INQUIRY REPORT

SUBJECT: A341 – OIL AND LINTERS DERIVED FROM INSECT-PROTECTED COTTON.

EXECUTIVE SUMMARY

- 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-protected cotton in the Table to clause 2 of Standard A18 – Food Produced Using Gene Technology;

- The Authority considered the Full Assessment report on Application A341 at ANZFA 55 in February 1999. The draft variation to the *Food Standards Code* was gazetted on 17 February 1999 and the period for public comment closed on 31 March 1999, although submissions were accepted beyond the closing date;

- The conclusion at full assessment of this application was that oil and linters derived from insect-protected cotton lines 531, 757 and 1076 can be regarded as substantially equivalent to oil and linters from unmodified cottonseed in respect of composition, safety, wholesomeness and end use;

- At Inquiry, issues raised in public submissions included:

  (i) Allergenic or toxic potential of food derived from Bt cottonseed;
  (ii) Increased levels of insecticide in the human diet;
  (iii) The presence of animal or insect genes in the food;
  (iv) The acceptance and credibility of the applicant's data;
  (v) Development of insect resistance to Bt proteins;
  (vi) Potential transfer of antibiotic resistance to intestinal microbes; and
  (vii) Labelling of oil and linters from Bt cottonseed.

- The conclusions of the Inquiry Report are:

  - cottonseed oil and linters derived from insect-protected cotton lines 531, 757 and 1076 are considered to be substantially equivalent to the oil and linters from conventional cottonseed in respect of their composition, safety, wholesomeness and end use. There are no additional public health and safety concerns associated with the use of oil and linters derived from insect-protected cottonseed;

  - while considerable general concern has been raised in public submissions regarding the use of gene technology in food production, there is no evidence that the consumption of oil and linters from the insect-protected cotton lines will lead to adverse health effects in humans;

  - oil and linters derived from insect-protected cotton lines 531, 757 and 1076 would not require labelling under the current provisions of Standard A18 as they can be regarded as substantially equivalent to oil and linters derived from conventional cottonseed. It is noted however that the labelling provisions of Standard A18 are still under consideration by ANZFSC. On resolution, these foods will be required to comply with the amended labelling provisions;

- the proposed amendment to list oil and linters derived from insect-protected cotton lines 531, 757 and 1076 in the Table to Standard A18 is consistent with ANZFA's section 10 objectives; and

- the regulatory impact analysis identified no disadvantages to either industry, government or consumers in the proposed amendment. The direct benefits of the proposed amendment primarily accrue to the cotton producers, with potentially a small benefit to the consumer. These benefits outweigh the costs associated with recommending against the amendment.

BACKGROUND

Standard A18 was adopted as a joint Australia New Zealand standard in July 1998 and came into effect on 13 May 1999. The standard prohibits the sale of food produced using gene technology unless it has first undergone a safety assessment by ANZFA and has been approved by the Australia New Zealand Food Standards Council (ANZFSC).

On 30 March 1999, ANZFSC approved a recommendation by ANZFA, under section 37 of the ANZFA Act, to allow foods produced using gene technology which were already in the marketplace, to remain on the market during the period of assessment by ANZFA providing they met specified criteria. The standard was amended to this effect by inserting clause 2A. These foods will, however, still undergo a rigorous safety assessment process.

CHANGES TO THE APPLICATION SINCE FULL ASSESSMENT

The applicant initially submitted information pertaining to four lines of cotton – lines 531, 757 and 1076 containing the *cry1Ac* gene and line 1849 containing the *cry2Aa* gene. The Full Assessment report to this application therefore included a safety assessment of both genes and their protein product and referred to all four cotton lines.

On 30 April 1999, the Authority subsequently received a request from the applicant to separate the two different genetic constructs into two separate applications for technical reasons associated with characterisation of Line 1849 containing the *cry2Aa* gene. This request was formally accepted by the Authority and the applicant was advised of a separate application number (A389) pertaining to cottonseed oil and linters derived from cotton line 1849, known as INGARD® cottonseed (Cry2Aa construct).

However, on 23 July 1999 the Authority again received advice from the applicant that a decision had been made not to proceed with commercialisation of cotton line 1849. Consequently, application A389 was withdrawn by the applicant, effective from that date. As a result of these changes to the original submission, this application now pertains only to lines 531, 757 and 1076 containing the *cry1Ac* gene construct.

SUBMISSIONS RECEIVED AT INQUIRY

The Authority considered 86 submissions pertaining to this application at Inquiry, with almost two thirds of these from New Zealand. Almost all of the submissions were opposed to the application due to ongoing concerns relating to the safety of the food both in the short and longer term, but also for a variety of environmental, ethical or philosophical reasons.

Although a significant proportion of these were detailed submissions, the technical information did not always relate specifically to food derived from Bt cotton, but often to unrelated genetic modifications in other plant crops or to broader issues relating to the use of biotechnology in food production.

The Full Assessment report to this application discussed both general issues concerning the use of biotechnology in food production as well as issues specifically relating to Bt cotton. In addition, previous reports such as the Full Assessment and Inquiry reports to Proposal P97 which established Standard A18, also contain detailed responses to issues which are being expressed as ongoing matters of concern in the current submissions. Some issues previously discussed include the use of antibiotic resistance marker genes and the potential for allergenicity of the new food.

A subset of the submissions contained comments on public health and environmental matters unrelated to food issues, but nevertheless served to illustrate a growing wariness in consumers to food regulation, which is being reflected globally. As a result of this broad public concern, the issues raised frequently had no direct relevance to the food products encompassed by this application, namely refined oil and processed fibre produced from insect-protected cottonseed. However, in response to the broad concerns expressed in a majority of the submissions, this report will revisit some of the more general issues concerning the safety of genetically modified foods but relate these more specifically to food derived from insect-protected (Bt) cottonseed.

Five of the submissions received were generally in favour of the application. These were received from the Western Australian Food Advisory Committee, Victorian Food Safety Council, Nestle Australia Ltd, the Food Technology Association of Victoria and the Australian Food and Grocery Council (AFGC). In addition, InforMed Systems Ltd together with the New Zealand Nutrition Foundation were not opposed to the application provided that particular scientific concerns in relation to the characteristics of the introduced genetic material were considered during the assessment. They noted also that the first genetically modified food applications to be assessed by ANZFA pertain to gene modifications which do not confer an immediate benefit to consumers, such as improved nutritional characteristics, or better sensory or storage characteristics.

ASSESSMENT OF ISSUES RAISED IN PUBLIC SUBMISSIONS AT INQUIRY

Allergenic or toxic potential of food derived from Bt cottonseed

The Australian Natural Therapies Association was particularly concerned with the possibility that new proteins in the food supply may pose allergy risks to consumers.
However, the submission also recognised that new proteins expressed in non-edible parts of the plant are not of concern in relation to food allergy. Similarly, the Environmental Health Branch of the South Australian Public and Environmental Health Service noted that the absence of protein or new genetic material in the oil and linters circumvents the concerns in relation to the potential for toxicity or allergenicity of the foods derived from Bt cotton. However, this submission also expressed the view that the data presented in the Full Assessment report did not demonstrate unequivocally that protein was absent in both the refined oil or processed fibre. Several other submitters noted that the Full Assessment report stated the detection limits of protein in the oil and linters from cotton line 531, but not specifically from the other cotton lines under assessment.

On a related issue, Go Mark Food Systems and Mr A. Ward were concerned with the possibility that the genetic modification could result in unintentional changes to existing components or inadvertently introduce a new allergenic protein to the food.

Evaluation

As detailed in the Full Assessment report, any potential for toxicity and allergenicity of this protein has been comprehensively discussed as part of the Authority's safety assessment process.

The potential for allergenicity arises from the presence of certain protein components in food and any evaluation of the allergic potential of this particular food must address the following matters. Firstly, a review of the history of use of the Cry1Ac protein and the Bt organism, including toxicology studies; secondly, whether consumption of the food derived from the cotton plant provides a significant level of exposure to seed protein; thirdly, whether the genetic modification has resulted in compositional changes in the food components of the cottonseed such that they may contain additional or altered compounds with a potential for allergenicity. This evaluation also includes a comparison of the physicochemical properties and sequence homology of the new protein with those of known allergens to test for similarities at the molecular level. The combined data from these tests provided a broad base of knowledge about the food under consideration and, in the case of this application, revealed no likely potential for allergenicity. It should be noted that the evaluation of all of these matters is a standard procedure during the course of the safety assessment of foods produced using gene technology.

(i) History of use

With respect to the potential toxicity of the food derived from Bt cottonseed, as recently as July 1997 the Environmental Health and Safety Unit (EHSU) of the Department of Health and Family Services reviewed toxicology data provided in support of the registration of the INGARD® gene in cotton. Part of this review was an assessment of a range of products in which the biological insecticide Bt is the active ingredient. Data were analysed from established toxicological studies carried out in different animal species including guinea pigs, rats, mice and rabbits. In addition, data from acute, short-term, sub-chronic and chronic experiments (up to 2 years) in several different species and via several different modes of administration were presented. Results from human studies, including workers and personnel involved in production, and monitored for 1-20 years were also available. Other human data consisted of completed extensive epidemiological studies on a large population of people (1.4 million) in the mid 1980s. Consistent with its use as an organic pesticide for over 30 years, commercial preparations of Bt are thus considered to be of very low or no toxicity to humans, other animal species, most beneficial insects and other non-target organisms.

Further, it should be noted that the Cry1Ac protein has been exempted by the National Registration Authority for Agricultural and Veterinary chemicals (NRA) 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 its demonstrated low toxicity and history of safe use. The public has thus been potentially exposed to Bt proteins in the diet through the consumption of commercially available fresh vegetables, either organically or conventionally grown, over a long period.

Another new protein expressed in the cottonseed is neomycin phosphotransferase II (NPT II) which is an enzyme which metabolises the antibiotic neomycin, as well as related antibiotics such as kanamycin, and thus confers resistance to these antibiotics. The health aspects of specific marker genes and the enzymes they produce are discussed in more detail below.

(ii) Exposure data

The data analysed at full assessment indicated that both of the introduced proteins were present at approximately 0.001% or less of fresh weight in the leaf and seed tissue of each of the insect-protected cotton lines. This represents a low level of expression and thus a very small fraction of the total protein in the seed. Furthermore, the oil and linters derived from the cottonseed undergo extensive processing and refinement which effectively eliminates all protein before they are used as food. Thus, humans are not considered to be exposed to any detectable cottonseed proteins, whether or not they are new proteins.

Plant protein was not able to be detected in refined oil to a sensitivity of 1.3 parts per million (ppm) total protein. The absence of protein in the oil is expected for all lines and all production batches since quality assurance measures ensure that all are subjected to identical processing treatments which eliminate the protein from the finished product. If any plant protein is present following these treatments, it is present at vanishing amounts which are below currently available analytical methods of detection. Consequently, from a food perspective, refined cottonseed oil can be regarded as a highly purified product.

As indicated in the full assessment, a low level of Cry1Ac protein was detected in raw cotton linters, most likely because of adventitious contamination with a small amount of hull material from the seed. However, the raw linters undergo extensive processing which removes any trace levels of seed protein and subsequent fractions were found to be analytically free of protein. In view of these results, the cleaned linters can also be regarded as a highly purified product.

(iii) Composition

Lastly, the compositional analyses of cottonseeds from the insect-protected lines in comparison with the control line do not indicate any change in constituents that represents a food safety concern. The theoretical possibility, however remote, that levels of a previously unknown toxin, allergen or antinutrient might be elevated as an unintended consequence of the modification is not supported by any of the technical data or information provided either by the applicant or in submissions. On the contrary, the nutritional study conducted over a period of four weeks in rats indicates that the insect-resistant line is equivalent to the normal line in its suitability to support growth and provide adequate nutrition.

Increased levels of 'insecticide' in the human diet

Several submitters, including Ms I. Bailey, expressed concerns in relation to human health from consuming foods containing what was referred to in the submissions as an 'insecticide', referring to the Bt protein. With similar concerns, Mr E. Dempsey asserts that genetic modification of crops to contain Bt protein will lead to higher levels of this pesticide in the human diet.

Evaluation

These concerns can be addressed in two ways. Firstly, the Bt protein has been extensively tested for toxicity in humans and other animals and there are no health and safety concerns associated with its use in agricultural situations. It has been used as an insecticidal agent by the organic farming industry for over 30 years. Secondly, the human food use of this plant is restricted to the oil extracted from the cottonseed and, to a lesser extent, to the linters (short fibres attached to the cottonseed). Following processing into food grade material, neither of these components of the plant contains sufficient Bt protein to be detected by sensitive analytical techniques, and therefore may be regarded as highly refined products. Consumers of the food obtained from Bt cotton are therefore not exposed to detectable amounts of proteins from the seed or other parts of the plant.

To summarise previous information, the Bt protein Cry1Ac, is a protein produced by the *Bacillus thuringiensis* (Bt) organism, a common soil microbe that has insecticidal properties (For reviews see Biocontrol Science and Technology, OECD Workshop, 1994 and Analytical Chemistry of *Bacillus thuringiensis*, Ed. L. Hickle and W. Fitch, 1990). It is termed a biopesticide because the bacteria which produce it occur naturally in the environment, in virtually all soils. Although it is effective at destroying certain insect pests, it is not chemically related to synthetic chemical pesticides. It is toxic only to certain Lepidopteran insects that express another protein (referred to as a receptor) in the insect intestinal wall which specifically binds to the Cry1Ac protein. As animals, including humans, lack the particular receptor protein in the intestine, the Bt protein does not elicit the same toxic effect as in Lepidopteran insects. The Cry1Ac protein ingested by animals is subjected to the same degradative processes as any other extraneous protein which may be consumed as or with food.

Presence of animal or insect genes in the food

As a vegetarian, Mr G. Clarke expressed a concern of consuming animal or insect genes present in some genetically modified plants.

Evaluation

Foods derived from Bt cotton lines 531, 747 and 1076 contain copies of new genetic sequences derived from bacteria, and regulatory sequences copied from a common plant virus, but not from animals or insects. In the consumption of fresh fruit and vegetables, consumers would be readily exposed to naturally occurring soil microbes and even common plant viruses that are widespread in the environment.

It is recognised and accepted that many in the community wish to make food choices for a variety of reasons based on philosophical, cultural, religious and ethical considerations. ANZFA's legal powers only allow consideration of whether the food products derived from Bt cottonseeds are as safe as the products derived from unmodified cottonseeds. In this regard, the presence of foreign genes from animals or insects is not an issue for concern in this case.

Acceptance and credibility of the applicant's data

Mr T. Jones and others expressed concerns with the acceptance and use of the applicant's data to conduct the safety assessment and were critical of the duration of the feeding study in rats.

Evaluation

(i) Data used in safety assessment

In accepting an application to vary Standard A18 in the Food Standards Code, ANZFA requires detailed scientific information relating to the genetic modification in the food crop as well as data to establish the safety of the modified food. In order to ensure that applicants submit sufficient and appropriate information, ANZFA has produced two detailed documents to assist applicants with their submissions – 'Format for Applying to Amend the Australian Food Standards Code - Food Produced Using Gene Technology' and 'Guidelines for the Safety Assessment of foods to be included in Standard A18 - Food Produced Using Gene Technology'. Together, these documents indicate the nature of the information required by ANZFA to complete a comprehensive safety assessment of the food, and ensure that the applicant is informed of their responsibilities in relation to the data they provided. The requirement for detailed molecular data relating to the genetic modification necessitates the information being supplied by the developers of the modification.

In the acceptance and assessment of the applicant's data relating to insect-protected cotton, ANZFA is using normal procedures consistent with those used by government agencies for regulation of food additives, drugs and agricultural and veterinary chemicals. Because of its very detailed nature, the scientific data on the composition and safety of the food must be provided by the applicant who is in turn directly responsible for the validity and accuracy of the information submitted. In the completion of the safety assessment, however, ANZFA relied also on a range of other reference material relevant to Bt cotton, including the toxicological assessment of the Bt organism completed by the Australian Commonwealth Health Department and information in the international scientific literature. Taken together, the material analysed formed the basis of ANZFA's recommendation at full assessment.

It is also a standard requirement that applicants are expected to demonstrate to ANZFA that the studies submitted in an application have been done according to internationally recognised principles of Good Laboratory Practice (GLP) and that the data presented accurately reflect the raw data generated during the studies. To demonstrate compliance with these principles, applicants generally provide Quality Assurance certification. In addition, the applicant is also required to make a Statutory Declaration that the data presented in an application fully set out the matters for consideration and is a truthful reporting of the analyses that were done. With respect to completed studies on the insect-protected cotton, the applicant submitted a complete set of analytical data with the required certification which ANZFA considers were in full compliance with the rigorous requirements set out in the guidelines for assessment of these foods under Standard A18.

(ii) Feeding study in rats

The results of the animal feeding study where rats were fed a diet containing either raw insect-protected cottonseed or raw unmodified cottonseed for a period of four weeks were discussed fully in the safety assessment and as a specific issue raised in submissions to the Full Assessment report. The small decrease in food consumption especially of the female rats at the highest dietary incorporation rate (10%) during the first week of the study is not considered to represent any health concerns. A difference in palatability is reasonable explanation for the observed transient difference which was not observed at the lower dietary incorporation rate (5%).

This interpretation of the results is consistent with the findings at the conclusion of the study. In summary, the study showed no treatment related differences or adverse signs of toxicity in the animals tested with the insect-protected cottonseed at either of the feeding rates.

The purpose of a short term feeding study such as this, is to provide information on the nutritional performance of the food in young animals rather than to provide a detailed toxicological profile. The relevance of the study has been questioned because the animals were fed raw cottonseed, which is not used for human consumption due to the presence of toxic substances in parts of the seed, for a period of only fourteen days. It is recognised that the value of the data from such a study is limited but it does nevertheless provide important information which is used in the safety assessment.

This application also serves to illustrate the difficulties of designing feeding experiments in animals with sufficient scientific rigor to yield meaningful data directly related to the substances being tested. As the major food in this instance is an oil, even basic nutritional feeding studies using the oil moiety alone would not be suitable. The lack of other dietary requirements in an oil-only diet would have inevitable detrimental effects on the test animals. Furthermore, the use of dietary supplements to substitute for deficiencies in the test diet contribute to the complexity of the experiment and may confound the interpretation of the results. Given the overall limitations that are inherent in the design of such experiments, the feeding of whole ground cottonseed to rats was appropriate in that any nutritional consequences of the consumption of this food were considered in terms of a comparison of effects between the insect-protected cottonseed and the conventional one.

Development of insect resistance to Bt proteins/Loss of effective use of Bt by organic farmers.

Mr E. Trevelyan, J. and R. Thornton and others expressed concerns that are primarily related to the potential environmental effects of this crop rather than to food safety. These were that the expression of Bt proteins in transgenic crops will hasten the onset of insect resistance to the Bt proteins, thereby rendering the use of this bacterial pesticide ineffective on target insect pests. As this is one of the permitted organic pesticides, insect resistance to Bt potentially compromises the pest management strategies of the organic farming industry.

Mr E. Dempsey and Dr M. Godfrey cite the Wingspread statement on the precautionary principle (Wingspread, Wisconsin, January 1999) for advocating a cautious approach to the widespread adoption of Bt engineered crops predominantly for these environmental reasons.

Evaluation

This is an environmental issue which is not immediately related to public health and food safety and therefore not an issue for which ANZFA has the legal powers to address. However, the following information provides an additional perspective that may allay some of the concerns.

Researchers and primary producers alike readily acknowledge the problem of the development of insect resistance, and various strategies have been developed to counter or delay the gradual acquisition of resistance in pest insects. It should also be noted that the Cry1Ac protein is only one of a number of proteins in this class of insecticidal endotoxins produced by the Bt organism. Resistance to one particular protein does not necessarily equate to resistance to the entire family of proteins, new members of which are still being found and described in the scientific literature.

Furthermore, resistance can occur in populations of insects for a number of reasons other than due to the selection pressure of the presence of Bt proteins (Ballester et al. 1994). It is also widely acknowledged that the degree of resistance brought about by selection pressure on the insects is biologically inevitable, even with restricted use of the commercial pesticide formulations. Scientific knowledge of these natural biological events does enable control and management strategies to be developed and implemented to minimise the impact of these occurrences.

Potential transfer of antibiotic resistance to gut microorganisms

Several submitters including Go Mark Food Systems raised the issue of the possibility of transfer of a functional antibiotic resistance marker gene to intestinal bacteria present in animals or humans following consumption of food containing such a gene.

However, the New Zealand Nutrition Foundation and Dr John Birkbeck of InforMed Systems Ltd noted specifically that the presence of the marker gene in this application did not, in their view, represent cause for particular safety concerns in view of the fact that it encodes for an enzyme (NPTII) which metabolises neomycin, an antibiotic not used in human therapeutics.

The National Council of Women of Australia and Ms E. Attwood provided a transcript of an article written by Dr Michael Antoniou, Senior Lecturer in Molecular Pathology, London, UK. This article discussed the use of a particular antibiotic resistance gene in the development of certain genetically modified crop lines and discussed the possible risk to the efficacy of the antibiotic in the event of the transfer of the resistance gene, consumed as part of a food, to the gene pool of microorganisms existing in the human or animal digestive tract.

The discussion was not focussed entirely on this issue and did not specifically discuss the marker genes of relevance to this application. Instead, it was a broad commentary on the safety of genetically modified foods which frequently confused the regulatory processes by which these foods are assessed for safety and thus made several erroneous conclusions. For example, Dr Antoniou cites the tragic human health effects in 1989 associated with the consumption of certain batches of a commercially prepared dietary supplement, tryptophan, promoted as a therapeutic agent for insomnia (see Mayeno and Gleich, 1994). Although he acknowledges that the presence of a subsequently identified toxic contaminant cannot be attributed to the genetically modified (GM) bacteria used in the production process, he nevertheless states that as the product was 99% pure and devoid of DNA, the supplement would be "passed as substantially equivalent" to the same substance derived from non GM bacteria. This assumption is incorrect for a number of important reasons.

Tryptophan is one of the basic set of amino acids present ubiquitously in all proteins. When used as a dietary supplement, it is consumed in amounts above those regarded as being associated with a normal diet and is regulated not as a food but as a complementary medicine under the TGA Act. It is therefore not appropriate to relate a regulatory procedure specifically designed to evaluate the safety of a *food*, consumed as part of a normal diet, to a substance which is clearly consumed in amounts intended to elicit some physiological response. The concept of s*ubstantial equivalence* does not apply to the assessment of a dietary supplement.

Other inaccuracies in the commentary indicate a lack of familiarity with the application of the tools used in the scientific safety assessment of foods. For instance, s*ubstantial equivalence* in relation to foods produced using gene technology is not based merely on the absence of new genetic material. Further, a determination of *substantial equivalence* does not obviate the requirement for a scientific safety assessment, but may be determined as a result of conducting one.

Background

Antibiotics are substances which interfere with the basic functioning of cells, and hence are most effective in interrupting the growth of rapidly dividing cells such as bacteria involved with infection. They are particularly useful in clinical situations to control bacterial infections in humans and other animals. They are typically classed into broad groups with similar chemical properties targeting particular types of bacteria. Many antibiotics are naturally occurring substances, e.g. penicillin, often produced by microorganisms (fungi, other bacteria) whose antibiotic properties have been discovered over decades of study in microbiology.

Resistance to antibiotics is also naturally occurring in bacteria. Through natural mutation frequencies and other mechanisms, bacteria develop protection to the chemical toxins (antibiotics) produced by their microbial relatives or competitors. It is known that random sampling of the environment generally recovers antibiotic resistant microorganisms at significant frequencies ranging from approximately 6% to 67%, depending on the antibiotic being tested (Kelly 1981).

A bacterial antibiotic resistance gene used as a marker gene in the laboratory encodes a bacterial protein which is able to specifically inactivate a particular antibiotic. The interaction between the protein and the antibiotic is relatively specific and resistance to one class of antibiotic has no effect on antibiotics of different chemical types.

Evaluation

This issue was raised previously by submitters and addressed in the Full Assessment report to this application. It is worth noting that not all foods produced using gene technology carry antibiotic resistance sequences. Although bacterial genes conferring antibiotic resistance are routinely used in the laboratory, the sequences are occasionally not transferred when generating the modified plant.

In this application, the *nptII* gene which encodes the selectable marker enzyme neomycin phosphotransferase II (NPTII), imparting resistance to the antibiotics neomycin and kanamycin, was needed to identify the correct laboratory intermediates and is present in the DNA segment transferred to the plant. Neomycin is not considered to be of clinical importance in the treatment of infections in humans. However, as kanamycin still has some limited therapeutic use, the potential for inactivation of an oral dose of this antibiotic by consuming food containing the *nptII* gene simultaneously with the antibiotic, is a potential food safety issue.

The Nordic Council of Ministers have published a recent comprehensive review of the use of antibiotic resistance genes and have thoroughly reviewed this gene in particular. Its use as a selectable marker gene in the laboratory and in a range of genetically modified foods has been well studied and the data published in a succession of scientific papers (for review see Health Effects of Marker Genes in Genetically Engineered Food Plants, The Nordic Council, 1996) This review concluded that the nptII gene and its protein product can be considered safe for use as a marker in the genetic transformation of food plants.

In addition, the *aad* gene which encodes the bacterial selectable marker enzyme aminoglycoside adenylyltransferase (AAD) is present under the control of a bacterial promoter. This enzyme, which confers resistance to spectinomycin or streptomycin, was also used to identify laboratory intermediates and has no function in the plant.

The lack of any expression of this gene in the cotton plants is confirmed by an ELISA specifically developed for the AAD protein. This gene and several others in the same family with specificity for aminoglycoside antibiotics is common and can be found at high frequency in natural populations of bacteria. Therefore, this gene and its protein product is not considered novel for humans and animals.

The possibility of transfer of antibiotic resistance sequences, contained in some genetically modified foods, to microorganisms inhabiting the human intestine is considered to be extremely small (ACNFP, 1994 and 1996). In part, this is due to the number and complexity of the events that would be necessary to occur in the human digestive system in order to achieve the genetic change in the bacteria within the gut.

Briefly, some of the necessary factors to be considered in this transfer are the amount of DNA present in the food itself (for instance, refined oils and sugars are not considered to contain any detectable amounts of DNA), the degree of digestion of any DNA present in the food (survival of sufficient amounts of DNA encoding an intact gene to the digestive processes), the competence of the bacteria to take up isolated fragments of DNA and lastly, the incorporation of these fragments into functional replicating units capable of being retained by bacterial cells. The potential frequency of any one of these necessary events is so low that, taken together, the cumulative limitations present an almost insurmountable technical barrier to the complete event. Moreover, without the continued selection pressure of the antibiotic substance itself, the bacteria would not be expected to maintain the resistance capability, adding another negative factor to any theoretical model of probability.

Since the completion of the full assessment report, a study has been described in which it was demonstrated that genetically modified bacteria can, at low frequency, transfer their antibiotic resistance genes to bacteria in an artificial gut (see New Scientist, January 1999). This research used a simulated digestive system to show that microbes in the simulated gut conditions were potentially exposed to DNA at a measurable frequency. It was claimed that because of the vast numbers of bacteria normally inhabiting the gut, these data suggest that some would be transformed. However, these results were obtained using antibiotic resistant bacteria, and therefore are not readily extrapolated to a situation where the antibiotic resistance sequence is merely present in a food. Whereas the interspecies transfer of DNA between bacteria is well described in the scientific literature, there are no reports of transformation of gut bacteria by ingested food. The researchers noted the results, however, in the context of the current precautionary approach with respect to the use of antibiotic resistance marker genes in biotechnology and advocated that more research in this area would be of immense use.

From research data and a wealth of scientific literature, it is widely demonstrated that antibiotic resistance in bacteria is a naturally occurring phenomenon, to the extent that bacteria with such properties are ubiquitous and normally inhabit the intestine of animals and humans (see Conner, 1997). The maintenance of particular antibiotic resistance phenotypes in certain bacterial pathogens is considered also to be a function of a number of medical and veterinary practices. The constant presence of some antibiotics in the environment has affected this natural process (see New Scientist, 25 April, 1998). In comparison to these pre-existing circumstances, the risk associated with direct gene transfer from the consumption of a genetically modified food is considered therefore to be extremely small.

On the basis of the information compiled on this issue, in the case of Bt cotton specifically, the absence of detectable DNA in the oil and linters obtained from the plant therefore means this small possibility is not of practical significance when considering the safety aspects of the foods.

Labelling of oil and linters from Bt cottonseed

The Food Technology Association of Victoria stated that labelling should be mandatory whenever this product is incorporated into any food, while InforMed Systems Ltd regarded labelling of this food as unnecessary on the basis that the oil and linters do not contain any DNA or protein.

The majority of submissions stated a clear preference for labelling of all foods produced using gene technology. On the basis of the conclusions of the assessment for this application, the current labelling provisions of Standard A18 would not require food derived from insect-protected cottonseed lines 531, 757, and 1076 to be labelled. However, the Australia New Zealand Food Standards Council (ANZFSC) confirmed its commitment to the labelling of all foods produced using gene technology at meetings held in August and October 1999. It is anticipated, therefore, that following Ministerial approval, foods covered by this application would be required to be labelled under the proposed amendments to Standard A18 still under consideration.

CHANGES TO FULL ASSESSMENT/RIS RESULTING FROM INQUIRY

The Office of Regulation Review in Australia suggested that the Regulatory Impact Statement (RIS) should consider the costs of developing and implementing an interim labelling requirement against the costs of non compliance with the decision by Health Ministers to include labelling for substantially equivalent foods. Such costs might be those associated with having to withdraw unlabelled products in the event of a decision to extend the labelling requirements of the standard.

However, as with the implementation of Standard A18, it is anticipated that any decision of ANZFSC to amend the labelling provisions, of necessity, would include a similar implementation period to allow the food industry to comply with amendments to the standard. This is regarded as an essential provision to ensure no disruption to the current availability of foods already in the market in Australia and New Zealand. In addition, the current standard does not present any impediment to labelling of foods produced using gene technology, if the manufacturer currently wishes to implement a voluntary system of labelling.

Notwithstanding that the labelling provisions of Standard A18 are not yet fully resolved, the public submissions have not raised any substantive issues which would result in an alteration to the conclusions made at Full Assessment.

CONCLUSIONS

- oil and linters derived from insect-protected cotton lines 531, 757, and 1076 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 in public submissions regarding the use of gene technology in food production, there is no evidence that the consumption of cottonseed oil and linters from the insect-protected cotton lines may lead to adverse health effects in humans;

- cottonseed oil and linters derived from insect-protected cotton lines 531, 757 and 1076 would not require labelling under the current provisions of Standard A18 as they can be regarded as substantially equivalent to oil and linters from conventional cottonseed. It is noted however that the labelling provisions of Standard A18 are still under consideration by ANZFSC. On resolution, these foods will be required to comply with the amended labelling provisions;

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

- the regulatory impact analysis identified no disadvantages to either industry, government or consumers in the proposed amendment. The direct benefits of the proposed amendment primarily accrue to the cotton producers, with potentially a small benefit to the consumer. These benefits outweigh the costs associated with recommending against the amendment.

References

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Attachments:

1. Proposed Draft Variation
2. Statement of Reasons
3. Executive Summary to the Full Assessment Report
4. Summary of Public Submissions

ATTACHMENT 1

DRAFT VARIATION TO THE AUSTRALIAN *FOOD STANDARDS CODE*

A341 - OIL AND LINTERS DERIVED FROM INSECT-PROTECTED COTTON

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

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

ATTACHMENT 2

STATEMENT OF REASONS

APPLICATION A341

FOR RECOMMENDING A VARIATION TO STANDARD A18 - FOOD PRODUCED USING GENE TECHNOLOGY - TO INCLUDE OIL AND LINTERS DERIVED FROM INSECT-PROTECTED COTTON LINES 531, 757 AND 1076 TO THE TABLE TO CLAUSE 2 OF THE STANDARD.

The Australia New Zealand Food Authority has before it an application received on 14 April 1997 from Monsanto Australia Ltd to amend the Australian *Food Standards Code* to include oil and linters derived from insect-protected cotton lines 531, 757 and 1076 to the Table to clause 2 of Standard A18 - Food Produced Using Gene Technology.

The Australia New Zealand Food Authority recommends the adoption of the draft variation for the following reasons:

- Cotton plants have been modified using gene technology to produce an insecticidal protein, Cry1Ac, derived from a common soil bacterium, *Bacillus thuringiensis* (known commercially as Bt). The protein is toxic to the two major insect pests of cotton crops, cotton bollworm and native budworm, both Lepidopteran species. The modification is primarily to assist in the agricultural production of this commodity crop;

- Assessment of the safety of the food derived from the cottonseed according to ANZFA's safety assessment guidelines and using all available data has not raised any public health and safety concerns;

- Analysis of the compositional data on the refined cottonseed oil and processed linters derived from the insect-protected lines found that these foods were substantially equivalent to the oil and linters derived from conventional cottonseed;

- Assessment of the issues raised in public submissions did not raise any new concerns in relation to public health and safety;

- As the cotton lines 531, 757 and 1076 have been found to be substantially equivalent to the unmodified counterpart, no labelling requirements have been recommended, in accordance with the current standard. It is recognised, however, that the situation is likely to change as a result of the current review of the labelling provisions for foods produced using gene technology.

The commencement date of the draft variation be the date of gazettal of the amendment to Standard A18.

REGULATION IMPACT

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

WORLD TRADE ORGANIZATION (WTO) NOTIFICATION

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

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

This variation to the *Food Standards Code* will allow cottonseed oil and linters derived from insect-protected cotton lines 531, 757 and 1076 to the Table to clause 2 of Standard A18 - Food Produced Using Gene Technology. Australia and New Zealand have previously notified the WTO in relation to matters concerning the implementation of Standard A18. These notifications included the temporary exemption of foods produced using gene technology, under the clause 2A amendment, for foods which are currently on the market, such as those encompassed by this application.

ATTACHMENT 3

EXECUTIVE SUMMARY FROM THE FULL ASSESSMENT REPORT
(completed in January 1999)

- Standard A18–Food 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;

- 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-protected cotton lines 531, 757, 1076 and 1849 in the Table to Clause 2 of Standard A18 – Food Produced Using Gene Technology;

- 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;

- 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;

- 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;

- 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;

- A full data package for insect-protected 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;

- The safety assessment found the following:

– 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);

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

– 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;

– 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 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;

– 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;

– 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 ;

– 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;

– the compositional analyses were comprehensive and indicate that there are some significant differences in composition between the insect-protected 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-protected cotton are considered to be equivalent to those of unmodified cotton; and

– a 14 day 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;

- On the basis of the safety assessment conducted, no potential public health and safety concerns were identified. Oil and linters derived from insect-protected 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;

- 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;

- The regulatory impact analysis concluded that, as oil and linters derived from the insect-protected 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-protected 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.

ATTACHMENT 4

SUMMARY OF PUBLIC SUBMISSIONS

A341 – OIL AND LINTERS DERIVED FROM INSECT-PROTECTED COTTONSEED

1. Dr Bernard Conlon (NZ)

- provides list of 20 concerned scientists supporting Dr Pusztai (UK) and calling for the safety and hazards presented by genetically modified crops to be properly assessed.

- the most significant aspect of Dr Pusztai's results is not that the snowdrop lectin adversely affected the laboratory rats, but that there was a difference between the rats treated with the genetically modified potatoes and those who received lectin in unmodified potatoes. There is an assertion that the observations in the animals were therefore due to the process of genetic engineering itself.

- states that the insect-protected cotton has not been tested for effects on the immune system or internal organs of laboratory animals.

- states that substantial equivalence means that the food does not have to be thoroughly tested. In addition, claims that the genetically modified potatoes used in Dr Pusztai's experiments were declared to be substantially equivalent and therefore the effects on the mammalian system would not have been discovered within the present regulatory framework.

- Approval for insect-protected cotton should be declined and the precautionary principle applied, placing the burden of proof of safety first.

2. Janine Kelly (NZ)

- strongly demands labelling for all genetically modified foods.

3. Janina Clark (Aust)

- demands labelling of all genetically modified foods including vegetable oils and sugars.

4. Go Mark Food Systems (Aust)

- supports an all-encompassing GMO labelling system.

- all current Monsanto applications for genetically modified foods should be rejected because:
  - long term safety issues are unresolved;
  - the regulatory framework is biased towards commercial interests;
  - the public's ability to assess the issues is very limited.

- concerned that the Quality Assurance Certification relating to the data presented in the applications is conducted by the applicant, Monsanto.

- the application should be rejected for the following additional reasons:

  - expresses concerns about the use of antibiotic resistance genes *nptII* and *aad* and states that alternatives are currently available;

- suggests the development of an Australian standard on acceptable selection markers;
- data provided only looks for known toxins, and does not sufficiently evaluate all the possible changes potentially arising from the insertion of the new genetic sequence;
- no human testing done;
- questions whether animal feed prepared from insect-protected cotton would effect meat products;

5. Garry Clarke (NZ)

- objects to genetically modified foods because of the presence of animal or insect genes in the food.

- all genetically modified foods must be labelled.

6. Pauline Bailey (NZ)

- wants withdrawal of all genetically modified foods from NZ until legally proven to be safe, including to future generations.

7. Marja Rouse (Aust)

- demands labelling of all genetically modified foods including oils, processing agents and enzymes.

- believes that the use of antibiotic (resistance) genes poses a threat to human health.

8. Dorothy Golder (NZ)

- strongly opposed to all genetically modified foods because believes them to be unsafe.

9. Colin Kell (NZ)

- expresses a complete lack of acceptance of ANZFA's assessment of both applications in terms of public health and safety.

- demands labelling of all genetically modified food products.

10. Gary Bilton (Aust)

- ANZFA's terms of reference are too narrow. Substantial equivalence should not be determined purely on scientific grounds.

- calls for comprehensive labelling of all genetically modified foods.

- genetically modified crops must be segregated.

11. Neil Farmiloe (NZ)

- opposed to application because considers safety testing to be inadequate, and does not trust data provided by the applicant.

12. I. A. Black (NZ)

- benefits of Bt bacteria will be lost if insect resistance develops due to genetic modification.

13. Nathan Kennerly (NZ)

- opposed to application on the grounds that the short and long term safety of eating such products is not established.

14. Home Economics Institute of Australia Incorporated

- believes that food containing oil or linters derived from insect-protected cottonseed should be labelled because, although not expected to contain any detectable genetic material, there is no guarantee that it is not present at all or that the product is totally unaffected by the genetic modification in the plant.

- consumer demands for labelling are not based solely on changes to the actual food, but include concerns over the possible environmental, economic and social consequences of the development of insect-protected cotton.

15. Brent Ferretii (NZ)

- opposed to the application because of perceived risks to human health.

16. Margaret Burn (NZ)

- opposed to the application because of view that the applicant is not a reliable source of data on which to base the safety assessment.

17. Maurilia (NZ)

- opposed to the application on the grounds that the foods cannot be guaranteed as safe.

18. J. Watt (NZ)

- opposed to the application because of concerns about the validity and integrity of the data provided by the applicant. Independent data should be required for proper assessment of the foods.

19. Ministry of Health (NZ)

- generally welcomes the pre-market safety assessment process adopted by ANZFA.

- the data presented from the animal feeding studies is problematic. In some cases the results generated more questions than answers and some experiments, which indicated a difference between the control and test groups, should have been repeated.

- suggests that ANZFA consider establishing independent ad hoc advisory panels for such controversial issues as genetically modified foods.

20. Dr Virginia Lubell (NZ)

- strongly opposes the application due to a belief that there is an unacceptable health risk in genetically modified foods.

21. Public Health Association of Australia Inc.

- ANZFA should give full consideration to the conclusions and recommendations of the Consensus Conference on Gene Technology in the Food Chain.

- ANZFA adopts a very narrow interpretation with respect to public health and safety, with less emphasis on longer term nutritional and other public health considerations e.g. environmental health.

- considers that it is necessary to obtain an independent safety evaluation using research not obtained from the applicant, to broaden the parameters of the evaluation.

- the application is not supported in the absence of amendments to Standard A18 being in place which reflect the ANZFSC decision in December on labelling. Accordingly, ANZFA is advised to impose interim labelling requirements under the special conditions column of the Table to clause 2 of the standard.

22. M. Hunt (NZ)

- opposed to the application and demands labelling of all genetically modified foods to provide complete information to the consumer

23. Sukyo Mahikari Australia Ltd

- opposed to the application on the basis of the claim that the assessment procedures are rather crude and do not adequately address the safety considerations of the effects of genetic manipulation. Refers to media reports of the laboratory data from Dr A. Pusztai.

24. Rex Warren - A.C.T.A. (Aust)

- opposed to the application because of the view that approval will lead to the consumption of foods with increased pesticides.

25. Consumers' Federation of Australia

- independent research should be conducted on this food before any approval .

- other feeding trials in a range of animals should be performed.

- believes that a system for monitoring any adverse reactions be established before the foods are assessed as safe for consumption.

- no approvals should be granted until the issue of labelling is resolved in line with the Health Ministers decision of December 1998.

26. Dr P. Butler (NZ)

- opposed to the application because it is asserted that the food poses risks from undetected toxins, allergens, antibiotic resistance factors and unpredictable immunological effects. It is further asserted that any risk beyond that for the non-genetically engineered soy and cottonseed oil is unacceptable and that these risks can only be quantified by long term human consumption studies.

- states that the genetic changes in the application affect the whole of the population but have no clearly defined benefits.

- believes that recent research by Dr Pusztai gives reason to apply the precautionary principle to the approval of these foods.

27. Australian GeneEthics Network

- opposed to the application because of the assertion that the tests conducted by the applicant are insufficient and not adequately documented to satisfy the rigorous standards employed by ANZFA.

- believes that the applicant is attempting to influence ANZFA on the labelling of genetically modified foods, and claims that the applicant is attempting to deliberately withhold information from consumers.

- provides data to support the assertion that the applicant's claim of significant agronomic benefits associated with the use of the insect-protected cotton plants is not supported by independent research.

- does not agree with the possibility that TBT issues are raised with the WTO in view of Australia's rights as signatories and believes that Australia is favoured in some international markets for growing non- genetically modified crops, e.g.. canola.

28. Dr F.E. Peters (Aust)

- is opposed to the application on the basis that the information provided by the applicant is insufficient to make an educated assessment of the potential risks to consumers posed by the foods.

29. Edwin Dempsey (NZ)

- opposed to the application on the basis that it may lead to increased insect resistance to Bt insecticide and thereby severely compromise the effective use of Bt by the organic industry.

- claims that Bt engineered plants will lead to higher levels of pesticide in the human diet.

- cites the Wingspread Statement on the Precautionary Principle which should be applied in consideration of the application.

30. Agriculture, Fisheries and Forestry Australia

- the importation requirements of Australia's trading partners must be considered in assessing the application.

31. Annie Stroh (NZ)

- opposed to the application on the belief that long term safety has not been established and demands a comprehensive labelling regime for all genetically modified foods.

32. T.T. Green (NZ)

- opposed to the application because of concerns about the long term effects of consuming foreign proteins, antibiotic resistance marker genes and viruses.

33. Jim Chapple (NZ)

- strongly opposed to the application and claims that ANZFA does not have a genuine consumer representative on the Board.

- demands verification that the data supplied was done according to good laboratory practice and that it was independently audited.

34. Daniel Harris (NZ)

- opposed to the application because does not accept the food is substantially equivalent or that safety issues are resolved.

- demands comprehensive labelling to enable consumers to decide whether to eat these foods.

35. Dr V. Lubell (NZ)

- opposed to the application and believes that trade considerations should be ignored completely in favour of public health and safety.

36. InforMed Systems Ltd (NZ)

- tentatively supports the application but is concerned about particular issues. Specifically these are:
  - there is no independent data supplied by the applicant;
  - questions the safety of using the cauliflower mosaic virus "as a transfer agent";
  - is concerned about the presence of the *aad* gene and its expression.

- on the basis of the claims that the food does not contain modified DNA or protein, generally supports ANZFA's conclusion that no special labelling requirements should apply.

37. Mike Gregory (NZ)

- opposed to the application on the grounds that the foods are potentially unsafe.

38. Dietitians Association of Australia

- does not support the application until full toxicological data is available for evaluation by ANZFA.

39. Home Economics Institute of Australia Consumer Affairs Standing Committee

- the level of consumer unease about the products indicates that comprehensive labelling is required.

40. Victorian Food Safety Council - Food Standards Sub-Committee, Department of Human Services (Aust)

- supports ANZFA's assessment and recommendation in relation to the application.

- queries whether there is any intention to conduct post market testing of the foods as is done for certain other foods.

41. Nestlé Australia Ltd.

- supports the application

42. B. Veitch (NZ)

- opposes the application for environmental reasons.

43. Native Forest Network (Aust)

- states that the Bt toxin has no history of safe use in the human food supply.

- the application should be rejected because it is claimed that the data presented by the applicant is anecdotal, unsubstantiated and unscientific.

- demands pre-market human testing, full labelling of all approved foods, public review of the toxicity of the Bt protein, consideration in the assessment process of cultural, social, ethnic diversity issues, an adverse reactions register, post-approval monitoring.

44. Stephen and Maxine Blackheath (NZ)

- all genetically modified foods, including refined food products, should be comprehensively labelled to enable monitoring of any adverse reactions.

- refers to a UK poll which reportedly concluded that a majority of consumers do not want genetically modified foods.

- believes that there is insufficient knowledge of the effects of the genetic modification on the crop plant to establish safety.

45. Safe Food Campaign (NZ)

- the application should be rejected because the scientific data provided by the applicant is believed to be inadequate and unsubstantiated.

- ANZFA's approach to assessment of the application is extremely narrow and does not enable fulfilment of obligations to stakeholders.

46. Rachel Kiel (NZ)

- opposed to the application because of concerns about safety of the foods.

47. D. Bailey (NZ)

- opposed to application because the food has no increased benefit to consumers.

48. Isobel Bailey (NZ)

- opposed to the application because of concerns about the long term safety of the food.

49. D. Davies-Payne (NZ)

- expresses a lack of confidence in safety assessments and does not support the concept of substantial equivalence.

- the foods encompassed by this application should carry a label and could be segregated if the political will existed.

50. E. Ponter (NZ)

- believes that ANZFA should take political, social, moral and ethical issues, as well as science, into consideration when assessing the application.

- opposed to the application on the grounds that there has been insufficient public debate on the issue in New Zealand.

- concerned that control over the production of food will be narrowed.

51. Raymond Vogt (NZ)

- concerned that no clinical studies have been done which involve testing the foods on humans in a controlled situation.

- raises concerns about the likelihood of a transfer of antibiotic resistance genes from some genetically modified foods to intestinal bacteria.

- calls for a rejection of the application until more research is done to assess the safety of genetically modified foods, and refers to research of Dr. Arpad Pusztai to support this view.

52. Dr. Peter Wills (NZ)

- believes that ANZFA has considered the matter very narrowly and should take factors other than science into consideration in the assessment process of the application.

- asserts an ANZFA bias in favour of approving applications for foods produced using gene technology.

- calls on ANZFA to devise a solution to the issue of genetically modified foods which will make it possible for those members of the public who wish to avoid such foods, to be able to do so easily.

- is philosophically opposed to the application and favours a ban on all genetically modified foods.

53. Dr. M.E. Godfrey (NZ)

- expresses serious concerns in relation to the scientific data submitted by the applicant and calls for independent research.

- states that the InGard cotton could result in the development of resistance in wild populations of insects and that consumers may develop adverse health effects due to continued low level exposure to the foods derived from the Bt crops.

- advocates the Precautionary Principle in relation to this application.

54. E. Trevalyan (NZ)

- believes that the application shows a disregard for organic farming practices and will lead more rapidly to insect resistance to Bt protein.

- opposed to the application and believes that New Zealand would have a food market advantage in the rejection of the technology.

55. Dr. Joan Chapple (NZ)

- opposed to the application although it was not specifically referred to in the expression of the necessity for long term independent scientific studies before acceptance that the foods are as safe as conventional types.

- believes mandatory labelling of all genetically modified food is a necessity.

- believes ANZFA places trade considerations above public health.

56. L.A. Birchall (NZ)

- is opposed to the application because of the view that independent assessment trials should be done in relation to the foods.

- demands that all food products, including oils, which contain genetic material from outside their particular species, be mandatorily labelled.

57. Neil and Barbara Mountier (NZ)

- strongly opposed to the application due to a lack of confidence in the assessment procedure adopted by ANZFA and the acceptance of the applicant's data.

- ANZFA appears to have ignored its section 10 objectives in recommending approval for the foods (considers the animal feeding studies inadequate to indicate wholesomeness).

- ANZFA appears to have ignored potential health and environmental risks associated with the application and there has been a lack of rigorous public debate and unbiased scientific examination of the issues.

- consumers' rights (supported by the New Zealand Bill of Rights 1991) are being breached by the introduction of genetically modified foods, unlabelled, into the market.

58. Timothy Jones (NZ)

- opposed to the application on the basis that ANZFA has not adequately researched the possible public health and safety effects of the foods and has accepted the scientific data provided by the applicant.

- the Precautionary Principle should apply to these foods.

- genetically modified foods should be subject to at least as stringent testing procedures as are new drugs and other pharmaceutical products. The cost of the testing should be borne by the applicant, but the applicant should have no role in designing the trials or selecting who will conduct them.

59. Nelson Environment Centre (NZ)

- opposes the application on environmental grounds and states that as InGard cotton is not grown in New Zealand, ERMA will not assess the environmental impacts of this product. Unless comprehensive labelling is adopted, consumers will be denied the right to choose between products for a variety of legitimate reasons.

- the feeding studies are inadequate to demonstrate wholesomeness of the food.

- cites the incident involving Showa Denko and the production of tryptophan as an example of genetically modified foods posing considerable potential safety problems.

- cites a recent article (New Scientist, January 30 1999) outlining research on the transferability of antibiotic resistance genes to microorganisms in the human intestine.

- cites articles raising concerns about the use of the CaMV promoter in relation to the generation of new viruses.

60. National Council of Women of Australia

- opposed to the application because of claims that the full assessment report did not adequately address concerns of consumers.

- advocates labelling of all genetically modified foods, including oils and sugars obtained from genetically modified plants.

- believes there is a need for clinical testing in human volunteers in a similar manner of testing applied to new drugs and pharmaceuticals.

- provides article which discusses potential health and safety issues concerning genetically modified foods, including the use of antibiotic resistance genes. The article states that "substantial equivalence" is conceptually flawed because of the potential for unknown effects due to the gene transfer.

61. Food Technology Association of Victoria Inc. (Aust)

- agrees with the addition of this product to the Standard.

- recommends mandatory labelling whenever the foods are incorporated into any other food products.

62. Office of Regulation Review (Aust)

- ANZFA should focus its assessment on safety of the foods.

63. Food Advisory Committee, Health Department of Western Australia

- agrees with the approval of this product and its inclusion in the standard.

- agrees with ANZFA's finding of substantial equivalence in respect of the composition, safety, wholesomeness and end use of the food.

- understands that foods derived from insect-protected cottonseed will be labelled because of the attitude expressed by some consumers.

64. Pam Atkinson (NZ)

- believes that there is no consumer support for the application and it should therefore be rejected.

65. Oraina Jones (NZ)

- considers that ANZFA should assess the wider implications of giving approval to the application, for example, the environmental impact.

- believes that an independent review of the data by unbiased scientists should occur before any approval is given.

66. Helmut Lubbers (NZ)

- opposes the application because the conclusions and recommendation of the full assessment report do not adhere to any of the section 10 objectives in relation to the protection of public health and safety, the promotion of fair trading in food and the promotion of trade and commerce in the food industry. The latter objectives are not fulfilled if approval results in the eventual loss of the organic farming industry to Australia and New Zealand.

- ANZFA's section 10 objectives should give scope to assess the broader implications (e.g.. environmental) of the application.

- the regulatory impact analysis fails to adequately address consumer interests and also neglects the impact on organic producers.

67. John Ibbotson (NZ)

- opposed to the application because of concerns the food may have on an existing allergy.

68. Jennifer Jane (NZ)

- opposed to the application on public health and safety grounds, human rights issues and on religious grounds.

- consumer rights to choose non-genetically modified foods are threatened by the application.

- calls for immediate and mandatory labelling of all genetically modified foods.

69. Canberra Consumers Inc. (Aust)

- questions the molecular characterisation of the genes transferred.

- concerned that the use of antibiotic resistance genes may lead to increased antibiotic resistance.

- questions the validity of the feeding study in relation to the safety assessment.

- ANZFA has not sufficiently justified its recommendation for approval of the application, either in demonstrating scientific rigour in the assessment or in the presentation of the findings.

70. Roger Knecht (NZ)

- the application should be rejected because of ongoing doubts about the safety of the foods. Because of the apparent rush to put the products in the market place, there has not been adequate scientific testing over a long period.

- concerned that the use of the Bt gene in transgenic crops may compromise the efficacy of Bt when used by organic food producers by increasing the number of resistant insects.

71. J. and R. Thornton (NZ)

- strongly opposed to the application because of safety fears and the environmental concern that use of InGard cotton may lead to insect resistance.

- states that acceptance of the applicant's scientific data is unethical and that the feeding trials were not adequate to satisfy safety concerns.

72. New Zealand Nutrition Foundation

- supports comments made by InforMed Systems.

73. Lynne Crooks (NZ)

- opposes the application for a variety of reasons concerning safety of the foods and the possible environmental impact of the technology.

74. Marie Clayton (NZ)

- opposed to the application and calls for comprehensive labelling.

75. Tracy Botica (NZ)

- opposed to the application on the grounds of possible detrimental health effects.

76. Noeline Gannaway (NZ)

- opposed to the application because of concerns about the long term health effects of the foods and disapproves of the use of the concept of substantial equivalence, stating that the term is unscientific.

- urges mandatory labelling for all genetically modified foods.

77. Jonathan Peter (Aust)

- opposed to the application because of health and environmental concerns.

- calls for comprehensive labelling of all genetically modified foods including oils and sugars derived from genetically modified crops.

78. F. Woodham (NZ)

- opposed to the application for health and environmental reasons.

79. Elaine Attwood (NZ)

- expresses criticisms about the feeding studies in relation to the possible chronic effects, and the issue of the use of antibiotic resistance genes in the constructs.

- states that ANZFA's interpretation of the decision made by Health Ministers in December is not consistent with press releases indicating that all genetically modified foods, including oils and sugars, should be labelled. Believes that the application should be rejected until the labelling issues are resolved.

- provides an article which discusses the possibility of producing toxins in genetically modified foods which would not necessarily be destroyed or removed during extensive processing to remove DNA.

80. R. Vogt (NZ)

- opposed to the application and submits discussion points relating to the safety of the foods written and submitted separately by the Australian GeneEthics Network.

81. Australian Food and Grocery Council

- supports approval of the application on the basis of the findings of the safety assessment conducted by ANZFA.

- does not support the mandatory labelling of substantially equivalent foods because of the view that this requirement is unnecessary, confusing to consumers, impractical, unenforceable and discriminates against packaged foods.

82. Dr. Nelum Devi Soysa (NZ)

- opposed to the application and believes that ANZFA should have adhered to the Precautionary Principle in the assessment of the application. In addition to a RIA, ANZFA should complete a Health Impact Assessment (HIA) and an Environmental Impact Assessment (EIA).

- criticises the process of public consultation throughout the setting up of the standard and the assessment of the application.

- questions the calibre of the animal and allergy testing, and the parameters examined in the safety assessment.

- expresses concern about the possibility of transferring antibiotic resistance to pathogenic bacteria in the human gut.

83. Australian Natural Therapies Association Ltd.

- opposed to the application for a variety of health associated reasons. Cites various written articles from different sources which range across such issues as the potential for causing allergic reactions, the (inadvertent) transfer of toxins, the undesirable environmental impacts of the particular genetic modification and the potential for the spread of diseases. The information provided relates to a range of examples of genetically modified organisms with predominantly medical and pharmaceutical applications.

84. South Australian Department of Human Services, Public and Environmental Health Service, Environmental Health Branch.

- ANZFA should ensure that foods which are similar are assessed via the same criteria.

- there is a lack of data relating to the expression of the gene fusion of the *cry2Aa* gene with an endogenous cotton gene.

- queries the effects of engineering of the *cry1Ac* and the *cry2Aa* genes on characteristics of the proteins expressed in the cottonseed.

- calls for scientific evidence that the cottonseed oil derived from the cotton lines does not contain any genetic material and questions the level of protein detectable in the cottonseed oil.

- states that there is community concern in relation to the concept 'substantial equivalence' and recommends that ANZFA need to define:

    - criteria which result in changes to composition or nutrition being 'significant';
    - threshold levels at which anti-nutritional factors or natural toxicants are considered 'significantly different'; and
    - the 'control' to be used in determining the normal range of values.

- disagrees that the evidence supports a finding of substantial equivalence and therefore states that cottonseed oil and linters derived from lines 531, 757, 1076 and 1849 should be labelled.

- supports approval of the application provided the above concerns can be addressed, and labelling is required from 13 May, 1999.

85. Peter Johnston (NZ)

- opposed to the application because of concerns primarily about the environmental impacts of the use of insecticidal proteins in transgenic crops and the consumption of the proteins by humans.

86. Australian Conservation Foundation Gold Coast Inc.

- opposed to the application for reasons outlined in the submission of the Australian GeneEthics Network.

ATTACHMENT 3

Comments on ANZFA Inquiry Report: A341-Oil and Linters derived from insect-protected cotton (7/12/99)

Associate Professor Brian R. Jordan

Thank you for inviting me to comment on the Inquiry Report A341. Overall, I feel that the inquiry report deals satisfactorily with the concerns raised. As I believe gene technology is a process and that this report is dealing with products, many of the frequent concerns over gene technology are not appropriate. I hope that the following comments are helpful:

- On p.9 of the inquiry report the short term feeding studies are discussed and especially the feeding of raw cottonseed. I did feel this was inappropriate and unlikely to give valuable information. What I could not understand was why a normal `healthy' balanced diet was not fed to the rats with a supplement of oil produced from GE plants or non GE oil. Certainly there may be some difficulties in such a diet, but surely it is a more realistic test. We have certainly used such diets. Does the applicant usually supply data on diets prepared by knowledgeable nutritionists? This would be useful, so as to provide data that could be assessed by experts.

- The above point also brings up the constant fear that the testing carried out by the company is in some way `fixed' (p.8). While, I appreciate the companies will be as thorough as possible, it is all about public perception and this is unlikely to be assured unless some independent analysis is carried out.

- The fatty acid analysis is routine and described on p.39 of the Full Assessment Report. I could not see any specific problem in the information provided. One cautionary note, however, the report states that the mean values were within the literature reported ranges. What literature? Is this the mean of all data on **cotton** oil? Oil composition could vary significantly throughout development or under different environmental situations. The test FA composition from GE plants must be compared to a set of FA data that is an appropriate control.

- Labelling on p.14. I cannot understand the need for labelling a product that is well characterised purely because it derived from a new technology. This is increased cost with little rationale. It surely would be better to get the public to understand the issue, rather than have this mandatory labelling.

ATTACHMENT 4

Comments on ANZFA Inquiry Report for Application A341 – Oil and linters derived from insect-protected cottonseed.

Associate Professor Richard T. Roush

Thanks very much for the opportunity to review the assessment of cotton seed oil and linters from Bt cotton. These are two more excellent reports, and I'd like to ask if I can get electronic copies of these and the Round-up Ready reports when the assessments can be circulated.
I noticed only one statement that is perhaps not very accurate: "The public has been readily exposed to Bt proteins" as on page 6 of the Inquiry report. Given the rapid degradation of Bt sprays even as measured by insect bioassays, and the washing and cooking of foods, I wonder if this is true and have never seen any data (as by antibody tests) for human exposure among the general public. Perhaps a more accurate statement would be that "At least some segments of the public have probably been exposed to Bt proteins in the diet".

I may be able to assist you on the subject of resistance management (page 10 of the Inquiry report). A key point often overlooked by the critics of this technology is that the pest species targeted by Bt cotton are only poorly controlled and rarely targeted by Bt sprays! For example, there are essentially no Bt sprays used against bollworms in the US or Australia. Thus, although there are obvious reasons for all of us to slow the evolutions of resistance to Bt cotton in the pests, even if resistance did occur, it would make little or no difference to the uses of Bt in conventional or organic agriculture.

Further, in contrast to Bt crops where resistance management strategies are already in place, the only cases of resistance in the field to Bt are as a result of the use of Bt sprays, for which neither organic growers nor the producers of Bt sprays have instituted ANY resistance management programs.

I note that the Australian GeneEthics Network (submission 27) disputed the claim of significant agronomic benefits from the Bt cotton. I and others have addressed this in discussions with Bob Phelps of GeneEthics on several occasions. First, the benefits offshore are very large and unambiguous. Second, even in Australia, Phelps seems to have consistently ignored the point that growers prefer to use Bt cotton not so much for their agronomic benefits, the limits of which they are well aware, but because it reduces their use of chemical pesticides.

As a last point, I think that your arguments about antibiotic resistance are excellent (page 13 of the Inquiry report), but wouldn't it also be true that existing resistant bacteria in the gut would be a far more readily available source of the resistance than any transgenic crop? It seems to me that this argument is implicit in your response, but could perhaps be more explicit.

The overall grammatical quality was also excellent, but I noticed some occasional glitches with that common bugbear of scientific discussions, confusion over whether "data" is singular or plural (e.g.., "Data was" rather than "Data were" on page 5 and "data reflects" rather than "data reflect" on page 8).

Congratulations on a job well done!
Sincerely,
Rick Roush
10 December 1999