

FSANZ RESPONSE TO ARTICLE ENTITLED “GE FOODS AND HUMAN HEALTH SAFETY ASSESSMENTS” BY DR JUDY CARMAN, SPOKESPERSON ON GE FOOD, PUBLIC HEALTH ASSOCIATION OF AUSTRALIA

Background

Dr Judy Carman, spokesperson on genetically modified (GM) foods for the Public Health Association of Australia (PHAA) has written an article “GE Foods and Human Health Safety Assessments” which has been placed on the PHAA and Greenpeace web sites. The article criticises the procedures used by Food Standards Australia New Zealand (FSANZ) to assess the safety of GM foods. The article makes several claims which, in FSANZ’s view, are unfounded.

This response addresses some of the major points raised by Dr Carman below in detail in order to reassure consumers that the FSANZ GM food safety process is comprehensive, rigorous and at the forefront of world’s best practice.

General Comments

FSANZ has taken a cautious approach in its assessment and approval processes for GM food. Industry must demonstrate to FSANZ and the Australia and New Zealand Food Regulation Ministerial Council (ANZFRMC) that products are safe for human consumption before they can be legally sold in Australia and New Zealand. Our own scientists evaluate all data submitted to FSANZ. FSANZ follows guidelines for assessing GM foods developed by the Codex Alimentarius Commission, FAO/WHO and OECD. These best-practice principles and processes have also been adopted in other countries including Canada, Japan and members of the European Union.

FSANZ staff are recognised internationally for their extensive expertise and leadership and have participated, by invitation, in many of the major international fora convened to consider the safety of GM foods and have contributed significantly to the development of international guidelines for the safety assessment of these foods. FSANZ believes that such invitations are in recognition of the expertise and leadership of our staff in this area.

Assertion: That FSANZ’s Safety Assessment Process for GM Foods is not scientifically comprehensive and consistent, and relies on data submitted by the applicants which is not published in peer reviewed journals.

FSANZ Comment

The Commonwealth Government, together with State, Territory and the New Zealand Governments have put in place Food Standard 1.5.2 - *Food Produced using Gene Technology* of the *Australia New Zealand Food Standards Code* which regulates the sale of foods produced using gene technology. The Food Standards Code has the force of law under the Food Acts of the Australian States and Territories and New Zealand. The approval process is open, consultative and based on a scientific risk assessment undertaken by FSANZ. Public comment is invited during the assessment process.

The assessment focuses on the altered DNA and new gene product(s), its properties including potential allergenicity, toxicity, compositional differences in the food and its history of use as a food or food product. Applicants are required to submit data that defines :

1. how the food crop was developed, including the molecular biological data which characterizes the genetic change;
2. composition of the novel food compared to non-modified counterpart foods;

3. nutritional information for the novel food compared to non-modified counterparts;
4. potential for new toxins; and
5. potential for causing allergic reactions.

Full details of the comprehensive data requirements are available from the *Guidelines for Amending the Food Standards Code, Standard 1.5.2 – Food Produced Using Gene Technology*. FSANZ receives the raw data from every experiment under these strict guidelines. This enables a more rigorous analysis of experimental outcomes than the summary data of the type submitted in support of publication of a scientific article in a peer reviewed journal. Thus, FSANZ is in a much better position to ensure the safety of GM foods than it would be if it received copies of articles published in journals. FSANZ also considers all relevant data available from the broad scientific literature and other food regulatory authorities, and maintains close links with international scientific and clinical bodies to gain access to research, trial and other reports relevant to the safety of GM foods. Additional research or testing can be required if FSANZ's scientists are not satisfied at any stage in the safety assessment process. Only if all of FSANZ's stringent criteria are met is a novel food allowed access to the Australian and New Zealand markets.

It is also important to note that this process of receiving raw data from every experiment is the normal process followed by all of the regulatory authorities involved in assessing data submitted in support of applications for approvals, including the Therapeutic Goods Administration (TGA) for medicines, the Australian Pesticide and Veterinary Medicine Authority (APVMA) for approval of agricultural and veterinary chemicals and National Industrial Chemicals Notification and Assessment Scheme (NICNAS) for industrial chemicals. In addition to internal peer review by the FSANZ scientific specialists, the safety assessments also undergo peer review by an independent panel of external experts who are considered leaders in this field. For data supplied by the applicant to be accepted as reliable, the relevant studies must have been conducted using internationally accepted protocols for research such as Good Laboratory Practice (GLP).

Assertion: In the case of the herbicide-tolerant canola, Dr Carman questions data submitted in laboratory rats which were fed canola mash.

FSANZ Response

- One of the specific comments in Dr Carman's article relates to a study provided by the applicant in which there was a small increase in liver weights in rats fed a diet of GM (glyphosate tolerant) canola meal. The applicant undertook **three** rat feeding studies. The first focused on unprocessed and processed canola meal, the second on processed canola meal. The first study showed no differences of any significance in liver weights between the glyphosate-tolerant canola and the parent line, although a minor difference in the group mean body weight for males was observed. However, the seed used in this study was found to be co-mingled with another line that was not under assessment. The study was repeated for the processed meal component and this study showed a small increase in liver weights compared to the control.
- FSANZ has pointed out in the safety assessment of foods derived from GM canola that approval has been recommended for oil derived from glyphosate-tolerant canola only. Canola meal is not normally considered to be a human food fraction due to the presence of natural toxicants (e.g. glucosinolates), and was evaluated to compare levels of major components to determine any potential unintended effects.
- All rapeseed (e.g. canola) contains natural toxins (e.g. erucic acid and glucosinolates) which are regulated by strict canola industry standards to very low levels. Furthermore canola oil is

a highly processed food in which glucosinolates present in the seed meal are removed. Thus GM canola oil is as safe as that produced from non-GM canola.

- Although liver weights were enlarged in rats fed GM canola meal, this difference was not considered biologically meaningful in the absence of any other behavioural or physical signs and these livers appeared normal when grossly examined. Based on the data submitted, the slight increase in liver weight was possibly attributable to a slightly higher level of glucosinolates in the GM canola meal. Glucosinolate is well known to cause liver enlargement (Hayes, Principles and Methods of Toxicology, 3rd Edition). Equally, and perhaps more likely, the slight increases in liver weight were due to chance. FSANZ scientists, the New Zealand Ministry of Health and the New Zealand Institute of Environmental Science and Research, the South Australian Department of Human Services, regulators in Japan, the UK and Canada, and members of FSANZ's panel of independent experts were satisfied with this evaluation.
- FSANZ concluded that there were no human health and safety concerns in relation to the feeding studies in rats fed on canola meal.
- Canola meal, rather than canola oil, was fed to rats because it would be impossible to feed rats enough oil to test without causing other dietary imbalances. Thus no meaningful information would result from this testing. Using canola meal in feeding studies provides a test for more compounds than are present in oil and is essentially a worst case scenario. In feeding studies on other animals, no adverse effects were observed.
- The third study submitted to FSANZ included an assessment of glyphosate-tolerant canola meal, control lines from around the world and rat chow as a negative control. Duplicate samples were prepared for all lines tested to determine the variation that may arise due to processing of the canola to canola meal. There were no mortalities and no adverse clinical signs that were considered treatment related in any group. There were no significant differences in body weight, cumulative weight gain, terminal body weights or food consumption for animals fed GM canola meal compared to the non-GM control canola meal. There were also no significant differences in absolute or relative liver or kidney weights between animals fed the GM canola meal compared to the non-GM canola meal or the population of canola varieties. Glucosinolate levels were within the acceptable normal range for all groups and there was no difference in glucosinolate levels between the GM and non-GM canola meals. This third study confirms the conclusion on the safety of the GM canola reached by FSANZ for the previous two studies.

Reference:

A W Hayes *Principles and Methods of Toxicology* Third Edition

Assertion : Concern that transgenic potatoes containing Bt protein may damage mouse digestive systems. Dr Carman references a study on structural changes in the ileum of mice fed on potatoes treated with δ endotoxins and transgenic potatoes (Fares and El-Sayed, 1998). She stated the following:

They used a (different) potato genetically engineered to produce a Bt toxin approved for human consumption in some countries and also used potatoes treated with the δ endotoxin believed to have the insecticidal properties of that GE potato. Both of these potatoes caused damage to the microscopic structure of the ileum (part of the small intestine) of mice. Mice fed the δ endotoxin had hyperplasia and other changes often considered to be precursors to cancer.

FSANZ Response

- A thorough examination of the information presented in this paper does not support Dr Carman's conclusion that GM food is less safe than conventional food. This paper showed that the GM potatoes were safer for mice digestive systems than conventional potatoes treated with the Bt protein.
- Bt is the abbreviated name given to the common bacterium *Bacillus thuringiensis*. The Bt protein is a δ endotoxin that exhibits insecticidal activity against lepidopteran insects. Organic farmers have used this bacterial organism for many years as an alternative to chemical insecticides. More recently the gene for this protein has been introduced into some plants, including potatoes, to help combat insect infestations and to reduce the need for chemical insecticides. δ endotoxin has probably always been present (in trace amounts) in the human diet due to the common presence of *Bacillus thuringiensis* in soil and water and on the surfaces of plants.
- Genes coding for Bt crystal proteins have recently been introduced into GM plants to protect them from insect attack. A large number of scientific studies have shown that Bt is not toxic to humans or other vertebrate animals. Rats, mice, rhesus monkeys and humans do not contain receptors for the bacterial proteins.
- In the study by Fares and El-Sayed, three groups of mice were fed one of the following three diets regimes; 1) conventional potatoes (control group), 2) conventional potatoes which had been treated with the Bt protein, or 3) genetically modified potatoes containing the Bt gene. After two weeks, the mice were dissected and their ileums were examined for any abnormalities. Cellular structures of the intestinal villi including the enterocytes, Paneth cells and mucous cells were examined. The results of the study showed that in mice that had been fed the GM potatoes, the cellular structures of the intestine showed some minor changes which were not significantly different to the control group of mice. However, mice that had been fed Bt treated conventional potatoes had more serious structural changes to the intestinal villi, including abnormally high numbers of enterocytes, which in many cases (50%) were multinucleated with the nuclei being hypertrophied and round, rather than the usual oval shape demonstrated by the control group of mice. In addition to this, consumption of Bt treated potatoes was possibly involved in hyperplastic development in the mice ileums.
- The authors concluded that transgenic crops developed for food production contain a variety of beneficial novel genes, conferring resistance to pests, herbicides and diseases. They recommend that all new food crops should be thoroughly assessed and found to be safe for human consumption before being released into the market. Indeed this is the case in Australia and New Zealand, as in many other countries, where this evaluation is performed by FSANZ. Under the FSANZ process, a robust and thorough safety assessment is conducted prior to any GM food being allowed into the food supply.
- Interpretation of this paper as evidence that GM foods are unsafe is either selective quoting or misinterpretation of the data. A complete assessment of the information presented in this paper does not support Dr Carman's conclusion that GM food is less safe than conventional foods, nor that GM potatoes are less safe than their conventional counterparts. Rather, it shows that the GM potatoes have a similar effect on the intestine of mice as the conventional potatoes.

Reference:

Fares, N H and El-Sayed, K (1998) Fine Structural Changes in the Ileum of Mice Fed on δ Endotoxin-Treated Potatoes and Transgenic Potatoes. *Natural Toxins* 6: 219-233.

Assertion: The need for long-term feeding studies: A number of comments referred to the perceived lack of long-term toxicity studies on GM foods and the perceived need for human studies.

FSANZ Response

- It is important to recognise that it is the food product itself, rather than the process through which it is made, that should be the focus of attention in assessing safety.
- Animal studies are a major element in the safety assessment of many compounds, including pesticides, pharmaceuticals, industrial chemicals and food additives. In most cases, the test substance is well characterised, of known purity and of no nutritional value, and human exposure is generally low. It is therefore relatively straightforward to feed such compounds to animals at a range of doses (some several orders of magnitude above expected human exposure levels) in order to identify any potential adverse effects. Establishing a dose-response relationship is a pivotal step in toxicological testing. By determining the level of exposure at which no adverse effects occur, a safe level of exposure for humans can be established which includes appropriate safety factors.
- By contrast, foods are complex mixtures of compounds characterised by wide variations in composition and nutritional value. Due to their bulk, they can usually be fed to animals only at low multiples of the amounts that might be present in the human diet. Therefore, in most cases, it is not possible or appropriate to conduct dose-response experiments for foods in the same way that these experiments are conducted for chemicals. In addition, a key factor to be considered in conducting animal studies on foods is the need to maintain the nutritional value and balance of the diet. One of the primary aims when designing an animal study to test the safety of a novel food or ingredient is to achieve a concentration of the GM food or ingredient in the diet which, at the highest level used in the study, does not cause nutritional imbalance or metabolic overload. A diet that is poorly balanced will compromise the interpretation of any feeding study, since the effects observed will confound and usually override any small adverse effect which may be related to a component or components of the food. Identifying any potentially adverse effects and relating these to an individual component or characteristic of a food can, therefore, be extremely difficult. Another consideration in determining the need for animal studies is whether it is appropriate from an ethical standpoint to subject experimental animals to such a study if it is unlikely to produce meaningful information.
- In any case, the objective of the toxicological studies is not to provide the sole basis of the safety assessment with, as an outcome, the derivation of a numerically expressed acceptable daily intake. Rather, they are intended to complement the information available on the nature, composition, expected use and exposure of the GM food to arrive at a reasonable certainty that no harm will result from intended uses under the anticipated conditions of consumption.
- In some instances it may be possible to focus animal studies on discrete components which are known to represent the only significant difference between the GM food and its traditional counterpart. If there is a need to examine the safety of a newly-expressed protein in a GM food, it is more appropriate to examine the safety of this protein alone in an animal study rather than when it is part of a whole food. For newly-expressed proteins in GM foods, the acute toxicity is normally examined in experimental animals. In some cases, studies up to 14 days have also been performed. In other cases, 3 month sub-chronic studies in rodent species have been performed. These can provide additional re-assurance that the proteins will have no

adverse effects in humans when consumed as part of a food. Such experiments can provide more meaningful information than feeding studies on the whole food. Additional re-assurance regarding the safety of newly-expressed protein can be obtained by examining the digestibility of the new protein in *in vitro* assays using conditions that simulate gastric fluid and intestinal fluid.

- While the possibility of an undetected increase in a toxic component in a new food cannot be entirely eliminated, the current safeguards make this quite unlikely and no toxicologically or nutritionally significant changes of this type are evident in the transgenic plants so far marketed for food production. This issue is addressed by considering levels of known toxins and the molecular biology which indicates the potential for new proteins. A continuing evolution of toxicological methodologies and regulatory strategies will be necessary to ensure that the present levels of safety of biotechnology-derived foods is maintained in the future.

Assertion: Substantial equivalence: Concerns were expressed regarding the use of the concept of substantial equivalence as part of the assessment process.

FSANZ Response

- In the system in place in Australia and New Zealand, all GM foods are subject to safety assessment prior to entering the market place. The safety assessment aims to identify hazards over and above hazards that may be found in the conventionally produced counterpart organism.
- The comparative approach, previously referred to as substantial equivalence, embodies the concept that GM foods can be assessed to a large extent by comparison to the benchmark of commonly consumed foods already regarded as safe (the traditional or non-modified counterpart) (World Health Organisation (WHO) 2000). This can include physical characteristics and compositional factors, as well as an examination of the levels of naturally occurring allergens, toxins and anti-nutrients. This allows the safety assessment to focus on any significant differences between the genetically modified food and its conventionally produced counterpart. Genotypic differences (i.e. differences at the DNA level) are not normally considered in a determination of substantial equivalence, if that difference does not significantly change the characteristics for composition of the new food relative to the conventional food.
- The comparative approach allows for an evaluation of the important constituents of a new food in a systematic manner while recognizing that there is general acceptance that normally consumed food produced by conventional methods is regarded by the community as safe. It is important to note that, although a GM food may be found to be different in composition to the traditional food, this in itself does not necessarily mean that the food is unsafe or nutritionally inadequate.
- The comparative approach was first espoused by a 1991 Joint Consultation of the Food and Agricultural Organisation (FAO) and the WHO where it was noted that the '*comparison of a final product with one having an acceptable standard of safety provides an important element of safety assessment*' (WHO 1991). Since this time, the concept has been internationally recognised and integrated into safety assessment procedures used by regulatory authorities worldwide. It has thus been in use for over ten years and has been an integral part of the safety assessment of more than 50 products. The Organisation of Economic Cooperation and Development (OECD) advocates an approach to safety assessment based on substantial equivalence as being '*the most practical to address the safety of foods and food components derived through modern biotechnology.*'

- Although the approach has attracted criticism, it remains the most appropriate mechanism for assessing the nutritional and food safety implications of foods produced using gene technology (WHO 2000). It is generally agreed also that continual review of the concept, in response to the criticism, provides a useful stimulus to ensure that the safety assessment procedures are kept at the forefront of scientific knowledge (Joint FAO/WHO Expert Consultation on Foods Derived from Biotechnology, Geneva, 2000; Expert Panel Report on the Future of Food biotechnology, Royal Society of Canada, 2000; Report of the New Zealand Royal Commission on Genetic Modification, 2001; Genetically Modified Plants for Food Use and Human Health – An Update. The Royal Society, London, 2002; the Society for Toxicology (2001), the American College of Nutrition (2002) *The Future of Food and Nutrition With Biotechnology*; the Institute of Food Technology (2000); American College of Medicine (2000), the Codex Alimentarius Commission Ad Hoc Taskforce on Foods Derived Using Biotechnology (2003); the OECD Taskforce on Novel Foods and Feeds (2000)).
- The recent report produced by the Canadian Royal Society (2000) endorses the use of substantial equivalence when it is used in an appropriate scientifically robust manner. Although Dr Carman states that the Canadian Royal Society is critical of substantial equivalence, the report states that there are two definitions – or two ways of using the concept. They disagree with one – where substantial equivalence is used as a decision point for determining the safety of GM foods. But they **endorse substantial equivalence** when it is used in the way that FSANZ uses it, i.e when it is used as a starting point for comparison with existing food as suggested by the FAO Expert Consultations.
- The substantial equivalence paradigm focuses attention on any safety issues associated with differences between a novel food and its most appropriate comparator. Each food needs to be evaluated on an individual basis with regard to the significance of any changes in relation to its composition or to its properties. If no significant compositional differences are observed, substantial equivalence directs primary attention to the safety of the newly introduced protein. If a difference is identified in comparison with the control line (in FSANZ's assessments so far any differences have been small but statistically significant differences) it then has to be evaluated for its biological or food safety significance. Typically, this is done by comparing the data obtained for the GM food to the natural range for the particular constituent measured in conventional varieties, usually by reference to data reported in the literature. If the difference exceeds natural variation then further assessment (nutritional, toxicological) would be required. If the difference does not exceed natural variation then further assessment would usually not be required. This is the standard approach (i.e. endorsed by the recent FAO/WHO Expert Consultation) used to detect unintended changes.
- It needs to be emphasized that identification of a difference does not necessarily equate to an adverse food safety outcome. Many differences are neutral with respect to food safety and are consistent with the natural variation that occurs in all food. During the assessment of the safety of the 21 GM foods already approved in Australia and New Zealand, FSANZ scientists have noted compositional changes between GM food and the control conventional counterpart food that, although different, represent only extremely small percentage changes and are not outside the range for natural variation.

References:

Royal Society (2002. Genetically Modified Plants for Food Use and Human Health – An Update. Policy Document 4/02. The Royal Society, London.

Royal Society of Canada (2001). Report of the Expert Panel on the Future of Food Biotechnology. Royal Society of Canada, Ottawa.

FAO/WHO (2000). Safety Aspects of Genetically Modified Foods of Plant Origin. Report of a Joint FAO/WHO Expert Consultation on Foods Derived from Biotechnology.

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Organisation of Economic Cooperation and Development (2000). Report of the Task Force for the Safety of Novel Foods and Feeds.

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Institute of Food Technology (2000). Expert Report on Biotechnology and Foods. Food Technology, 54, 1-56.

Kuiper et al., (2001) . Assessment of the food safety issues related to genetically modified foods. The Plant Journal, 27(6), 503-528.

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Society of Toxicology Position Paper (2001). The Safety of Foods Produced Through Biotechnology.

Assertion: Concern that novel DNA in GM foods may not be digested and may be taken up by bacteria in the digestive system or by cells in the intestinal epithelium (either directly or via the intestinal microflora). Dr Carman quotes from a study reported in the Guardian that a relatively large proportion of genetically modified DNA survived the passage through the small bowel after a meal of a burger containing GM soy and a milkshake.

FSANZ Response:

- The study by Netherwood et al, which was reported in the Guardian on 17 July 2002 showed that up to 3.7% of a novel gene survived passage through the small bowel after a meal of GM soy products. An equal amount of endogenous soybean DNA survived also. No intact novel DNA was found in the faeces of volunteers with intact gastrointestinal tracts. Contrary to Dr Carman's interpretation of the results of this study, the authors conclude that the data presented in this study support the view that GM foods do not represent a significant risk to human health through gene transfer to either the intestinal epithelium or the microflora within the human intestine.
- The study consisted of seven ileostomists and twelve volunteers with intact gastrointestinal tracts. The 19 subjects were each given a meal consisting of a burger and a milk shake both containing GM soy products. The GM soy contained a novel gene, *epsps*, which confers tolerance to the herbicide glyphosate. To investigate whether the *epsps* gene survived passage through the small bowel, digesta was collected from the seven ileostomists every 30 minutes for 6 hours following the meal and tested for the presence of the *epsps* gene and the endogenous soya lectin gene. The data showed the amount of the *epsps* gene remaining in the digesta varied between the seven subjects but its persistence was similar to that of the endogenous soya lectin gene. This demonstrates that the *epsps* gene was degraded at a rate similar to the normal soybean DNA. To determine whether the novel gene and other soybean DNA survives passage through the complete gastrointestinal tract, faeces from the 12 volunteers with intact digestive

systems were examined for the presence of the *epsps* gene. The *epsps* gene was not detected in any of the twelve subjects, demonstrating that the DNA, although surviving passage through the small bowel, is completely degraded in the large intestine.

- The study also examined the digesta from the ileostomists and the faeces from the healthy volunteers for the presence of bacteria containing the novel gene. Microbes from the ileal digesta samples were cultured in media containing glyphosate, the herbicide to which *epsps* confers tolerance. It was found that a very small proportion of the intestinal microflora contained the *epsps* gene derived from the GM soy burger. In the subjects with intact gastrointestinal tracts, none of the endogenous bacteria in the faeces were found to contain the *epsps* gene from the GM soy. This indicates that either the *epsps* - containing bacterium in the small bowel of the ileostomists did not survive passage through the human colon or that in intact digestive systems gene transfer from plant material to the intestinal microflora does not occur at the same frequency as in the ileostomists.
- Another area of concern with the inclusion of GM foods in the human diet is that novel DNA might be transferred, via bacteria to the intestinal epithelium. The possibility of this was assessed by incubating common gut bacteria containing an antibiotic resistance gene with cultured intestinal cells *in vitro*. 10^7 intestinal cells, at various stages of differentiation were incubated with either plasmid DNA containing the antibiotic resistance gene or with 1000 fold excess of the common gut bacteria containing the same plasmid DNA. When plasmid DNA alone was used, antibiotic resistance cells were generated at a frequency of 1 in 3000. In contrast, no antibiotic resistant cells were generated when intestinal cells were incubated with bacteria containing the plasmid DNA. These data indicate that gene transfer from GM plants to the intestinal epithelium, either directly or via the intestinal microflora, is unlikely to occur.

Reference:

Netherwood, T., Martin-Orue, S. M., O'Donnell, A. G., Gockling, S., Gilbert, H.J. and Mathers, J.C. Transgenes in genetically modified Soya survive passage through the human small bowel but are completely degraded in the colon.

Assertion: In work on compositional analyses of the GE foods, often only the compositions of amino acids were given in the ANZFA reports, and not even the fatty acids (the components of fat). Moreover, when a scientific journal would normally require most of the number, mean, standard deviation, 95% confidence interval of the mean, nature of the statistical test (eg t-test) and a p-value, never more of these than the number and mean were given for any analyses, thereby preventing others from reviewing the data and doing sample size calculations.

FSANZ Response

- FSANZ maintains a public register of all the scientific data provided (other than a very small amount of data classified commercial-in-confidence) and invites two rounds of public comment to obtain the views of interested parties and carefully considers them when making a recommendation to Health Ministers. All of the technical information supplied to FSANZ including the results from field and laboratory analyses, toxicity studies, bioinformatics studies, comprehensive molecular and compositional analyses, and animal feeding studies, but excluding a small amount of commercially confidential information, is available to be publicly viewed upon request at FSANZ offices in both Canberra and New Zealand. All relevant studies are available publicly to allow the appropriate sample size calculations to be made. Normal data required by FSANZ as a

minimum includes information on the nature of the statistical tests used, the number of samples taken, the mean and standard deviation. FSANZ encourages those interested to view the data and make comments concerning the science in its two rounds of public consultation.

Assertion: That statistically significant differences in some of the nutrient levels between GM plants and non-GM plants have not been rigorously investigated in the safety assessment of some GM foods and that the differences may be due to potentially harmful novel proteins.

...statistically significant differences were still found with some foods (eg eight of the amino acids measured in corn line MON810 were significantly different to the control corn) but were then ascribed to natural variation and were not investigated further, even though such significant amino acids differences could also signal the production of potentially harmful novel proteins.

FSANZ Response:

- The composition and nutrient levels in plants are highly variable and depend on a variety of factors including weather conditions, rainfall, soil type, soil quality, growing season, location and orientation of plots. Significant differences in composition can be found between, for example, plants harvested from two different field sites planted with an identical variety of conventional (non-GM) corn.
- When assessing a GM food to determine its safety for human consumption, FSANZ reviews a substantial amount of statistical data relating to nutrients present in the GM food compared to the non-GM counterpart food, and compares these to the literature range of values for nutrients in that type of food. Often over 40 different nutrients and anti-nutrients are analysed, depending on the commodity type. Given the accepted level of variation that can occur within any particular plant line, some statistically significant differences in some nutrients are expected when comparing two closely related lines such as a GM and the non-GM control line. It is therefore normal that some variation is found between GM and non-GM plants, even when cultivated under the same field conditions.
- The goal of the safety assessment is to determine whether any of these differences are significant with respect to food safety. Where differences between lines are observed, the levels of that nutrient in the GM line are then compared to the appropriate reference standard. The reference is an established range for that nutrient or component based on a large number of measurements from many different varieties generated over time. Where the measurement of a particular component falls within the reference range, there are generally no food safety concerns.
- The FSANZ assessment also considers whether any observed difference is likely to be due to the genetic modification or to natural variation, based on the statistical pattern of data across multiple testing sites in different geographical locations. In the case of corn line MON810 where eight of the eighteen amino acids were found to be statistically different to the non-GM control corn line, all of the observed differences were within the range of natural variation found in conventional corn (FSANZ 2000). In addition, there was no pattern of change but rather a random distribution of differences between the lines. Thus, it was appropriate to conclude that the nutritional value of corn line MON810 was similar to conventional corn lines.

- It is also important to note that the overall amino acid composition would not be likely to indicate the presence of a potentially harmful novel protein. All proteins of biological origin are composed of the same suite of amino acids and, unless a new protein was in great abundance and had a distinctive amino acid composition, this would not be reflected in the amino acid analysis, but would be likely to be detected in other analytical methods.
- In addition to the nutrient analysis of every GM food and the analysis of the potential for novel proteins to be toxic or allergenic, feeding studies with animals including chickens, pigs, and cows have determined that food derived from corn line MON810 is as nutritious and wholesome as food from other commercially available corn lines (Mireles, et al 2000; Weber et al, 2000; Hendrix et al, 2000; Russell et al, 2000a&b; Faust & Spangler, 2000).
- The observed differences in amino acid levels (and in other nutrient levels) are explained by natural variation between plants and, although they may be statistically significant, the small percentage differences are not of biological or nutritional significance and are therefore not of concern with respect to food safety.

References:

Faust MA and SM Spangler. 2000. Nutritive value of silage from MON810 Bt and non-Bt near isogenic corn hybrids. Abstract 301 presented at the Midwestern Section ASAS and Midwest Branch ADSA 2000 Meeting, Des Moines, IA.

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