TE MANA WHAKARITE KAI
MO AHITEREIRIA ME AOTEAROA

FULL ASSESSMENT REPORT AND REGULATORY IMPACT ASSESSMENT

A341û OIL AND LINTERS DERIVED FROM INSECT RESISTANT COTTON

EXECUTIVE SUMMARY

ò Standard A18ûFood Produced using Gene Technology was adopted as a joint Australia New Zealand standard in July 1998 and is due to come into effect on 13 May 1999. After that time, the sale of food produced using gene technology will be prohibited unless the food is listed in the Table to the Standard;

ò The Australia New Zealand Food Authority (ANZFA) received an application from Monsanto Australia Ltd on 14 April 1997 to amend the *Food Standards Code* to include oil and linters derived from insect resistant cotton lines 531, 757, 1076 and 1849 in the Table to Clause 2 of Standard A18 û Food Produced Using Gene Technology;

ò The principal food products extracted from the cotton are refined cottonseed oil and fibre. Cottonseed oil is a premium quality oil that may be used in a variety of foods including frying oil, mayonnaise, salad dressings, etc. The fibre is obtained from the linters that are removed from the cottonseed during delinting. The linters consist primarily of cellulose and are used as high fibre dietary products, sausage casings and viscosity enhancers in products such as ice cream and salad dressings;

ò Lepidopteran insects are the main insect pests of cotton in Australia, infecting up to 100% of the planted hectares and involving significant costs to growers in the application of chemical pesticides. The applicant has developed plant lines, known commercially as INGARD cotton, which contribute to the control of the lepidopteran insects by producing one of two insecticidal proteins derived from the soil bacterium *Bacillus thuringiensis* subsp *kurstaki,* (B.t.k.). The cotton lines are also known as Bt cotton, denoting the donor organism of the new proteins;

ò The cotton lines 531, 757, 1076 and 1849 have each had three new genes transferred to them. All contain the bacterial genes *nptII* and *aad,* which encode the selectable marker enzymes neomycin phosphotransferase II and aminoglycoside adenylyltransferase, respectively. These selectable marker genes enable the selection of plant cells that have been transformed with new genes.

As well, each line carries one of two genes, *cry1Ac* or *cry2Aa* which encode the insecticidal proteins Cry1Ac and Cry2Aa, respectively;

- ò To be active against the target insect, the insecticidal proteins must be ingested. In the insect gut, the proteins bind to separate specific receptors on the insect mid-gut, insert into the membrane and form ion-specific pores. These events disrupt the digestive processes and cause the death of the insect;

- ò A full data package for insect resistant cotton lines 531, 757, 1076 and 1849 was submitted by the applicant for assessment. Quality Assurance certification stated that the studies were done in accordance with Good Laboratory Practice and that the information presented in the application accurately reflects the raw data generated during the studies;

- ò The safety assessment found the following:

    - û of the three genes transferred into cotton lines 531, 757, 1076 and 1849, only the *cry1Ac* or *cry2Aa* and the *nptII* genes are expressed in the plant. The newly expressed proteins are neomycin phosphotransferase II (NPTII) and the insecticidal proteins, Cry1Ac (line 531, 757 and 1076) or Cry2Aa (line 1849);

    - û the bacterial gene *aad* is also present in the cotton lines, but lacks the gene elements necessary for expression in plants;

    - û the cotton lines containing the *cry1Ac* gene and the *cry2Aa* gene will be cross-bred, to develop cotton varieties containing both genes, in order to have two insecticidal mechanisms of action in the same plant line;

    - û the molecular and genetic analyses provided by the applicant indicate that the introduced genes have been stably integrated into the plant genome and are stably inherited from one generation to the next;

    - û the newly expressed proteins Cry1Ac and Cry2Aa and the NPTII enzyme have been evaluated for their potential to be toxic or allergenic to humans. A range of analyses including acute toxicity tests using mice for Cry2Aa, amino acid comparisons with known toxins and allergens and examination of digestion of the proteins in simulated digestive systems, indicate no increased potential for toxicity or allergenicity in humans;

    - û as a result of extensive processing, neither refined cottonseed oil nor processed linters contain protein or genetic material. Protein was not detected in refined cottonseed oil to a sensitivity of 1.3 ppm total protein, for line 531. Similarly, Cry1Ac was not detected in raw cotton fibre, cleaned cotton fibre or cleaned linters, also due to the processing which removes the contaminating hulls;

- û the presence of the two bacterial antibiotic resistance genes in the Bt cotton is not considered to increase the potential for gene transfer to microorganisms of the human gut or to increase the risk of the development of antibiotic resistance among pathogenic bacteria. Antibiotic resistant microorganisms are already naturally abundant in the human gut and, in the scientific literature, the possibility of this type of gene transfer is considered to be virtually zero ;

- û in line 1849, a copy of the cry2Aa gene is fused to a cotton gene, resulting in a hybrid gene. This hybrid gene has been characterised by the applicant and appears not to be expressed;

- û the compositional analyses were comprehensive and indicate that there are some significant differences in composition between the insect resistant cotton lines and the comparator. However, for most constituents, these values are within the literature reported ranges. Furthermore, as many of the compounds measured are not constituents of either the refined oil or fibre, the differences are not relevant in relation to the food uses of the cottonseed. The oil and linters derived from the insect resistant cotton are considered to be equivalent to those of unmodified cotton; and

- û a 4 week rat feeding study using raw, ground cottonseed from line 531 at differing concentrations, found that the Bt cottonseed is essentially equivalent to the control line C312 in terms of its wholesomeness;

- ò On the basis of the safety assessment conducted, no potential public health and safety concerns were identified. Oil and linters derived from insect resistant cotton lines 531, 757, 1076 and 1849 can be regarded as substantially equivalent to the oil and linters from conventional cotton varieties in respect of their composition, safety, wholesomeness and end use;

- ò Under Standard A18, as currently drafted, oil and linters derived from cotton lines 531, 757, 1076 and 1849 would not require labelling as they can be regarded as substantially equivalent to the oil and linters from conventional cotton varieties. As a result of a recent decision in December of the Australia New Zealand Food Standards Council (ANZFSC), Ministers have indicated that foods which do not contain genetically modified material should be exempt from a mandatory labelling requirement. Therefore, under proposed amendments to Standard A18, it is unlikely that cottonseed oil or linters would require labelling once these amended provisions take effect, as neither the oil nor the linters contains any detectable genetically modified material;

- ò The regulatory impact analysis concluded that, as oil and linters derived from the insect resistant cotton lines do not pose any greater risk to public health and safety than oil or linters from conventional cotton, an amendment to the *Food Standards Code* to list oil and linters derived from insect resistant cotton lines 531,

757, 1076 and 1849 in the Table to the Standard is necessary, cost effective and of benefit to industry, government and consumers.

BACKGROUND

Standard A18

On 30 July 1998, the Australia New Zealand Food Standards Council (ANZFSC) agreed to adopt Standard A18 for the regulation of foods produced using gene technology.

In Australia, the Standard was gazetted on 13 August 1998. In New Zealand, the decision was gazetted, as a mandatory standard, on 20 August 1998. The Standard will come into effect in both countries on 13 May 1999, nine months after the Australian gazettal date, to allow the Australia New Zealand Food Authority (ANZFA) time to consider applications for food already in the market place, prior to implementation of Standard A18.

Under Standard A18, the sale of food produced using gene technology is prohibited unless they are included in the Table to Clause 2 of the Standard and comply with any special conditions so listed in the Table. The Standard requires that a pre-market safety assessment be conducted before consideration be given to listing in the Table. In addition, the Standard contains a provision for labelling of food that contains new or altered genetic material and which is no longer substantially equivalent to its conventional counterpart. Specifically, the Standard will require labelling of food where the nature of the food has been significantly changed with respect to its nutritional quality, composition, allergenicity, or end use. The Council, at its meeting on 30 July 1998, deferred the decision regarding mandatory labelling for foods which are substantially equivalent.

On 17 December 1998, ANZFSC decided that the mandatory labelling requirements should be extended to foods produced using gene technology that are also substantially equivalent. Specifically, it was decided that:

(a) food that is known to contain genetically modified material must be labelled; and

(b) where there is uncertainty about the foodÆs contents, it must be labelled as æmay contain genetically modified materialÆ.

ANZFSC recognised that there are many foods, such as oils and sugars, which can be made from genetically modified crops but which can be virtually identical to their conventional counterparts. ANZFSC has agreed that these products should be exempt from a labelling requirement. ANZFA is in the process of developing an appropriate amendment to Standard A18. A timetable for the implementation of these new provisions has yet to be determined.

Application A341

On 14 April 1997, the Authority received an application from Monsanto Australia Limited to amend the *Food Standards Code* to include oil and linters derived from insect resistant cotton lines 531, 757, 1076 and 1849 in the Table to Clause 2 of Standard A18 - Food Produced Using Gene Technology.

The principal food product extracted from the cottonseeds is the edible oil which is used in a variety of foods including frying oil, salad and cooking oil, mayonnaise, salad dressing, shortening, margarine and packing oil. Linters (short fibres that remain attached to the extracted seed) may also be used as a cellulose base in such products as paper, high fibre dietary products, casings for sausages, as well as a viscosity enhancer in toothpaste, ice cream and salad dressings. Cotton seed meal and hulls are primarily used as animal feed.

Lepidopteran insects are the main insect pest of cotton in Australia. During the growing season, other insects (including mites, thrips, mirids and aphids) are also present, but the primary infestations are due to cotton bollworm (*Helicoverpa armigera*) and native budworm (*Helicoverpa punctigera*), both Lepidopteran species. These pests infest up to 100% of the planted hectares and significant costs are associated with attempts at chemical control.

The applicant has developed genetically modified cotton plants, known commercially as INGARD cotton, that are resistant to infestations of both native budworm and cotton bollworm. These cotton varieties were first grown commercially in Australia in 1996 and in 1997 comprised 15% of the Australian cotton acreage. Currently, cotton is not grown in New Zealand.

The crop protection is conferred by the transfer to the cotton of one of two genes from the soil bacterium *Bacillus thuringiensis* subsp. *kurstaki*. These genes are known as either the *cry1Ac* or *cry2Aa* gene and produce insecticidal crystal proteins, otherwise known as deltaûendotoxins. To be active against the target insect, the proteins must be ingested. In the insect gut, the protein binds to specific receptors on the insect midgut, inserts into the cell membrane and forms ionûspecific pores. These events disrupt the digestive processes and cause the death of the insect. The protein products of *cry1Ac* and *cry2Aa* have slightly different sites of action on the surface of the cell.

The applicant intends that plants containing the *cry1Ac* gene and the *cry2Aa* gene will be cross-bred with each other, to develop cotton varieties that contain both genes. The purpose of this is to delay the development of resistance in target insect populations by having two insecticidal mechanisms of action in the one plant line.

OBJECTIVE

The objective, in addressing the issue of permitting the sale of food from insect resistant cotton, is to allow innovation in the food industry without compromising public health and safety or the provision of information to consumers to enable informed choice.

RELEVANT PROVISIONS

Australian *Food Standards Code*

Food produced using gene technology is currently provided for in Standard A18. This Standard will come into effect on 13 May 1999. Following a decision of the Australia New Zealand Food Standards Council (ANZFSC) in December 1998, amendments to the labelling provisions of Standard A18 are proposed. The procedure and timing for implementation of these proposed new labelling provisions has yet to be determined.

New Zealand *Food Regulations*

As a result of the Agreement in 1995 between the Governments of Australia and New Zealand, a joint *Australia New Zealand Food Standards Code* is being developed by the Authority. The decision of ANZFSC to adopt Standard A18 was gazetted in New Zealand, as a mandatory standard, on 20 August 1998 and will apply in both countries on the same day, that is 13 May 1999.

Codex Standards

There are currently no Codex provisions relating to the preûmarket assessment or labelling of foods produced using gene technology. Draft Codex recommendations for the Labelling of Food Obtained through Biotechnology (proposed draft amendment to the General Standard for the Labelling of Prepackaged Foods) are at Steps 3 and 5 of the Codex process.

PUBLIC CONSULTATION

The Authority has received a total of six applications from Monsanto Australia Ltd for a variety of foods produced using gene technology. Due to commonalities in these applications, a combined preliminary assessment report was prepared. The Authority released the combined preliminary assessment report for public comment on 28 October 1998 and submissions were accepted until 23 December 1998. Each application, however, is to be assessed individually at Full Assessment. A total of 58 submissions relating to the six applications in the combined Preliminary Assessment were received primarily from individuals, consumer organisations and special interest groups from both New Zealand and Australia.

OPTIONS including alternatives to regulation

As Standard A18 requires preûmarket assessment of foods produced using gene technology it is not appropriate to consider nonûregulatory options. Only two regulatory options will be considered.

Option 1 - No approval

The status quo would be maintained and no specific approval would be given in the *Food Standards Code* for refined oil and fibre from insect resistant cotton lines 531, 757, 1076, and 1849. This would need to be based on an identified public health and safety concern.

Option 2 - Approval

The *Food Standards Code* would be amended to include the oil and linters from insect resistant cotton lines 531, 757, 1076, and 1849 in the Table to Clause 2 of Standard A18. No special labelling conditions are proposed, as these foods are considered to be within the category of foods which are exempt from mandatory labelling requirements, as decided by ANZFSC in December 1998.

IDENTIFICATION OF AFFECTED PARTIES

Parties affected by the options listed above include:

- consumers
- State, Territory and New Zealand Health Departments
- Australian Quarantine and Inspection Service
- manufacturers and producers of food products that are likely to be made using refined cottonseed oil or processed linters from insect resistant cotton
- suppliers of cottonseed oil and linters to manufacturers.

ASSESSMENT

1. Summary and Conclusions of the Safety Assessment (see Attachment 3)

Insect resistant cotton lines 531, 757, 1076 and 1849 contain three new genes. These are:

- the *cry1Ac* or *cry2Aa* genes derived from the soil bacterium *Bacillus thuringiensis* subspecies *kurstaki*. These genes encode the insecticidal proteins, Cry1Ac and Cry2Aa, which bind to specific receptors on the midgut of lepidoptera species causing the insect larvae to stop feeding and die;

- the *nptII* gene encodes the selectable marker enzyme neomycin phosphotransferase II and confers resistance to the aminoglycoside antibiotics. This gene is used as a marker of plant cell transformation and has no other function in the plant; and

ò The *aad* gene encodes the bacterial selectable marker enzyme aminoglycoside adenylyltransferase and confers resistance to the antibiotics spectinomycin and streptomycin. This gene is used in the cloning processes prior to transfer of the genes to the plant cell. It is not expressed in the plants.

Considerable data has been presented by the applicant to establish that food derived from the insect resistant cotton lines is equivalent to the parental cotton line Coker C312 in all respects apart from the expression of the *cry1Ac* or *cry2Aa* genes and the *nptII* gene. This data included molecular and genetic analyses of the new insect resistant cotton lines, an examination of the potential for the newly expressed proteins to be toxic or allergenic to humans, compositional analyses of the insect resistant cotton lines, and an animal feeding study to establish the wholesomeness of insect resistant cotton line 531 in comparison to conventional cotton varieties.

The molecular and genetic analyses provided by the applicant indicate that the introduced genes have been stably integrated into the plant genome and are stably inherited from one generation to the next.

The new proteins which are expressed in the insect resistant cotton lines are neomycin phosphotransferase II and the insecticidal proteins, Cry1Ac (line 531, 757 and 1076) or Cry2Aa (line 1849). In line 1849, a copy of the *cry2Aa* gene was found to have fused to a cotton gene, resulting in a hybrid gene. This hybrid gene was characterised by the applicant and appears not to be expressed, however, this finding requires confirmation. As refined cottonseed oil and processed linters do not contain any detectable protein, the expression of this gene is not a concern, provided cottonseed is not intended for human consumption. Therefore, in the absence of confirmation of the lack of expression of the hybrid gene it is recommended that approvals for food use be restricted to cottonseed oil and linters.

The applicant submitted data which showed that the newly expressed proteins, Cry1Ac, Cry2Aa and neomycin phosphotransferase II, had been evaluated for their potential to be toxic or allergenic to humans. This included acute toxicity tests using mice for Cry2Aa, comparison of the amino acid sequence of the proteins with known toxins and allergens, and examination of digestion of the proteins in simulated mammalian digestive systems. Furthermore, additional evidence is available from the literature which indicates that the family of *B. thuringiensis* deltaûendotoxins are highly specific for particular gut receptors and these are absent in nonûtarget species including humans. Therefore, the evidence does not indicate that there is any potential for neomycin phosphotransferase II or the Cry1Ac or Cry2Aa proteins to be either toxic or allergenic to humans. Furthermore, these proteins are expressed to relatively low levels in the cotton and cannot be detected in either the refined oil or fibre.

As two antibiotic resistance genes (*aad* and *nptII*) were transferred to the insect resistant cotton lines, the potential for transfer of these genes from ingested material to microorganisms of the human gastrointestinal tract was considered. The presence of these genes in the insect resistant cotton lines was not considered to increase the

potential for transfer to microorganisms of the human gut or to increase the risk of the development of antibiotic resistance among pathogenic bacteria. This is because the human gut already naturally contains a large number of antibiotic resistant microorganisms and the risk of transfer of these genes from ingested material to gut bacteria is generally accepted in the literature to be virtually zero. Furthermore, refined cottonseed oil and fibre do not contain any detectable nucleic acid.

The compositional analyses were comprehensive and indicate that there are some significant differences in composition between the insect resistant cotton lines and the comparator. However, with the exception of carbohydrate (where there is no available information on the normal ranges for commercial cotton varieties) which was significantly decreased in relation to the comparator, these values were within the literature reported ranges. Furthermore, as many of the compounds measured are not constituents of either the refined oil or fibre, these differences are of no concern, provided cottonseed is not intended for human consumption. The refined cottonseed oil and fibre derived from the insect resistant cotton are considered to be equivalent to that of unmodified cotton.

Animal feeding studies using raw, ground cottonseed were presented for insect resistant cotton lines 531. However, as raw, ground cottonseed is not intended for human consumption, this study is considered to have little relevance to humans. Nevertheless, the feeding study indicates that cottonseed from insect resistant cotton line 531 is essentially equivalent to that of the control line C312 in terms of its wholesomeness.

In conclusion, no public health and safety concerns have been identified in this assessment. Both refined cottonseed oil and fibre derived from insect resistant cotton lines 531, 757, 1076 and 1849 can be regarded as substantially equivalent to the refined oil and fibre derived from conventional cotton varieties in respect to composition, safety, wholesomeness and end use.

2. Issues Raised By Public Submissions

A total of 58 submissions were received in response to the section 14 Gazette Notice, of which 51 relate to this application. Very few of the submissions specifically addressed any of the details of the individual applications or provided the Authority with any additional information. Rather, the majority of submissions made general statements against the use of gene technology in association with food, asserted that food produced using this technology is unsafe for human consumption and expressed opposition to any amendment to Standard A18 to permit the sale of such food. A summary of the submissions is attached (Attachment 4).

GENERAL ISSUES RAISED BY SUBMISSIONS

The general issues raised by these submissions have previously been addressed by the Authority in Proposal P97 and are also common to each of the six Monsanto applications referred to in the preliminary assessment. The general issues therefore, have been addressed in an attachment (Attachment 5) to the full assessment of this application, and to each of the remaining applications. Only those issues raised in submissions that are specific to this application are addressed below.

SPECIFIC ISSUES RAISED BY SUBMISSIONS

1. *Feeding studies*

The Consumer Food Network, the Natural Law Party and E. Attwood express concern about the safety of INGARD cottonseed as a source of food because of the results of the animal feeding study 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. A more detailed account of the study is in Attachment 3 - Safety assessment of oil and linters derived from insect resistant cotton, which forms part of this assessment. As noted in the safety assessment, food consumption was decreased slightly and a proportion of the animals exhibited decreased body weight gains in the first week of the study.

Evaluation

Ten male and female rats were fed rodent chow containing 0, 5 and 10% (wt/wt) of raw, ground cottonseed from either INGARD cotton or the C312 control for 4 weeks. At the highest dietary incorporation rate (10%), body weight gain (males) and body weight and body weight gain (females) was slightly, but statistically significantly lower during the first week of study for rats fed INGARD cottonseed meal. For the remainder of the study, there were no statistically significant differences in either parameter for either of the groups. The explanation offered by the applicant to account for the observation, is a slightly reduced palatability of INGARD cottonseed in comparison with the control. As noted in the Safety Assessment, this may be due to slightly increased levels of sterculic acid in unprocessed cottonseed derived from line 531, as used in the study.

The explanation of reduced palatability is reasonable given that there were no observed differences in feeding at the lower concentration of 5% INGARD cottonseed, and that by the end of the 4 week study period, the initial differences had disappeared.

The tissue analysis and post mortem studies on these animals indicated no treatment related differences between the INGARD cotton and control groups. In the absence of any such findings or adverse signs of toxicity, the results do not suggest any connection between a transient difference in weight gain in some animals and any

potential health hazard from the consumption of the INGARD cottonseed.
The likely explanation of a reduced palatability accounts for the initial differences observed and is also compatible with the observed lack of any adverse findings at the end of the study.

It is noted that the feeding study provided raw, ground whole cottonseed including the hulls and meal to the animals. The only components of the cottonseed used for human consumption are the refined edible oil and processed fibres from the linters. Following extensive processing, as well as removal of genetic material and protein from the cottonseed oil, the removal or inactivation of the cyclopropenoid fatty acids (including sterculic acid) results in a product which has a long history of safe use as a food for human consumption. Moreover, the edible fractions of cottonseed derived from INGARD cotton are equivalent to those extracted from conventional cotton lines.

2. *Toxicity and allergenicity of the insecticidal crystal 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.

Evaluation

While it is correct that the B.t.k. proteins, Cry1Ac and Cry2Aa, are not commonly used directly as a food or in a feed source, they are nevertheless ubiquitous in nature and are commonly present as contaminants on food and other animal feed consumed. The donor organism *Bacillus thuringiensis* subsp. *kurstaki (*B.t.k.), which produces the two insecticidal proteins, is the basis of microbial formulations which have been commercially available for Lepiodopteran 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 proteins produced by the INGARD cotton lines are almost identical (greater than 99.4%) to that found in nature and in commercial B.t.k. formulations. Further, it should be noted that the B.t.k. proteins have been exempted from the requirement to establish a maximum residue limit (MRL) when present in INGARD cotton (or when used as a topical application on food crops) because of their low toxicity. It is therefore concluded that there are no adverse implications from food products derived from cottonseed containing these proteins.

Although cottonseed oil and cotton fibre do not contain any detectable protein, if the B.t.k. proteins were consumed, the above information indicates a long history of safe use in association with food crops. Furthermore, neither Cry1Ac nor Cry 2Aa share the biochemical properties common to known allergenic proteins. On the basis of the biochemical profile of the two B.t.k. proteins therefore, there is no scientific evidence to indicate that either of the proteins are potentially allergenic.

3. *Presence of new allergens or toxicants in the refined oil and processed fibres*

Comments from the Western Australian Food Advisory Committee, the National Council of Women of Australia, and B. Thrussell question the applicant's claim that extensive processing of the cottonseeds completely removes protein and genetic material. Hilde and Kristin Knorr, and Elaine Attwood were concerned with the possibility of any new allergic responses to the consumption of foods obtained from INGARD cotton.

Evaluation

Cottonseed oil and fibre are the only cotton products used for human food. Compositional data for cottonseed oil shows that the cottonseed oil does not contain protein or genetic material due to the processing steps. Specifically, these steps include hulling, flaking, heating, extraction, deodorising and bleaching. Refined oil from both line 513 and C312 showed no detectable protein at a sensitivity of 1.3 ppm of total protein. This data supports previous reports which also concluded that there was no protein in cottonseed oil.

Similarly, based on the compositional analysis of the cellulose fibre and the extensive processing at alkaline pH and high temperatures used to produce the fibre prior to food use, fibres for food use are not expected to contain any detectable genetic material or protein. The biochemical methods used to measure total protein (Bradford method) and specific protein (ELISA-Enzyme-Linked Immunosorbent Assay) are well established and validated methods for the measurement of protein from animal and plant tissues.

Although there are no predictive assays available to definitively predict the allergenic potential of substances, certain common biochemical features of known allergens are widely recognised. Most allergens are present as major protein components in the specific food whereas it has been demonstrated that refined oil does not contain appreciable amounts of protein. Moreover, it has been shown that individuals who are allergic to peanuts are able to consume peanut oil without it illiciting an allergic response. These results support the other scientific evidence of no detectable protein in refined oil. There is therefore no evidence which indicates that individuals are likely to be at risk from consuming food derived from INGARD cotton.

In summary, humans are not expected to be exposed to either the genes or expressed proteins of INGARD cotton as the only cotton fractions known to be used for human food are the oil and cellulose from the linters. Neither of these fractions contain either the genes or proteins.

4. *The levels of pesticides in foods derived from INGARD crops*

E. Attwood disputes the applicant's claim that the use of INGARD cotton varieties leads to a substantial reduction in the use of chemical pesticides, and therefore has concerns about the level of residual pesticides in foods derived from these crops.

Evaluation

The risk associated with the presence of chemical residues in food is managed through the establishment of maximum residue limits (MRLs).

In Australia, MRLs are recommended by the National Registration Authority for Agricultural and Veterinary Chemicals (NRA) following an evaluation of actual field trials. In addition, an evaluation of toxicological and other safety data is undertaken by the Chemicals and Nonûprescription Drugs Branch of the Commonwealth Department of Health and Aged Care to determine that likely human levels of exposure will not result in adverse health effects.

ANZFA is responsible for incorporating Australian MRLs into the *Food Standards Code* and, in cooperation with these other government bodies, for ensuring that food containing such residues is safe for human consumption under foreseeable dietary conditions. The values set for MRLs define a legal limit above which residues should not occur if the chemical is used according to good agricultural practice. The MRLs set for chemical residues in the *Food Standards Code* are set well below the level at which adverse health effects may occur.

The setting of MRLs is outside the Agreement between Australia and New Zealand for the development of a joint *Food Standards Code*. The TransûTasman Mutual Recognition Arrangement, which came into effect between Australia and New Zealand in July 1998, however, allows for the mutual recognition of MRLs between the two countries. That is, if MRLs differ, products imported from New Zealand into Australia need only comply with the New Zealand MRLs and vice versa. In New Zealand, there is also recognition of Codex MRLs for imported foods.

Consequently, food derived from insect resistant cotton will have to comply with any appropriate MRLs in Australia and New Zealand.

ANZFA Section 10 Objectives

Protection of public health and safety

A safety assessment of insect resistant cotton lines 531, 757, 1076 and 1849 has been done according to ANZFAÆs safety assessment guidelines using data submitted by the applicant and other relevant information. This assessment concluded that there would be no additional public health and safety concerns associated with the consumption of refined oil and processed fibre from the insect resistant cotton lines. Oil and fibre from these lines can be regarded as substantially equivalent to oil and

fibre from conventional cotton plants in respect of their composition, safety, wholesomeness and end use.

Provision of adequate information relating to food to enable consumers to make informed choices and to prevent fraud and deception

Under the current provisions which do not mandate the labelling of foods that are deemed to be substantially equivalent (such as the refined oil and processed fibre from the insect resistant cotton lines), the onus is very much on the consumer to seek out additional information about these products. Much of this information is available in the public domain and can be readily obtained from ANZFA, government information programs such as Gene Pool in New Zealand, and from the food industry. In addition, the use of negative claims is not prohibited by Standard A18 provided such claims are not false, misleading or deceptive. Therefore, those in the community wishing to avoid these products altogether will be able to do so by accessing the alternative products that have been produced without the use of gene technology.

The recent decision by ANZFSC to amend the current labelling requirements to include mandatory provisions for substantially equivalent foods is not likely to affect the labelling of the food derived from insect resistant cotton, namely the refined cottonseed oil and processed fibre. This is because Health Ministers have agreed such products would be exempt from mandatory labelling requirements as neither the oil nor the fibre contain protein to a level of detection of 1.3 ppm or any detectable genetic material.

Promotion of fair trading in food

Approval for the sale of refined cottonseed oil and processed fibre from insect resistant cotton lines 531, 757, 1076 and 1849 will mean that all manufacturers and food producers in Australia and New Zealand are free to use such products should they wish to do so. Therefore, the proposed amendment should not impact on fair trading in food.

Promotion of trade and commerce in the food industry

The insect resistant cotton lines represent a technological advance in agricultural cropping systems which allows cotton growers access to cotton varieties that can resist infestation by insects and consequently enable them to use a range of practices in pest management, including a reduction in the amount of pesticides that must be used in crop. The insect resistant cotton does not offer any technological advantage to the food industry as the processing, storage, and nutritional characteristics of the oil and fibre remain unchanged. Therefore, the insect resistant cotton lines are grown along with conventional cotton varieties and the seeds obtained from the crops are not segregated. Consequently, this objective is not directly relevant to this application. However, the approval of foods that have been produced using new technologies will indirectly lead to the promotion of trade and commerce in the food industry by encouraging innovation.

Promotion of consistency between domestic and international food standards

There are no international (ie., Codex) food standards for foods produced using gene technology, therefore an amendment to the *Food Standards Code* will not contribute to the promotion of consistency between domestic and international standards. However, insect resistant cotton is grown commercially by some of AustraliaÆs and New ZealandÆs major trading partners (United States, Canada). Approval in Australia and New Zealand will lead to harmonisation with our trading partners and will facilitate trade in foods containing these products.

4. Regulatory Impact Analysis

Option 1û not permit the sale of oil and linters derived from INGARD cotton lines from 13 May 1999.

GOVERNMENT Commonwealth, New Zealand Health Departments, State/Territory Health Departments, local government, Australian Quarantine and Inspection Service	**Benefits** ò no benefits were identified	**Costs** ò the government may be open to challenge under WTO as a prohibition on the sale of oil or linters derived from INGARD cotton could restrict imports of manufactured food products into Australia and New Zealand. ò a prohibition on food use in Australia and New Zealand could affect acceptability of Australian cottonseed in export markets such as Japan, Korea and Taiwan. ò there may be technical and resource implications for enforcement agencies in enforcing a prohibition at the import barrier.
INDUSTRY manufacturers and producers of food products containing either refined cottonseed oil or cellulose fibre from insect resistant cotton varieties, food importers and exporters,	**Benefits** ò no benefits were identified	**Costs** ò food manufacturers and producers will be unable to use the processed food fractions of the cottonseed derived from the INGARD crops, requiring segregation of transgenic seed from unmodified seed at harvest and necessitating a duplication of storage and handling facilities. ò restricted access to raw materials and restricted access to export markets

CONSUMERS	**Benefits** **ò** no benefits were identified	**Costs** **ò** could lead to decreased

		availability of certain food products **ò** increased costs to consumers because manufacturers and producers may have to source their raw commodities from other suppliers

Option 2ûamend the Food Standards Code to permit the sale of oil and linters derived from INGARD cotton lines.

GOVERNMENT Commonwealth, New Zealand Health Departments, State/Territory Health Departments, local government Australian Quarantine and Inspection Service	**Benefits** ò increased innovation and competitiveness by the food industry has the potential to benefit the economy	**Costs** ò minor costs associated with amending the *Food Standards Code*
INDUSTRY manufacturers and producers of food products containing either refined cottonseed oil or cellulose fibre from insect resistant INGARD« varieties, food importers and exporters, cotton producers	**Benefits** ò manufacturers and producers will have continued access to raw materials and therefore continued access to export markets ò 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 ingredients derived from the insect resistant INGARD cotton lines ò cotton growers would have unrestricted markets for cottonseed obtained from the insect resistant lines	**Costs** ò no costs were identified
CONSUMERS	**Benefits** **ò** assurance of the availability of food products derived from cottonseed oil and linters	**Costs** **ò** consumers will be unable to specifically choose between cottonseed products derived from insect resistant cotton and those products derived from conventional cotton.

Evaluation of the regulatory impact

Option 1

This option will prohibit the sale of cottonseed oil and linters when Standard A18 comes into effect on 13 May 1999. A recommendation by ANZFA against inclusion of these food products from insect resistant cotton would need to be based on an identified public health and safety concern.

The safety assessment has found that the refined cottonseed oil and processed fibre from the linters are equivalent in terms of their composition, safety, wholesomeness and end use to those obtained from unmodified cottonseed. On this basis therefore, there are no public health and safety concerns which could support this option.

A prohibition on food products derived from insect resistant cotton would mean that the food fractions of the cottonseed, namely the edible oil and processed linters, would be deemed unsuitable for human consumption. At the point of harvest, this would require segregation of genetically modified and unmodified seeds, necessitating separate handling and storage facilities. The proportion of Bt cotton currently grown in Australia is approximately 15% of the total cotton acreage, and therefore a reduction in the availability of raw materials is likely to restrict supplies to manufacturers of products which use the cottonseed oil in blended vegetable oil and as an ingredient in certain processed foods. Consumers may also experience reduced availability of certain products and/or increased costs.

There are potential trade implications as INGARD cotton is currently used without restriction in the USA and Canada and segregation of INGARD cottonseed is not required, nor are foods derived from the cotton required to be labelled. In addition, regulatory approval for end-use of Bt cottonseed has been obtained in Japan. If different regulatory requirements were imposed in Australia, these could be expected to restrict trade and impose costs on both imports and exports. Currently, a significant proportion of cottonseed grown in Australia is exported to countries such as Japan, Korea and Taiwan for oil extraction and animal feed. Differing export and domestic requirements for INGARD cottonseed would pose additional handling costs and possibly reduce Australia's competitiveness in the export market.

The only potential benefits recognised in this option are to that proportion of consumers who are opposed to gene technology, and who wish to avoid foods produced using gene technology. This option is not considered therefore to be a viable option, as the potential costs identified for government, industry and consumers outweigh any benefits to those consumers who wish to avoid foods produced using gene technology.

Option 2

This option will result in permitting the sale of refined cottonseed oil and processed fibre derived from the insect resistant cotton lines specified in this assessment. The safety assessment has concluded that these food products are equivalent to those obtained from the non-transgenic cotton and therefore do not pose any greater risk to public health and safety when consumed as food. On the basis of these findings, this is the Authority's preferred option.

The benefits of this option primarily accrue to the agricultural sector, the food industry and government. There is an indirect social benefit if a wider interpretation of the environmental benefits ensuing from the proposed reduction in chemical pesticide usage is taken into consideration.

The government will benefit because this decision will serve to give encouragement to agricultural sectors that technological innovations in the development of food crops will be accepted by the government. This could lead to greater certainty in the food industry, and greater competition and investment in agriûfood businesses. The food industry will benefit because there will be no risk of disruption to their businesses and manufacturers and producers can continue to access the necessary raw materials for their products. Cotton producers will benefit in having a more comprehensive pest resistance management strategy aimed at preventing or postponing insects developing resistance to B.t. proteins. Agricultural workers are expected to benefit from reduced exposure to pesticides and pesticide spray solutions used specifically for *Helicoverpa* spps.

In addition, consumers will have the knowledge that the refined oil and fibre of the cottonseed derived from the insect resistant plants have been subjected to a scientific safety assessment and found to be suitable for human consumption.

The only cost that could be identified, apart from that to government for amending the *Food Standards Code* , is to those consumers wishing to totally avoid eating food produced using gene technology. These consumers will be restricted to alternative markets, such as organic foods, which have reduced variety and tend to be more expensive.

Conclusion of the regulatory impact analysis

Consideration of the regulatory impact for this application concludes that, as the consumption of food products derived from insect resistant cottonseed does not pose any greater risk to public health and safety than those obtained from conventional cottonseed, Option 1, to not permit their sale, is not a viable option. Therefore, the preferred option is to amend the *Food Standards Code* to permit the sale of oil and linters derived from insect resistant cotton lines 531, 757, 1076 and 1849.

It is concluded from the regulatory impact analysis that the proposed amendments to the *Food Standard Code* are cost effective in that the potential benefits for industry, government and consumers, outweigh the potential costs.

CONCLUSIONS OF THE FULL ASSESSMENT

It is concluded that:

- oil and linters derived from insect resistant cotton lines 531, 757, 1076 and 1849 are considered to be substantially equivalent to those derived from conventional cotton lines in respect of their composition, safety, wholesomeness and end use;

- while considerable general concern has been expressed regarding the use of gene technology in food production, there is no evidence that the oil and linters from the insect resistant cotton lines will cause adverse health effects in humans;

- on the basis of the recent ANZFSC decision to require mandatory labelling on foods which do, or may, contain genetically modified material, it is not envisaged that the refined oil or processed fibre from the cottonseed, or any processed product using these as ingredients, would require labelling. The reason for this is that neither the oil nor the fibre contains any detectable genetically modified material;

- the proposed amendment is consistent with ANZFA's section 10 objectives;

- the benefits of the proposed amendment primarily accrue to the cotton producers, food industry and government, with potentially a small benefit to the consumer. These benefits outweigh the costs associated with recommending against the amendment.

WORLD TRADE ORGANISATION (WTO) NOTIFICATION

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

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

This matter does not need to be notified to the WTO as an Sanitary and Phytosanitary (SPS) notification or a Technical Barriers to Trade (TBT) notification because the proposed variation to the *Food Standards Code* constitutes a minor technical change and will have no effect on trade issues for either technical or sanitary reasons.

Attachments to the Report:

1. Draft Variation to the Australian *Food Standards Code*
2. Explanatory Notes
3. Safety Assessment
4. Public Comment Received
5. General Issues Raised

Attachment 1

DRAFT VARIATION TO THE AUSTRALIAN FOOD STANDARDS CODE

A341 - OIL AND LINTERS DERIVED FROM INSECT RESISTANT COTTON

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

Oil and linters derived from insect resistant cotton lines 531, 757, 1076 and 1849.

Attachment 2

DRAFT EXPLANATORY NOTES

DOCUMENT AVAILABLE SEPARATELY

SAFETY ASSESSMENT
A341û OIL AND LINTERS FROM INSECT RESISTANT COTTON

BACKGROUND

Monsanto Australia Ltd have made an application to ANZFA to vary Standard A18 to include food from insect resistant cotton lines in the Table to the standard. The insect resistant cotton lines described in the application are not intended to be used themselves in commercial production. Their insect resistant trait has been transferred into commercial cotton varieties by traditional breeding techniques.

The cotton which is the subject of this application is known commercially in Australia as æINGARD cottonÆ or æBt cottonÆ. The term æBt cottonÆ denotes that the soil bacteria *Bacillus thuringiensis* is the source organism for the genes conferring resistance to the insect pests. The insect pests in question are larvae of the moths *Helicoverpa punctigera* and *H. armigera* û otherwise known as native budworm and cotton bollworm, respectively.

Following advice from the Genetic Manipulation Advisory Committee, the National Registration Authority for Agricultural and Veterinary Chemicals registered the INGARD gene as a plant pesticide (Approval No. 48296/01, 48404) in Australia. Cotton varieties containing this gene were first grown commercially in Australia in 1996 and in 1997 comprised 15% of the Australian cotton acreage.

The only human food products obtained from the cotton are cottonseed oil and linters. Cotton seed oil is a premium quality oil that may be used in a variety of foods including frying oil, mayonnaise, salad dressing, shortening, margarine and packing oil. Linters are short fibres removed from the cottonseed during delinting. After extensive processing at alkaline pH and high temperatures, the linters can be used as high fibre dietary products, sausage casings and viscosity enhancers in ice cream and salad dressings. The linters consist primarily of cellulose (>99%).

DESCRIPTION OF THE MODIFICATION

Cotton lines 531, 757, 1076 and 1849 were generated by transformation of the parental cotton line (*Gossypium hirsutum* L. cv Coker C312) using *Agrobacterium*ûmediated transformation. The following genes were transferred:

Table 1: Genes transferred to insectûresistant cotton lines

gene	line 531	line 757	line 1076	line 1849
cry1Ac	_	_	_	ù
cry2Aa	ù	ù	ù	_
nptII	_	_	_	_
aad	_	_	_	_

Genes for the insect resistance trait

The *cry1Ac* gene encodes the Class I (*Lepidoptera*ûspecific) crystal protein (Cry1Ac) and the *cry2Aa* gene encodes the Class II (*Lepidoptera*ûspecific) crystal protein (Cry2Aa). Both proteins are also referred to as deltaûendotoxins and are produced by the soil bacterium *Bacillus thuringiensis* subspecies *kurstaki*. During sporulation, *B. thuringiensis* produces cytoplasmic inclusions containing one or more of the insecticidal crystal proteins. Most crystal proteins are synthesised intracellularly as inactive protoxins that spontaneously form small crystals, approximately 1 Ám in size. Upon ingestion by susceptible insects, the highly alkaline pH of the midgut promotes solubilisation of the protoxinûcontaining crystals. The protoxin is activated by trypsinûlike gut proteases which cleave off domains from the carboxyû and aminoû termini leaving a proteaseûresistant core which is the active toxin. The now active toxin binds to a glycoprotein receptor on the surface of midgut epithelial cells. When about eight of these 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. The Cry1Ac and Cry2Aa proteins are structurally and functionally similar, but bind to different glycoprotein receptors in the midgut.

To improve the expression of the bacterialûderived *cry1Ac* and *cry2Aa* genes in plant cells, their DNA sequence was modified to reflect the codon preference of transfer RNAs in plant cells. The amino acid sequence encoded by the genes, however, remained virtually the same.

The applicant intends that plants containing the *cry1Ac* gene and the *cry2Aa* gene will be crossed, to develop cotton varieties that contain both genes. The purpose of this is to delay the development of resistant populations of target insects by having two insecticidal mechanisms of action in the one plant line.

Selectable marker genes

The *nptII* gene encodes the selectable marker enzyme neomycin phosphotransferase II and confers resistance to the aminoglycoside antibiotics, kanamycin, and neomycin. The *aad* gene encodes the bacterial selectable marker enzyme aminoglycoside adenylyltransferase and confers resistance to the antibiotics spectinomycin and streptomycin.

Controlling sequences

In lines 531 and 757, both the *cry1Ac* gene and the *nptII* gene are under the control of the 35S promoter derived from cauliflower mosaic virus. In line 1076 and 1849, the *cry1Ac* and *cry2Aa* genes are under the control of the 35S promoter derived from figwort mosaic virus. Therefore, the *cry* genes and the *nptII* gene would be expected to be expressed in all four cotton lines. The *aad* gene is under the control of a bacterial promoter, therefore, would not be expected to be expressed in any of the cotton lines.

Molecular analyses

The cotton lines were subjected to several rounds of selfûfertilisation and backûcrossing. Molecular analysis of these lines, using Southern blot analysis, indicates that the transferred genes are stably integrated into the plant genome. A summary of the molecular characterisation of each line is given below.

Line	Characterisation
531	Two TûDNA inserts (one incomplete) in close proximity in the plant genome in a head to tail arrangement. The incomplete TûDNA insertion contains the 3Æ end of the *cry1Ac* gene, and lacks the insecticidally active 5Æ end of the gene. The *cry1Ac* gene segregated in a manner consistent with a single active copy of the gene. The *cry1Ac* gene was stably transferred with crossing.
757	Two TûDNA inserts (one incomplete) at separate sites into the plant genome. The incomplete TûDNA insertion lacks the 5Æ end of the *cry1Ac* gene as well as the promoter sequences, therefore its expression would be improbable. The segregation data supports the presence of a single active *cry1Ac* gene.
1076	Two TûDNA inserts (one incomplete) in tandem at a single genetic locus in the plant genome. Incomplete TûDNA insertion contains only a partial *cry1Ac* gene and no promoter sequences therefore expression of the second copy of this gene would be improbable.
1849	Two TûDNA (one incomplete) inserts into the plant genome. The incomplete TûDNA insertion only contains a partial copy of the *cry2Aa* gene. The partial *cry2Aa* gene is truncated at the 3Æ end and is fused to host DNA, resulting in a chimaeric gene. Immunoblot analyses did not reveal any detectable protein product from this chimaeric gene. Segregation analysis is consistent with a single active copy of the *cry2Aa* gene inserted in the genome.

ISSUES IN SAFETY ASSESSMENT

There are two food products obtained from Bt cotton, namely, vegetable oil and fibre. The vegetable oil is the major food product for human consumption. The Bt cotton has been assessed according to the safety assessment guidelines developed by ANZFA. Although the primary food products for human consumption are refined oil and fibre, the data presented relates primarily to cottonseed, therefore, safety

assessment issues relate to Group D foods. The following issues were considered relevant for a safety assessment:

(i) General safety issues:

- û history of use of the cotton plant as a source of vegetable oil and fibre for human food use;
- û expression of new genetic material;
- û potential toxicity of newly expressed proteins;
- û immunological effects; and
- û transfer of novel genetic material to gut microflora.

(ii) Compositional analyses:

- û proximate analysis for major constituents; and
- û critical nutrients, anti-nutritional factors, and natural toxicants.

(iii) Ability to support typical growth and wellûbeing.

Each of these issues are discussed below.

(i) General safety issues

History of use of the cotton plant as a source of vegetable oil and fibre for human food use

Cotton seed is processed into four major products ù oil, meal, hulls, and linters. Of these, only oil and linters are intended for human consumption. These products are routinely used in food and have a history of safe use.

Expression of new genetic material

Of the three genes transferred into cotton lines 531, 757, 1076, 1849, only the *cry1Ac* or *cry2Aa* and the *nptII* genes are expressed in the plant. The *aad* gene, which encodes the enzyme aminoglycoside adenylyltransferase, is under the control of a bacterial promoter, therefore, would not be expected to be expressed in the plant. The lack of *in planta* expression of aminoglycoside adenylyltransferase was confirmed using ELISA, sensitive down to 7.5 ng/g tissue weight in leaf and 5 ng/g tissue weight in seed.

The *nptII* gene is a selectable marker gene which expresses the enzyme neomycin phosphotransferase II. This enzyme catalyses the phosphorylation of neomycin using ATP, as well as related antibiotics such as kanamycin, thereby inactivating it and preventing the antibiotic from killing the cell in which it is expressed. It is used as a positive selection for those plant cells which have been transformed with the vector and, therefore, the gene of interest, in this case the *cry1Ac* or *cry2Aa* genes.

The *cry1Ac* gene used to produce lines 531, 757 and 1076 is an artificial gene constructed by combining the first 1398 nucleotides of the *cryIAb* gene with nucleotides 1399 to 3534 of the naturally occurring*cry1Ac* gene. With the exception of the nucleotides coding for 6 amino acids, the *cryIAb* region is identical to the analogous region of the *cry1Ac* gene. The protein encoded by the*cry1Ac* portion of this artificial gene is identical to the Cry1Ac crystal protein present in nature with the exception of one amino acid. This amino acid is not present in the active proteaseûresistant core of the crystal protein, therefore does not affect the specificity of the protein. Overall, the Cry1Ac deltaûendotoxin expressed by lines 531, 757 and 1076 is near natureûidentical (99.4% homologous) to the naturally occurring Cry1Ac deltaûendotoxin produced by *B. thuringiensis* subsp *kurstaki*.

Analyses of leaf and seed tissue from the cotton lines demonstrated that both the deltaûendotoxin proteins and neomycin phosphotransferase II are expressed at low and relatively consistent levels in lines 531, 757, 1076 and 1849 (Table 2).

Table 2: Protein expression levels in the insect resistant cotton lines

	Expression levels	
	Ág/g fresh weight	**% fresh weight**
Line 531		
Cry1Ac crystal protein	<10	<0.001
Line 757		
Cry1Ac crystal protein	12.7 and 9.9	_0.001
neomycin phosphotransferase II	6.9 and 3.3	<0.001
Line 1076		
Cry1Ac crystal protein	12.2 and 12.7	0.001
neomycin phosphotransferase II	16.3 and 7.9	<0.002
Line 1849		
Cry2Aa crystal protein	16.9û36.5	<0.004
neomycin phosphotransferase II	8.2û23.5	<0.003

Detection of protein in refined cottonseed oil and linters

Protein was not able to be detected in refined oil down to a sensitivity of 1.3 ppm total protein in cotton line 531, confirming reports that refined cottonseed oil does not contain any detectable protein.

An insect bioassay with a sensitivity of 1 ng/ml diet was used to test for the presence of Cry1Ac in linters from line 531. A low level of Cry1Ac was detected in raw cotton linters, probably because raw linters would contain a small amount of hull material. However, Cry1Ac was not able to be detected in raw cotton fibre, cleaned cotton fibre or cleaned linters, indicating that processing of the raw linters removes any of the trace levels of protein from the contaminating hulls. Protein could also not be detected using harsh protein extractions and immunoblot analysis of the linter fractions.

Expression of genetic material other than the intended change

In line 1849, a copy of the *cry2Aa* gene was found to have fused to a cotton gene during the gene transfer, resulting in a hybrid gene. This hybrid gene appears not to be expressed because immunoblots are negative for this protein. However, this finding requires further confirmation using RNA analyses. As refined oil and processed linters have been shown to contain no detectable protein, the expression of this gene would not be a concern, provided cottonseed is not intended for human consumption.

Potential toxicity of newly expressed proteins

The potential for toxicity of the newly expressed proteins was examined. Additional information was also available from the literature on the relative toxicity of these proteins.

Cry1Ac and Cry2Aa

These crystal proteins are virtually identical to the proteins 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 (eg, in this case specific to the lepidoptera) and there is no evidence that they are active against nonûtarget insects, birds, fish or mammals. This lack of activity against nonûtarget species appears to be due to an absence of specific gut receptors (Frick 1995). The binding of the deltaûendotoxin to specific gut receptors appears to be a preûrequisite for toxicity.

Toxicology data provided in support of the registration of the *cry1Ac* gene by the NRA was assessed by the Chemicals and Nonûprescription Drugs Branch of the Therapeutic Goods Administration. Poisonings scheduling was not considered necessary, in view of the low toxicological hazard posed by the Cry1Ac delta endotoxin and also because the product will be used in a way which precludes human exposure. That is, the proteins are not able to be detected in the products used in food, namely refined cottonseed oil and processed linters.

In addition, the amino acid sequence of Cry2Aa was compared with the amino acid sequences of known protein toxins in public domain databases (eg, EMBL, GenBank). The only significant homologies detected were with other *B. thuringiensis* insecticidal crystal proteins.

The acute oral toxicity of Cry2Aa was studied in mice using doses up to 4000 mg/kg. Mice were observed for up to 9 days after dosing. No adverse findings that could be related to the treatment were found.

Neomycin phosphotransferase II

Neomycin phosphotransferase II is ubiquitous in the environment and is also naturally produced by many common bacteria of the human digestive system. In conditions that simulate the human digestive system, the enzyme is rapidly inactivated by stomach acid and digestive enzymes. In addition, the enzyme has also been shown to be heat labile, therefore, would be expected to be inactivated with heat processing. This enzyme has no significant homology with any known toxins.

Neomycin phosphotransferase II has been granted approval by the United States Food and Drug Administration (FDA) for use as a processing aid in tomatoes, canola and cotton.

Immunological effects

Data was provided on the potential for allergenicity of the newly expressed proteins in all four lines.

Cry1Ac and Cry2Aa

Although there are no predictive assays available to assess the allergenic potential of proteins, a number of characteristics are common among many of the allergens that have been characterised. For instance, known allergens tend to be glycosylated proteins with a molecular weight of 10û70KDa. In addition, they tend to be heat stable as well as resistant to peptic and tryptic digestion and the acid conditions of the stomach and be present at high concentrations in the ingested food. The Cry1Ac and Cry2Aa crystal proteins were evaluated below against these criteria.

The full length Cry1Ac and Cry2Aa proteins are proteolytically cleaved to 67 kDa and 50 kDa proteins, respectively. This fits within the size range of known allergens. The biological activity of these proteins is reported to be destroyed with processing of the seed to extract the oil, although a small amount of the inactive protein can still be detected in the processed meal. Studies using simulated gastric systems indicate that these proteins are readily digested by the proteases that are present in mammalian gastric fluids (halfûlife of 15 seconds for Cry2Aa and less than 30 seconds for Cry1Ac). Also, at least 97% of the functional bioactivity of the Cry2Aa protein is lost within 60 seconds in simulated gastric fluids. In a simulated intestinal system, these proteins are rapidly converted to the proteaseûresistant core and are not further degraded, although with Cry2Aa bioactivity was found to decrease by 95% in 24 hours. Cry1Ac protein purified from the cottonseed was shown to not be glycosylated as would be expected given that neither the *cry1Ac* or *cry2Aa* genes were constructed with leader peptides that would enable transportation to the endoplasmic reticulum. Both proteins were found not to have any significant homology to any know protein allergens and are only present in cottonseed at very low levels. Furthermore, these proteins were not able to be detected in either refined

cottonseed oil or processed linters using a very sensitive bioassay for insecticidal activity.

Neomycin phosphotransferase II

The use of the enzyme as a processing aid has previously been evaluated by the FDA. The FDA concluded that this enzyme does not have any of the recognised characteristics of food allergens or any attributes that would distinguish it toxicologically from other phosphorylating enzymes in the food supply (FDA 1994).

Transfer of novel genetic material to gut microflora

The cotton lines all contain copies of the *nptII* gene, which confers resistance to kanamycin and neomycin, and the *aad* gene, which confers resistance to streptomycin and spectinomycin. The *aad* gene is not expressed in the plants.

The potential for transfer of antibiotic resistance genes from ingested material to microorganisms of the human gastrointestinal tract was considered by a Workshop conducted by the World Health Organisation in 1993 (WHO 1993). This issue was considered because of the question of whether the transfer of such genes could affect the therapeutic efficacy of antibiotics. This workshop concluded that there was no recorded evidence of transfer of genes from plants to microorganisms in the gut and also that such transfers would be extremely unlikely given the complexity of the steps required.

The following points are considered relevant to consideration of this issue:

1. Antibiotic resistant bacteria are found normally in the environment and the human gut because of the constant presence of antibiotics in the human environment (Levy 1984, Levy *et al* 1988). Therefore, the transfer of antibiotic resistance genes to pathogenic bacteria is more likely from these sources (Connor 1997);

   eg., û it has been estimated that the average person ingests over $1 \infty 10^6$ kanamycin resistant microorganisms daily as a natural component of food, especially raw vegetables (Flavell *et al* 1992);

   û about $1 \infty 10^{12}$ kanamycin resistant bacteria are thought to naturally inhabit the gut of each person at one time or another (Flavell *et al* 1992);

2. The horizontal transfer of genetic material from plants to bacteria has never been demonstrated (Pittard 1997);

3. Refined cottonseed oil and fibre do not contain any detectable nucleic acid.

Therefore, the presence of copies of the *nptII* gene and the *aad* gene in the insect resistant cotton lines is not considered to pose any additional risk to public health and safety in relation to the development of antibiotic resistant pathogenic bacteria.

Conclusions regarding general safety issuesù Seed from the cotton, *Gossypium hirsutum* L., is the traditional source of cottonseed oil and fibre for human consumption and has a history of safe use for these purposes. The insect resistant cotton lines express two new proteins: either Cry1Ac (lines 531, 757 and 1076) or Cry2Aa (line 1849); and neomycin phosphotransferase II. In line 1849, a copy of the *cry2Aa* gene was found to have fused to a cotton gene, resulting in a hybrid gene. This hybrid gene was characterised by the applicant and appears not to be expressed, however, this finding requires confirmation. As refined cottonseed oil and fibre do not contain any detectable protein, the expression of this gene would not be a concern, provided cottonseed is not intended for human consumption. The evidence does not indicate that there is any potential for Cry1Ac, Cry2Aa or neomycin phosphotransferase II to be either toxic or allergenic to humans. Furthermore, the proteins are expressed at relatively low levels in the cotton and cannot be detected in either the refined oil or fibre. The presence of the *nptII* gene and the *aad* gene, conferring resistance to antibiotics, in the cotton lines is not considered to increase the risk of the development of antibiotic resistance among pathogenic bacteria. Furthermore, refined cottonseed oil and fibre do not contain any detectable nucleic acid.

(ii) Compositional analyses

Compositional analyses were done on the seed and processed fractions of seed (meal, toasted meal and oil) from insect resistant cotton lines 531, 757, 1076 and 1849 and comparison was made to the seed and processed fractions of seed from the parental Coker C312 cultivar. The Coker C312 cultivar is an older cotton variety which has been superseded by other cultivars, however, it is still considered to be a commercially acceptable cultivar.

Lines 531, 757, 1076 and C312 were grown at six separate field locations in the United States in 1993. Lines 1849 and C312 were grown at six different field sites in the United States in 1994 and 1995. Each of the different sites are located in major cotton growing regions and are representative of various local growing practices. These locations are reported to provide a variety of environmental conditions and insect pressures. Insect resistant cotton and the control cotton (C312) were grown under the same conditions at each location.

Proximate analysis for major constituents

The mean levels of major constituents (protein, total fat, carbohydrate, moisture, ash, crude fibre and calories) were measured in cottonseed from all four lines.

In the case of lines 531 and 757, no significant differences with the comparator C312 were found with respect to any of the major constituents measured in the proximate analysis. No significant differences were also observed in relation to protein, ash

and moisture between line 1076 and the comparator C312. This was also the case for line 1849 which was also equivalent to the comparator with respect to calories.

Statistically significant differences were found between line 1076 and the comparator C312 with respect to total fat, carbohydrate and calories. However, the mean values reported for total fat and calories all fall within the range reported for the comparator. Statistically significant differences were also found between line 1849 and the comparator C312 with respect to protein, crude fibre, and carbohydrates. However, the mean values reported for crude fibre and protein all fall within or very near the ranges reported for the comparator or the ranges reported for commercial cotton varieties. Normal ranges for carbohydrates in commercial cotton varieties are not available because this constituent is not one normally measured for commercial varieties. Mean carbohydrate levels in lines 1849 and 1076 are outside the range reported for the comparator C312. As carbohydrate values for commercial cotton varieties are not available the significance of this cannot be commented on. However, this is not considered to be of concern as cottonseed is not intended for human consumption.

Critical nutrients, antiûnutritional factors and natural toxicants

Amino acids analysis

Amino acid analyses were done on whole cottonseed from all four lines. Of the 18 amino acids analysed, mean levels of several amino acids in cottonseed from some of the cotton lines were found to be statistically significantly different to the mean levels obtained for the comparator C312. The amino acids were glutamic acid, valine, methionine, isoleucine, tyrosine, lysine, histidine and arginine in lines 757 and 531 and serine, glycine, methionine, cystine and lysine in line 1849. In most cases, however, the mean values fell within or very near the literature reported ranges for amino acid levels in commercial cotton varieties. The exceptions were: lysine which was significantly increased in lines 531, 757 and 1849; and glutamic acid which was significantly decreased in lines 531 and 757. In all these cases, however, the mean levels of these substances were also significantly different between the comparator C312 and the literature reported ranges for commercial cotton varieties. Therefore, these differences cannot be directly attributable to the transfer of new genes and may instead be the result of natural variability within cotton varieties.

Overall, the amino acid composition of the seed from cotton lines 531, 757, 1076 and 1849 can be regarded as similar to the composition of seed from the comparator C312.

Fatty acid analysis

Fatty acid analysis was done on seed from all four cotton lines. Components measured were myristic acid (C14:0), pentadecanoic acid (C15:0; except for line 531), palmitic acid (C16:0), palmitoleic acid (C16:1), heptadecanoic acid (C17:0) stearic acid (C18:0), oleic acid (C18:1), linoleic (C18:2), and linolenic (C18:3), arachidic acid (C20:0; except for lines 757 and 1076), behenic (C22:0; except for lines 757 and 1076), and lignoceric acid (C24:0; except for lines 757 and 1076).

For the majority of fatty acids analysed, no statistically significant differences were found between the insect resistant cotton lines and the comparator C312. The exceptions were for myristic, stearic and oleic acid for line 531, myristic and palmitoleic acid for line 1076, and linoleic acid for the 1995 testing of line 1849. In all these cases, however, the mean values reported were within the literature reported ranges.

Therefore, the fatty acid content of seed from the insect resistant cotton lines is equivalent to that of the other commercial varieties of cotton. These components are considered to be of most importance as it is the oil which is the major food product for human consumption.

Gossypol analyses

Gossypol is a biologically active terpenoid aldehyde substance that is present in discrete glands in various plant tissues, including seed. The presence of gossypol in cottonseed limits its use as a protein source in animal feed, except for cattle. However, the removal or inactivation of gossypol during processing enables the use of some cottonseed meal for fish, poultry and pigs. The gossypol that partitions into the oil is essentially completely eliminated during subsequent refining of the oil. The reduction of free gossypol in oil is a measure of the food quality and processing efficiency.

Data was presented on both total and free gossypol levels for all four insect resistant cotton lines. The mean gossypol levels obtained for seed from the insect resistant cotton were mostly equivalent to those obtained for the comparator C312. The exception was for a statistically significant decrease in mean total gossypol level for line 1076. This mean value, however, was within the normal range of values for the comparator as well as commercial cotton varieties. There was no detectable gossypol in refined oil and the amount of free gossypol was reduced to trace levels in the toasted meal for both lines.

Cyclopropenoid fatty acids

The cyclopropenoid fatty acids are toxicants and comprise malvalic, sterculic, and dihydrosterulic acids. The cyclopropenoid fatty acids inhibit the biodesaturation of stearic acid to oleic acid, and this is reported to lead to adverse biological effects (Gunstone *et al* 1994). For example, pink colouration of egg whites has been associated with the feeding of sterculic acid to chickens. The cyclopropenoid fatty acids are destroyed either by hydrogenation or by heating the oil in the presence of free fatty acids for deodorisation purposes (Gunstone *et al* 1994). The presence of cyclopropenoid fatty acids in cottonseed limits its use as a protein source in animal feed, except for cattle. However, its removal or inactivation during processing enables the use of some cottonseed meal for fish, poultry and pigs.

Analyses were done on malvalic acid, sterculic acid and dihydrosterulic acid for all four cotton lines. The literature reported ranges for these compounds are quite variable and, for the most part, the mean values reported for these three fatty acids in the insect resistant cotton lines are within these ranges.

The mean level for sterculic acid in line 1849 in the 1994 planting (mean value of 0.473%, range 0.197û1.03%) appeared to be significantly increased in relation to the comparator C312 (mean value of 0.269%, range 0.201û0.335%) but was within the literature reported ranges for sterculic acid in commercial cotton varieties (0.08û0.56%). In addition, this increase in sterculic acid did not appear to be associated with any concomitant increase in the stearic acid levels or decrease in the oleic acid levels.

As the cyclopropenoid fatty acids are destroyed during processing to produce oil, and differences in their levels does not appear to have affected the levels of some of the key fatty acids in cotton, these differences are not considered to pose a public health and safety concern.

Aflatoxin analyses

Aflatoxins are a group of mycotoxins produced by the *Aspergillus flavus* and *A. parasiticus* and are potent animal toxins and carcinogens and have been epidemiologically implicated as environmental carcinogens in humans. Cotton seed is one of the commodities most commonly contaminated by aflatoxins. Cotton that is damaged by moth larvae is more susceptible to infection by *Aspergillus* fungi. This infection is often initiated through larval damage that occurs in the field rather than in storage.

For the most part, there were no significant differences in aflatoxin levels between the insect resistant cotton lines and the comparator. The exception was that occasionally, the control cotton line was found to have significantly higher aflatoxin levels than the insect resistant cotton lines, as might be expected given it would be more susceptible to insect damage.

Conclusions regarding compositional analysesùLine C312 is an appropriate comparator for insect resistant cotton lines 531, 757, 1076 and 1849 because it is a commercially acceptable variety and is the variety that was initially transformed. Some significant differences in composition between the insect resistant cotton lines and the comparator were found. However, with the exception of carbohydrate (where there is no available information on the normal ranges for commercial cotton varieties) which was significantly decreased in relation to the comparator, these values were within or very near the literature reported ranges. As these constituents were measured in whole cottonseed, and it is only refined cottonseed oil and fibre which are intended for human consumption, these differences are not of concern. Fatty acid analysis of the cottonseed indicates that there are no significant differences in the levels of fatty acids. Refined cottonseed oil and fibre from the insect resistant cotton are considered to be equivalent to that of unmodified cotton.

(iv) Ability to support typical growth and well-being

A feeding study in rats was done to establish the wholesomeness of cottonseed derived from insect resistant cotton. This study was not designed specifically as a toxicity test but serves to indicate whether there are unknown factors present in the cottonseed which affect animal growth and wellûbeing. Feed efficiency analyses (feed consumed/weight gained) were done.

Rat 4-week feeding study with raw, ground cottonseed

Groups of rats (10/sex/group) were fed *ad libitum* rodent chow containing unprocessed cottonseed meal at 0, 5, or 10% (w/w) from either insect resistant cotton line 531 or from C312 control cotton for approximately 4 weeks. Animals were observed for adverse signs twice daily and body weights were recorded weekly. Kidneys, testes and liver were collected and weighed at the end of the study and tissues retained for analyses.

There were no treatmentûrelated deaths and no adverse signs of toxicity in any group. Food consumption was decreased slightly for rats of both sexes fed 10% line 531 relative to C312 during the study but was only statistically significant for females in the first week of the study. Diets containing line 531 appeared to be slightly less palatable than diets containing line C312 at the 10% incorporation rate and resulted in statistically significant decreased body weight gains in the first week of the study. This may be due to slightly increased levels (nonûsignificant) of sterculic acid in unprocessed cottonseed derived from line 531.

For the remainder of the study, there were no statistically significant differences in body weight or body weight gain for male or female rats receiving either 5 or 10% raw cottonseed in their diet. Post mortem examination did not reveal any treatment related findings and organ weights were comparable to control line C312.

Conclusions regarding ability to support typical growth and well beingù As raw, ground cottonseed is not intended as a food for human consumption the relevance of this study to humans is questionable. However, the result of the rat feeding study indicates that cottonseed from insect resistant cotton line 531 is essentially equivalent to that of the control line C312 in terms of its wholesomeness.

SUMMARY AND CONCLUSIONS

Insect resistant cotton lines 531, 757, 1076 and 1849 contain three new genes. These are:

ò the *cry1Ac* or *cry2Aa* genes derived from the soil bacterium *Bacillus thuringiensis* subspecies *kurstaki*. These genes encode the insecticidal proteins, Cry1Ac and Cry2Aa, which bind to specific receptors on the midgut of lepidoptera species causing the insect larvae to stop feeding and die;

ò the *nptII* gene encodes the selectable marker enzyme neomycin phosphotransferase II and confers resistance to the aminoglycoside antibiotics.

This gene is used as a marker of plant cell transformation and has no other function in the plant; and

ò The *aad* gene encodes the bacterial selectable marker enzyme aminoglycoside adenylyltransferase and confers resistance to the antibiotics spectinomycin and streptomycin. This gene is used in the cloning processes prior to transfer of the genes to the plant cell. It is not expressed in the plants.

Considerable data has been presented by the applicant to establish that food derived from the insect resistant cotton lines is equivalent to the parental cotton line Coker C312 in all respects apart from the expression of the *cry1Ac* or *cry2Aa* genes and the *nptII* gene. This data included molecular and genetic analyses of the new insect resistant cotton lines, an examination of the potential for the newly expressed proteins to be toxic or allergenic to humans, compositional analyses of the insect resistant cotton lines, and an animal feeding study to establish the wholesomeness of insect resistant cotton line 531 in comparison to conventional cotton varieties.

The molecular and genetic analyses provided by the applicant indicate that the introduced genes have been stably integrated into the plant genome and are stably inherited from one generation to the next.

The new proteins which are expressed in the insect resistant cotton lines are neomycin phosphotransferase II and the insecticidal proteins, Cry1Ac (line 531, 757 and 1076) or Cry2Aa (line 1849). In line 1849, a copy of the *cry2Aa* gene was found to have fused to a cotton gene, resulting in a hybrid gene. This hybrid gene was characterised by the applicant and appears not to be expressed, however, this finding requires confirmation. As refined cottonseed oil and processed linters do not contain any detectable protein, the expression of this gene is not a concern, provided cottonseed is not intended for human consumption. Therefore, in the absence of confirmation of the lack of expression of the hybrid gene it is recommended that approvals for food use be restricted to cottonseed oil and linters.

The applicant submitted data which showed that the newly expressed proteins, Cry1Ac, Cry2Aa and neomycin phosphotransferase II, had been evaluated for their potential to be toxic or allergenic to humans. This included acute toxicity tests using mice for Cry2Aa, comparison of the amino acid sequence of the proteins with known toxins and allergens, and examination of digestion of the proteins in simulated mammalian digestive systems. Furthermore, additional evidence is available from the literature which indicates that the family of *B. thuringiensis* deltaûendotoxins are highly specific for particular gut receptors and these are absent in nonûtarget species including humans.

Therefore, the evidence does not indicate that there is any potential for neomycin phosphotransferase II or the Cry1Ac or Cry2Aa proteins to be either toxic or allergenic to humans. Furthermore, these proteins are expressed to relatively low levels in the cotton and cannot be detected in either the refined oil or fibre.

As two antibiotic resistance genes (*aad* and *nptII*) were transferred to the insect resistant cotton lines, the potential for transfer of these genes from ingested material to microorganisms of the human gastrointestinal tract was considered. The presence of these genes in the insect resistant cotton lines was not considered to increase the potential for transfer to microorganisms of the human gut or to increase the risk of the development of antibiotic resistance among pathogenic bacteria. This is because the human gut already naturally contains a large number of antibiotic resistant microorganisms and the risk of transfer of these genes from ingested material to gut bacteria is generally accepted in the literature to be virtually zero. Furthermore, refined cottonseed oil and fibre do not contain any detectable nucleic acid.

The compositional analyses were comprehensive and indicate that there are some significant differences in composition between the insect resistant cotton lines and the comparator. However, with the exception of carbohydrate (where there is no available information on the normal ranges for commercial cotton varieties) which was significantly decreased in relation to the comparator, these values were within the literature reported ranges. Furthermore, as many of the compounds measured are not constituents of either the refined oil or fibre, these differences are of no concern, provided cottonseed is not intended for human consumption. The refined cottonseed oil and fibre derived from the insect resistant cotton are considered to be equivalent to that of unmodified cotton.

Animal feeding studies using raw, ground cottonseed were presented for insect resistant cotton lines 531. However, as raw, ground cottonseed is not intended for human consumption, this study is considered to have little relevance to humans. Nevertheless, the feeding study indicates that cottonseed from insect resistant cotton line 531 is essentially equivalent to that of the control line C312 in terms of its wholesomeness.

In conclusion, no public health and safety concerns have been identified in this assessment. Both refined cottonseed oil and fibre derived from insect resistant cotton lines 531, 757, 1076 and 1849 can be regarded as substantially equivalent to the refined oil and fibre derived from conventional cotton varieties in respect to composition, safety, wholesomeness and end use.

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PUBLIC COMMENT RECEIVED
A341 - OIL AND LINTERS DERIVED FROM INSECT RESISTANT COTTON

Jean Adams (Aust)

- ò does not want these experimental foods in the common food supply until they have been longûterm tested for undesirable sideûeffects related to public health, environmental damage to species
- ò questions the legality of forcing such genetically modified foods onto the public and the intention to remove labelling of such foods

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

- ò knowledge about the nature of the promoter genes and the type of antibiotic resistance genes is crucial to a proper assessment
- ò the applications should be rejected because most of the New Zealand population do 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)

- ò is against the amendment to the *Food Standards Code* to permit the foods in the applications.
- ò 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.
- ò consumer choice is being violated.
- ò because it is a new science, potential problems or long term implications are yet to be made apparent.

Elaine Attwood (Aust)

- ò supports Option 1 in the combined Preliminary Assessment - that is, to maintain the status quo and not approve any of the six applications
- ò 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
- ò re: A355, A362 and A346ûgenetically modified material will enter the food chain via cottonseed meal and hulls and corn waste being fed to animals
- ò re: A363 û canola free of genetic modification would be marketable overseas
- ò re: A341 û 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
- ò trade considerations should not prevail over consumer rights to have all genetically modified foods labelled as such.

Australian GeneEthics Network

- ò MonsantoÆs proposals should all be rejected as inadequate
- ò there should be preûmarket human testing to provide data for a precautionary approach on safety and nutritional efficacy
- ò there should be full labelling of all approved foods in keeping with the Ministerial decision
- ò there should be public review of the MRLs for Roundup in these foods
- ò 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
- ò an adverse reactions register should be established to enable systematic monitoring of any impacts of these foods

- ò 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
- ò GMAC's assumption that AQIS's regulations would keep imported soy out of the Australian environment does not apply to the other commodities applied for, and the geographical limits and performance of Bt cotton need public review
- ò Monsanto has not studied the dietary implications of these products and presents no evidence that it considered the diversity of diets among different cultures, social or ethnic groups
- ò 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
- ò RR canola and cottonseed 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
- ò 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.
- ò 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 (mouse) testing of the products has been done, whole genetically engineered soybean, corn, canola or cotton were not checked in simulated gastric and intestinal fluids
- ò 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." 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)
- ò these foods will be in 60û80% of all processed foods therefore freedom to choose will be compromised
- ò 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
- ò support the submissions of the Natural Law Party and Clive Elwell

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

Jim Chapple (NZ)
- ò 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
- ò very strongly objects to the term "substantially equivalent" as a play on words
- ò genetically modified foods are not identical to their conventional counterpart and therefore all such products must carry labelling

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

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

Clive Elwell (NZ)

- ò 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, the danger of allergic reactions, and genetically modified food is insufficiently tested and so cannot be regarded as safe for human consumption.
- ò the foods cannot be sufficiently tested because its impossible to carry out appropriate tests, the tests that are carried out are limited and inappropriate.

ConsumersÆ Federation of Australia Inc.

- ò not supportive of these applications being approved at this stage
- ò questions the safety of soya milk as infant food because of the presence of trypsin inhibitor and other antiûnutrients after heat processing, and also the presence of isoflavones.
- ò refers to an analysis done by Professor M. Wahlqvist (but provides no reference to a publication) which has shown that the isoflavone levels may differ from the levels in conventional soybeans
- ò application A338 does not provide sufficient evidence of antiûnutrients to prove that the soybeans are safe for processing into infant formula. In light of this interprets ANZFAÆs 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
- ò no evidence in present by the applicant about glyphosate residues in A338, A362, and A363, despite a specific requirement to do so in ANZFAÆs safety assessment guidelines
- ò donÆt accept the assertion by the applicant that there is only one novel protein in the Roundup Ready soybeans
- ò donÆt 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
- ò traces of the introduced proteins could be present in coldûpressed 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
- ò the approval of Roundup Ready maize will facilitate even greater use of high fructose corn syrups in Australian processed foods. The endûresult of this could well be that consumption of such highûenergy products by Australians will rise and that the current excessive levels of nutritional diseases such as obesity, diabetes and heart disease will increase further
- ò ANZFA needs to be satisfied that antiûnutrient levels in canola are safe and that they will not rise over time.
- ò expresses concern about the decreased weight gain by laboratory rats in the first week of a 4 week feeding trial with INGARD cottonseed. Believes that further feeding trials on a range of animals should be performed before this product is released.
- ò ask that approval of foods produced using gene technology 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
- ò a system for monitoring adverse reactions to these foods should be established before they are released into the diet of Australians
- ò Approval and release of these foods should not occur until the system of labelling agreed to by Health Ministers is established.
- ò Australia should not be bullied by other countries to accept their exports of unsegregated mixtures of genetically modified and nonûmodified foods

Francela Davies (NZ)

- ò 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
- ò wants ANZFA to address the long term effects of the consumption of foreign proteins, antibiotic resistant marker genes and viruses

- ò as there is no evidence that these foods are contributing anything positive to the food or the environment requests that the applications are declined

Food Technology Association (FTA) Victoria Inc.
- ò the risk assessment must be completed and reported to ANZFA stakeholders prior to any decision on the Applications
- ò it is unclear from Standard A18 as to the labelling that would apply to these products
- ò wants to know what special conditions might apply to these products
- ò the option to not amend the *Food Standards Code* and permit the sale of these foods is the preferred option
- ò 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)
- ò share the same concerns as expressed in the submission of the Natural Law Party and Clive Elwell
- ò glyphosate has not been included among the residues tested for and are not aware of any program that monitors for glyphosate residues in food
- ò Treaty of Waitangi obligations have not been considered in ANZFA processes
- ò the New Zealand Bill of Rights provides that no New Zealand may be subjected to experimentation without providing informed consent therefore full disclosure labelling of all transgenic foods and ingredients is the only way this can begin to be achieved
- ò Monsanto has not done any long term studies on health effects
- ò 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)
- ò supports labelling of all food containing genetically engineered products
- ò there may be risks of toxic or allergic reactions
- ò oppose the transfer of genetic material between different species as unethical and potentially unsafe

Goodman Fielder (Aust)
- ò is fully supportive of developments in the agriûfood industry through the application of gene technologies provided that consumer benefits are clearly defined and communicated
- ò 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

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

Martin Hartman and Cornelia Baumgartner (NZ)
- ò object to genetically modified foods
- ò call for mandatory labelling of all genetically modified foods

Karen Hunt (NZ)
- ò demands that all genetically modified foods be labelled

- ò states that consumer rights are violated if products are deemed substantially equivalent and consequently are not subject to mandatory labelling

InforMed Systems Ltd (NZ)
- ò the transfer of EPSPS genes to soybean, maize, cotton and canola are acceptable without prejudice as to whether these foods should require labelling
- ò the transfer of the gox gene to canola is also acceptable
- ò the use of the cry1Ac gene is also acceptable
- ò noted that no mention was made of any maker genes in the applications for soybeans, corn or canola
- ò 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.
- ò notes that none of these 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)
- ò genetically engineered foods have not been adequately tested for their benefits or side effects to human health
- ò what are the long term effects of the consumption of foreign proteins, antibiotic resistant marker genes and viruses
- ò has Monsanto supplied any evidence of long term trials
- ò requests that the application be declined as the foods are not contributing in any way to the food supply or environment

Colin Kell (NZ)
- ò criticises some of the wording used in the preliminary assessment report
- ò claims that genetically altering food decreases their nutritional value
- ò the application provides no proof that glyphosate does not cause long term effects
- ò there has been insufficient testing of these genetically modified foods
- ò balanced information on genetic modification needs to be made available and the rights of everyone taken into consideration
- ò imported commodities should be segregated at source
- ò 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)
- ò concerned about the depth of investigation into the safety of genetically modified foods and the lack of concern by regulatory authorities for the opinions of informed members of the general public and scientists.
- ò ANZFA puts too much faith in the integrity of companies who are producing genetically modified foods.
- ò the timing of the deadline for public submissions is unfortunate as most potential submitters would be pressed for time
- ò urges ANZFA to consider the longûterm implications of allowing the sale of genetically modified foods.
- ò if they are allowed, they should all be labelled.

Kristen Khaine (NZ)
- ò 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 data
- 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
- demand that all food with a genetically modified 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

- ò 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. The foods should be labelled because of this
- ò ANZFA has not taken into consideration the considerable consumer backlash that is occurring.
- ò there must be scientific certainty that humans are not exposed to any newly expressed proteins
- ò objects to the commercial in confidence aspects of A362
- ò concerned about the feeding of the genetically modified seeds to animals as this is another source for these products entering the human food supply
- ò there is no justification for using glyphosateûtolerant canola
- ò Australia should be able to prohibit the import of genetically modified foods if it wishes
- ò 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)

- ò 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 preûmarket testing or screening for risk factors associated with this technology and that unlabelled products deprive individuals of their basic freedom of choice
- ò rejects the premise of substantial equivalence on the grounds that differences at the DNA level make them substantially different
- ò concerned about the potential for increased glyphosate levels.
- ò the effects of glyphosate on health and on phytoestrogens in genetically engineered soy has not been addressed
- ò genetically engineered soy contains genes from a virus, a soil bacterium and from petunia, none of which has been in our food before
- ò the technology is being introduced in the total absence of an informed public debate about the general acceptance of GMO technology
- ò 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
- ò 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
- ò no further applications should be considered until proper public debate has occurred

New Zealand Nutrition Foundation

- ò submission identical to InforMed Systems Ltd

Office of Regulation Review (Aust)

- ò comments on the preparation of the RIS for the full assessment report
- ò ANZFA should discuss in the background section why such products as the Roundup Ready soybeans which previously entered the commercial markets without segregation from the nonûtransgenic counterpart need now go through an approval process. Is it to address health and safety and/or consumer information concerns?
- ò 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
- ò the material present in the sections on potential regulatory impacts and identification of affected parties should be summarised in the RIS in matrix form
- ò 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)

- ò 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
- ò all genetically modified foods should be labelled in order for consumers to choose
- ò 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)

- ò all genetically modified food should be labelled so that there can be post-market monitoring for new allergens or toxic effects in consumers
- ò strongly opposed to the technology because of a range of concerns about public health and safety
- ò raised a number of concerns in relation to Application A338, specifically that:
  - û the bacterial EPSPS is unlike any protein that human have eaten and there is no reliable method for predicting its allergenic potential;
  - û a major allergen, trypsin inhibitor was found to be 26.7% higher in transgenic soybeans;
  - û the compositional analyses of the soybeans were not done on soybeans that had been treated with the herbicide;
  - û there were significant increases compared to controls in the milk fat of cows fed transgenic soybeans; and
  - û the applicant did not submit any data on glyphosate residues in the transgenic soybeans.

Sara Parsons (NZ)

- ò objects to the applications because she is a vegetarian.
- ò it is harmful to be introducing genetically modified soybeans, corn, canola oil and cottonseed into the NZ food chain.
- ò these products are a threat to the safety and well being of animals and humans and are of no benefit to society.
- ò the testing of genetically modified foods on animals and the harm that may be caused to animals in the wider environment is unacceptable.
- ò 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)

- ò is concerned about the importation of unlabelled genetically modified food
- ò 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)

- ò opposes all six applications on the grounds that the genetically engineered crops pose a major environmental hazard and human health hazard
- ò claims that the technology promotes unsustainable farming practices
- ò believes consumers have the fundamental right to be informed about all the ingredients in foods and therefore demands mandatory labelling
- ò 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)

- ò is opposed to the foods which are the subject of MonsantoÆs 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.
- ò if NZ remains GMOûfree is represents an opportunity to create a niche market.
- ò 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.
- ò ANZFA should address the large public concern associated with the introduction of genetically modified foods onto the market.

Emma Subue-Timson (Aust)

- ò 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. 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
- feeding experiments in cows indicate a change in the milk fat production in animals fed on Roundup Ready soybeans versus non-transgenic soybeans, possibly due to elevated oestrogens. Very concerned about the potential health effects, particularly in children, of higher levels of oestrogens.
- 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)

- ò opposes approval for the applications on the grounds that genetically modified foods have not undergone an independent scientific testing
- ò calls for a moratorium on genetically modified foods in NZ for ethical and religious reasons
- ò demands mandatory labelling of all genetically modified foods
- ò 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

- ò a safety assessment of the foods is lacking along with the absence of any supporting scientific evidence
- ò postûmarket 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
- ò the claim that CP4 EPSPS is destroyed in heat processing requires independent scientific validation and it is unclear from ANZFAÆs papers whether this evidence has been provided and reviewed.
- ò 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 of comprehensive a scientific evaluation of these products
- ò 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
- ò given the heightened public concern about genetically modified foods it is essential that scientific information relating to compositional variance due to novel gene expressions, toxicology, potential for allergenicity, nutritional and dietary properties for each of foods proposed by Monsanto be publicly available and a full safety evaluation be undertaken
- ò The Committee recommends the adoption of Option 1 at this time

S. and L. Wintergraas

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

GENERAL ISSUES RAISED BY PUBLIC SUBMISSIONS

A total of 58 submissions were received by the closing date of 23 December 1998, in response to the section 14 Gazette Notice. The majority of submissions made statements against the use of gene technology, asserted that food produced using this technology is unsafe for human consumption and expressed opposition to any amendment to Standard A18 to permit the sale of such food. An evaluation of the issues raised by the submissions appears below. Where possible, individual submitters or organisations are identified, however where a large number of submissions addressed the same issue, it was not possible to list the submitters individually.

GENERAL ISSUES RAISED BY SUBMISSIONS

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 longûterm 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, æsafeÆ 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 preûmarket 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.

New technologies, including gene technology, are assessed therefore, in part, by a comparison to the benchmark of commonly consumed foods which 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. Substantial equivalence

J. Chapple (NZ) and N. Green (NZ) objected to the use of æsubstantial equivalenceÆ as a means of establishing the safety or otherwise of foods produced using gene technology. The Natural Law Party (NZ) submitted that they reject the premise of substantial equivalence on the grounds that differences at the DNA level make foods substantially different.

Evaluation

The concept of æsubstantial equivalenceÆ has been internationally recognised and embraced as a valuable tool in the safety assessment of foods produced using gene technology. This concept was first espoused by a Joint Consultation of the Food and Agricultural Organisation (FAO) and the World Health Organisation (WHO) in 1991 where it was established that the *comparison of a final product with one having an acceptable standard of safety provides an important element of safety assessment.*

Since the establishment of that principle, work by the OECD on food safety and biotechnology has also focussed on this concept. The OECD advocates an approach to safety assessment based on substantial equivalence as being ôthe most practical to address the safety of foods and food components derived through modern biotechnologyö.

Substantial equivalence embodies the concept that if a new food or food component is found to be substantially equivalent to an existing food or food component, it can be treated in the same manner with respect to safety as its traditional counterpart. Substantial equivalence encompasses both phenotypic[1] characteristics and compositional comparisons. Genotypic differences (ie differences at the DNA level) are not normally considered in a determination of substantial equivalence if that difference does not significantly change the composition of the new food relative to the conventional food.

The concept of substantial equivalence provides a commonsense approach to the evaluation of a food produced using gene technology. It allows the evaluator to determine in a systematic fashion if there have been any significant changes to important constituents of a new food. It is also important to note that, although a particular food or food component may be found to be not substantially equivalent to an existing food or food component, this does not necessarily mean that it is unsafe. Such a food will need to be evaluated on the basis of its composition and properties.

[1] χηαραχτεριστιχσ τηατ αρε ωισιβλε

3. Labelling of foods produced using gene technology

A majority of submissions focussed on this issue. Specifically, the submitters expressed a desire that all foods produced using gene technology be labelled, regardless of whether or not 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 ôright to knowö arguments. It was stated that full labelling will enable identification and possible avoidance of such foods in the market place.

Evaluation

In the development of Standard A18, the Authority recommended that foods produced using gene technology, that are no longer substantially equivalent to their conventional counterparts, be labelled. This recommendation was adopted by ANZFSC and Standard A18 was gazetted in August 1998, to come into effect in May 1999. In December 1998, ANZFSC decided that foods produced using gene technology that are substantially equivalent should also be subject to mandatory labelling, with the exception of certain products that are highly refined and purified and contain no new or altered genetic material, such as oils and sugars. The Authority is currently preparing an amendment to Standard A18 to this effect.

4. Timing of assessment of applications

C. Elwell (NZ), Berylla (NZ), Friends of the Earth (NZ), the Consumers' Federation of Australia Inc. and the National Council of Women of Australia suggested in their submissions that genetically modified foods should not be introduced until the recent labelling decision of Health Ministers is implemented. The Australian GeneEthics Network submitted that all approved foods should be labelled in keeping with the ANZFSC decision.

Evaluation

The implementation timetable for the new labelling provisions agreed to by ANZFSC on 17 December 1998 has yet to be determined. Standard A18 comes into effect on 13 May 1999 from which point on any food produced using gene technology will be prohibited unless it is listed in the table to the standard. Currently, Standard A18 only provides for mandatory labelling in circumstances where the food is not substantially equivalent to its conventional counterpart.

5. The nutritional value of food produced using gene technology

C. Kell (NZ) submitted that the genetic alteration of food decreases its nutritional value. No supporting information was provided by the submitter.

Evaluation

The assessment of food produced using gene technology by ANZFA will entail an assessment of any intentional or unintentional compositional changes that have occurred to the food. This assessment will take into account the major constituents of the food (fat, protein, carbohydrate, fibre) 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 and there are examples where genetic modification is being used to improve the nutritional value of food. Therefore, it does not necessarily follow that genetically modified foods will have reduced nutritional value. This will be assessed by ANZFA on a caseûbyûcase basis.

6. Public consultation and information about gene technology

M. and J. Gregory (NZ) submitted that the public has not been properly consulted or informed by government or ANZFA on the introduction of foods produced using gene technology. J. Adams (Aust), R. Anderson (NZ), N. Green (NZ), C. Elwell (NZ), Berylla (NZ) and Friends of the Earth (NZ) also submitted that there has been very little opportunity for public debate on the issue of genetically modified foods. The Natural Law Party (NZ) submitted that no further applications should be considered until there has been proper public debate.

A submission from Goodman Fielder (Aust) stated that it is fully supportive of developments in the agriûfood industry through the application of gene technologies provided that consumer benefits are clearly defined and communicated. They urged ANZFA to undertake wider consultation with all affected parties including growers, crushers (in the case of oilseeds), food industry users and consumers before these modified plants are introduced. They appreciate that regulation of markets is not within ANZFAÆs area of responsibility, but would like ANZFA to at least 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, therefore, the New Zealand community had not been consulted on this matter by the Authority until after that time. Consequently, Standard A18 only underwent 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 ANZFA only undertook one round of public comment in New Zealand for the development of Standard A18, there is further opportunity for public consultation in the context of the current applications to vary Standard A18. This will involve two rounds of public comment. Furthermore, all the documentation (except for commercial in confidence information) relating to these applications will be 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 potential sources of information about gene technology are available to consumers in New Zealand. These include:

- The æGene PoolÆ which is an information resource established by the Gene Technology Information Trust, with initial funding from the Association of Crown Research Institutes in New Zealand. The function of the Gene Pool is ôto ensure the widespread dissemination of balanced, accurate, credible and timely information about gene technologyö. The Gene PoolÆs information resources include a website, a repository of publications, regular newsletter, fact sheets about various issues, a list of professionals available for public speaking engagements, and resources for schools and other learning institutions; and

- The Environmental Risk Management Authority (ERMA), which is a statutory authority set up by the New Zealand Government to administer the *Hazardous Substances and New Organisms (HSNO) Act 1996*. It is the body that 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.

7. Maori beliefs and values

C. Elwell (NZ), Berylla (NZ) and Friends of the Earth (NZ) submitted 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 nonûMaori, is held. In support, C. Elwell provided a copy of a report to the ERMA from a Maori advisory committee (Nga Kaihautu Tikanga Taiao) formally established under the *Hazardous Substances and New Organisms (HSNO) Act 1996* to advise on how to take account of issues of concern to Maori.

Evaluation

This is an issue that was also raised in a consideration of a proposal for the development of Standard A18. Then 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.
The report provided by C. Elwell indicates that the Nga Kaihautu is opposed, in principle, to any research that seeks to artificially modify the genome of an individual organism or species.

This issue appears to be of importance to the Maori. This, however, raises the question of the appropriate means of giving consideration to such issues. Both New Zealand and Australia have established mechanisms for the scrutiny of proposals to introduce viable new genetic material into the respective countries. As indicated above, this is the role of ERMA in New Zealand (and the Genetic Manipulation Advisory Committee and the associated arrangements to establish a Gene Technology Office in Australia). Issues of cultural belief and values concerning the use of genetically modified organisms should be dealt with in that context rather than through ANZFA processes given the statutory requirement that ANZFA focus upon the protection of public health and safety, consumer information, fair trading, industry development and international trade considerations. It would be inconsistent with the objectives of good government, administrative efficiency and clarity over responsibilities for two agencies to have overlapping responsibilities for this (or any other) matter.

8. Sources of genes being used to modify the crops

C. Kell (NZ) submitted that the applicant has failed to disclose the source of genes being used to modify the crops in question and goes on to state that ôit is a known fact that genes from animals and fish are being used.ö

Evaluation

The applications carry full details of the source of all the genes used in the modifications. None of the genetically modified plants in question have had either animal or fish genes transferred into them.

9. Environmental concerns

A number of submitters (N. Mc Rae *et al*, M. Rouse, C. Taylor, M. Karas, S. Parsons, J. Adams, W. Borst, B. Thrussell and A. Ward) have raised concerns that genetically modified crops may pose a risk to the environment. The Australian GeneEthics Network submitted that ôall proposals should be submitted for Genetic Manipulation Advisory Committee (GMAC) assessment and recommendation..".

Evaluation

These issues are considered in the assessment processes of GMAC in Australia and ERMA in New Zealand. The Authority has neither the expertise nor the mandate to

assess matters relating to environmental risks resulting from the release of food produced using gene technology into the environment.

Currently, there are no formal mechanisms in place for the coordination of assessments and approvals of gene technology products by the various regulatory agencies in Australia. ANZFA, at this stage, also has no formal links with ERMA. However, informal links exist between ANZFA and other regulatory agencies and a large degree of information sharing occurs. It is highly unlikely that the Authority would make a recommendation for 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.

10. Creation of market monopoly

J. Chapple (NZ) submitted that he is strongly opposed to the application on the grounds that approval of these foods may create a market monopoly for the applicant in the supply of agrochemicals. The Commerce Commission of NZ, on the other hand, stated that the applications do not raise any issues on which they would wish to comment.

Evaluation

The AuthorityÆs role is to develop and vary food standards and in so doing to ensure that public health and safety is protected and that consumers are provided with sufficient information to make informed choices about that food. It is not appropriate for the Authority to influence the market in these matters. Allegations of antiûcompetitive practice are more appropriately dealt with by other government bodies.

11. Toxins and allergens

R. Anderson (NZ), Consumers' Federation of Australia Inc. and N. Gannaway (NZ) expressed concerns about the risks of the introduction of new toxins or allergens.

Evaluation

It is possible to develop foods containing new toxins or allergens by gene technology or by traditional breeding techniques. It is also possible to use these techniques to develop foods specifically lacking such compounds. The advantage of gene technology is that the 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.

12. Antibiotic resistance

W. Borst (NZ), R. Anderson (NZ), F. Davies (NZ), O. Jones (NZ) and B. Thrussell (NZ) raised concerns about increased antibiotic resistance resulting from the use of gene technology. InforMed Systems Ltd (NZ) and the New Zealand Nutrition Foundation stated that it would be reassuring if independent biomedical advice were available to reassure us 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

This issue arises because of the use of antibiotic resistance marker genes in the generation of genetically modified plants. Antibiotic resistance genes are often linked to the gene of interest which is being transferred. They enable the initial selection of the engineered cells by exposing them to antibiotic selection. Those cells that contain the antibiotic resistance marker gene will be able to survive and divide in the presence of the antibiotic. Those cells that do not contain the antibiotic resistance marker gene, and hence do not contain the gene of interest, will die in the presence of the antibiotic.

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.

The World Health Organisation considered this issue in 1993 at a Workshop on the health aspects of marker genes in genetically modified plants. It was concluded at that Workshop that there is no recorded evidence of transfer of genes from plants to microorganisms in the gut and also that such transfers would be extremely unlikely given the complexity of the steps required. Antibiotic resistant bacteria are ubiquitous and normally inhabit the gut of animals and humans. The transfer of antibiotic resistance genes is much more likely to arise from this source rather than from ingested genetically modified food.

13. Viral recombination

W. Borst (NZ), F. Davies (NZ) O. Jones (NZ) and A. Ward (Aust.) all expressed concern about the long term effects of transferring viral sequences to plants.

Evaluation

The issue is one which is commonly raised as many of the genes that are transferred to plants are linked to a plant virus promoter. Promoters are controlling DNA sequences which act like a switch and enable the transferred genes to be expressed (ie 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 virusûresistant, 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 caseûbyûcase 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.