FOOD STANDARDS
Australia New Zealand
Te Mana Kounga Kai – Ahitereiria me Aotearoa

7 May 2010
[11-10]

APPLICATION A1021
FOOD DERIVED FROM HERBICIDE-TOLERANT MAIZE LINE DP-098140-6
APPROVAL REPORT

Executive Summary

Purpose

Food Standards Australia New Zealand (FSANZ) received an Application from Pioneer Hi-Bred International, Inc. (Pioneer), a DuPont Company, on 20 January 2009. The Applicant requested a variation to Standard 1.5.2 – Food produced using Gene Technology, in the *Australia New Zealand Food Standards Code* (the Code), to permit the sale and use of food derived from a new genetically modified (GM) variety of maize[1], herbicide-tolerant maize line DP-098140-6.

The Application was assessed under the General Procedure.

Safety Assessment

Maize line DP-098140-6 has been genetically modified for tolerance to the broad-spectrum herbicide glyphosate and to acetolactate synthase (ALS)-inhibiting herbicides. Tolerance is conferred by expression in the plant of two novel proteins: GAT4621 and ZM-HRA. The GAT4621 protein confers tolerance to glyphosate-containing herbicides by acetylating glyphosate and thereby rendering it non-phytotoxic. The ZM-HRA protein is a modified maize ALS enzyme that is able to function in the presence of the ALS-inhibiting class of herbicides, thereby conferring tolerance to those herbicides.

FSANZ has completed a comprehensive safety assessment of food derived from maize line DP-098140-6 (see **Supporting Documents 1[2] and 2[3]**). This assessment included consideration of (i) the genetic modification to the plant; (ii) the potential toxicity and allergenicity of the novel proteins; (iii) the composition of maize DP-098140-6 compared with that of conventional maize varieties; and (iv) the potential toxicity of two novel herbicide residues, *N*-acetyl glyphosate (NAG) and *N*-acetyl aminomethylphosphonic acid (*N*-acetyl AMPA).

[1] Also known as corn
[2] SD1 Safety Assessment for A1021
[3] SD2 Assessment of Glyphosate Residues for A1021

No public health and safety concerns have been identified in this pre-market safety assessment of food derived from maize DP-098140-6, including with regard to NAG and *N*-acetyl AMPA, which are less toxic than glyphosate itself.

On the basis of the available evidence, including detailed studies provided by the Applicant, food derived from herbicide tolerant maize line DP-098140-6 is considered as safe and wholesome as food derived from other commercial maize varieties.

Labelling

Labelling addresses the objective set out in paragraph 18(1)(b) of the *Food Standards Australia New Zealand Act 1991* (FSANZ Act); that is, the provision of adequate information relating to food to enable consumers to make informed choices. The general labelling requirements will provide consumers with information about the GM status of foods.

In accordance with general labelling provisions, food derived from herbicide-tolerant maize line DP-098140-6, if approved, would be required to be labelled as genetically modified if novel DNA and/or novel protein is present in the final food. Studies conducted by the Applicant show that novel proteins are present in the grain.

In addition to this, maize DP-098140-6 has elevated levels of several acetylated amino acids. Standard 1.5.2 states that there could be additional labelling requirements for GM food where *the genetic modification has resulted in one or more significant composition or nutritional parameters having values outside the normal range of values for existing counterpart food not produced using gene technology*. FSANZ has examined this issue and is not recommending any additional labelling requirements for foods derived from maize DP-098140-6 as the elevated components are not considered *significant composition or nutritional parameters* based on their demonstrated safety, low levels, lack of nutritional impact, and presence in other commonly consumed foods.

Impact of regulatory options

Following completion of the safety assessment, two regulatory options were considered: (1) rejection of the Application; or (2) approval of food derived from maize DP-098140-6.

Following analysis of the potential costs and benefits of each option on affected parties (consumers, the food industry and government), option 2, approval of this Application is the preferred option. Under option 2, the potential benefits to all sectors outweigh the costs associated with the approval.

Assessing the Application

In assessing the Application and the subsequent development of a food regulatory measure, FSANZ has had regard to the following matters as prescribed in section 29 of the *Food Standards Australia New Zealand Act 1991* (FSANZ Act):

- whether costs that would arise from a food regulatory measure, developed or varied as a result of the Application, outweigh the direct and indirect benefits to the community, Government or industry that would arise from the development or variation of the food regulatory measure

- whether there are other measures that would be more cost-effective than a variation to Standard 1.5.2 that could achieve the same end

- any relevant New Zealand standards including those for residue limits (see Section 6.1)

- any other relevant matters.

Decision

To approve the draft variation to Standard 1.5.2 – Food produced using Gene Technology, to include food derived from herbicide-tolerant maize line DP-098140-6 in the Table to clause 2.

Reasons for Decision

The development of a variation to the Code to give approval to the sale and use of food derived from herbicide-tolerant maize line DP-098140-6 in Australia and New Zealand is proposed on the basis of the available scientific evidence, for the following reasons:

- the safety assessment did not identify any public health and safety concerns associated with the genetic modification used to produce herbicide-tolerant maize line DP-098140-6

- the novel herbicide residues generated on maize DP-098140-6 plants following glyphosate application are less toxic than glyphosate and pose no food safety concern

- labelling of foods derived from maize line DP-098140-6 will be required if novel DNA and/or protein is present in the final food

- a regulation impact assessment process has been undertaken that fulfils the requirement in Australia and New Zealand for an assessment of compliance costs. The assessment concluded that the preferred option is Option 2, a variation to the Code

- there are no other measures that would be more cost-effective than a variation to Standard 1.5.2 that could achieve the same end.

Consultation

Public submissions were invited on the Assessment Report between 16 December 2009 and 10 February 2010. Comments were specifically requested on the scientific aspects of this Application, in particular, information relevant to the safety assessment of food derived from herbicide-tolerant maize line DP-098140-6. A total of 13 submissions were received. A summary of these is provided in **Attachment 2** to this Report.

As this Application was assessed as a General Procedure, there was one round of public comment following the preparation of an Assessment Report. Responses to the Assessment Report were used to develop this Approval Report for the Application. The main issues raised in public comments are discussed in the Approval Report.

CONTENTS

SUPPORTING DOCUMENTS

The following material which was used in the preparation of this Approval Report is available on the FSANZ website at http://www.foodstandards.gov.au/standardsdevelopment/applications/applicationa1021food4210.cfm:

SD1: Safety Assessment Report: Application A1021 – Food Derived from Herbicide-Tolerant Maize Line DP-098140-6

SD2: Assessment of Glyphosate Residues for A1021

INTRODUCTION

On 20 January 2009, Pioneer Hi-Bred International, Inc. (Pioneer), a DuPont Company, submitted an Application seeking approval for food derived from herbicide-tolerant maize line DP-098140-6 (also referred to as maize 98140) under Standard 1.5.2 – Food produced using Gene Technology, in the *Australia New Zealand Food Standards Code* (the Code).

Maize 98140 has been genetically modified for tolerance to the broad-spectrum herbicide glyphosate and to acetolactate synthase (ALS)-inhibiting herbicides. Protection is conferred by expression in the plant of two novel proteins: GAT4621 (glyphosate acetyltransferase) and ZM-HRA (modified version of a maize ALS). The GAT4621 protein, encoded by the *gat4621* gene, confers tolerance to glyphosate-containing herbicides by acetylating glyphosate and thereby rendering it non-phytotoxic. The ZM-HRA protein, encoded by the *zm-hra* gene, is able to function in the presence of the ALS-inhibiting class of herbicides, thereby conferring tolerance to those herbicides.

The dual herbicide tolerance traits of maize DP-098140-6 are intended to enable growers to choose an optimal combination of the herbicides to manage weed populations. The first glyphosate-tolerant maize line was made available to North American farmers in 1998. Extending tolerance to ALS-inhibiting herbicides is intended to provide growers with an additional management tool for weeds that are difficult to control with glyphosate alone.

FSANZ completed a full scientific evaluation of food derived from maize 98140 according to FSANZ guidelines[4] to assess its safety for human consumption. The Assessment Report was released in December 2009 and public comment was sought on the safety assessment and proposed recommendations. Comments received were considered in completion of this Approval Report.

1. The Issue

The Applicant has developed GM maize line DP-098140-6 that is tolerant to the broad-spectrum herbicide glyphosate and to ALS-inhibiting herbicides. Pre-market approval is necessary before this product may enter the Australian and New Zealand food supply. An amendment to the Code granting approval to food derived from maize 98140 must be approved by the FSANZ Board, and subsequently notified to the Australia and New Zealand Food Regulation Ministerial Council (Ministerial Council). An amendment to the Code may only be gazetted once the Ministerial Council process has been finalised.

Maize line DP-098140-6 was originally intended to be grown for production in North America. Because of commercial reasons, the Applicant has advised that production in North America will not proceed however production in other regions is still a possibility. Before release onto commercial agricultural markets, the Applicant is seeking regulatory approval for maize DP-098140-6 in key trading markets for maize, including Australia and New Zealand. This is necessary because once it is cultivated on a commercial-scale, maize products imported into Australia and New Zealand could contain ingredients derived from maize 98140 as a result of comingling practices at harvest or later processing stages. The Applicant has therefore sought the necessary amendments to Standard 1.5.2 to include food derived from maize line DP-098140-6 prior to any decision to commercialise this line.

The Application was assessed under the General Procedure.

[4] FSANZ (2007). Safety Assessment of Genetically Modified Foods – Guidance Document. http://www.foodstandards.gov.au/_srcfiles/GM%20FINAL%20Sept%2007L%20_2_.pdf

2. Current Standard

2.1 Background

Approval of GM foods under Standard 1.5.2 is contingent upon completion of a comprehensive pre-market safety assessment. Foods that have been assessed under the Standard, if approved, are listed in the Table to clause 2 of the Standard.

2.2 Overseas approvals

Submissions on maize line DP-098140-6 have been made to the appropriate agencies for food, feed and environmental approvals in the United States (Food and Drug Administration, Department of Agriculture) and Canada (Health Canada and the Canadian Food Inspection Agency). The Canadian Food Inspection Agency approved maize 98140 for growing and for animal feed in August 2009. Health Canada approved food from maize 98140 in September 2009. The United States Food and Drug Administration (USFDA) completed its regulatory review in September 2008[5]. Regulatory submissions for food import approvals have also been made in the European Union[6]. The Applicant has advised that further submissions for import approvals in key international markets will also be made.

In December 2009, the US Environmental Protection Agency (US EPA) amended the tolerance (i.e. maximum residue limits) for herbicide residues on maize 98140 treated with glyphosate to include the novel metabolite *N*-acetyl glyphosate.

3. Objectives

In developing or varying a food standard, FSANZ is required by its legislation to meet three primary objectives which are set out in section 18 of the FSANZ Act. These are:

- the protection of public health and safety; and
- the provision of adequate information relating to food to enable consumers to make informed choices; and
- the prevention of misleading or deceptive conduct.

In developing and varying standards, FSANZ must also have regard to:

- the need for standards to be based on risk analysis using the best available scientific evidence;
- the promotion of consistency between domestic and international food standards;
- the desirability of an efficient and internationally competitive food industry;

[5] FDA (2008) *Biotechnology Consultation Note to the File BNF No. 000111*. Center for Food Safety and Applied Nutrition, U.S. Food and Drug Administration. http://www.fda.gov/Food/Biotechnology/Submissions/ucm155603.htm.

[6] Pioneer Hi-Bred International Inc. (2007) Summary of the Application for Authorisation of Genetically Modified 98140 Maize and Derived Food and Feed in Accordance with Regulation (EC) 1829/2003 http://www.gmo-compass.org/pdf/regulation/maize/98140_mais_application_foodfeed.pdf

- the promotion of fair trading in food;

- any written policy guidelines formulated by the Ministerial Council.

4. Assessment Questions

In completing the assessment of this application, a number of questions have been addressed:

Based on information provided by the Applicant on the nature of the genetic modification, the molecular characterisation, the characterisation of the novel proteins, the compositional analysis and consideration of any nutritional issues, is food derived from maize line DP-098140-6 comparable to food derived from conventional varieties of maize in terms of its safety for human consumption?

As novel herbicide residues are generated on maize DP-098140-6 plants following glyphosate application, how does the safety of these metabolites compare to that of glyphosate?

Is other information available, including from the scientific literature, general technical information, independent scientists, other regulatory agencies and international bodies, and the general community, that should be taken into account in this assessment?

Are there any other considerations that would influence the outcome of this assessment?

RISK ASSESSMENT

Food derived from herbicide-tolerant maize line DP-098140-6 has been evaluated according to the safety assessment guidelines prepared by FSANZ and is provided in **Supporting Documents 1 and 2**. The summary and conclusions from the safety assessment and the assessment of glyphosate residue levels are presented below.

In addition to information supplied by the Applicant, other available resource material including published scientific literature and general technical information was used in this assessment.

5. Risk Assessment Summary

5.1 Safety Assessment Process

In conducting a safety assessment of food derived from maize line DP-098140-6, a number of criteria have been addressed including: a characterisation of the transferred genes, their origin, function and stability in the maize genome; the changes at the level of DNA, protein and in the whole food; detailed compositional analyses; evaluation of intended and unintended changes; and the potential for the newly expressed proteins to be either allergenic or toxic in humans.

The safety evaluation of maize 98140 has included an assessment of the levels of two novel herbicide residues, namely *N*-acetyl glyphosate (NAG) and *N*-acetyl aminomethylphosphonic acid (*N*-acetyl AMPA), generated on these plants following glyphosate application.

A safety assessment of NAG and *N*-acetyl AMPA was previously conducted as part of the assessment of Application A1006 – Food derived from Herbicide-tolerant Soybean line DP-356043-5[7].

[7] Application A1006 – Food derived from Herbicide-tolerant Soybean Line DP-3560435
http://www.foodstandards.gov.au/foodstandards/applications/applicationa1006food3900.cfm

The safety assessment applied to food from maize line DP-098140-6 addresses only food safety and nutritional issues. It does not address any risks related to the release into the environment of GM plants used in food production, the safety of animal feed or animals fed with feed derived from GM plants, or the safety of food derived from the non-GM (conventional) plant.

5.2 Outcomes of the Safety Assessment

Maize 98140 contains two novel genes, *gat4621* and *zm-hra*. Detailed molecular analyses indicate that one copy of each novel gene has been inserted at a single site in the plant genome and the genes are stably inherited from one generation to the next. No antibiotic resistance marker genes are present in maize 98140.

Maize 98140 expresses two novel proteins: GAT4621 and ZM-HRA. The GAT4621 sequence is based on the GAT enzyme sequences from three strains of the bacterium *Bacillus licheniformis* that were optimised for enhanced glyphosate acetylation activity. The amino acid sequence of GAT4621 is 75-78% identical to each of the three native GAT enzymes from which it was derived. GAT4621 is 147 amino acids in length and has an approximate molecular weight of 17 kDa. The GAT4621 protein is expressed at low levels in maize 98140 grain, with a mean concentration of 7.7 ng/mg of tissue (dry weight).

The ZM-HRA protein is a modified version of the native ALS (acetolactate synthase) from maize. The ZM-HRA protein is characterised by two specific amino acid changes in the mature ALS protein that are known to confer tolerance to sulfonylurea herbicides. The ZM-HRA protein is 638 amino acids in length with a predicted molecular weight of 69 kDa. Following transport into the chloroplast and cleavage of the transit peptide, the mature protein is 598 amino acids with a predicted molecular weight of 65 kDa. The ZM-HRA protein is expressed at low levels in maize 98140 grain, with a mean concentration of 0.34 ng/mg of tissue (dry weight).

Both proteins conform in size and amino acid sequence to that expected, do not exhibit glycosylation, and demonstrate the expected enzymatic activity.

Bioinformatic studies with the GAT4621 and ZM-HRA proteins confirmed the absence of any biologically significant amino acid sequence similarity to known protein toxins or allergens. Digestibility studies demonstrated that both proteins would be rapidly degraded following ingestion, similar to other dietary proteins. Acute oral toxicity studies in mice with both proteins also confirmed the absence of toxicity. Taken together, the evidence indicates that neither protein is toxic nor likely to be allergenic in humans.

Compositional analyses were conducted to establish the nutritional adequacy of maize 98140, and to compare it to a non-transgenic conventional maize under typical cultivation conditions. For the majority of components, there are no compositional differences of biological significance in forage or grain from transgenic maize 98140, compared to the non-GM control.

In an *in vitro* study, the GAT4621 enzyme was shown to acetylate several amino acids.

Consequently, in maize 98140, the levels of *N*-acetylglutamate (NAGlu), *N*-acetylaspartate (NAAsp), *N*-acetylthreonine (NAThr), *N*-acetylserine (NASer), and *N*-acetylglycine (NAGly) are elevated compared with conventional maize. NAAsp levels are increased by around 450-fold and NAGlu around 160-fold. Increases in NAThr, NAGly and NASer are smaller at around 17-fold, 3-fold and 2-fold, respectively. These five acetylated amino acids account for only 0.5% of the total amino acid content in maize 98140 grain.

Both NAGlu and NAAsp were found to be present in a number of common foods, indicating that they are normal components of human diets. NAThr, NASer and NAGly are also present in conventional maize so these compounds are also considered not to be novel. Acetylated amino acids are readily metabolised in humans and raise no safety or nutritional concerns.

Based on these conclusions, the introduction of herbicide-tolerant maize 98140 into the food supply would not be expected to have any nutritional impact. This was supported by the results of a feeding study, where no differences in health and growth performance were found between broiler chickens fed diets containing either maize 98140 meal or those fed conventional maize meal diets. Similarly, a 90 day toxicity study concluded that there were no diet related adverse effects in rats fed a diet containing maize 98140.

Two novel residues are generated on maize 98140 plants following glyphosate application, namely NAG and *N*-acetyl AMPA. While NAG is the predominant residue detected on commodities derived from maize 98140 plants that have been treated with glyphosate, parent glyphosate, *N*-acetyl AMPA and aminomethylphosphonic acid (AMPA) are also detectable. FSANZ has recently conducted an assessment to establish the safety of these novel compounds, and to consider whether the current requirements for glyphosate from a safety perspective are appropriate. Using a weight-of-evidence approach, NAG and *N*-acetyl AMPA were concluded to be less toxic than glyphosate, which itself has low toxicity potential. On this basis, the establishment of a new acceptable daily intake (ADI) for glyphosate and its residues, or a separate ADI for NAG and *N*-acetyl AMPA was considered unnecessary.

5.3 Conclusions

No potential public health and safety concerns have been identified in the assessment of herbicide tolerant maize line DP-098140-6. On the basis of the data provided in the present Application, and other available information, food derived from maize line DP-098140-6 is considered as safe and wholesome as food derived from conventional maize varieties.

The metabolite residues generated by glyphosate-treated maize 98140 plants are considered less toxic than glyphosate, which itself is considered to be of very low potential toxicity in animals. Hence, there is no increase in overall toxicity arising from the presence of glyphosate residues on maize 98140, and the current ADI for glyphosate is considered to be protective of public health and safety.

RISK MANAGEMENT

6. Issues raised

6.1 Impact on Other Standards

As part of its pre-market safety assessment of food derived from herbicide-tolerant GM crops, FSANZ has regard to the generation of new residues or increased concentrations of known residues on the crop, following application of the herbicide.

The potential toxicity of any new residues that have not previously been assessed is relevant to food safety and could also have implications for the existing glyphosate Maximum Residue Limits (MRLs)[8].

[8] The MRL is the maximum concentration of a residue, resulting from the registered use of an agricultural or veterinary chemical legally permitted or recognised as acceptable in or on a food, agricultural commodity, or animal feed.

The purpose of these MRLs is to ensure the legitimate and safe use of agricultural chemicals on commodities grown in, or imported into, Australia or New Zealand.

In Australia, the MRLs for agricultural and veterinary chemical residues present in food are listed in Standard 1.4.2, an Australia only Standard. There is a glyphosate MRL of 0.1 mg/kg for cereal grains in Standard 1.4.2 of the Code and the applicant has provided information to indicate that this MRL is appropriate for maize 98140 (see **Supporting Document 2**[9]). The current MRL Standard of the Australian Pesticides and Veterinary Medicines Authority (APVMA) also contains an MRL of 0.1 mg/kg for cereal grains. For both the FSANZ and APVMA MRL standards, the residue definition for glyphosate is the sum of glyphosate and AMPA metabolite, expressed as glyphosate.

In New Zealand, MRLs are established by the Agricultural Compounds and Veterinary Medicines Group (ACVMG) within the NZ Food Safety Authority (NZFSA). There is no MRL for glyphosate on maize currently listed in the New Zealand MRL Standard[10], however, there is a provision for residues of up to 0.1 mg/kg for agricultural compound/food combinations not specifically listed. In addition, the New Zealand MRL Standard recognises Codex standards for imported food. The Codex MRL for glyphosate in maize is 5 mg/kg (the Codex and New Zealand residue definition only includes parent glyphosate).

A safety assessment of residues of glyphosate and its metabolites NAG, AMPA and *N*-acetyl AMPA was previously conducted as part of the Assessment of Application A1006 – Food derived from herbicide-tolerant Soybean line DP-356043-5. The same residues are produced in/on maize 98140 and the levels of these residues are provided in **Supporting Document 2**[10]. It is concluded that glyphosate is the only toxicologically-significant compound of the four residues considered as part of the current assessment. On this basis, the current residue definition for glyphosate in Standard 1.4.2, the sum of glyphosate and AMPA expressed as glyphosate, remains appropriate from a safety perspective.

FSANZ also acknowledges that there is a need to consider the existing MRLs and residue definition for glyphosate from a compliance perspective.

In the case of maize 98140, the United States Environmental Protection Agency (US EPA) has recently amended the existing tolerances[11] for glyphosate residues to include the combined residues of the herbicide glyphosate and its metabolite *N*-acetyl-glyphosate[12].

While noting the US EPA decision, FSANZ considers that the costs of amending the existing residue definition for glyphosate solely in relation to maize 98140 outweigh the benefits of pursuing such an amendment to Standard 1.4.2. There is no approval or any application under consideration to grow maize 98140 plants in Australia or New Zealand. Therefore, food commodities derived from maize 98140 will only be present in foods in Australia or New Zealand if they are imported as food or food ingredients. In addition, the presence of NAG and *N*-acetyl AMPA raises no safety concerns. On this basis, FSANZ proposes that the existing glyphosate residue definition for cereal grains should apply, that is, the sum of glyphosate and AMPA metabolite, expressed as glyphosate.

Also, as stated above, the Applicant has indicated that maize 98140 is no longer planned for commercial growing in North America but that commercial production in other locations is a possibility.

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[9] SD2 Assessment of Glyphosate Residues for A1021.
[10] http://www.nzfsa.govt.nz/policy-law/legislation/food-standards/bn-08-213-nz-mrl-fs-2009-consolidation.pdf
[11] The term 'tolerances' is used in the United States and is equivalent to the term Maximum Residue Limit in Australia.
[12] http://edocket.access.gpo.gov/2009/E9-30053.htm

Maize line DP-098140-6 also carries a second genetic modification conferring tolerance to ALS-inhibiting herbicides. Soybean line DP-356043-5 is the only other GM line that FSANZ has previously assessed that is tolerant to ALS-inhibiting herbicides (Application A1006). If approved, maize line DP-098140-6 would need to comply with the existing MRLs in the Code.

6.2 Risk Management Strategy

If approved, food derived from herbicide-tolerant maize line DP-098140-6 will be required to be labelled as genetically modified if novel DNA and/or novel protein is present in the final food. Studies conducted by the Applicant show that novel proteins are present in the grain. Highly refined products, such as maize oil, are exempt from this general labelling requirement if they do not contain novel protein or DNA.

Standard 1.5.2 also contains provision for additional labelling requirements in cases where *the genetic modification has resulted in one or more significant composition or nutritional parameters having values outside the normal range of values for existing counterpart food not produced using gene technology.* In developing the GM food labelling standard, it was recognised that there may be instances where additional labelling would be appropriate, for example where a property or characteristic of the food means that it is no longer equivalent to an existing counterpart food (Proposal P97).

As discussed in Section 5.2, the levels of five acetylated amino acids are increased in maize 98140. These five acetylated amino acids account for only 0.5% of the total amino acid content in maize 98140 grain. Although elevated compared to the conventional counterpart, these constituents remain minor components of maize 98140. Acetylated amino acids are normal constituents of commonly eaten foods and are readily metabolised. In this case, these components are not considered to be *significant composition or nutritional parameters* for the purposes of labelling GM foods.

Labelling is intended to address the objective set out in paragraph 18(1)(b) of the FSANZ Act; the provision of adequate information relating to food to enable consumers to make informed choices.
Labelling for changes in the levels of acetylated amino acids would be unlikely to provide consumers with useful information, particularly as the changes are of no safety or nutritional consequence and do not change the nature of the food. In this context, additional labelling is likely to be confusing and potentially misleading to consumers. The general labelling provisions of the Standard would provide consumer information on the GM status of the food.

The costs to the agricultural and food industry sectors of applying additional labelling requirements in the absence of a clear consumer benefit were also considered. Maize 98140 has been approved for cultivation and as food in the United States. The USFDA has not imposed a requirement for labelling of maize 98140 and maize 98140 will be treated as for other GM maize varieties. In order to comply with any additional labelling requirements in Australia and New Zealand, maize 98140 would need to be segregated from other maize, including other GM maize, varieties. This would involve considerable additional costs associated with food production, which could be passed on to consumers.

7. Options

There are no non-regulatory options for this Application. The two regulatory options available for this Application are:

7.1 Option 1 – Reject the Application

Reject the Application, thus maintaining the *status quo*.

7.2 Option 2 – Develop a food regulatory measure

Proceed to development of a food regulatory measure to vary Standard 1.5.2 to permit the sale and use of food derived from herbicide-tolerant maize line DP-098140-6, with or without specified conditions in the Table to clause 2 of the Standard.

8. Impact Analysis

In the course of developing food regulatory measures suitable for adoption in Australia and New Zealand, FSANZ is required to consider the impact of all options on all sectors of the community, including consumers, the food industry and governments in both countries. The regulatory impact assessment identifies and evaluates, though is not limited to, the costs and benefits of the regulation, and its health, economic and social impacts.

8.1 Affected Parties

The affected parties may include the following:

- Consumers of maize-containing food products, particularly those concerned about the use of biotechnology to generate new crop varieties.

- Industry sectors:

  - food importers and distributors of wholesale ingredients
  - processors and manufacturers of maize-containing food products
  - food retailers.

- Government:

  - enforcement agencies
  - National governments, in terms of trade and World Trade Organization (WTO) obligations.

Maize line DP-098140-6 has been developed primarily for agricultural production overseas and, at this stage, the Applicant has no plans for cultivation of this variety in either Australia or New Zealand. The cultivation of maize 98140 in Australia or New Zealand could have an impact on the environment, which would need to be independently assessed by the Office of the Gene Technology Regulator (OGTR) in Australia, and by various New Zealand government agencies including the Environmental Risk Management Authority (ERMA) and the Ministry of Agriculture and Forestry (MAF) before commercial release in either country could be permitted.

8.2 Benefit Cost Analysis

8.2.1 Option 1 – Reject the Application

Consumers: Possible restriction in the availability of imported maize products to those products that do not contain maize line DP-098140-6.

No impact on consumers wishing to avoid GM foods, as food from maize line DP-098140-6 is not currently permitted in the food supply.

Potential increase in price of imported maize foods due to requirement for segregation of maize line DP-098140-6.

Government: Potential impact if considered inconsistent with WTO obligations but impact would be in terms of trade policy rather than in government revenue.

Industry: Possible restriction on imports of maize food products once maize line DP-098140-6 is commercialised overseas.

Potential longer-term impact - any successful WTO challenge has the potential to impact adversely on food industry.

8.2.2 Option 2 – Develop a draft regulatory measure

Consumers: Broader availability of imported maize products as there would be no restriction on imported foods containing maize line DP-098140-6.

Potentially, no increase in the prices of imported foods manufactured using comingled maize products.

Appropriate labelling would allow consumers wishing to avoid GM maize products to do so.

Government: Benefit that if maize line DP-098140-6 was detected in maize imports, approval would ensure compliance of those products with the Code. This would ensure no potential for trade disruption on regulatory grounds.

Approval of maize line DP-098140-6 would ensure no conflict with WTO responsibilities.

This option could impact on monitoring resources, as certain foods derived from maize line DP-098140-6 will be required to be labelled as genetically modified and there are likely to be increased costs associated with the additional monitoring required to ensure compliance with the labelling provisions of the Code.

Industry: Importers of processed foods containing maize derivatives would benefit as foods derived from maize line DP-098140-6 would be compliant with the Code, allowing broader market access and increased choice in raw materials.

Retailers may be able to offer a broader range of maize products or imported foods manufactured using maize derivatives.

Possible cost to food industry as some food ingredients derived from maize line DP-098140-6 would be required to be labelled as genetically modified.

8.3 Comparison of Options

As food from herbicide-tolerant maize line DP-098140-6 has been found to be as safe as food from conventional varieties of maize, Option 1 is likely to be inconsistent with Australia's and New Zealand's WTO obligations.

Option 1 would also offer little benefit to consumers, as approval of maize line DP-098140-6 by other countries could limit the availability of imported maize products in the Australian and New Zealand markets. In addition, Option 1 would result in the requirement for segregation of any products containing maize 98140 from those containing approved maize varieties, which would be likely to increase the costs of imported maize foods.

As the novel herbicide residues generated on maize 98140 plants following glyphosate application are less toxic than glyphosate itself, glyphosate is considered the only toxicologically-significant residue associated with maize 98140 plants. Detection and measurement of glyphosate residues on material derived from maize 98140 plants is adequate from a safety perspective.

Based on the conclusions of the safety assessments, the potential benefits of Option 2 outweigh the potential costs. A variation to Standard 1.5.2 giving approval to herbicide-tolerant maize line DP-098140-6 is therefore the preferred option.

COMMUNICATION AND CONSULTATION STRATEGY

9. Communication

FSANZ applied a communication strategy to this Application that involved advertising the availability of the assessment report for public comment in the national press and placing the report on the FSANZ website. This Approval Report will also be available to the public on the FSANZ website.

This Approval Report and the decision of the FSANZ Board to approve the variation to Standard 1.5.2 will be notified to the Ministerial Council. If the approval of food derived from maize line DP-098140-6 is not subject to a request by the Ministerial Council for the FSANZ Board to review its decision, the Applicant and stakeholders, including the public, would be notified of the gazettal of the variation to the Code in the national press and on the website.

10. Consultation

10.1 Public Consultation

The Assessment Report was advertised for public comment between 16 December 2009 and 10 February 2010. Comments were specifically requested on the scientific aspects of this Application, in particular, information relevant to the safety assessment of food derived from herbicide-tolerant maize line DP-098140-6. As this Application was assessed under a General Procedure, there was one round of public comment.

A total of 13 submissions were received. A summary of these is provided in **Attachment 2** to this Report. FSANZ has taken the submitters' comments relevant to food safety into account in preparing the Approval Report for this Application. The Office of the Gene Technology Regulator in Australia and the Ministry of Agriculture and Forestry in New Zealand are the agencies responsible for any issues of public concern regarding the growing of GM crops and the environment.

Responses to general issues raised, such as the safety of GM food, GM food labelling, the nature and source of data used to inform the Safety Assessment, are available from the FSANZ website (see Table 1). In relation to the data required for an assessment, it should be noted that the data submitted by an Applicant and the conduct of the studies are subject to strict requirements outlined in the *Application Handbook*[13].

[13] http://www.foodstandards.gov.au/foodstandards/changingthecode/applicationshandbook.cfm

In turn, these requirements are guided by concepts and principles developed through the work of the OECD, FAO, WHO and the Codex Alimentarius Commission in relation to the assessment of GM foods.

Table 1: Sources of information, available on the FSANZ website, regarding GM Food

Issue	General area of FSANZ website where information can be found	Specific web link
Safety of GM food	Safety Assessment of Genetically Modified Foods	http://www.foodstandards.gov.au/_srcfiles/GM%20Foods_text_pp_final.pdf
	Frequently Asked Questions on GM foods	http://www.foodstandards.gov.au/foodmatters/gmfoods/frequentlyaskedquest3862.cfm
Labelling of GM food	Appendix 3: Safety Assessment of Genetically Modified Foods	http://www.foodstandards.gov.au/_srcfiles/GM%20Foods_text_pp_final.pdf
	Frequently Asked Questions on GM foods Part III. Labelling of GM Foods	http://www.foodstandards.gov.au/foodmatters/gmfoods/frequentlyaskedquest3862.cfm
	GM Labelling Review Report	http://www.foodstandards.gov.au/newsroom/publications/gmlabellingreviewrep2460.cfm
Long term feeding studies	Section 7.6: Safety Assessment of Genetically Modified Foods	http://www.foodstandards.gov.au/_srcfiles/GM%20Foods_text_pp_final.pdf
	Role of animal feeding studies in the safety assessment of genetically modified foods	http://www.foodstandards.gov.au/consumerinformation/gmfoods/roleofanimalfeedings3717.cfm
Data used to inform the Safety Assessment	Food Matters • GM Foods	http://www.foodstandards.gov.au/foodmatters/gmfoods/

In relation to the data required for an assessment, it should be noted that the data submitted and the conduct of the studies are subject to strict requirements outlined in the *Application Handbook.*

The main issues raised in submissions are discussed below.

10.1.1 Safety of GM food

One private submitter suggests that food derived from maize 98140 or any genetically modified organism (GMO) may accelerate the ageing process in cells or have a degenerative effect on neural function. Several submitters raise the issue of the safety of GM foods in general and as evidence allude to research carried out on other GM crops, e.g. a paper by Spiroux de Vendômois et al. (2009)[14] regarding GM corn lines NK603, MON810 and MON863.

10.1.1.1 Response

There is no evidence in the scientific literature to suggest that consumption of food derived from any GMO, including GM maize, has been implicated in cell ageing or loss of cognitive function.

[14] Spiroux de Vendômois J, Roullier F, Cellier D and Séralini G-E, A Comparison of the Effects of Three GM Corn Varieties on Mammalian Health. *Int J Biol Sci.* 5:706-726.

FSANZ has assessed the Spiroux de Vendômois et al. paper[15] and concluded that the authors have misrepresented the toxicological significance of their results by placing undue emphasis on the statistical treatment of data, and failing to take other relevant factors into account. Despite claims to the contrary, no new evidence of adverse effects has been put forward by this research. A 2010 report by the GMO Panel of the European Food safety Authority[16] has similarly concluded that the authors' claims about toxicity are not supported by the data.

It should also be noted that it is not appropriate to draw conclusions on the safety of food from a specific GM maize based on data obtained from another GM maize with differing genetic modifications. The safety of a GM food should be assessed on a case-by-case basis using specific evidence from a variety of experimental approaches.

10.1.2 Future findings that may influence an approval decision

Two private submitters and the Hon. Lynn MacLaren MLC are concerned about further GM approvals being made until the findings of the Review of Food Labelling Law and Policy are released, and the findings of research conducted by Dr Judy Carman become publicly available.

10.1.2.1 Response

The labelling Review committee is expected to provide its final report to the Ministerial Council in December 2010 and to COAG in early 2011.[17]

The previous West Australian Government commissioned Dr Judy Carman to undertake some animal feeding studies on GM foods.
While there has been some publicity surrounding possible work being undertaken by Dr Carman, there is as yet no evidence that this work has been progressed, and it is the understanding of FSANZ that any findings have not yet been published.

FSANZ has a statutory obligation to consider all applications seeking to amend the Code. Further, there is a statutory timeframe associated with this consideration and FSANZ therefore cannot hold up a consideration process on the grounds that information may become available at a future point. In the case of food derived from maize 98140, FSANZ considers that sufficient evidence has been provided to allow completion of a safety assessment.

However, FSANZ remains open to receive or review any new information pertinent to the GM applications that have been approved, or are in the process of being considered. If necessary, FSANZ would not hesitate to withdraw an approval or not approve a GM food where the decision could be supported by robust scientific evidence.

10.1.3 The agricultural plausibility of the herbicide spray regimens

The New Zealand Food Safety Authority (NZFSA) asks for comment on the agricultural plausibility of the herbicide spray regimes used in the studies submitted by the Applicant.

[15] http://www.foodstandards.gov.au/scienceandeducation/factsheets/factsheets2009/fsanzresponsetoseral4647.cfm
[16] http://www.efsa.europa.eu/en/events/event/gmo100127-m.pdf
[17] http://www.foodlabellingreview.gov.au

10.1.3.1 Response

Even though consideration of the plausibility of the herbicide spray regimens is not the mandate of FSNAZ, details of the herbicide spray regimens, such as the concentrations and timing of applications, were included in the study reports provided by the Applicant. Only one study employed a spray regimen which was not consistent with the usage directions described on the herbicide product label. In this study, described in Supporting Document 2 of the Assessment Report, maize 98140 was treated with glyphosate at 5-times the label application rate; however, there were no detectable residues of glyphosate, *N*-acetyl glyphosate, AMPA, or *N*-acetyl AMPA found in refined maize oil or starch derived from the grain.

10.1.4 Comment

NZFSA notes that the maize-expressed and *E. coli*-expressed GAT4621 and ZM-HRA proteins were analysed using matrix-assisted laser desorption/ionisation mass spectrometry (MALDI-MS) following enzymatic digestion and that the *E. coli* expressed proteins were also analysed by electrospray ionisation mass spectrometry (ESI-MS). NZFSA asks why the maize expressed proteins were not also analysed by ESI-MS.

10.1.4.1 Response

It is likely that the purity of the maize expressed protein samples was considered insufficient to attempt characterisation using the ESI-MS technique which is more prone to be adversely affected by sample contamination.

10.1.5 Comment

NZFSA asks for clarification on the presentation of tabular data comparing analytical results from maize subjected to various herbicide treatment regimens, in particular why some results appear to be aggregated into a single treatment category while others have been kept separate.

10.1.5.1 Response

Results for herbicide treatments regimens have not been aggregated in the tables presented. In some studies the maize plants were either untreated or were treated with glyphosate and two ALS inhibiting herbicides, while for other studies maize plants were either untreated, treated with glyphosate only, treated with ALS herbicides only, or treated with glyphosate and ALS herbicides. The presentation of data in the tables accurately represents these different herbicide treatment regimens.

10.1.6 Benefit Cost analysis

Queensland Health requests more quantitative detail to support the conclusions of the Benefit Cost Analysis in the Assessment Report.

10.1.6.1 Response

The Benefit Cost Analysis included in the Assessment Report is not intended to be an exhaustive, quantitative dollar analysis of the options and, in fact, most of the impacts that are considered cannot be assigned a dollar value. Rather, the analysis seeks to highlight the qualitative impacts of criteria that are relevant to each option.

These criteria are deliberately limited to those involving broad areas such as trade, consumer information and compliance and do not, for example include any consideration of the impact of growing the crop (either to the farmer or to the environment).

10.1.7 Detection methodology

The Soil and Health association of NZ is concerned that there are no diagnostic tools available for detection of GM foods by consumer advocates and dietary and health practitioners.

10.1.7.1 Response

As part of the Application, the Applicant is required to confirm the availability of detection methodology for the GM food. For maize line 98140, this methodology involves the use of the polymerase chain reaction for DNA detection. The method is currently under evaluation by the European Commission Joint Research Centre. The status of the validation process can be found at http://gmo-crl.jrc.ec.europa.eu/statusofdoss.htm. Because of the technology involved, these detection methods are generally restricted to specialist laboratories. This is no different from the routine testing of food samples for a variety of chemicals or organisms, which is done by specialist laboratories.

10.1.8 Enforcement costs

Queensland Health has concerns about the impact on monitoring resources if the Application is approved.

10.1.8.1 Response

FSANZ believes it is important to recognise that, because GM foods are continually entering international trade, the costs of monitoring are largely unavoidable and will arise irrespective of whether or not GM foods are approved in Australia and New Zealand.

In the case of approved GM foods, monitoring is required to ensure compliance with the labelling requirements, and in the case of GM foods that have not been approved, monitoring is required to ensure they are not illegally entering the food supply.
The costs of monitoring are thus expected to be comparable, whether a GM food is approved or not. Any regulatory decision take by FSANZ is therefore unlikely to significantly affect the cost impact on jurisdictions, in terms of their responsibilities to enforce the Code.

10.1.9 Long-term feeding studies

The Food Technology Association of Australia (FTAA) states that a possible anomaly might exist in that long-term feeding studies for genetically modified food are only for a maximum of 14 days whereas for a similar type of food ingredient, i.e. enzymes, long-term feeding trials are conducted for 3 months (12 weeks). FTAA considered that long-term feeding studies would be of a standardised length.

10.1.9.1 Response

There is no particular duration specified for feeding studies; however, such studies are usually longer than 14 days. For example, this application included a 42-day feeding study in broiler chickens and a 90-day study in rats.

10.2 World Trade Organization (WTO)

As members of the WTO, Australia and New Zealand are obligated to notify WTO member nations where proposed mandatory regulatory measures are inconsistent with any existing or imminent international standards and the proposed measure may have a significant effect on trade.

The inclusion of food derived from maize 98140 in the Code would have a trade enabling effect as it would permit any foods containing this variety of maize to be imported into Australia and New Zealand and sold, where currently they would be prohibited. For this reason it was determined there was no need to notify this Application as a Sanitary and Phytosanitary (SPS) measure in accordance with the WTO Agreement on the Application of SPS Measures.

CONCLUSION

11. Conclusion and Decision

Decision

To approve the draft variation to Standard 1.5.2 – Food produced using Gene Technology, to include food derived from herbicide-tolerant maize line DP-098140-6 in the Table to clause 2.

11.1 Reasons for Decision

The development of a variation to the Code to give approval to the sale and use of food derived from maize line DP-098140-6 in Australia and New Zealand is proposed on the basis of the available scientific evidence, for the following reasons:

- the safety assessment did not identify any public health and safety concerns associated with the genetic modification used to produce herbicide-tolerant maize line DP-098140-6
- food derived from maize line DP-098140-6 is equivalent to food from the conventional counterpart and other commercially available maize varieties in terms of its safety for human consumption and nutritional adequacy
- the herbicide residues generated on maize 98140 plants following glyphosate application are less toxic than glyphosate
- labelling of certain foods derived from herbicide-tolerant maize line DP-098140-6 will be required where novel DNA and/or protein is present in the final food
- a regulation impact assessment process has been undertaken that fulfils the requirement in Australia and New Zealand for an assessment of compliance costs. The assessment concluded that the preferred option is Option 2, the development of a food regulatory measure
- there are no other measures that would be more cost-effective than a variation to Standard 1.5.2 that could achieve the same end.

12. Implementation and Review

The FSANZ Board's decision will be notified to the Ministerial Council. Following notification, the proposed variation to the Code is expected to come into effect on gazettal, subject to any request from the Ministerial Council for a review of FSANZ's decision.

ATTACHMENTS

1. Draft variation to the *Australia New Zealand Food Standards Code*
2. Summary of issues raised in public submissions

Attachment 1

Draft variation to the *Australia New Zealand Food Standards Code*

Section 87(8) of the FSANZ Act provides that standards or variations to standards are legislative instruments, but are not subject to disallowance or sunsetting

To commence: on gazettal

[1] ***Standard 1.5.2*** *of the Australia New Zealand Food Standards Code is varied by inserting in the* Table to clause 2 –

Food derived from herbicide-tolerant corn line DP-098140-6	

Attachment 2

Summary of Public Submissions on Assessment Report

Submitter	Comments by submitter
Colin Thomson (San Diego Tortilla Factory Pty Ltd)	• States that long term effects of GM foods on animals and human are unknown. • States that Australian crops should be protected from potential cross contamination by GM crops.
Christine Bennett (Private)	• States that GM foods have disastrous effects on the Australian environment and our domestic food supply. • States that GM crops adversely affect bee colonies.
David Savill (Private)	• Under current labelling laws there is no guarantee that food is GM free. • No long term health studies have been conducted by independent scientists with no financial interest in genetic engineering technologies. • Scientific analysis has been performed by the Applicant and not a truly independent third party.
Paul Elwell-Sutton (Private)	• Opposes the approval of food derived from maize 098140 on the grounds that there is little or no long term evidence to demonstrate the absence of any degenerative or abnormal effects on cellular ageing and/or neuronal development as a result of consumption of food derived from GM organisms. • States that the absence of a robust food labelling protocol in New Zealand deprives consumers of the right to avoid buying GM foods.
Shirley Collins (Private)	• States that an embargo should be placed on GM food until outstanding issues are resolved concerning: – Labelling, especially with regard to any findings of the current labelling review – Safety of GM food to humans (cites, in particular, a paper by Spiroux de Vendômois et al (2009) on GM corn lines NK603, MON810, and MON863. Also makes reference to a forthcoming paper by Dr Judy Carman).
New Zealand Food Safety Authority	• Concurs with the conclusions that 'food derived from dual-herbicide tolerant maize line DP-098140-6 is considered as safe and wholesome as food derived from other commercial maize varieties'. • Requested comment on several minor points: (i) the agricultural plausibility of the herbicide spray regimes; (ii) the reason(s) why *E. coli* expressed proteins, but not maize expressed proteins, were examined using electrospray ionisation mass spectrometry; and (iii) reason(s) for variability in the presentation of data in some tables.
Michelle Denise (Private)	• Requests deferral of a decision on the Application until the outcomes of the current labelling review are known and the findings of a research paper by Dr Judy Carman are published.
Ryan Hamilton (Private)	• Is against the approval of any GM food. • Requests clear labelling of GM food.
Australian Food & Grocery Council	• Supports the Application on the basis that there is no identified risk to public health and safety.

Submitter	Comments by submitter
Environmental Health Unit, Queensland Health	• Requests the outcomes of submissions to other agencies, particular that of the US FDA. • Requests any relevant additional information provided to overseas agencies by the Applicant. • States that the cost-benefit analysis appears to be limited in detail. Requests elaboration on how it was concluded that 'the potential benefits ...outweigh the potential costs'. Also requests any available information relative to quantitative values assigned to the costs or benefits to the various stakeholders. • Is concerned that a decision to approve food derived from maize line DP-098140-6 will impact on monitoring resources in Queensland.
The Hon Lynn MacLaren, Member for South Metropolitan Legislative Council, Parliament of WA	• Requests deferral of a decision on the Application until the outcomes of the current labelling review are known and the findings of a research paper by Dr Judy Carman are published. • Expresses concern that the scientific studies accompanying the Application are not independent. • States that decisions on food safety must be based on hard evidence data not assumptions. • States that there is no reliable scientific evidence that GM foods are safe. • Suggests that there should be mandatory labelling in Australia of all foods derived from gene technology.
The Soil and Health Association of New Zealand	• Opposes approval of the Application on a number of grounds: – Inadequate safety testing – Lack of independent studies – Lack of long term testing – Lack of diagnostic tools for detecting the presence of the GM food – The Application is deficient in many consumer, practitioner and health parameters.
Food Technology Association Australia	• Supports the Application. • Stated that a possible anomaly might exist in that long-term feeding studies for genetically modified food are only for a maximum of 14 days whereas for a similar type of food ingredient, i.e. enzymes, long-term feeding trials are conducted for 3 months (12 weeks). It was thought that long-term feeding trials would be of a standardised length.