FINAL RISK ANALYSIS REPORT

APPLICATION A346

Food produced from insect-protected corn line MON 810

Note:

This report is the "Inquiry" as referred to in Section 17 of the *Australia New Zealand Food Authority Act (1991)* and sets out the reasons for making a recommendation to the Australia New Zealand Food Standards Council under Section 18 of the Act.

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EXECUTIVE SUMMARY

Background

ANZFA received an application from Monsanto Australia Limited on 12 August 1997 for the approval of food derived from insect-protected corn line MON 810. This corn has been genetically modified to confer protection against lepidopteran pests, and is known commercially as Yieldgard corn. This report describes the scientific assessment of the application.

Issues addressed during assessment

(i) Safety evaluation

Insect-protected corn line MON 810 has been evaluated according to ANZFA's safety assessment guidelines. The process involves an extensive analysis of the nature of the genetic modification together with a consideration of general safety issues, toxicological issues and nutritional issues associated with the new GM food. This approach establishes whether or not a food produced from GM corn is as safe and nutritious as food produced from non-GM varieties.

The detailed information available on the genetic modification used to produce Yieldgard corn indicates that no unintentional changes have taken place at the molecular level and that the novel genetic material is stably inserted and maintained over several generations.

Data on the potential toxicity and allergenicity of the protein encoded by the transferred gene have been reviewed, and indicate that the new protein expressed in insect-protected corn is non-toxic and unlikely to have allergenic effects.

Compositional analyses demonstrate no significant differences between insect-protected corn and its conventional counterparts. This constitutes further evidence that no unintentional effects have occurred as a result of the genetic modification.

In assessing all of the above data, ANZFA has concluded that insect-protected corn line MON 810 does not raise any public health and safety concerns.

(ii) Labelling

On the basis of the data considered in the safety evaluation, food derived from insect-protected corn line MON 810 was found to be substantially equivalent to food derived from non-GM corn. No mandatory labelling is therefore required, although this may change when the proposed changes to the labelling provisions of Standard A18 have been finalised.

(iii) Public submissions

The assessment of this application underwent two rounds of public comment. Fifty-eight submissions were received in the first round and 26 were received in the second round. The majority of submissions in both rounds of consultation were not supportive of the application. Those opposing the application did so primarily on the basis that they perceive GM food to

be unsafe. The food safety concerns raised in submissions have been addressed in the draft safety assessment report.

Conclusions

ANZFA considers that food derived from insect-protected corn line MON 810 is as safe for human consumption as food from other commercial corn varieties, and therefore recommends that the Australian *Food Standards Code* be amended to give approval to the sale of such food in Australia and New Zealand. Based on the data submitted in the present application, ANZFA is also proposing that, as insect-protected corn is substantially equivalent to non-GM corn, no mandatory labelling be required, although this may change when the proposed changes to the labelling provisions of Standard A18 have been finalised.

INTRODUCTION

The Australia New Zealand Food Authority (ANZFA) is a bi-national statutory body responsible for making recommendations on food standards which, when approved by the Australia New Zealand Food Standards Council (ANZFSC), are adopted by reference and without amendment into food law. ANZFA is currently working to establish a joint Australia New Zealand Food Standards Code that will apply in both countries. In the interim, a system of dual standards operates for the majority of the food standards. Standard A18 has been accepted by New Zealand, and currently applies in both countries.

Standard A18 was adopted by ANZFSC as a joint Australia/New Zealand standard in July 1998 and came into force on 13 May 1999. Under this Standard, the sale of food produced using gene technology is prohibited unless the food is included in the Table to clause 2 of the Standard. The Standard requires that a pre-market safety assessment be conducted on all foods produced using gene technology. However, the Standard provides an exemption for those foods currently on the market provided that an application was accepted by ANZFA on or before 30 April 1999, that the food is lawfully permitted in a country other than Australia or New Zealand, and that ANZFSC has not become aware of evidence that the food poses a significant risk to public health and safety.

BACKGROUND TO THE APPLICATION

ANZFA received an application from Monsanto Australia Ltd on 12 August 1997 to amend the Australian *Food Standards Code* to include food produced from insect-protected corn line MON 810 in the Table to clause 2 of Standard A18 – Food Produced using Gene Technology.

The insect-protected corn under consideration is known commercially as Yieldgard corn and is protected from attack by lepidopteran pests, particularly the European Corn Borer. The corn was developed by Monsanto Ltd for cultivation in the United States. Products derived from Yieldgard corn may have been imported into Australia and New Zealand since December 1996.

The genetic change involved in the modification is the incorporation of a gene, *cry 1A(b),* from the soil bacterium *Bacillus thuringiensis* subsp. *kurstaki.* The gene codes for a protein that is toxic to Lepidoptera, and the modified corn is thus protected from attack by these types of insect pests.

Yieldgard corn is not currently grown in either New Zealand or Australia. However, domestic production of corn in both countries is supplemented by a small amount of imported corn-based products, largely as high-fructose corn syrup, which is not currently manufactured in either Australia or New Zealand. Such products are processed into breakfast cereals, baking products, extruded confectionary and corn chips. Other corn products, including maize starch, are also imported. This is used by the food industry for the manufacture of dessert mixes and canned foods.

The main benefits of insect-protected corn are agronomic in nature, and are therefore likely to accrue mainly to the primary producer. Target pests, in particular the European Corn Borer, should be cheaper and easier to control, with lower expenditure on labour and pesticides and

higher overall crop yields. More general benefits may flow to the community as a result of reduced primary production costs.

PUBLIC CONSULTATION

The Authority received the first six applications for foods produced using gene technology from Monsanto Australia Ltd. Due to commonalities in these applications, a combined Notice of Application (formally referred to as the Preliminary Assessment Report) was advertised on 28 October 1998, which called for public comment on the applications. A total of 58 submissions were received in response to the combined Notice of Application, of which 53 relate to this application. The submissions were primarily from individuals, consumer organisations and special interest groups from both New Zealand and Australia. The submissions are summarised in Attachment 5.

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 Technological 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 changes to Standard A18 are considered to raise potential Technical Barrier to Trade or Sanitary/Phytosanitary matters and were therefore notified to the WTO.

ISSUES ADDRESSED IN THE ASSESSMENT OF THE APPLICATION

1. Safety assessment

The safety assessment was performed according to the safety assessment guidelines prepared by ANZFA[1] and considered the following issues: (1) the nature of the genetic modification; (2) general safety issues such as novel protein expression and the potential for transfer of novel genetic material to cells in the human digestive tract; (3) toxicological issues; and (4) nutritional issues.

Nature of the genetic modification

One gene has been transferred to insect-protected corn line MON 810 using the particle bombardment method - *cry1(A)b*.

The *cry1(A)b* gene is one of several isolated from *B. thuringiensis*, which encode a group of toxins known as the *Bt* toxins. These toxins are selectively active against several groups of insects such as moths and butterflies, beetles, and flies and mosquitos. The *Bt* toxin produced by the *cry1(A)b* gene is known as Cry1(A)b and is selectively active against lepidopteran

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

insects. The protein becomes active against the target insect through ingestion. In the insect gut, the protein binds to specific receptors on the insect midgut, inserts into the cell membrane and forms ion–specific pores. These events disrupt the digestive processes and cause the death of the insect.

Through various laboratory investigations the transferred gene was found to be stably integrated as a single insert, and maintained in corn plants over multiple generations.

General safety issues

Corn represents 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.

The toxin expressed in the modified corn was found to be identical to that occurring naturally, and equivalent to that produced for use as the biopesticide that is widely used by the organic food industry. The expression level of the protein was low, constituting less than 0.001% of the total protein. The level varied depending on the plant part, with levels highest in the leaves (9.35 μg/g) and relatively low in the grain (0.31 μg/g) and pollen (0.09 μg/g).

Although the plasmids used in the transformation process of Yieldgard corn contain the antibiotic resistance gene *nptII*, the gene was not transferred to the modified plant. The impact on human health from its potential transfer to gut micro-organisms was therefore not considered.

Toxicological issues

The presence of naturally-occurring toxins and allergens in insect-protected corn line MON 810 was investigated, as well as the potential toxicity and allergenicity of the Cry1(A)b protein.

Corn contains no naturally-occurring toxins or allergens, and as noted above has a long history of safe use.

The potential toxicity of the novel protein, Cry1(A)b was assessed using acute oral toxicity testing in mice. No adverse findings were seen in the animal studies, and the novel protein was found to be identical to that present in *B. thuringiensis* formulations that have been used commercially for many years to control insect pests. These formulations have been used with no evidence of toxicity to humans, or non-target species of insects, birds, fish or mammals. On the basis of these various pieces of evidence, it can be concluded that Cry1(A)b, as expressed in insect-protected corn line MON 810, is non-toxic to humans.

The novel protein is also unlikely to be allergenic to humans. As already discussed, it has a long history of safe use, and shares no characteristics or similarity with known allergens. In laboratory tests it was also found to be rapidly digested in conditions that mimic human digestion.

Nutritional issues

Detailed compositional analyses were carried out to establish the nutritional adequacy of insect-protected corn, and to compare it to non-modified control lines. Constituents analysed were carbohydrates, fatty acids, amino acids, calcium and phosphorus, and tocopherols. Proximate analysis of total protein, fat, moisture, ash, total carbohydrates and calories was also carried out. Analyses confirmed that insect-protected corn line MON 810 is compositionally equivalent to other commercial corn lines. Animal feeding studies were not considered essential in this case because sufficient information had been provided about the genetic modification and the composition of the food. However, Monsanto have decided to conduct feeding trials, which are expected to be completed by late 2000. Although not considered essential for the safety assessment of insect-protected corn line MON 810, this work will be reviewed by ANZFA as additional supporting data when it becomes available.

Conclusion

Insect-protected corn line MON 810 is equivalent to other commercially available corn in terms of its safety and nutritional adequacy.

2. Labelling of food produced from insect-protected corn

Clause 3 of Standard A18 prescribes mandatory labelling of a food produced using gene technology, when it contains new or altered genetic material, and where it is not substantially equivalent in any characteristic or property of the food. As Yieldgard corn has been found to be equivalent to non-GM varieties there is no requirement for mandatory labelling under the current standard.

It should be noted, however, that the labelling provisions in Standard A18 are in the process of being amended and may result in the mandatory labelling of some Yieldgard corn food products.

3. Issues arising from public submissions

3.1 General issues

Six applications including this application were advertised together and most of the comments received did not specifically address an individual application. Many of the submissions received in both the first and second rounds of public comment raised issues of a general nature relating to gene technology or issues that had already been addressed in the safety assessment report (see Attachment 2). A discussion of some of the general issues in relation to gene technology that were raised in public submissions can be found in Attachment 6.

3.2 Specific issues

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

(i) Feeding studies

Both the Consumer's Federation of Australia and the Natural Law Party express possible concerns over the safety and/or palatability of Yieldgard Corn, based on the results of feeding studies carried out with INGARD cottonseed. This product, dealt with separately under Application A341, is similar to Yieldgard corn in that it too produces insecticidal proteins

derived from B.t.k. In feeding studies with INGARD cottonseed, where rats were fed a diet containing either raw INGARD cottonseed or raw seed from the C312 control cotton at varying concentrations for a period of 4 weeks, food consumption was decreased slightly and a proportion of the animals exhibited decreased body weight gains in the first week of the study. The Consumer's Federation of Australia suggest that in the light of these results, similar feeding studies should be carried out with Yieldgard corn before release of the product.

Response

A full evaluation of the results of this feeding study can be found in the safety assessment report for Application A341. The overall conclusion was that the applicant's explanation of reduced palatability, rather than any direct toxic effect was reasonable. Tissue analysis and post mortem studies indicated no treatment-related differences between the INGARD cotton and control groups. The palatability issues appear to be due to compounds specific to cottonseed, and it is not expected that similar results would be seen with corn. For explanation of other toxicity issues, please see the safety assessment at Attachment 2. As mentioned above, Monsanto are in fact presently undertaking feeding studies with Yieldgard corn. While not considered essential for the safety assessment, the data will be reviewed by ANZFA when available as additional supporting data.

(ii) Toxicity and allergenicity of Bt-proteins

The Australian GeneEthics Network states that the *Bt* insecticidal proteins have no history of safe use in the animal and human food supplies and their long-term impacts are unknown.

Response

While it is correct that the *B.t.k.* protein Cry1A(b) is not commonly used directly as a food or in a feed source, it is nevertheless ubiquitous in nature and commonly present as a contaminant on food. The donor organism *Bacillus thuringiensis* subsp. *kurstaki (B.t.k.)*, which produces the insecticidal protein, is the basis of microbial formulations that have been commercially available for Lepidopteran insect control for over 30 years. These microbial formulations have been used on a wide variety of crops, including fresh produce like lettuce and tomato, with no reported allergenic responses. The protein produced by Yieldgard corn is identical to that found in nature and in commercial *B.t.k.* formulations. On the question of possible immunological effects, Cry1A(b) shares no biochemical properties common to known allergenic proteins. On the basis of the biochemical profile of the *B.t.k.* protein therefore, there is no scientific evidence to indicate that either of the proteins are potentially allergenic. It is therefore concluded that there are no likely adverse effects of consuming food products derived from corn containing these proteins.

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

(i) The New Zealand Ministry of Health have requested that the animal feeding studies that are currently being conducted should be assessed once completed. The National Council of Women of Australia, the Dietition's Association of Australia, the Canberra Consumer, the (New Zealand) Environment and Scientific Research Institute and the South Australian Department of Human Services do not believe the genetically modified insect-protected corn in this application should be approved until after the feed studies have been assessed.

Response

Monsanto are completing a feeding study using corn from insect protected corn line MON 810 and ANZFA is anticipating a report by the end of 2000. This data will be assessed once available. As it was concluded that feeding studies were not required for this application, given the information provided on the nature of the modification as well as the compositional analysis of nutrients and potential anti-nutrient factors, this application can proceed and the additional information assessed when available.

(ii) Angela Hough from the University of Auckland advised of some minor corrections in the safety assessment.

Response

The corrections have been made in the safety assessment.

4. Risk management

Under Standard A18, a GM food must undergo a safety assessment in accordance with ANZFA's safety assessment guidelines. The requirement for the food to be labelled must also be assessed in accordance with the labelling criteria specified in clause 3 of the standard.

On the basis of the conclusions from the safety assessment report, together with a consideration of the public submissions, it is proposed that Table 1 to clause 2 of Standard A18 be amended to include food from insect-protected corn line MON 810. The proposed amendment is provided in Attachment 1.

In relation to labelling of the food, the safety assessment report found that food from insect-protected corn line MON 810 is substantially equivalent to from other commercially available corn in terms of its safety and nutritional adequacy. Therefore, under the current standard, no mandatory labelling is required, although this may change when the proposed changes to the labelling provisions of Standard A18 have been finalised.

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

REGULATORY IMPACT ASSESSMENT

The benefits and costs associated with the proposed amendment to Standard A18 have been analysed in a draft Regulatory Impact Statement (Attachment 3). The benefits of the proposed Standard A18 amendment to approve food from insect-protected corn line MON 810 primarily accrue to the food industry and government, with potentially a small benefit to the consumer.

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

CONCLUSIONS

ANZFA recommends the adoption of the draft variation (Attachment 1) for the following reasons:

- The introduced gene in insect-protected corn line MON 810 is not considered to produce any increased public health and safety risk;

- Insect-protected corn line MON 810 is equivalent to other commercial varieties of corn in terms of its safety and nutritional adequacy;

- Based on the data submitted in the present application, food derived from insect-protected corn line MON 810 does not require labelling under the current provisions of Standard A18 as it is substantially equivalent to food derived from non-GM corn. Proposed amendments to the labelling provision of Standard A18 currently under consideration could result in some Yieldgard corn food products being labelled in the future; and

- The benefits to government, consumers and industry associated with the proposed amendment outweigh the costs.

ATTACHMENTS

1. Variation to the Australian *Food Standards Code*
2. Final 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 AUSTRALIAN FOOD STANDARDS CODE

A346 - FOODS FROM INSECT-PROTECTED CORN

To Commence: on gazettal

Standard A18 *is varied by inserting into Column 1 of the Table to clause 2 -*

Food derived from insect-protected corn line MON 810.

If Standard 1.5.2 has been adopted by the Ministerial Council at the time this recommendation is considered, the following applies -

To Commence: on gazettal

Standard 1.5.2 *is varied by inserting into Column 1 of the Table to clause 2 -*

Food derived from insect-protected corn line MON 810.

ATTACHMENT 2

FINAL SAFETY ASSESSMENT REPORT

A346 – FOOD DERIVED FROM INSECT-PROTECTED CORN LINE MON 810

SUMMARY AND CONCLUSIONS

The insect-protected corn line MON 810 has been assessed by ANZFA to evaluate its safety in food products. A number of criteria are used in this assessment including a characterisation of the genes, their origin and function, the changes at the DNA, protein and whole food levels, stability of the introduced genes in the corn genome, compositional analyses, evaluation of intended and unintended changes and the potential allergenicity or toxicity of the newly expressed proteins.

Nature of the modification

One genetically modified corn line (MON 810) was generated by the transfer of the *cry1*A(b) gene into the parental line (genotype Hi-II) and confers protection against attack from insects. The protein product is an insecticidal crystal protein, whose toxic effect is specific to Lepidopteran insects, in this case the European Corn Borer. No other genes were transferred to the corn plant. The introduced gene for *cry1*A(b) was found to be stably integrated into the corn plant genome and is phenotypically and genetically stable over multiple generations.

General safety issues

This *Bacillis thuringiensis* (Bt) insecticidal protein has a long history of use in agriculture as a biopesticide and no evidence of adverse health effects has emerged. The newly expressed Cry1A(b) protein was detected in corn leaf, kernels, whole plant and pollen in very small amounts (>0.001% total protein).

The insect-protected corn line MON 810 does not contain any antibiotic resistance genes and therefore poses no risk to the development of antibiotic resistant pathogenic bacteria.

Toxicological issues

Data for the newly expressed Cry1A(b) endotoxin in the insect-protected corn line MON 810 has been evaluated for its potential toxicity to humans. No signs of toxicity were observed among mice following acute oral doses up to 4000 mg/kg Cry1A(b) of the endotoxin and no significant similarity to the amino acid sequence of known toxins was identified.

An examination of the digestion of the proteins in simulated mammalian digestive systems resulted in rapid digestion of the proteins. Additionally, the protein does not have chemical or physical characteristics that are typical of known food allergens. Amino acid sequence analysis did not reveal any similarities to known allergens.

Therefore, the evidence does not indicate that there is any potential for the protein to be toxic or allergenic to humans.

Nutritional Issues

Comprehensive nutrient analyses did not indicate any significant differences in the levels of major constituents, nutrients or anti-nutritional factors between insect-protected corn line MON 810 and the control corn lines. The major components assessed on corn kernels were

proximate (protein, fat, moisture, calories, carbohydrates and ash), amino acids, fatty acids, inorganic components, carbohydrate and tocopherols. The level of the anti-nutrient trypsin inhibitors was also analysed.

These analyses confirm that insect protected corn line MON 810 is nutritionally and compositionally comparable to other corn lines and that no health or safety risks are posed by consuming food derived from the genetically modified corn.

Conclusion

No potential public health and safety concerns have been identified in the assessment of insect protected corn line MON 810. Based on the data submitted in the present application, food derived from this corn line can be regarded as equivalent to food derived from conventional corn in respect of its composition, safety and end use.

1. BACKGROUND

Monsanto Australia Ltd have made an application to ANZFA to vary Standard A18 to include food derived from insect-protected corn in the Table to the standard.

The insect-protected corn plants are known commercially as Yieldgard corn as they are protected against attack from Lepidopteran attack, particularly the European Corn Borer. The corn was developed by Monsanto Ltd for cultivation in the United States. Products derived from corn harvested from these plants may have been imported into Australia and New Zealand.

Domestic production of corn in both countries is supplemented by a small amount of imported corn-based products, largely as high-fructose corn syrup, which is not currently manufactured in either Australia or New Zealand. Other products include maize starch which is used by the food industry for the manufacture of dessert mixes and canned foods and corn-based ingredients processed into breakfast cereals, baking products, extruded confectionary and corn chips.

2. DESCRIPTION OF THE MODIFICATION

Monsanto submitted the following report in support of their application:

J. Kania, P. Keck, E. Levine and P.R. Sanders. 1995. Molecular analysis of insect-protected maize line MON 810. Monsanto Company, USA 63198.

2.1 Methods used in the genetic modification

Using particle bombardment, the parental corn line (genotype Hi-II) was simultaneously transformed with two plasmids:

i) PV–ZMBKO7 which contains:

- the *cry1*A(b) gene for insect resistance; and
- the *npt*II gene for antibiotic resistance;

ii) PV-ZMGT10 which contains:

- *the* gox *gene for glyphosate tolerance;*
- *the CP4 EPSPS gene for glyphosate tolerance; and*
- *the* npt*II gene for antibiotic resistance.*

Both the gox and CP4 EPSPS genes allow the selection of transformed plants under application of glyphosate (Barry et al, 1992). The bacterial nptII gene is a marker used to select transformed bacteria from non-transformed bacteria during the DNA cloning and recombination steps undertaken in the laboratory prior to transformation of the plant cells (Bevan et al, 1983).

Transformation with and selection for these plasmids resulted in line MON 810 which is the subject of assessment. The transformations resulted in the transfer of only one gene - the *cry1*A(b) gene from *Bacillus thuringiensis* subsp. kurstaki strain HD-1.

No genes conferring glyphosate tolerance or antibiotic resistance were transferred to line MON 810.

2.2 Function and regulation of the novel gene

Although there was the potential for the transfer of four genes into the corn lines, only one gene, the *cry1*A(b) gene was transferred into line MON 810.

All genes require regulatory sequences that allow them to be transcribed into RNA and then translated into a protein product which are outline in Table 1. These sequences are termed promoter, terminator or polyadenylation sequence and enhancer sequence. A promoter is the key control element that enables a gene to be transcribed into messenger RNA (mRNA) and a terminator is a DNA (polyadenylation) sequence which stops the transcription of mRNA. These sequences can be unique in each organism and thus regulatory elements that already exist in plants are often used in gene constructs to enable functioning in the plant.

Table 1. Description of the gene transferred to corn Line MON 810

	Gene	**Promoter**	**3' untranslated region**	**Enhancer**
	cry1A(b)	E35S	NOS 3'	*hsp70*
Source of sequence	*Bacillus thuringiensis*	Cauliflower Mosaic Virus	*Agrobacterium tumefaciens*	Maize

The cry1*A(b) gene includes the following regulatory elements:*

(i) the 35S promoter region of the cauliflower mosaic virus (CaMV);

(ii) the intron from the maize *hsp70* gene (heat shock protein); and

(iii) the 3' untranslated region of the nopaline synthase gene (NOS 3') from the Ti plasmid of *Agrobacterium tumefaciens*. The NOS 3' sequence provides the polyadenylation signal for stable expression.

The CaMV E35S promoter enables the constitutive, high-level expression of the

*cry*1A(b)gene. It is widespread in nature and is often present in many plants (Odell *et al*, 1985). The enhancer region of a maize intron for the *hsp70* gene is present to increase the levels of gene transcription (Rochester *et al*, 1986). The NOS 3' sequence is present to stop the transcription of the gene by providing a mRNA polyadenylation signal (Fraley *et al*, 1983).

The Cry1A(b) gene

Bacillus thuringiensis (Bt) is the accepted name for a range of soil dwelling, aerobic spore-forming bacteria that form a crystal protein during sporulation that is toxic to insects. Studies of the physical properties of the crystal protein structure and screening of many Bt strains have revealed that there are a multitude of crystal types and subsequent spectrum of activity. It is widely accepted that there are four major classes of the crystal protein genes (cry) that are Lepidoptera specific (cry1), Lepidoptera and Diptera specific (cry2), Coleoptera specific (cry3) and Diptera specific (cry4) (Drummond and Pinnock, 1991; Cooper 1991; Noteborn *et al*, 1995).

The cry1A(b) gene relevant to this application, encodes a nature identical Cry1A(b) insecticidal crystal protein, whose toxic effect is specific to Lepidopteran insects. During sporulation, B. thuringiensis produces cytoplasmic inclusions containing one or more of the insecticidal crystal protein or delta–endotoxin. Most crystal proteins are synthesised intracellularly as inactive protoxins that spontaneously form small crystals, approximately 1 µm in size. Upon ingestion by susceptible insects, the highly alkaline pH of the midgut promotes solubilisation of the protoxin–containing crystals. The protoxin is then activated by trypsin–like gut proteases which cleave off domains from the carboxy– and amino– termini leaving a protease–resistant core which is the active toxin. The now active toxin binds to a highly specific glycoprotein receptor on the surface of midgut epithelial cells in the insect. When about eight of these core proteins aggregate together, they form a pore through the cell membrane. These cells eventually swell and burst, causing loss of gut integrity and resulting in larval death within 1 to 2 days (Cooper, 1991; Hofte and Whitely, 1989).

The cry1A(b) gene sequence was modified to increase the levels of expression in corn (Perlak et al, 1991). The native gene contained A+T rich regions that could be potential polyadenylation sites and codons that are not frequently used in plant genes thus impairing its expression in the plant. The cry1A(b) gene sequence was modified to reflect plant codon usage therefore allowing efficient expression in the plant.

2.3 Characterisation of the genes in the plant

Southern blot analysis is used to detect the presence of specific DNA sequences and to establish the mode, number and stability of inserted DNA (Lewin, 1997). In line MON 810, Southern blot analysis was used to demonstrate that there was a single DNA copy of the *cry1*A(b) gene, of approximately 5.5 Kb inserted into corn line MON 810. Southern blot analysis did not detect the presence of the *nptII* gene nor any DNA from plasmid PV-ZMGT10 (ie. the CP4 EPSPS, *gox* and *nptII* genes) suggesting that only the *cry1*A(b) gene had been inserted in corn line MON 810.

2.4 Stability of the genetic changes

The stability of inserted DNA was demonstrated using ELISA analysis and insect feeding

assays. Segregation analysis for line MON 810 is consistent with a stable, single dominant gene segregating according to Mendelian genetics. The insect-protected phenotype and inheritance pattern have been consistent over multiple generations.

Conclusion

Insect-protected corn line MON 810 was generated using the particle bombardment transformation system to transfer the *cry*1A(b) gene to corn. No other genes were transferred during transformation. The DNA has transferred into the corn genome as a single and stable DNA insert.

3. GENERAL SAFETY ISSUES

The corn used in compositional analyses to assess the safety of the inserted DNA was grown at six locations throughout the USA. The insect-protected corn has been evaluated against the safety assessment guidelines developed by ANZFA (ANZFA, 1999). As the data presented is for the whole kernel, the safety assessment issues relate to Group D foods – food ingredients.

Monsanto submitted the following reports in support of their application:

K.A. Croon *et al* , 1995. Safety, compositional and nutritional aspects of insect-protected corn line MON 801: conclusion based on studies and information evaluated according to FDA's policy on foods from new plant varieties. Submitted to FDA on September 15, 1995

K.A. Croon, P.R. Saunders and R.L. Fuchs. 1996. Safety, compositional and nutritional aspects of insect-protected corn line MON 809 and MON 810: Conclusion based on studies and information evaluated according to FDA's policy on foods from new plant varieties. Monsanto # 96-102F

The insect-protected corn is largely imported for processing into a diverse range of products including breakfast cereals, baking products, extruded confectionary and corn chips. Maize starch is used by the food industry for the manufacture of dessert mixes and canned foods. The corn products that Australia and New Zealand currently import are largely highly processed products, particularly high fructose corn syrup. It is noted that the import of corn products may significantly increase in the future.

3.1 History of the use of corn as a food source

Corn is widely cultivated on nearly every continent and represents a staple food for a significant portion of the world's population. Most of the corn consumed by humans are corn-based food items rather than whole kernel or processed corn. These products are routinely used in food and have a long history of safe use.

The largest use of corn in the USA is as animal feed for cattle, chickens and pigs.

3.2 Nature of the novel protein

The *cry1A*(b) gene is derived from the soil bacterium *Bacillus thuringiensis* subsp. *kurstaki* (*B.t.k*) strain HD-1 (Fischoff *et al,* 1987). It encodes a full length *B.t.k* DH-1 (ie Cry1A(b)) protein of 1156 amino acids (131 kDa). Upon digestion by trypsin, an active trypsin-resistant protein of approximately 600 amino acids is produced (63 kDa).

The *cry*1A(b) gene sequence in insect protected corn line MON 810, has been modified to improve the expression in the plant. Expression of the *cry1A*(b) results in a full length delta–endotoxin that is identical to the one produced by *B. thuringiensis* subsp *kurstaki*, strain HD-1 (*B.t.k* HD-1). Under digestive conditions, the full length delta-endotoxin is cleaved to produce the active trypsin-resistant core protein. Both the full length delta–endotoxin and smaller trypsin resistant core protein produced in line MON 810 are identical to the naturally occurring full length Cry1A(b) delta–endotoxin and the cleaved active core protein produced by *B. thuringiensis* subsp *kurstaki*.

This trypsin resistant core protein is equivalent to the *E. coli* produced B.t.k. HD-1 (trypsin resistant core protein) which is widely used as a biopesticide.

3.3 Expression of novel protein in the plant

Two techniques are widely used to detect and quantify the products of genes (ie proteins) that are present in the tissue analysed. Enzyme linked immuno-sorbent assay (ELISA) is a highly sensitive technique that can detect the presence of a protein approximately to a sensitivity of 10-100 ρg. Western blot analysis is a highly specific technique also used for the detection of proteins (Lewin, 1997). Both techniques were used to analyse protein expression in leaf, kernel, whole plant tissue and pollen from the insect-protected corn line.

Cry1A(b)

ELISA and western blot analyses of leaf, kernel, whole plant tissue and pollen from the insect-protected corn line MON 810 demonstrated that the Cry1A(b) delta–endotoxin protein is expressed at very low levels in all tissues tested (Table 2) and constitutes less than 0.001% of the total protein in each tissue. The *cry1*A(b) gene is the only gene expressed in line MON 810 and was expressed highest in the leaves (Table 2).

Table 2: Protein expression levels in the insect-protected corn lines as determined by ELISA analysis

Corn Line MON 810	**Mean expression levels and ranges (µg/g fresh weight) [1]**							
	Leaf		**Grain**		**Whole Plant[2]**		**Pollen[3]**	
	Mean	Range	Mean	Range	Mean	Range	Mean	Range
Cry1A(b)	9.35	7.93-10.34	0.31	0.19-0.39	4.15	3.65-4.65	0.09	na
CP4 EPSPS	nd[4]	-	nd	-	nd		na	-
GOX	nd	-	nd	-	nd		na	-
nptII	na[4]	-	na	-	na		na	-

[1]Values are means from six plant samples ie. n=6. One plant is taken from each site unless otherwise noted.
[2]Values are means from sample(s) from replicate plant samples.
[3]Values are means from sample(s) from one site only (n=6).
[4]na: not assayed; nd: not detected; -: not applicable.

CP4 EPSPS, GOX and nptII Proteins

CP4 EPSPS and GOX proteins were not detected by ELISA or western blot analysis in leaf, kernel and whole plant tissue from corn line MON 810, confirming the results from the Southern blots which indicated that these genes had not been transferred.

Given that the *nptII* gene was not detected by Southern blots and that it is under the control of a bacterial promoter, it is not expected to be expressed in the transformed plant cells (WHO, 1993) and no analysis were done to detect this protein.

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

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

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

The major concern in relation to the transfer of novel genetic material to gut microorganisms is with antibiotic resistance genes.

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). There are concerns, however, that there could be horizontal gene transfer of the antibiotic resistance gene from ingested food to gut microorganisms and that if the microorganisms are able to express the transferred resistance gene this could lead to an increase, in the gastrointestinal tract, of microorganisms resistant to a specific antibiotic. This, in turn, might lead to an increased potential for the transfer of the antibiotic resistance gene to pathogenic microorganisms, thus compromising the therapeutic use of such antibiotics. There are further concerns that, if the antibiotic resistance gene is expressed in the plant, the expressed protein, when ingested, could inactivate oral doses of the antibiotic to which it confers resistance.

The insect-protected corn line MON 810 does not contain an antibiotic resistance gene as indicated by the Southern blot experiments and therefore no protein product from this gene is possible. The only gene transferred is the insect-protection cry1A(b) gene which is not considered to pose any health risk. Additionally, the products from insect-protected corn are largely consumed as processed corn products and the processing is likely to destroy the function of any DNA present in the food.

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

It is equally unlikely that novel genetic material will transfer from GM foods to human cells via the digestive tract. In considering the potential impact on human health, it is important to note that humans have always consumed large amounts of DNA as a normal component of food and there is no evidence that this consumption has had any adverse effect on human

[3] Food and Agriculture Organization.

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.

Conclusion

The experiments show that the *cry*1A(b) gene is expressed in insect-protected corn line MON 810 and is expressed at relatively low levels in leaves, kernels and at a virtually negligible level in pollen. Given the history of safe use of Bt in agriculture and that it has been considered non-toxic to humans and other non-target organisms, the transfer of the *cry*1A(b) to corn is not considered to risk public health and safety.

4. TOXICOLOGICAL ISSUES

Monsanto submitted the following reports in support of the application:

T.C. Lee and M. Bailey. 1995. Assessment of the equivalence of *B.t.k*. HD-1 Protein produced in several insect-protected corn lines and *Escherichia coli*. Monsanto Company, USA 63198. 95-040E

T.C. Lee, M. Bailey, S. Sims, J. Zeng, C.E. Smith, A. Shariff, L.R. Holden and P.R. Sanders. 1995. Assessment of the equivalence of *Bacillus thuringiensis* susp. kurstakis HD-1 Protein produced in *Escherichia coli* and European corn borer resistant corn. Monsanto Company, USA 63198.

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 newly-expressed protein

The crystal protein produced by insect-protected corn line MON 810 is identical to the protein produced by the *B. thuringiensis* formulations that have been used commercially for many years to control insect pests. There is no evidence from this history of use that there is any associated toxicity to humans. The toxicity of these proteins is very specific to Lepidoptera and there is no evidence that they are active against non–target insects, birds, fish or mammals (Drummond and Pinnock, 1991). This lack of activity against non–target species appears to be due to a number of factors including physical differences in the gut environment and an absence of specific gut receptors (Frick 1995) in other organisms. The binding of the delta–endotoxin to specific gut receptors appears to be a pre–requisite for toxicity (Cooper, 1991).

Monsanto submitted the following reports in support of the application:

J. Astwood. 1995. *Bacillus thuringiensis* susp. kurstakis HD-1 insecticidal protein (*B.t.k*. HD-1 protein) is homologous to proteins of the *Bacillus thuringiensis* insecticidal crystal protein gene family, but not to protein toxins found in public domain sequence databases. Monsanto Company, USA 63198. MSL-14283

M.W. Naylor. 1992. Acute oral toxicity study of *B.t.k*. HD-1 tryptic core protein in albino mice. Monsanto Company, USA 63198. MSL-11985

The potential for toxicity of the newly expressed proteins, Cry1A(b), were evaluated based on:

. the amino acid sequence similarity with known toxins
. acute toxicity testing in mice.
. the resistance to digestion by proteases and acids in the model digestive/gastric system
. their presence as a major protein component in a specified food.

An amino acid sequence comparison of the Cry1A(b) to a database of known allergens detected significant similarities only to other *B. thuringiensis* insecticidal crystal proteins.

An acute oral toxicity study was done to assess the potential mammalian toxicity of the Cry1A(b) protein. The test protein was produced by fermentation in *E. coli* because the plant lines did not express enough protein for purification of large quantities for toxicity testing. Data was presented to indicate that the bacterially produced Cry1A(b) protein is equivalent to the plant produced Cry1A(b) protein in terms of its molecular mass and immunological cross-reactivity. Therefore the *E. coli* produced Cry1A(b) protein is a suitable substitute for plant produced Cry1A(b) in toxicity testing.

The Cry1A(b) core protein (B.t.k. HD-1 trypsin resistant core protein) was administered to groups of ten CD-1 mice/sex using doses up to 4000 mg/kg body weight. These doses are well above the level of expression found in insect-protected corn plants (refer to Table 2) and represent a test using 200-1000 fold increase in amount of protein that would be expected by consuming the genetically modified plants. A group of mice (vehicle control group) were administered 4000 mg/kg bovine serum albumin and another control group (also termed vehicle control group) were administered 66.66 mg/kg carbonate buffer.

Clinical observations were performed and body weights and food consumption were determined. One female mouse belonging to the vehicle control died during the test — on day 1. The death of the control female was considered a result of the intubation procedure. As there were no deaths in other treated mice, or at higher exposure levels, the death is not considered to be treatment related. All surviving animals were necropsied at study termination (8-9 days). Mice were observed up to 9 days after dosing and no treatment related effects on body weight, food consumption, survival, or gross pathology were observed for mice administered the B.t.k HD-1 core protein.

4.3 Levels of naturally occurring allergenic proteins

There are no naturally occurring allergenic proteins known to occur in corn (Wright, 1987).

4.4 Potential allergenicity of novel proteins

The Cry1A(b) protein expressed in insect-protected corn plants is identical to the protein contained in microbial formulations that have been used on crops for 30 years (Milner, 1991). The protein assessed in this application is a very safe form of insect control from the human or animal consumption view point, as the acidic pH in the animal digestive system does not permit processing of the delta-endotoxins to an active form (Vandemark, 1999). This effectively provides a mechanism for a specificity of action against only Lepidopteran insects. Also, in its long history of use, there have been no reported allergenic responses for this protein.

Monsanto submitted the following reports in support of the application:

J. Astwood. 1995. *Bacillus thuringiensis* susp. kurstakis HD-1 insecticidal protein (*B.t.k*. HD-1 protein) shares no significant sequence similarity with proteins associated with allergy or Coeliac disease. Monsanto Company, USA 63198. MSL-14172

J.E. Ream and R.L. Fuchs. 1994. Assessment of the in vitro digestive fate of *Bacillus thuringiensis* susp. kurstakis HD-1 protein. Monsanto Company, USA 63198.

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 Cry1A(b) protein is evaluated for potential allergenicity against these criteria: size, digestive degradation and sequence similarity to known allergens.

The Cry1A(b) core protein has a molecular weight of 63 kDa, which is in the size range of known allergens.

The amino acid sequence of the Cry1A(b) protein was compared to the amino acid sequences of 219 known allergens present in public domain databases (eg GenBank, EMBL, Swissprot, PIR). No biologically significant homology was found with any of these known allergens.

The digestibility of Cry1A(b) *B.t.k* HD-1 protein was determined experimentally using *in vitro* mammalian digestion models. Purified Cry1A(b) trypsin-resistant core protein (63 kDa) was added to simulated gastric and intestinal fluids and incubated at 37ºC. The protein used was from the same batch that had been produced in *E. coli* for acute toxicity testing in mice. The degradation of the protein in the digestion fluid was assessed over time by Western blot analysis. An insect bioassay was used as an additional means of monitoring *B.t.k* HD-1 degradation in the digestion fluids. The simulated digestion fluids were prepared according to procedures outlined in the United States Pharmacopeia (1990).

The 63 kDa *B.t.k* HD-1 core protein was shown to be rapidly degraded in the simulated gastric system. It was 90% degraded after 2 minutes incubation in the simulated gastric fluid as determined by Western blot analysis. Bioactivity of the *B.t.k* HD-1 protein also dissipated readily with up to 90% dissipated after 2 minutes incubation in the simulated gastric fluid.

In the simulated intestinal fluid, the *B.t.k* HD-1 protein did not degrade substantially after approximately 19.5 hours incubations as assessed by both Western blot analysis and insect bioassay. The stability of the trypsin-resistant core protein in the intestinal system is expected as other *Bacillus* insecticidal proteins have been shown to be resistant to digestion by serine proteases (Hofte and Whitely 1989), like trypsin which is the predominant proteolytic component in the intestinal fluid.

The *B.t.k* HD-1 Cry1A(b) protein does not possess the characteristics typical of many known allergens nor does it show significant homology to known allergens. Furthermore, the Cry1A(b) protein is rapidly digested in conditions that mimic human digestion.

Conclusions

The evidence does not indicate that there is any potential for the Cry1A(b) protein to be either toxic or allergenic to humans. The source of the cry1A(b) gene has a long history of use on food crops as a biopesticide and no evidence of adverse effects. The Cry1A(b) protein has no amino acid similarity to known allergens or toxins. Additionally, the protein is expressed at a relatively low level in the corn and is rapidly digested in model digestive systems.

5. NUTRITIONAL ISSUES

A range of analyses were performed on the insect protected corn line MON 810. The proximate analysis, amino acid composition and fatty acid profiles of the genetically modified and control corn tissue and kernels were analysed under GLP at Corning Hazelton Inc (Madison, Wisconsin) using recognised published methods in accordance with the Association of Official Analytical Chemists (AOAC, 1990).

Monsanto submitted the following reports in support of their application:

P.R. Sanders. 1995. Compositional analyses of insect-protected corn line MON 810 from the 1994 field trials. Monsanto Company, USA 63198. MSL-14384

P.R. Sanders, E.N. Elswick, M.E. Groth and B.E. Ledesma. 1995. Evaluation of insect-protected corn line MON 810 in 1994 US field trials. Monsanto Company, USA 63198.

P.R. Sanders, D.M. Henning and M.E. Groth. 1996. Compositional analyses of insect-protected and insect-protected Roundup Ready corn lines from the 1994 US Field Trials. Monsanto Company, USA 63198.

Sanders and Patzer, 1995. Compositional analyses of MON 801 grain and silage from the 1993 and 1994 US field test locations. Study no. 94-01-39-08, an unpublished study conducted by Monsanto Company.

5.1 Nutrient analysis

Compositional analyses were done on the insect-protected corn line and comparisons were made to the control line (818 which is derived from the Hi-II) and lines of similar genetic background (MON 800/801) that have been previously reported by the applicant and is listed in the reports above (Sanders and Patzer, 1995). Line MON 810 was grown in six field locations in 1994 according to quality assurance guidelines. Seed grown from each of the six sites was analysed and the data subject to statistical analyses. The corn kernels were analysed for compositional quality characteristics according to GLP using standardised analytical methods.

Proximate analysis for major constituents

Proximate analyses were done on corn kernels. Components measured were protein, fat, moisture, calories, carbohydrates and ash and these values are found in Table 3.

As a percentage of dry weight, the component analyses for line MON 810, are approximately:

protein 13.1%; fat 3.0%; moisture 12.4%; calories 408 Kcal/100g; ash 1.6%; and carbohydrate 82.4%. In all of the component analyses of line MON 810, there were no significant differences between the insect-protected corn and the control line.

Table 3: Mean values and ranges of Proximate Analyses for corn trials

	Control[2]		MON 810[2]	
	mean	**range**	**mean**	**range**
Protein[1]	12.8	11.7-13.6	13.1	12.7-13.6
Fat[1]	2.9	2.6-3.2	3.0	2.6-3.3
Ash[1]	1.5	1.5-1.6	1.6	1.5-1.7
Carbohydrate[1]	82.7	81.7-83.8	82.4	81.8-82.9
Calories Kcal/100g[1]	409	406-410	408	407-410
Moisture	12.0	10.6-14.2	12.4	11.0-14.4

[1]Data as a percentage of dry weight.
[2]Value is the mean of six samples (n=6), one from each of six sites.

Amino acid analysis

Amino acid analyses were done on insect-protected corn kernels. Of the 18 amino acids analysed, the values were comparable for the insect-protected corn and control line, with few exceptions (Table 4).

In line MON 810, the mean values for eight amino acids were significantly different from the values for the control line ($p>0.05$) but were within the values reported in the literature (Watson, 1982; Watson, 1987) or for a corn line with a similar genetic background (Table 4) and thus were not considered to represent a meaningful difference.

Table 4: Profile of the amino acid levels that were significantly different to control

Amino Acid	MON 810[1]	Control (818)	Literature Range[2]	Lines 800/801[3]
cysteine	2.0	1.9	1.2-1.6	1.9-2.3
tryptophan	0.6	0.6	0.5-1.2	0.5-0.6
histidine	3.1	2.9	2.0-2.8	2.8-3.3
phenylalanine	5.6	5.4	2.9-5.7	5.2-5.6
alanine	8.2	7.8	6.4-9.9	7.8-8.2
proline	9.9	9.6	6.6-10.3	9.0-9.4
serine	5.5	5.2	4.2-5.5	5.5-6.1
tyrosine	4.4	4.0	2.9-4.7	3.8-4.3

[1]All values shown are percentage of total protein present
[2]Watson, 1982; Watson 1987.
[3]Lines of a similar genetic background evaluated by the applicant (Sanders and Patzer, 1995)

Fatty acid analysis

Corn oil is an excellent source of polyunsaturated fatty acids, with a high level of the essential fatty acid linoleic acid (18:2). In addition, it has naturally low levels of the saturated fatty acids, palmitic acid (16:0, 11%) and stearic acid (18:0, 2%). Corn kernels from insect protected and control corn lines were subject to analysis to determine the fatty acid profile. The components measured that were within the detectable limits of the assay were palmitic acid (C16:0), stearic acid (C18:0), oleic acid (C18:1 cis), linoleic (C18:2), and linolenic (C18:3). The fatty acids which were not detectable in the assay were: caprylic, capric, lauric,

myristic, myristoleic, pentadecanoic, heptadecanoic, eicosadienoic, eicosatrienoic and arachidonic. There were no statistically significant differences between line MON 810 and the control line (Table 5).

Table 5: Fatty acid composition of corn kernels[1]

Fatty Acid	Control		MON 810		Literature Range[2]
	Mean	Range	Mean	Range	
Linoleic (18:2)	63.0	61.8-64.6	62.6	59.5-64.7	35-70
Oleic (18:1)	22.8	21.6-23.9	23.2	21.5-25.4	20-46
Palmitic (16:0)	10.5	10.2-10.7	10.5	10.2-11.1	7-19
Stearic (18:0)	1.8	1.8-1.9	1.9	1.7-2.1	1-3
Linolenic (18:3)	0.9	0.8-0.9	0.8	0.7-0.9	0.8-2

[1]Value of fatty acid is % of total lipid. n=6
[2]Watson, 1982; Watson 1987.

Inorganic components analysis

Inorganic component analysis was done on corn kernels. Like other cereal grains, corn is very low in calcium, and low in other minerals including phosphorus, potassium and magnesium. The components measured were percentage calcium and phosphorus. The value for phosphorus for the insect-protected corn line was not significantly different to the control line. The value for calcium in insect-protected corn line MON 810 (0.0036%) was significantly different to the control corn line (0.0033%) but was not considered to represent a biologically meaningful difference as the value was within the range reported by the applicant for control corn lines with a similar genetic background (0.0030 – 0.0040%) (Sanders and Patzer, 1995).

Table 6: Analysis of Carbohydrates, Tocopherols and Inorganic components of corn kernels[1]

Component	Control		MON 810		Literature Range[2]
Inorganic	**Mean**	**Range**	**Mean**	**Range**	
% Phosphorus	0.348	0.327-0.363	0.358	0.334-0.377	0.26-0.75
% Calcium	0.0033	0.0029-0.0037	0.0036	0.0033-0.0039	0.01-0.1
Carbohydrates					
% Starch	66.9	64.6-69.0	67.6	65.3-69.7	64-78.0
% Crude Fibre	2.4	2.3-2.5	2.6	2.5-2.8	2.0-5.5
Sugars g/100g					
Fructose	0.27	0.22-0.40	0.32	0.23-0.35	
Glucose	0.41	0.34-0.46	0.44	0.34-0.47	
Sucrose	0.93	0.68-1.11	0.93	0.79-1.12	
Phytic Acid	0.84	0.79-0.91	0.86	0.81-0.91	0.7-1.0
Tocopherols					
alpha	10.9	9.9-12.1	10.4	9.7-11.3	3.0-12.1
beta	7.5	7.0-7.9	8.5	8.1-9.2	
gamma	21.6	18.8-27.8	20.2	15.3-24.8	

[1]Values on a dry weight basis. n=6, one sample from each field site.
[2]Watson, 1982; Watson 1987. Literature ranges provided if available.

Carbohydrate analysis

The carbohydrate components starch, crude fibre, sugars and phytic acid were evaluated in corn kernels (Table 6). The values for all components in the insect-protected corn line except crude fibre value were not significantly different to the control line. The value for crude fibre in line MON 810 (2.6%) was significantly different to the control line (2.4%) but is not considered to represent a biologically meaningful difference as it is within the range reported in the literature (2.0-5.5%) (Watson, 1982).

Tocopherol analysis

Tocopherols are naturally present in corn oil and have vitamin E potency (Watson, 1987). The values for alpha and gamma tocopherol levels in line MON 810 were not significantly different to the control line. The value for beta tocopherols in line MON 810 (8.5%) was significantly different to the control line (7.5%) but was within the range reported for corn lines with a similar genetic background (beta: 7.9-10.7%). There is no published literature for beta tocopherol levels in corn.

5.2 Levels of anti-nutrients

Corn contains few natural toxins or 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). As there are no routine analytical methods for the assessment of trypsin inhibitor activity in corn, the method developed for their study in soybeans was used (AOCS method Ba 12-75, 1997 modified).

The data for trypsin inhibitors was generated from a different set of field trials. Kernel samples were collected from seven hybrid MON 810 corn corn lines from seven field trials in the USA and untransformed control corn samples taken from the seven USA field trials and thirteen commercial hybrid corn plants in Italy and France. The analyses were independently conducted at the Covance Laboratories, Inc., Madison, Wisconsin. The range of values measured for corn from line MON 810 fell within the ranges reported for the control line.

Table 7: Analysis of trypsin inhibitor levels[1]

	Control[2]	**MON 810[2]**
Trypsin Inhibitor	1.63-5.28	2.35-5.54

[1]Values are Trypsin Inhibitor Units/ milligram dry weight basis.
[2]Control n=20; MON 810 n=7, one sample from each of 7 USA field sites.

Analytical methods for analysis of chymotrypsin inhibitors in corn are not known. There was no evidence in the literature searches conducted to indicate that chymotrypsin inhibitors could be a significant anti-nutrient component of the corn grain.

5.3 Ability to support typical growth and well-being

In the evaluation of the safety of genetically modified foods, the requirement for feeding studies is determined on a case by case basis by ANZFA. The nutritional information required depends on the nature of the food and the particular genetic modification. Compositional and other data is sought from the applicant to ensure that the nutritional status

of the consumer is not compromised by the substitution of less nutritious food varieties. Generally this can be assured by careful compositional analysis of nutrients and potential anti-nutrient factors. In some cases, it may be necessary to examine nutrient bioavailability using animal models.

The applicant did not submit feeding studies data for insect-protected corn. Nutritional qualities for the insect-protected corn lines were determined by compositional analyses of the major components of the kernel and these were found to be comparable to the conventional control lines. Acute oral toxicity studies (mice gavage studies) indicated that the newly expressed proteins were not toxic and no significant similarity to known allergens or toxins was found. Additionally, these proteins have been shown to be rapidly degraded in model digestive systems.

There is a long history of safe use of corn based food products and also of the Bt delta-endotoxins as a biopesticide on food crops. Given that Bt proteins have been well characterised and that they are present in the insect-protected corn lines in very minute amounts, there is no evidence to indicate that they will cause a toxic or allergenic reaction. It has also been demonstrated that the genes have been stably introduced into the corn genome. On the basis of the data available, the assessment of feeding studies were not considered essential for the safety assessment of insect-protected corn line MON 810.

Monsanto have informed ANZFA that they have decided to conduct feeding trials for insect-protected corn which are expected to be finalised in late 2000. While not essential for the safety assessment, the data will be reviewed when available as additional supporting data.

Conclusion

Analysis of the compositional data of the kernel indicates that there were few significant differences in the levels of major constituents, nutrients, anti–nutritional factors or natural toxicants between insect-protected corn line MON 810 and the control corn line. The differences that were noted were not considered to represent a meaningful difference because the values were consistent with the values reported in the literature or for a control corn line with a similar genetic background and thus were considered to represent the natural variability that exists within corn.

Acknowledgement

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ATTACHMENT 3

REGULATORY IMPACT ASSESSMENT

Regulatory Impact Assessment

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

Identification of affected parties

1. Governments in Australia and New Zealand

2. Consumers in Australia and New Zealand

3. Manufacturers, producers and importers of food products

Options

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

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

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

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

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

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

Conclusion of the regulatory impact assessment

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

ATTACHMENT 4

WORLD TRADE ORGANIZATION 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 phyto sanitary 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.

It is considered that these Full Assessments do constitute a potential Technical Barrier to Trade or a Sanitary/Phytosanitary matter. Matters raised in these Full Assessments therefore will be notified to the WTO.

ATTACHMENT 5

SUMMARY OF PUBLIC SUBMISSIONS

FIRST ROUND PUBLIC SUBMISSIONS

The Authority received the first six applications for foods produced using gene technology from Monsanto Australia Ltd. Due to commonalities in these applications, a combined Notice of Application (formally referred to as the Preliminary Assessment Report) was advertised on 28 October 1998, which called for public comment on the applications. A total of 58 submissions were received in response to the combined Notice of Application, of which 53 relate to this application.

Jean Adams (Aust)

- does not want these experimental foods in the common food supply until they have been long–term tested for undesirable side–effects related to public health or to environmental damage;
- questions the legality of forcing such genetically modified foods onto the public and the intention to remove labelling of such foods.

Robert Anderson (member of Physicians and Scientists for Responsible Application of Science and Technology)

- knowledge about the nature of the promoter, genes and the type of antibiotic resistance genes is crucial to a proper assessment;
- the applications should be rejected because most of the New Zealand population does not want to eat genetically engineered food. There are real dangers of allergic reactions, the Maori people are opposed to genetic engineering and these products are all an unknown risk to human health because they have not been tested.

Aoraki Greens and the Organic Garden City Trust (NZ)

- opposed to the amendment to the *Food Standards Code* to permit the foods in the applications;
- claim there is no alternative but to decline the acceptance of these products until they are clearly labelled and can be differentiated from their conventional counterparts;
- believe consumer choice is being violated;
- consider that because the science is new, potential problems or long term implications are yet to be made apparent.

Elaine Attwood (Aust)

- supports Option 1 in the combined Preliminary Assessment - that is, to maintain the status quo and not approve any of the six applications;
- re: A338 - considers 4 weeks of laboratory animal testing inadequate and doubts the applicant's claim that the need for herbicide will be reduced. Comments on proposed increase in the MRL for glyphosate;
- re: A355, A362 and A346–genetically modified material will enter the food chain via cotton seed meal and hulls and corn waste being fed to animals;
- re: A363 – canola free of genetic modification would be marketable overseas;

- re: A341 – the results of laboratory feeding studies in rats are of concern. Long term safety is uncertain and therefore the genetically modified cotton should not be permitted;
- trade considerations should not prevail over consumer rights to have all genetically modified foods labelled as such.

Australian GeneEthics Network

- Monsanto's proposals should all be rejected as inadequate;
- there should be pre–market human testing to provide data for a precautionary approach on safety and nutritional efficacy;
- there should be full labelling of all approved foods in keeping with the Ministerial decision;
- there should be public review of the MRLs for Roundup in these foods;
- there should be public review of the toxicity of the quantities of Bt toxins likely to enter the human and animal food supplies, taking cultural, social, ethnic and age diversity into account;
- an adverse reactions register should be established to enable systematic monitoring of any impacts of these foods;
- all proposals should be submitted for GMAC assessment and recommendation including an updated and public review of Bt cotton and Roundup Ready soy for environmental and health impacts;
- GMAC's assumption that AQIS regulations would keep imported soy out of the Australian environment does not apply to the other commodities, and the geographical limits and performance of Bt cotton need public review;
- Monsanto has not studied the dietary implications of these products and presents no evidence that the company considered the diversity of diets among different cultures, social or ethnic groups;
- RR soy and corn crops are very different in containing novel DNA, proteins at elevated levels, and new levels of synthetic chemical residue not in food before;
- RR canola and cotton seed oils are so extensively processed before human consumption that no DNA or proteins will remain. This ignores, for example, the use of whole seeds for sprouting, the inclusion of whole seeds in uncooked foods, and the cold pressing of oils;
- Bt cotton and corn are substantially equivalent to parental lines in composition, safety and wholesomeness, yet Bt has never been in the food supply in such quantities before;
- the toxicological studies of RR foods are brief and insufficient as no chemical residue studies are cited, proteins created by inserted genes have only been checked against known protein toxins and allergens, no human, and very few animal testing of the products has been done, whole genetically engineered soybean, corn, canola or cotton were not checked in simulated gastric and intestinal fluids;
- no toxicological studies were carried out on the Bt crops as Monsanto asserts that "regulatory agencies world-wide have determined that the use of registered B.t.k products pose no significant risks to human health, non-target organisms or the environment." Believes this is grossly misleading as it refers to the topical use of a whole organism which quickly disappears from the environment following spraying, whereas Bt crops express large amounts of toxin throughout their systems.

Berylla (NZ)

- these foods will be in 60–80% of all processed foods therefore freedom to choose will

be compromised;
- as these foods will also be fed to animals, choices will be restricted even further and if the animals were eaten then the degree of risk will increase;
- support the submissions of the Natural Law Party and Clive Elwell.

Willi Borst (NZ)
- wants all genetically modified foods to be labelled and if not they should all be banned;
- concerned about antibiotic resistance, viral recombination and environmental pollution;
- all genetically modified food should be deemed unsafe until proven otherwise;
- submits that ANZFA not amend the *Food Standards Code* to permit foods derived from genetically modified crops.

Jim Chapple (NZ)
- strongly opposed to all six applications on the grounds that approval of these foods may create a market monopoly for the applicant in the supply of agrochemicals and that gene technology is potentially unsafe;
- very strongly objects to the term "substantially equivalent" as a play on words;
- genetically modified foods are not identical to their conventional counterpart and therefore all such products must carry labelling.

Commerce Commission (NZ)
- no issues raised by the applications on which the Commission has any comments.

Consumers' Association of South Australia Inc. (Aust)
- supports comments made by Elaine Attwood.

Clive Elwell (NZ)
- the applications should be rejected because Maori people find genetic engineering in conflict with their beliefs and values, the overwhelming majority of people in Australia and New Zealand do not want to eat genetically modified food, there is a danger of allergic reactions, and genetically modified food is insufficiently tested and so cannot be regarded as safe for human consumption;
- the foods cannot be sufficiently tested because it is impossible to carry out appropriate tests; the tests that are carried out are limited and inappropriate.

Consumers' Federation of Australia Inc.
- not supportive of these applications being approved at this stage;
- questions the safety of soya milk as infant food because of the presence of trypsin inhibitor and other anti–nutrients after heat processing, and also the presence of isoflavones;
- refers to a reference (no details supplied) which has shown that the isoflavone levels may differ from the levels in conventional soybeans;
- application A338 does not provide sufficient evidence of anti-nutrients to prove that the soybeans are safe for processing into infant formula. In light of this, interprets ANZFA's safety assessment guidelines as requiring a full toxicological and nutritional assessment of the soybeans. Believes these concerns are serious enough to warrant a recall of foods containing Roundup Ready soy ingredients;
- no evidence is presented by the applicant on glyphosate residues in A338, A362, and A363, despite a specific requirement to do so in ANZFA's safety assessment guidelines;

- does not accept the assertion by the applicant that there is only one novel protein in the Roundup Ready soybeans;
- does not believe that testing for homology of protein structure is a sufficient test for allergenicity. At the very least these foods should be fed to human volunteers in closely monitored trials before they are released generally;
- traces of the introduced proteins could be present in cold–pressed oils at levels sufficient to precipitate allergic reactions, if there is an allergic potential. At the very least, such oils should carry precautionary labels warning of the possibility of allergic reactions;
- the approval of Roundup Ready maize will facilitate even greater use of high fructose corn syrups in Australian processed foods. The end result of this could well be that consumption of high energy products by Australians will rise and that the current excessive levels of nutritional diseases such as obesity, diabetes and heart disease will increase further;
- ANZFA needs to be satisfied that anti–nutrient levels in canola are safe and that they will not rise over time;
- expresses concern about the decreased weight gain by laboratory rats in the first week of a 4 week feeding trial with INGARD cotton seed. Believes that further feeding trials on a range of animals should be performed before this product is released;
- approval of foods produced using gene technology should be deferred until a national coordinating system for regulatory approvals is in place so that a global assessment of their likely impacts can be made;
- a system for monitoring adverse reactions to these foods should be established before they are released into the diet of Australians;
- approval and release of these foods should not occur until the system of labelling agreed to by Health Ministers is established;
- Australia should not be bullied by other countries to accept their exports of unsegregated mixtures of genetically modified and non–modified foods.

Francela Davies (NZ)

- concerned about the addition of food additives in the form of genetically engineered foods that have not been given adequate testing of their benefits or side effects to human health;
- wants ANZFA to address the long term effects of the consumption of foreign proteins, antibiotic resistant marker genes and viruses;
- the applications should be rejected because there is no evidence that these foods are contributing anything positive to the food supply or the environment.

Food Technology Association (FTA) Victoria Inc.

- the risk assessment must be completed and reported to ANZFA stakeholders prior to any decision on the Applications;
- it is unclear from Standard A18 as to the labelling that would apply to these products;
- wants to know what special conditions might apply to these products;
- the option to not permit the sale of these foods is the preferred option;
- the application needs more detail and background information such as a Full Assessment report, details on special conditions and labelling and a complete risk assessment.

Friends of the Earth (NZ)

- share the same concerns as expressed in the submission of the Natural Law Party and Clive Elwell;
- glyphosate has not been included among the residues tested, and there is no awareness of any program that monitors for glyphosate residues in food;
- Treaty of Waitangi obligations have not been considered in ANZFA processes;
- the New Zealand Bill of Rights provides that no New Zealand may be subjected to experimentation without providing informed consent, therefore full disclosure of all transgenic foods and ingredients via labelling is the only way this can begin to be achieved;
- Monsanto has not done any long term studies on health effects;
- submit that ANZFA should approve these foods for a period of 6 months only conditional on a requirement for immediate, prominent labelling of all food products and a warning logo. This should be followed by a moratorium on any further approval of genetically engineered foods.

Noeline Gannaway (NZ)
- supports labelling of all food containing genetically engineered products;
- there may be risks of toxic or allergic reactions;
- oppose the transfer of genetic material between different species as unethical and potentially unsafe.

Goodman Fielder (Aust)
- is fully supportive of developments in the agri–food industry through the application of gene technologies provided that consumer benefits are clearly defined and communicated;
- urges ANZFA to undertake wide consultation with all affected parties, including growers, crushers (in the case of oilseeds), food industry users and consumers before these modified plants are introduced.

Nathan Green (NZ)
- objects vehemently to the further introduction of genetically modified foods, specifically the applications by Monsanto;
- there have not been sufficient tests to prove safety;
- NZ should exploit the GMO free market opportunities;
- there has not been adequate public debate on the introduction of genetically modified foods;
- does not agree with the concept and use of substantial equivalence.

Mike and Jeanne Gregory (NZ)
- the public has not been properly consulted or informed by Government or ANZFA on the introduction of genetically modified foods;
- strongly opposed to genetically modified foods on grounds that these are not adequately tested;
- there is significant and growing scientific concern worldwide about the technology and the processes undertaken to evaluate the safety of genetically modified foods;
- NZ would have a market advantage if genetically engineered foods were prohibited altogether.

Martin Hartman and Cornelia Baumgartner (NZ)
- object to genetically modified foods;

- call for mandatory labelling of all genetically modified foods.

Karen Hunt (NZ)
- demands that all genetically modified foods be labelled;
- states that consumer rights are violated if products are deemed substantially equivalent and consequently are not subject to mandatory labelling.

InforMed Systems Ltd (NZ)
- the transfer of EPSPS genes to soybean, maize, cotton and canola is acceptable;
- the transfer of the gox gene to canola and the use of the cry1Ac gene are also acceptable;
- noted that no mention was made of any maker genes in the applications for soybeans, corn or canola;
- noted that the nptII gene is used in cotton and one insect resistant corn variety. Considers that there are remaining questions with regard to the use of antibiotic resistance genes. It would be reassuring if independent biomedical advice were available to reassure us that this does not pose a risk to the future use of these or related antibiotics in the management of human disease;
- notes that none of the modified plants provides any nutritional or functional benefit for the consumer. It is unfortunate that the first applications should not demonstrate benefits to the consumer, who may thus feel that failure to permit the use of such foods will have no measurable effect on them.

Oraina Jones (NZ)
- genetically engineered foods have not been adequately tested for their benefits or side effects to human health;
- what are the long term effects of the consumption of foreign proteins, antibiotic resistant marker genes and viruses;
- questions whether Monsanto supplied any evidence of long term trials;
- requests that the application be declined as the foods are not contributing in any way to the food supply or environment.

Michael Karas (Aust)
- is opposed to applications A338, A355, A362 and A363 because they are for herbicide resistant crops;
- is concerned about the potential for Roundup residues to be increased in human food supply;
- is concerned about the out–crossing of herbicide resistant crops to create ‘super–weeds’.

Colin Kell (NZ)
- criticises some of the wording used in the preliminary assessment report;
- claims that genetically altering food decreases the nutritional value;
- the application provides no proof that glyphosate does not cause long term effects;
- there has been insufficient testing of these genetically modified foods;
- balanced information on genetic modification needs to be made available and the rights of everyone taken into consideration;
- imported commodities should be segregated at source;
- the applications do not indicate the source of the genes being used - believes that genes from fish and animals are being used which is unethical and against nature.

Janine Kelly (NZ)
- concerned about the depth of investigation into the safety of genetically modified foods and the apparent lack of concern by regulatory authorities for the opinions of informed members of the general public and some scientists;
- ANZFA puts too much faith in the integrity of companies who are producing genetically modified foods;
- urges ANZFA to consider the long–term implications of allowing the sale of genetically modified foods;
- if they are allowed, they should all be labelled.

Kristen Khaine (NZ)
- consumer rights include the choice not to eat any genetically modified foods, therefore labelling is of paramount importance;
- trade barrier issues are secondary to public health and safety.

Hilde and Kristin Knorr (Aust)
- advocate a prohibition on genetically modified foods altogether, but otherwise strongly demand mandatory labelling.

Susie Lees (NZ)
- not enough information has been provided in these applications;
- the public do not want to eat these products;
- if the products are approved, we will be at risk of unknown toxins and allergens.

Margaret and Leonard Krohn (Aust)
- opposed to genetically modified foods on the grounds that insufficient scientific testing has been done and the effects on public health are unknown.

C. Lamprecht (Aust)
- concerned about the possible detrimental health effects of genetically modified foods;
- concerned about increased pesticide residues in food;
- advocates full mandatory labelling of all genetically modified foods.

Hannah Levy (Aust)
- strongly opposed to genetically modified foods because of the limited knowledge concerning the risks associated with the technology;
- demands full labelling.

Mahikari Australia
- strongly advocates the mandatory labelling of all foods or food ingredients produced using gene technology to allow consumer choice;
- disagrees with validity of "substantial equivalence" as a basis for labelling because of a lack of scientific rigor;
- completely opposed to all six applications because of the potential long term risks;
- concerned about increased levels of glyphosate in food;
- considers gene technology unethical;
- considers the outcomes of gene technology scientifically unpredictable because of the possibility that DNA can readily transfer between species.

Nadine McRae and others (NZ)

- opposes all of the six applications on the grounds that gene technology is unpredictable, unsafe and harmful to the environment;
- demands that all food with some genetically modified food content be labelled.

National Council of Women of Australia

- requests that ANZFA maintain the status quo and not amend Standard A18 to permit the sale of the indicated foods;
- no deliberations on applications should be made under this Standard until the situation with labelling is resolved;
- there is no mention of monitoring pesticide residue increase in the final product as a result of a greater tolerance to what is an obvious need to increase the pesticide used;
- for the soybean applications there should be absolutely no doubt about the safety of the source of the soybean if it is to be used in the Australian food supply;
- only two out of the six foods have been tested by feeding to laboratory animals and then only for 6 weeks;
- no evidence was provided about herbicide residue levels in any of the soybean foods despite there being an application to increase the MRL for glyphosate in soybeans;
- although the CP4 EPSPS protein may be inactivated on processing, the application does not take into account the use of raw soybeans to grow sprouts. This could represent an allergy problem and therefore the foods should be labelled;
- ANZFA has not taken into consideration the considerable consumer backlash that is occurring;
- there must be scientific certainty that humans are not exposed to any newly expressed proteins;
- objects to the commercial-in-confidence aspects of A362;
- concerned about the feeding of genetically modified seeds to animals as this is another source for these products entering the human food supply;
- there is no justification for using glyphosate–tolerant canola;
- Australia should be able to prohibit the import of genetically modified foods if it wishes;
- if ANZFA allows genetically engineered foods to be imported into Australia unlabelled, consumers will be affected by a lack of choice.

Natural Law Party (NZ)

- in the absence of a moratorium on genetically modified food, demands labelling of all genetically modified foods on the grounds that there has been no long term pre–market testing or screening for risk factors associated with this technology and that unlabelled products deprive individuals of their basic freedom of choice;
- rejects the notion of substantial equivalence on the grounds that differences at the DNA level make them substantially different;
- concerned about the potential for increased glyphosate levels;
- the effects of glyphosate on health and on phytoestrogens in genetically engineered soy has not been addressed;
- genetically engineered soy contains genes from a virus, a soil bacterium and from petunia, none of which has been in our food before;
- the technology is being introduced in the total absence of an informed public debate about the general acceptance of GMO technology;
- believe that there is significant potential for environmental or health disasters associated with the current introduction of this technology. Believes that serious

liability implications exist and need to be explored;
- recommends that, until long term independent safety and risk assessment studies on genetic technology in food production have been completed and their safety to human health and the ecosystems that support human life is established, approvals for these foods should be declined;
- no further applications should be considered until proper public debate has occurred.

New Zealand Nutrition Foundation
- submission identical to InforMed Systems Ltd

Office of Regulation Review (Aust)
- comments on the preparation of the RIS for the full assessment report;
- ANZFA should discuss, in the background section of the report, why products such as the Roundup Ready soybeans, which previously entered the commercial markets without segregation from the non–transgenic counterpart, now require an approval process. Questions whether the regulation is to address health and safety and/or consumer information concerns;
- the problem section of the RIS should outline the characteristics of food produced using gene technology and why these characteristics might give rise to the need to list special conditions. The RIS should specifically canvass the possible special conditions which could apply and fully discuss the varying costs and benefits that each set of conditions entails;
- the material present in the sections on potential regulatory impacts and identification of affected parties should be summarised in the RIS in matrix form;
- when the RIS is fully developed it will need to include a conclusion section which summarises the views elicited from the main affected parties, a conclusion and recommendation option section which states what the preferred option is and why this option was accepted and the others rejected, and an implementation and review section which outlines how the proposal will be administered, implemented and enforced.

Martin Oliver (Aust)
- opposes all six applications on the grounds that the long term safety of eating foods from herbicide tolerant or insect resistant crops has not been adequately established;
- all genetically modified foods should be labelled in order for consumers to choose;
- claims that the foods have not been tested for any health impact on humans.

The Pacific Institute of Resource Management/Revolt Against Genetic Engineering (NZ)
- all genetically modified food should be labelled so that there can be post-market monitoring for new allergens or toxic effects in consumers;
- strongly opposed to the technology because of a range of concerns about public health and safety;
- raised a number of concerns in relation to Application A338 specifically:
  - the bacterial EPSPS is unlike any protein that humans have ever eaten and there is no reliable method for predicting its allergenic potential;
  - a major allergen, trypsin inhibitor was found to be 26.7% higher in transgenic soybeans;
  - the compositional analyses of the soybeans were not done on soybeans that had been treated with the herbicide;
  - there were significant increases compared to controls in the milk fat of cows fed

transgenic soybeans; and
– the applicant did not submit any data on glyphosate residues in the transgenic soybeans.

Sara Parsons (NZ)
- objects to the applications because she is a vegetarian;
- it is harmful to be introducing genetically modified soybeans, corn, canola oil and cottonseed into the NZ food chain;
- these products are a threat to the safety and well being of animals and humans and are of no benefit to society;
- the testing of genetically modified foods on animals and the harm that may be caused to animals in the wider environment is unacceptable;
- the lack of labelling of genetically modified foods means that NZ consumers have no way of making appropriate choices if they wish to avoid eating such foods which may cause allergic reactions and offend ethical beliefs.

Eric Phimister (NZ)
- is concerned about the importation of unlabelled genetically modified food;
- does not wish to consume soybeans with a higher pesticide level than the previously allowed maximum. This alone should make it not substantially equivalent.

Marja Rouse (Aust)
- opposes all six applications on the grounds that the genetically engineered crops pose a major environmental hazard and human health hazard;
- claims that the technology promotes unsustainable farming practices;
- believes consumers have the fundamental right to be informed about all the ingredients in foods and therefore demands mandatory labelling;
- the safety assessment for the applications should not be based on information provided by the applicant in these cases, as the company has a vested interest in having the applications approved.

Dean Scahill (NZ)
- is opposed to the foods which are the subject of Monsanto's applications on the grounds that the costs in terms of potential risk to health, risk to organic crop contamination, and current inability of consumers to identify such foods, greatly outweighs the benefits;
- if NZ remains GMO–free is represents an opportunity to create a niche market;
- a labelling system should be developed which would provide consumers with a choice so that they can retain the right to not eat genetically modified food should they choose;
- ANZFA should address the large public concern associated with the introduction of genetically modified foods onto the market.

Emma Subue-Timson (Aust)
- opposed to foods produced using gene technology on the grounds that the technology contravenes nature.

Christine Taylor (Aust)
- opposes all applications because of the presence of new genes, new proteins and increased herbicide residues in genetically modified foods;
- concerned about the potential for herbicide resistance genes to transfer to other plant species, creating undesirable effects.

Bridget Thrussell (NZ)
- supports regulatory option 1- to not permit the sale of any of the foods in the applications;
- no long term safety tests have been done;
- worried about antibiotic resistance increasing because of the antibiotic resistance marker genes in A355;
- concerned about gene transfer between Roundup Ready canola and other Brassicas.

E.M. Trevelyan (NZ)
- does not believe that genetically modified foods can be assessed as safe because of the possibility of "gene flow";
- crops containing the Bt gene will inevitably lead to resistant insect populations;
- envisages an enormous marketing advantage to NZ if it maintains a clean, green image by not allowing genetically modified food onto the market;
- all genetically modified food products should be labelled.

Richard van Wegen (Aust)
- supports the restricted use of genetically modified plants for food production;
- strongly supports mandatory labelling as a democratic right to make informed decisions about food purchases.

Arnold Ward (Aust)
- opposed to all applications on the grounds that long term safety has not been established;
- ANZFA only concerns itself with public safety rather than adopting a 'holistic' approach which takes into consideration the broader issues to do with genetic engineering
- Roundup herbicide contains other chemicals which are harmful. Considers that the acceptable daily intake of glyphosate does not take into account the higher toxicity of the surfactant POEA in Roundup, on individuals with increased susceptibility such as children, immune compromised individuals or the elderly;
- notes examples of scientific evidence which show glyphosate can increase levels of plant oestrogens, which are known to affect humans. Very concerned about the potential health effects, particularly in children, of higher levels of oestrogens;
- feeding experiments in cows indicate a change in the milk fat production in animals fed on Roundup Ready soybeans versus non-transgenic soybeans;
- where resistance to Bt toxin occurs because of a widespread use of insect resistant crops, this would mean that organic farmers, who now rely on Bt formulations, could lose an important pest control agent;
- expresses concern about the possibility of recombination and horizontal gene transfer resulting in environmental catastrophies;
- glyphosate does not degrade in soils as efficiently as claimed by the applicant;
- all transgene products should be given the same testing applicable to pharmaceuticals;
- the seeds from genetically engineered crops could spread due to natural disasters;
- plant viruses can acquire viral DNA from a transgenic plant;
- Bt cotton is not very effective in controlling bollworm infestations;
- calls for a moratorium of 10 years on the introduction of genetically modified foods.

Joyce Weatherhead (NZ)

- opposes approval for the applications on the grounds that genetically modified foods have not undergone an independent scientific testing;
- calls for a moratorium on genetically modified foods in NZ for ethical and religious reasons;
- demands mandatory labelling of all genetically modified foods;
- believes that approval for herbicide resistant soybeans will result in a huge increase in the level of contaminating herbicides in foods derived from these crops.

Western Australian Food Advisory Committee

- a safety assessment of the foods is lacking along with the absence of any supporting scientific evidence;
- post–market monitoring to confirm the results of risk assessment and establish evidence of a safe history of use is an unacceptable alternative to a full scientific evaluation, with the results being available for public scrutiny;
- the claim that CP4 EPSPS is destroyed in heat processing requires independent scientific validation and it is unclear from ANZFA's papers whether this evidence has been provided and reviewed;
- insufficient evidence has been provided in the discussion document to support claims that these products are safe or that the Authority has undertaken a rigorous analysis or comprehensive scientific evaluation of these products;
- the issue of decreased availability of food choices in the marketplace listed under both Options 1 and 2 is not nearly as important as the safety issue;
- given the heightened public concern about genetically modified foods it is essential that scientific information relating to compositional variance due to novel gene expression, toxicology, potential for allergenicity, nutritional and dietary properties for each of the foods proposed by Monsanto, is publicly available;
- the Committee recommends the adoption of Option 1 at this time.

S. and L. Wintergraas

- ANZFA should stop all genetically engineered foods from entering into any food products in NZ, as it will destroy the clean green image;
- ANZFA is not able to guarantee safety of these foods - cites DDT, nuclear power and antibiotics as examples;
- ANZFA should protect the consumer, not big business.

SECOND ROUND PUBLIC SUBMISSIONS

The Authority received four applications from Monsanto Australia Ltd. (A346, A355, A362, A363) and one from Dupont/Pioneer (A387) for foods produced using gene technology. A draft Risk Analysis Report (formally referred to as the Full Assessment Report) was released for a 10 week period of public comment on 19 June 2000. At the end of the public comment period (30 August) a total of 26 submissions had been received.

J Coburn (NZ)

- does not want these experimental foods in the common food supply until they have been long–term tested for undesirable side–effects related to public health;
- questions the fairness of the ANZFA response to the concerns expressed in the first round of public submissions;
- comments on the risk of spread of antibiotic resistance due to the use of antibiotic

resistance marker genes;
- objects to any trace of herbicide residues in general;
- submits that the Draft Regulatory Impact Assessment is flawed.

Commerce Commission (NZ)
- concerned that labelling and advertising of GM foods is not misleading or deceptive;
- concerned whether by-products from the processing of GM foods could be fed to animals.

National Agenetic Awareness Alliance (Aus)
- believe that there has been no independent scientific research conducted by ANZFA in the risk assessment process;
- request ANZFA to set up analytical techniques to measure DNA or protein in GM-crop-derived oils;
- object to the use of viral promoters such as cauliflower mosaic virus (CaMV) promoter
- believe that GM crops yield less than conventional crops and require more herbicides.

InforMed Systems (Aus)
- comment that the use of antibiotic resistance marker genes should be phased out;
- the absence of any perceived benefit to the consumer of the modifications is not relevant to their safety, but can only increase public resistance to the technology.

Food Technology Association (Aus)
- recommend long-term feeding trials;
- question whether all "novel chemicals" have been "identified/discovered".

Australian GeneEthics Network
- recommends rejection of all applications on GM food;
- Monsanto's proposals should all be rejected as inadequate;
- questions the relevance of substantial equivalence;
- believes ANZFA should adopt the precautionary principle in its risk assessment process;
- suggest that insect-resistant crops should be considered an insecticide;
- labelling of GM food should be encouraged;
- believes the research conducted by Ewen and Pusztai should be considered in the assessments;
- objects to the use of antibiotic resistance marker genes;
- believes precautionary principle should be applied to the use of viral promoter sequences;
- recommend long-term feeding studies be undertaken;
- believe that gene silencing and its potential repercussions are not fully understood;
- state that ANZFA needs to take into account the variation in diet between different cultural and ethical groups.

Environmental Health Branch – SA Department of Human Services (Aus)
- state that the approval of a food produced using gene technology for human consumption in Australia should not depend on the GMO from which it is derived being cleared for general release in Australia. However, if clearance for general release of a GM crop is sought from GMAC and rejected, ANZFA should take account of the reasons for rejection in assessing any application received by the Authority in relation

to any food produced using gene technology for human consumption derived from the GM crop.
- applicants should identify which food products produced using genetic modification contain novel DNA and/or protein so labelling requirements can be determined;
- draft variations to Standard A18 should be specific as to which foods are permitted.

National Council of Women of Australia
- believe that the safety evaluation used by ANZFA is not the best suited to the evaluation of GM food;
- do not support the concept of substantial equivalence;
- objects to the use of antibiotic resistance marker genes;
- believe that animal feeding studies and human feeding studies should be conducted before GM foods are approved;
- post-market surveillance should be carried out since there is no long-term history of safe use of novel foods;
- all food derived from, or processed using genetic engineering, whether any DNA or protein remains in the finished product or not, should be labelled.
- believe that many statements made in the reports are not decisive;
- believe that the public's concerns are being over ridden by trade and other commercial interests;
- want the Office of the Gene Technology Regulator to be the overall regulator on all gene technology matters;
- believes that ANZFA does not deal with the issue of potential allergenicity appropriately; unknown allergens are not tested for;
- states that the Regulatory Impact Assessments for the applications are misleading and that there are no benefits to consumers;
- warn about the risks of using viral promoters such as CaMV;
- support continuing public consultation and information regarding gene technology;
- object to any chemical residues in foods.

Australian Competition & Consumer Commission
- the Commission believes that consumers have a right to purchase products that reflect their own personal preferences. Consumers must be able to rely on disclosures on packaging in order to make purchasing decisions;
- the Commission recommended the delay in the approval of the applications until the ANZFSC labelling decision of 28 July;
- column 2 of the table to clause 2 of Standard A18 could be used to require positive initiatives be undertaken by the applicant such as public information about the food in question or GMOs generally.

Institute of Environmental Science & Research Limited (NZ)
- ESR believe the ANZFA safety assessment process is consistent with current international "best practice" for this area;
- ESR's review of the data supporting the applications for approval of GM foods concluded that there was no reason to disagree with the ANZFA assessment that these foods are safe for human consumption;
- Greater toxicological testing is desirable to improve the data supporting the safety of GM foods, although it is acknowledged that there are practical difficulties in testing whole foods.

Consumers' Institute of New Zealand Incorporated

- expressed concerns over whether ANZFA had established that the evidence provided by the applicant has not been superceded by subsequent research;
- audit processes should be established to ensure that if new knowledge suggests there is any risk associated with the foods that approval can quickly be withdrawn;
- ongoing monitoring of the long-term effects of the foods should also be established;
- expressed concern on the lack of independent verification of testing carried out by the developers of the products;
- believe the concept of substantial equivalence is not rigorous;
- comment that the language in the risk analysis documents gives the impression that uncertainty remains about the products;
- believe that GM foods should be treated in the same way as medicines in relation to tests required to establish safety.

G C Morgan (NZ)

- raised concerns regarding the use of pesticides on crops;
- comments that there is little evidence of any benefit of the introduction of GM foods to the consumer.

Consumers' Association of South Australia Inc. (Aus)

- strongly support the submission of the National Council of Women.

Dieticians Association of Australia

- supports full labelling of GM food;
- comments that the broader environmental impacts of GM foods are not being addressed in the evaluations of the applications;
- believes that the recent decision on labelling of foods produced using gene technology should be extended further to require labelling of purified foods from GM sources, such as oils from glyphosate tolerant canola, even if there are no nutritional or safety concerns with the food;
- noted that very few of the studies that are relied upon in the evaluations have been published in peer-reviewed journals;
- comment that for a number of the applications there are no feeding studies.

I P Hancox (NZ)

- expressed general concerns regarding the environmental impact of GM foods.

P Gilgenberg (NZ)

- expressed general concerns regarding the safety of GM foods.

Food Technology Association of Victoria Inc (Aus)

- recommend long-term feeding trials;
- labelling of foods noting the presence of a GMO should only apply where more than 1% of any food contains a GMO present.

Canberra Consumers Incorporated (Aus)

- comments that none of the reports were peer reviewed;
- expressed concern over the use of antibiotic resistance marker genes;
- recommend long-term feeding trials;
- expressed concerns that GM foods used as stock feeds for animals are not safe for

livestock.

National Council of Women of New Zealand (Te Kaunihera Wahine O Aotearoa)

- the Council recommends that where substantial differences are detected in GM foods these products must be labelled;
- the Council advocate that an adequately funded independent scientific body to evaluate data be established as soon as possible.

University of Auckland, Food Science Postgraduate Programme (NZ)

- recommend long-term studies be conducted
- expressed concern over the use of antibiotic resistance marker genes;

Monsanto Australia Limited

- there are many formulations of the herbicide Roundup and not all have the surfactant POEA in them;
- some formulations e.g. Roundup Biactive is actually registered for use in waterways because the surfactant is approved with a good aquatic toxicological profile;

Arnold Ward (Aus)

- believes that ANZFA largely ignores submissions from the general public and is in league with large biotechnology companies;
- believes that there is a conspiracy between ANZFA and the US government and the FDA regarding the introduction of GM foods;
- wants ANZFA to exercise the precautionary principle and not approve GM food until it is proven to be safe;
- states that GM foods may not be as nutritional as conventional foods;
- objects to the concept of substantial equivalence;
- recommends long-term feeding studies in animals and human studies be conducted;
- recommends caution on the use of promotors such as CaMV;
- recommends that GM foods be treated the same as drugs in terms of testing requirements.

Carolyn Kitson (NZ)

- recommends that ANZFA guidelines for data requirements on safety of GM foods be consistent for every application.

Ministry of Health (NZ)

- considers the ANZFA safety assessment process is consistent with international “best practice” in this area and that all the applications were subject to this process;
- in relation to the assessments themselves, and by way of summary, MoH agree with the conclusion reached in each assessment, that these foods are safe for human consumption;
- the concentration of newly expressed proteins were generally very low as the refinement processes involved removal of these proteins;
- consider that the applications closely considered the potential allergenicity of the newly expressed proteins on the basis of the physical and chemical nature of these proteins, and the similarity of their amino acid sequence with known allergens;
- compositional analyses of the nutrients in control and GM food indicated no substantial differences in the levels of major nutrients; and

- toxicological effects of the modified foods were evaluated (although the estimated dietary intakes of the newly expressed proteins were not determined).

The following submissions were received after the end of the consultation period of 30 August 2000:

Public Health Association of Australia (PHAA) (part submission received 28 September 2000)

- believe that all studies submitted by industry should first be published by peer reviewed journals before undergoing the regulatory process;
- believe that there is a conflict of interest in an applicant company doing its own safety assessments and studies should be reproduced by independent laboratories;
- comment that the statistical analyses on the compositional studies is inadequate;
- contend that these foods undertake at least thorough animal testing, and at least the first phase of the four phases of a clinical trial before being released;
- contend that the issue of likely horizontal gene transfer has not been adequately resolved.

Australian Food and Grocery Council (received September 2000)

- The AFGC supports approval of each the applications A346, A355, A362, A363 and A387 on the basis that they do not raise any public health and safety concerns;
- Labelling of these foods should be according to the 28 July decision of the ANZFSC to enable consumers to make an informed choice.

ATTACHMENT 6

GENERAL ISSUES RAISED IN PUBLIC COMMENTS

The majority of submissions received in response to the Section 14 Gazette Notice, expressed general views against the use of gene technology and asserted that food produced using this technology is unsafe for human. A number of general issues were raised in these submissions and 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 is to establish that the new food is at least as safe as existing foods. 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 consistent with international protocols developed by these bodies.

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 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 studies on foods is the need to maintain the nutritional value and balance of the diet. A diet that is poorly balanced will compromise the interpretation of any feeding study, since the effects observed will confound and usually override any small adverse effect which may be related to a component or components of the food. 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 case, studies up to 14 days have also been performed. These can provide additional re-assurance that the proteins will have no adverse effects in humans when consumed as part of a food. Such experiments can provide more meaningful information than experiments on the whole food. Additional re-assurance regarding the safety of newly-expressed protein can be obtained by examining the digestibility of the new protein in *in vitro* assays using conditions which simulate the human gastric system.

3. *Substantial equivalence*

A number of submitters expressed concern regarding the use of the concept of substantial equivalence as part of the assessment process. Some rejected 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.

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*.'
The concept has been internationally recognised and embraced as a valuable tool in the safety assessment of foods produced using gene technology. The OECD also advocates an approach to safety assessment based on substantial equivalence as being '*the most practical to address the safety of foods and food components derived through modern biotechnology*.'

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

A small number of submitters expressed 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 expressed 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 raised concerns about increased antibiotic resistance resulting from the use of gene technology. Some felt that it would be reassuring if independent biomedical advice were available to reassure 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 expressed 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 focussed on this issue. Specifically, the submissions called for the labelling of all foods produced using gene technology, regardless of whether they are substantially equivalent to conventional foods. The submitters based their demands for full labelling on the presumption that all foods produced using gene technology are unsafe and on consumer "right to know" arguments. It was stated that full labelling was the only means of identification of foods produced using gene technology available to consumers.

Evaluation

The existing Standard A18 already makes provision for mandatory labelling of genetically modified foods that are substantially different from their conventional counterparts. However, ANZFA is committed to implementing the in-principle decision of ANZFSC Health Ministers of August 1999 to require labelling of all genetically modified foods, including those that are substantially equivalent in composition to the unmodified form. In conjunction with a task force of officials from State and Territory Health Departments and the New Zealand Ministry of Health, ANZFA developed draft revision to Standard A18 in October 1999 that requires labelling of other categories of genetically modified foods. At the Ministers request this draft was circulated for public review and a cost-benefit analysis of full labelling was commissioned. The task force considered both public comments and the cost-benefit analysis in finalising their recommendations to Ministers, which were delivered in May 2000. Ministers are to meet to resolve the issue in July 2000 following whole-of-government consideration of the issue. It is therefore expected that, following a decision and legal amendments to the standard, labelling requirements will be implemented that will apply to all current and subsequent applications.

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 is in the process of preparing a public discussion paper on the safety assessment process for GM foods. This will be 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.

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 in the assessment processes of GMAC in Australia and the Environmental Risk Management Authority (ERMA) in New Zealand. The Authority does not have the mandate to assess matters relating to environmental risks resulting from the release of food produced using gene technology into the environment. However, links exist between ANZFA and other regulatory agencies in both Australia and New Zealand, and a large degree of information sharing occurs. ANZFA would not recommend the approval of a food produced using gene technology if the genetically modified organism from which it was derived did not have the appropriate clearance for general release from either GMAC (or its successor) or ERMA, as appropriate.

The regulatory system in Australia will comprise the existing regulators 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)
- 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).

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

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

In Australia a new Office of the Gene Technology Regulator (OGTR) will complement the existing arrangements. OGTR will supersede the existing arrangements under the Genetic Manipulation Advisory Committee (GMAC), which advises on research and environmental release of GMOs. OGTR will regulate all GMOs and any ‘gap’ products (i.e. products for which no other regulator has responsibility).

All GM food is assessed and regulated by the Australia New Zealand Food Authority (ANZFA) under the direction of Commonwealth, State and Territories Health Ministers and the New Zealand Health Minister, sitting as Australia New Zealand Food Standards Council (ANZFSC).

There will be an interface between ANZFA and OGTR. Consequential amendments proposed to the ANZFA Act arising from the draft Gene Technology Bill 2000 will establish a statutory interface between OGTR and ANZFA. This will involve amendments to the ANZFA Act requiring the Authority to advise OGTR of recommendations to ANZFSC regarding the standard for foods produced using gene technology (currently Standard A 18).

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.

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 Food Regulations (1984) in New Zealand.