin concentration, PAT degradation appeared complete. When 0.001 times the standard pepsin concentration was used, a significant amount of PAT remained after a 2-minute incubation period. This concentration was thus selected for the enzyme inactivation studies.

The enzyme activity of PAT decreased to 56% of initial values after a 10-minute incubation at 37^{o}C. This reflects the thermal sensitivity of the enzyme above 35^{o}C, and would represent the maximum activity were gastric pH or pepsin to have no effect on PAT activity. Immediately after addition to SGF without pepsin, PAT activity decreased to 2.6% of the initial activity, and reached zero by 1 minute. When pepsin was included in the SGF, the initial activity was even lower. Activity was not restored by neutralisation, indicating that inactivation of the PAT enzyme was irreversible. The half-life of the PAT protein in SGF containing 0.0032 mg/mL was between 1 and 2 minutes.

This study demonstrates that the PAT protein is readily digested in the gastric environments and is not likely to be allergenic.

(iii) Comparison of PAT with known allergens

No similarity was found between the sequence of the PAT protein and sequences of known allergens in a search of public databases. Additionally, acetyltransferases in general have no similarity to any reported mammalian allergens.

4.5 Conclusion regarding toxicological issues

These studies indicate that the PAT protein loses enzymatic activity immediately upon exposure to gastric pH, and that the protein is readily digested in the stomach. The PAT protein is present at very low levels in the kernel, is readily digested and does not show any similarity with known allergens. Therefore it is highly unlikely that the PAT protein would be toxic or allergenic to humans.

5. NUTRITIONAL ISSUES

5.1 Nutrient analysis

The overall nutritional composition of corn line T25, including any changes resulting from the genetic modification, has been assessed. The composition of the food derived from corn line T25 has been compared with other commercial varieties of the crop. The major components examined were protein, moisture, ash, fibre, fat, carbohydrates, calcium, phosphorous, fatty acids and amino acid composition. Where there are statistically significant differences between the genetically modified and the conventionally bred crop, further comparisons can be made with values available in the literature to determine whether the parameter is within the normal range for non-transformed lines. As T25 is marketed as a herbicide-tolerant variety, the impact of glufosinate ammonium application on the biochemical composition of kernels has been assessed.

Studies submitted by Aventis:

Van Wert S (1999). Composition and nutrition of corn grain: a comparison of transgenic hybrids T25-2 and T25-5 in Canada and in the USA. Performing laboratory: Woodson-Tenent Laboratories Inc, Technical Assessment Systems Inc. Report No. C003219.

Van Wert S (1996). Composition of whole fractions of glufosinate resistant corn untreated and treated with glufosinate: Transformation event T25. Performing laboratory: AgrEvo USA Company, Willmington DE, United States. Report No. A55781.

Analysis of corn grown in the USA and Canada

The composition of two hybrids derived from transformation event T25 (T25-2 and T25-5) was assessed. Plants were grown in two sets of field trials: the first field trial was conducted over two consecutive years in 1994–95 in the USA (hybrid T25-2) and the second field trial was conducted at two sites (Breslau and Ridgetown, Ontario) in Canada in 1995 (hybrid T25-5). The genetically modified hybrid T25-2 was developed by backcrossing the original transformant to another inbred. T25-2 was backcrossed to this inbred three times in 1994 and four times in 1995. These hybrids are considered to have 87.5% and 93.25% genetic homology, respectively.

The genetically modified hybrid T25-5 was developed by backcrossing the original transformant four times to another inbred and has approximately 93.25% genetic homology. The genetically modified lines and their non-genetically modified counterparts are not true isolines but are considered genetic counterparts.

At each location, genetically modified plants and their respective non-genetically modified counterparts were planted in a randomised block design. Plants were harvested at maturity and at least three representative samples from each site, for each genetic background, were analysed. Analysis included moisture, fat, protein, fibre, ash, carbohydrate (by calculation), fatty acid composition, amino acid composition and minerals.

The samples of genetically modified and non-genetically modified corn were collected and nutrient analyses data was analysed statistically using SYSTAT software. The data was analysed using multiple comparisons (i.e. between sites or years, within country and combined countries) to determine any significant differences between the genetically modified and non-genetically modified counterparts.

In separate analyses of the data from each of the USA and the Canadian field trials, there were some significant differences between genetically modified and control corn lines. The values for all components are listed in Tables 3 (USA data) and Table 4 (Canadian data). The United States Department of Agriculture's Handbook 8 values for these components have also been listed as a reference.

USA

Significant differences in the proximate parameters protein and carbohydrate, in the fatty acids C18:3 and C20:0, in the minerals calcium and phosphorus and in seven amino acids (Table 3) were observed between the genetically modified T25-2 and control corn line. Additional statistical analyses of the data, separating data according to year, determined that there was an effect of season on many of these nutrient parameters. The data was collected

over two years, with different environmental conditions each year (temperature, rainfall, soil moisture and type). Additionally, these differences between the genetically modified and non-genetically modified corn were not consistent between years. Although these differences were identified as statistically significant, they are all within the range given in the United States Department of Agriculture's Handbook 8.

Table 3: Proximate, fatty and amino acid and mineral values for T25-2 and control grain grown in USA

Parameter[1]	Control	Transgenic	USDA HB-8[2]	Range[3]
Protein*	8.3 ± 0.6	10 ± 1.0	9.42 ± 0.89	9.0-11.2
Carbohydrate*	86.0 ± 0.8	84 ± 1.0	74.26	73.5
Fat	4.4 ± 0.1	4.6 ± 0.3	4.74 ± 0.91	4.1-4.8
Crude Fibre	2.6 ± 0.5	2.7 ± 0.6	2.90 ± 0.28	2.1-2.6
Ash	1.3 ± 0.2	1.5 ± 0.1	1.20 ± 0.14	1.4-2.0
C16:0	9.2 ± 0.2	9.3 ± 0.2	na	10.7-11.5
C18:0	2.5 ± 0.2	2.4 ± 0.2	na	2.2-4.1
C18:1	31.7 ± 0.8	31.8 ± 0.9	na	14-64; 24.5-27.
C18:2	54.3 ± 1.0	54.2 ± 1.3	na	19-71; 51.8-58.
C18:3*	1.0 ± 0.05	0.92 ± 0.04	na	0.5-2.0; 0.8-1.1
C20:0*	0.54 ± 0.01	0.51 ± 0.03	na	0.2
Calcium*	0.0051 ± 0.007	0.0141 ± 0.0007	0.007 ± 0.002	0.007- 0.05
Phosphorus*	0.286 ± 0.007	0.331 ± 0.001	0.210 ± 0.076	0.20-0.32
Alanine	0.53 ± 0.06	0.63 ± 0.1	0.61	na
Arginine*	0.28 ± 0.02	0.37 ± 0.05	0.41	na
Aspartic acid*	0.45 ± 0.04	0.55 ± 0.09	0.57	na
Cysteine	0.16 ± 0.02	0.18 ± 0.01	0.15	na
Glutamic acid	1.2 ± 0.1	1.3 ± 0.6	1.53	na
Glycine*	0.28 ± 0.02	0.32 ± 0.02	0.33	na
Histidine*	0.23 ± 0.02	0.27 ± 0.03	0.25	na
Isoleucine	0.20 ± 0.02	0.26 ± 0.06	0.29	na
Leucine	0.78 ± 0.09	0.98 ± 0.25	1.00	na
Lysine*	0.21 ± 0.01	0.25 ± 0.02	0.23	na
Methionine	0.17 ± 0.02	0.18 ± 0.03	0.17	na
Phenylalanine	0.30 ± 0.04	0.37 ± 0.09	0.40	na
Proline	0.56 ± 0.05	0.65 ± 0.2	0.71	na
Serine	0.35 ± 0.03	0.42 ± 0.07	0.39	na
Threonine*	0.26 ± 0.02	0.30 ± 0.04	0.31	na
Tryptophan	0.042 ± 0.008	0.050 ± 0.006	0.057	na
Tyrosine	0.12 ± 0.03	0.16 ± 0.05	0.33	na
Valine*	0.30 ± 0.02	0.37 ± 0.05	0.41	na

[1] Proximates and minerals expressed on a dry weight basis; fatty acids as percent of total lipids and adjusted for moisture. Amino acids reported as a % total protein.

[2] Values reported in Handbook 8, the United States Department of Agriculture (USDA), 1989. SD not available for fatty and amino acid values in the USDA HB-8.

[3] Wright, 1987 in Corn chemistry and technology, 1987, Watson SA and Ramstad PE (eds), American Association of Cereal Chemists, St. Paul, Minnesota, USA; Ensminger *et al*, 1990; Macgregor, 1989; Perry 1988

[4] HB-8 lists values for fatty acid values adjusted for moisture.

*Significantly different from non-genetically modified counterpart.

Canada

T25-5 corn grown in Canada showed significant differences in the fatty acids C18:1, C18:2 and C20:0, and in the amino acid cystine (Table 4). C18:2 was at a higher level in the transgenic than in the isogenic corn, whereas C18:1 and C20:0 were lower in the transgenic samples. Additional statistical analyses of the data, separating data according to sites, determined that there was an effect of location on some of these nutrient parameters. The samples were collected from two sites, with different environmental conditions at each site (temperature, rainfall, soil moisture and type).

Table 4: Proximate, fatty and amino acid and mineral values for T25-5 grain and control corn grown in Canada

Parameter[1]	Control	Transgenic	USDA HB-8[2]	Range[3]
Protein*	10.3 ± 0.5	10.1 ± 0.5	9.42 ± 0.89	9.0-11.2
Carbohydrate*	83. ± 0.5	83.7 ± 0.7	74.26	73.5
Fat	4.4 ± 0.2	4.7 ± 0.2	4.74 ± 0.91	4.1-4.8
Crude Fibre	2.6 ± 0.3	2.5 ± 0.3	2.90 ± 0.28	2.1-2.6
Ash	1.35 ± 0.05	1.41 ± 0.04	1.20 ± 0.14	1.4-2.0
C16:0	11.2 ± 0.4	11.8 ± 0.9	na	10.7-11.5
C18:0	1.9 ± 0.1	2.0 ± 0.1	na	2.2-4.1
C18:1*	29.0 ± 3.0	23.8 ± 0.7	na	14-64; 24.5-27.
C18:2	55.0 ± 3.0	60.0 ± 2.0	na	19-71; 51.8-58.
C18:3	1.2 ± 0.2	1.2 ± 0.1	na	0.5-2.0; 0.8-1.1
C20:0*	0.50 ± 0.03	0.46 ± 0.02	na	0.2
Calcium	0.0042 ± 0.0006	0.005 0.001	0.007 ± 0.002	0.007- 0.05
Phosphorus	0.29 ± 0.03	0.30 ± 0.03	0.210 ± 0.076	0.20-0.32
Alanine	0.60 0.05	0.60 0.06	0.61	na
Arginine	0.32 0.04	0.32 0.03	0.41	na
Aspartic acid	0.54 0.06	0.50 0.05	0.57	na
Cysteine*	0.15 ± 0.01	0.16 ± 0.01	0.15	na
Glutamic acid	1.5 ± 0.1	1.4 ± 0.2	1.53	na
Glycine	0.29 ± 0.02	0.28 ± 0.03	0.33	na
Histidine	0.25 ± 0.02	0.23 ± 0.02	0.25	na
Isoleucine	0.27 ± 0.02	0.26 ± 0.03	0.29	na
Leucine	1.02 ± 0.07	1.00 ± 0.11	1.00	na
Lysine	0.23 ± 0.02	0.22 ± 0.02	0.23	na
Methionine	0.15 ± 0.02	0.16 ± 0.02	0.17	na
Phenylalanine	0.40 ± 0.03	0.38 ± 0.03	0.40	na
Proline	0.69 ± 0.07	0.65 ± 0.08	0.71	na
Serine	0.40 ± 0.04	0.39 ± 0.04	0.39	na
Threonine	0.30 ± 0.03	0.28 ± 0.03	0.31	na
Tryptophan	0.052 ± 0.006	0.0049 ± 0.003	0.057	na
Tyrosine	0.16 ± 0.01	0.16 ± 0.01	0.33	na
Valine	0.35 ± 0.03	0.34 ± 0.03	0.41	na

[1] Proximates and minerals expressed on a dry weight basis; fatty acids as percent of total lipids and adjusted for moisture. Amino acids reported as a % total protein.

[2] Values reported in Handbook 8, the United States Department of Agriculture (USDA), 1989. SD not available for fatty and amino acid values in the USDA HB-8.

[3] Wright, 1987 in Corn chemistry and technology, 1987, Watson SA and Ramstad PE (eds), American Association of Cereal Chemists, St. Paul, Minnesota, USA. Ensminger *et al*, 1990; Macgregor, 1989; Perry 1988;

[4] HB-8 lists values for fatty acid values adjusted for moisture

*Significantly different from non-genetically modified counterpart.

The lack of consistent differences between the wild-type hybrids and their modified counterparts suggests that these effects are likely to be due to normal variation, rather than an effect of the genetic modification. The genetic makeup and environmental conditions can affect the composition and nutrient levels of corn. Furthermore, the differences observed are small and would not represent a difference that is nutritionally significant.

Combined USA and Canada

Data from all field trials were combined and analysed for significant differences between the genetically modified T25 corn line and its non-genetically modified counterpart. The results from this analysis are listed in Tables 5a-d. The ranges for each component as listed in the USDA Handbook-8 (HB-8) are given.

Table 5a: Proximate, amino and fatty acid and mineral values for kernels from T25 and control corn grown in USA and Canada

Parameter[1]	Control	Transgenic	USDA HB-8[2, 4]	Range[3]
Protein	10.18 ± 0.66	10.06 ± 1.09	9.42 ± 0.89	9.0-11.2
Carbohydrate	84.08 ± 0.66	84.09 ± 1.18	74.26	73.5
Fat*	4.39 ± 0.13	4.50 ± 0.12	4.74 ± 0.91	4.1-4.8
Crude Fibre	2.50 ± 0.36	2.37 ± 0.25	2.9 ± 0.28	2.1-2.6
Ash	1.34 ± 0.05	1.34 ± 0.05	1.20 ± 0.14	1.4-2.0
Moisture % H_2O	18.45 ± 3.29	20.77 ± 5.02	10.37 ± 3.28	7-23
C16:0*	11.13 ± 0.32	11.58 ± 0.51	na	10.7-11.5
C18:0*	2.00 ± 0.26	2.45 ± 0.15	na	2.2-4.1
C18:1*	29.22 ± 2.57	25.92 ± 0.69	na	14-64; 24.5-27.
C18:2*	55.05 ± 2.35	57.37 ± 1.37	na	19-71; 51.8-58.
C18:3	1.23 ± 0.16	1.20 ± 0.13	na	0.5-2.0; 0.8-1.1
C20:0	0.51 ± 0.03	0.51 ± 0.03	na	0.2
Calcium	0.0056 ± 0.0027	0.0072 ± 0.0026	0.007 ± 0.002	0.007- 0.05
Phosphorus*	0.3005 ± 0.0263	0.3200 ± 0.0221	0.210 ± 0.076	0.20-0.32
Alanine	0.61 ± 0.04	0.60 ± 0.06	0.61	na
Arginine	0.32 ± 0.04	0.30 ± 0.04	0.41	na
Aspartic acid	0.55 ± 0.05	0.50 ± 0.05	0.57	na
Cysteine	0.16 ± 0.02	0.16 ± 0.02	0.15	na
Glutamic acid	1.44 ± 0.13	1.38 ± 0.15	1.53	na
Glycine	0.30 ± 0.03	0.30 ± 0.05	0.33	na
Histidine	0.25 ± 0.01	0.24 ± 0.02	0.25	na
Isoleucine	0.26 ± 0.03	0.24 ± 0.04	0.29	na
Leucine	1.01 ± 0.09	0.95 ± 0.14	1.00	na
Lysine*	0.23 ± 0.02	0.21 ± 0.02	0.23	na
Methionine	0.17 ± 0.04	0.17 ± 0.02	0.17	na
Phenylalanine	0.40 ± 0.04	0.36 ± 0.04	0.40	na
Proline	0.70 ± 0.06	0.65 ± 0.07	0.71	na
Serine	0.41 ± 0.02	0.39 ± 0.03	0.39	na
Threonine	0.30 ± 0.02	0.28 ± 0.02	0.31	na
Tryptophan	0.05 ± 0.01	0.05 ± 0.00	0.057	na
Tyrosine	0.16± 0.01	0.15 ± 0.02	0.33	na
Valine	0.35 ± 0.04	0.32 ± 0.03	0.41	na

[1] Proximates and minerals expressed on a dry weight basis; fatty acids as percent of total lipids and adjusted for moisture. Amino acids reported as a % total protein.

[2] Values reported in Handbook 8, the United States Department of Agriculture (USDA), 1989
[3] Wright, 1987 in Corn chemistry and technology, 1987, Watson SA and Ramstad PE (eds), American Association of Cereal Chemists, St. Paul, Minnesota, USA. Ensminger *et al*, 1990; Macgregor, 1989; Perry 1988;
[4] HB-8 lists fatty acid values adjusted for moisture only, no standard deviation available for amino acids
*Significantly different from non-genetically modified counterpart.

Overall there were no significant differences in the proximate variables or minerals between genetically modified corn line T25 and its non-genetically modified counterpart. A significant difference was noted in the crude fat value, which was higher in the genetically modified corn. There were also differences between several fatty acids: values were higher in the genetically modified corn for C16:1, C18:0, C18:2 and lower for C18:1. The only amino acid showing a significant difference was lysine, which was lower in the genetically modified corn than in the control line corn. The value for phosphorous was higher in genetically modified corn. Location was found to have a significant effect on some of these parameters. These differences are all small and are not considered to be biologically or nutritionally significant. Additionally, all nutrient values are similar to the values for USDA HB-8 or literature ranges for corn.

Analysis of GA treated corn

During the 1994 USA field trial of corn hybrid T25-2 at a site in Indiana, plants were also treated with glufosinate ammonium. The experimental design consisted of three treatments (T25-2 not treated with glufosinate ammonium, T25-2 treated with glufosinate ammonium and non-transgenic), with three or four replications.

The treated T25-2 corn received one application of 400 gm glufosinate ammonium/hectare at growth stage V5. Grain was harvested at maturity. All compositional variables, with the exception of fatty acids, were adjusted for moisture prior to statistical analysis. Plants were harvested at maturity and at least three representative samples from each site, for each genetic background, were analysed.

There were no significant differences (P=0.05) between the treated and untreated transgenic corn (Table 6). Thus, the application of glufosinate ammonium on the genetically modified corn line does not appear to have an effect on the final composition of the corn kernel.

There were some significant differences between either the treated or untreated transgenic corn to the non-transgenic counterpart, which are indicated in Table 6. Although statistically significant differences were seen between the transgenic and the non-transgenic counterpart, all means observed fall within reported literature ranges and are not nutritionally significant.

5.2 Levels of anti-nutrients

Corn contains few anti-nutrients. The anti-nutrients trypsin and chymotrypsin inhibitors are present in corn at very low levels that are not considered nutritionally significant (Wright 1987).

5.3 Ability to support typical growth and wellbeing

In assessing the safety of food produced using gene technology, 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.

Table 6: Proximate, amino and fatty acid and mineral values for kernels from treated and untreated T25 corn and control corn grown in the USA[1]

Parameter[1]	Control	T25-2 untreated	T25-2 GA-treated	USDA HB-8[2, 4]	Range[3]
Protein*	6.81 ± 0.50	7.87 ± 1.15	9.22 ± 0.39	9.42 ± 0.89	9.0-11.2
Carbohydrate*	74.64 ± 2.29	73.50 ± 1.53	71.43 ± 0.40	74.26	73.5
Fat	3.76 ± 0.09	3.93 ± 0.20	4.20 ± 0.13	4.74 ± 0.91	4.1-4.8
Crude Fibre	2.60 ± 0.29	2.70 ± 0.29	2.43 ± 0.21	2.9 ± 0.28	2.1-2.6
Ash*	1.02 ± 0.10	1.21 ± 0.12	1.15 ± 0.06	1.20 ± 0.14	1.4-2.0
Moisture % H_2O	13.77 ± 2.51	12.72 ± 1.77	14.00 ± 0.33	10.37 ± 3.28	7-23
C16:0	9.11 ± 0.24	9.16 ± 0.21	8.88 ± 0.06	na	10.7-11.5
C18:0*	2.63 ± 0.02	2.24 ± 0.17	2.15 ± 0.03	na	2.2-4.1
C18:1	32.27 ± 0.53	31.37 ± 1.10	32.28 ± 0.31	na	14-64; 24.5-27.
C18:2	53.50 ± 0.43	54.83 ± 1.45	54.32 ± 0.18	na	19-71; 51.8-58.
C18:3*	1.03 ± 0.04	0.94 ± 0.03	0.88 ± 0.01	na	0.5-2.0; 0.8-1.1
Alanine	0.49 ± 0.04	0.55 ± 0.08	0.66 ± 0.06	0.61	na
Arginine*	0.26 ± 0.01	0.36 ± 0.06	0.33 ± 0.03	0.41	na
Aspartic acid*	0.43 ± 0.03	0.50 ± 0.08	0.60 ± 0.06	0.57	na
Cysteine	0.15 ± 0.01	0.17 ± 0.02	0.16 ± 0.01	0.15	na
Glutamic acid	1.13 ± 0.10	0.24 ± 0.29	1.60 ± 0.15	1.53	na
Glycine*	0.27 ± 0.14	0.32 ± 0.03	0.32 ± 0.02	0.33	na
Histidine*	0.21 ± 0.01	0.26 ± 0.04	0.28 ± 0.02	0.25	na
Isoleucine	0.19 ± 0.03	0.21 ± 0.05	0.25 ± 0.01	0.29	na
Leucine	0.73 ± 0.09	0.81 ± 0.17	1.03 ± 0.05	1.00	na
Lysine*	0.20 ± 0.01	0.25 ± 0.02	0.26 ± 0.01	0.23	na
Methionine	0.15 0.005	0.15 ± 0.02	0.15 ± 0.01	0.17	na
Phenylalanine*	0.28 ± 0.03	0.33 ± 0.07	0.41 ± 0.01	0.40	na
Proline	0.53 ± 0.05	0.54 ± 0.16	0.69 ± 0.06	0.71	na
Serine	0.33 ± 0.03	0.37 ± 0.06	0.44 ± 0.04	0.39	na
Threonine*	0.24 ± 0.02	0.28 ± 0.04	0.30 ± 0.03	0.31	na
Tryptophan	0.040 ± 0.008	0.050 ± 0.008	0.047 ± 0.006	0.057	na
Tyrosine*	0.10 ± 0.01	0.14 ± 0.05	0.14 ± 0.00	0.33	na
Valine	0.30 ± 0.03	0.34 ± 0.05	0.35 0.03	0.41	na

[1] Proximates, amino acids and minerals expressed on a dry weight basis; fatty acids as percent of total lipids and adjusted for moisture. Amino acids reported as a % total protein.
[2] Values reported in Handbook 8, the United States Department of Agriculture (USDA), 1989
[3] Wright, 1987 in Corn chemistry and technology, 1987, Watson SA and Ramstad PE (eds), American Association of Cereal Chemists, St. Paul, Minnesota, USA. Ensminger *et al*, 1990; Macgregor, 1989; Perry 1988;
[4] HB-8 lists fatty acid values adjusted for moisture only, no standard deviation available for amino acids
*Either the treated or non-treated genetically modified corn was significantly different from non-genetically modified counterpart – note: there were no significant differences between the treated and untreated genetically modified corns.

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 corn line T25, the extent of the compositional and other data provided in the application is considered adequate to establish the safety of the food. Nonetheless, Aventis also provided an animal feeding study to compare the wholesomeness of corn line T25 with conventional corn hybrids. Although not considered essential for establishing safety in this instance, this animal feeding study has been reviewed as additional supporting data.

Study submitted by Aventis:

Leeson D (1996). The effect of glufosinate resistant corn on the growth of male broiler chickens. Performing laboratory: Department of Animal and Poultry Sciences, University of Guelph, Ontario, Canada. Report No. C-5-96I.

Two hundred and eighty commercial strain Ross x Ross male broiler chickens were weighed and allocated at random to 1 of 2 treatment groups, replicated 4 times, 35 birds per replicate. Birds were reared on 1 of 2 diets, *ad libitum*; a commercial corn hybrid or genetically modified corn line T25.

Each diet was a conventional corn-soybean type, prepared for starter, grower and finisher periods. The source of corn for the first diet (commercial corn hybrid) was the University of Guelph, for the second (glufosinate ammonium tolerant corn), the source was Aventis, USA. Birds were fed starter diets to 18 days, grower diets from 18–32 days, and finisher diets from 32–42 days of age. At 18, 32 and 42 days, feed intake was measured and all birds weighed individually. All occurrences of mortality were submitted for post mortem examination. On day 42, 8 birds were randomly selected from each group for processing.

Variables considered for analysis were initial body weight; 18, 32 and 42 day body weight; 0–18, 18–32 and 32–42 day body weight gain, feed intake; and feed intake:body weight gain. Carcass characteristics considered were chilled carcass weight; abdominal fat pad weight; total deboned breast meat yield and abdominal fat pad as a percent of carcass weight; and deboned breast meat yield as a percent of carcass weight. Percent mortality over the experimental period was calculated. Significance was accepted at $P<0.05$.

The source of corn in the starter, grower and finisher diets had no effect on body weight, feed intake, feed intake:body weight gain or percent mortality over the experimental period ($P>0.05$). The mortality rate of 7.14 ± 5.47% was normal for this fast-growing strain of bird, with normal values being 5 – 8%. Carcass characteristics measured and calculated were unaffected by source of corn in the experimental diets.

Herbicide-tolerant corn was comparable in feeding value for 0–42 day broilers, relative to commercially available corn. The results indicate that the nutritive value of the herbicide-tolerant corn hybrid is equivalent to a commercially available corn hybrid and also supports the conclusion of the compositional analyses that there are no biologically significant differences between corn line T25 and other commercial varieties of corn.

5.4 Conclusions regarding nutritional issues

The nutritional qualities of glufosinate ammonium tolerant corn line T25 were determined by compositional analyses of the major components of the kernels and these were found to be comparable in all respects to the conventional corn lines.

There is a long history of safe use of corn. Based on the data submitted in the present application, grain derived from corn line T25is nutritionally and compositionally comparable to that from conventional corn and is not considered to pose a risk to human health and safety.

REFERENCES

Alexander, R.J. 1987 Corn dry milling: processes, products and applications. *in* Corn: Chemistry and Technology. ed. Watson, S.A. and Ramstead, P.E. American Association of Cereal Chemists Inc, St Paul, Minnesota. pp 351-376

ANZFA 1999. Guidelines for the safety assessment of foods to be included in Standard A18 — Food Produced Using Gene Technology.

Calva JJ, Sifuentes-Osbornio J and Ceron C 1996. Antimicrobial resistance in fecal flora: longitudinal community-based surveillance of children from urban Mexico. Antimicrobial Agents and Chemotherapy 40:1699-1701.

Ensminger, Oldsfield and Heinemann 1990. Feedsand Nutrition 2nd Edition. Ensminger Publishing Company, Clovis, Ca. USA

Hammond BG and Fuchs RL 1998. Safety evaluation for new varieties of food crops developed through biotechnology. In: Thomas JA (ed.) Biotechnology and safety assessment. Taylor and Francis, Philadelphia.

Jones DD and Maryanski JH 1991. Safety considerations in the evaluation of transgenic plants for human food. In: Levin MA and Strauss HS (eds) Risk assessment in genetic engineering. New York: McGraw-Hill.

Lehrer, S.B., W.E. Horner and Reese, G. 1996. Why are some proteins allergenic? Implications for biotechnology. *Crit Rev Food Sci Nutr 36*: 553-564.

Lehrer SB and Reese G 1998. Food allergens: implications for biotechnology. In: Thomas JA (ed.) Biotechnology and safety assessment. Taylor and Francis, Philadelphia.

Macgregor. 1989. Directory of Feeds and Feed Ingredients. Hoard and Sons Company.

May, J.B. 1987 Wet milling: processes and products. *in* Corn: Chemistry and Technology. ed. Watson, S.A. and Ramstead, P.E. American Association of Cereal Chemists Inc, St Paul, Minnesota. pp 377-397

Noteborn HP, Bienenmann-Ploum ME, van den Berg JH, Alink GM, Zolla L, Reynaerts A, Pensa M and Kuiper HA 1995. Safety assessment of the *Bacillus thuringiensis* insecticidal crystal protein CryIA(b) expressed in transgenic tomatoes. In: Genetically modified foods. American Chemical Society Symposium Series 605. Engal K-H, Takeoka GR and Teranishi R (eds) American Chemical Society, Washington, DC.

Odell, J.T., Nagy, F. and Chua, N-H. (1985). Identification of DNA sequences required for activity of the cauliflower mosaic virus 35S promoter. *Nature* **313:** 810-812.

Perry. 1988. Corn as a Livestock Feed; Corn and Corn Improvement. In: Corn and Corn Improvement, Sprague and Dudley (eds). Agronomy Monographs No .18. American Society of Agronomy.

Piertrzak, M, Shillito DS, Hohn T, and I Potrykus. 1986. Expression in plants of two bacterial antibiotic resistance genes after protoplast transformation with a new plant expression vector. Nucleic Acids Research 14:5857-5868.

Rogers, J. 1990 What food is that? and how healthy is it? Weldon Publishing, Sydney p 326-327

Sanders PR, Lee TC, Groth ME, Astwood JD and Fuchs RL 1998. Safety assessment of insect-protected corn. In: Thomas JA (ed.) Biotechnology and safety assessment. Taylor and Francis, Philadelphia.

Stewart GJ and Carlson CA 1986. The biology of natural transformation. Annual Review of Microbiology, 40:211-235.

Strauch E., Wohlleben, W. and A. Puhler. 1988. Cloning of a phosphinothricin N-acetyl transferase gene from *Streptomyces viridochromogenes* Tü4994 and its expression in *Streptomyces lividans* and *Escherichia coli*. Gene 63:65-77

Taylor S.L. and S.B. Lehrer. 1996. Principles and characteristics of food allergens. ***Crit Rev Food Sci Nutr*** **36** Suppl: S91-S118.

Wohlleben, W., W. Arnold, I. Broer, D. Hilleman, E. Strauch and A. Puhler. 1988. Nucleotide sequence of the phosphinothricin-N-acetyltransferase gene from a *Streptomyces viridochromogenes* T494 and its expression in *Nicotiana tabacum*. Gene 70:25-37.

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

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

Wright, K.N. (1987). Nutritional properties and feeding value of corn and its by-products. In: *Corn: Chemistry and Technology*. S.A. Watson and P.E. Ramsted (Eds.), American Association of Cereal Chemists, Inc. St. Paul, MN, USA.

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[5]. This is equivalent to 0.51% of turnover in Australia and 0.19% in New Zealand.

[5] 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

The draft risk analysis report for Applications A372, A375, A378 and A379 were advertised together on the 7 March 2001. Many submitters provided comment on the four applications in one submission or the submissions were general comment on GM foods, rather than specific comments on each individual application. Submissions from both rounds of consultation have been summarised in this attachment and a response to many of the general comments are addressed either in the safety assessment report or in Attachment 6.

SUMMARY OF FIRST ROUND PUBLIC 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. A378

- 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

B. 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 are 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 CP4 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.

▪ **ATTACHMENT 6**

GENERAL ISSUES RAISED IN PUBLIC COMMENTS

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 irrespective of the type of food concerned or the particular genetic modification. 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 Organisation (WHO)/Food and Agriculture Organisation (FAO) and the Organisation for Economic Cooperation and Development (OECD). The Authority 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 joint 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[6], 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)

[6] 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).*