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[20-09]

APPLICATION A1018 FOOD DERIVED FROM HIGH OLEIC ACID SOYBEAN LINE DP-305423-1 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 22 September 2008. 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 soybean, high oleic acid soybean line DP-305423-1.

The Application was assessed under the General Procedure.

Safety Assessment

Soybean line DP-305423-1 has been genetically modified (GM) with a partial gene sequence (fragment) designed to decrease the expression of the endogenous soybean fatty acid desaturase gene (*gm-fad2-1*). This leads to the production of seeds that have a higher concentration of oleic acid (C18:1) and a correspondingly lower concentration of linoleic acid (C18:2). The purpose of this change in fatty acid profile is to provide a stable vegetable oil that is suitable for frying applications without the need for hydrogenation. Soybean line DP-305423-1 also contains a modified version of a soybean acetolactate synthase (*als*) gene (*gm-hra*). The GM-HRA enzyme can function in the presence of the ALS-inhibiting class of herbicides, thereby conferring a degree of tolerance to those herbicides. However, the transcript of this gene was used as a selectable marker to identify genetically modified plants during their initial development in the laboratory and commercial levels of herbicide tolerance have not been conferred on soybean DP-305423-1.

FSANZ has completed a comprehensive safety assessment of food derived from soybean line DP-305423-1 (see **Supporting Document 1**¹). This assessment included consideration of (i) the genetic modification to the plant; (ii) the potential toxicity and allergenicity of the novel proteins; and (iii) the composition of soybean DP-305423-1 compared with that of conventional soybean varieties. The potential nutritional impact of the altered fatty acid profile was also assessed.

¹ SD1 Safety Assessment for A1018

No public health and safety concerns have been identified in this pre-market safety assessment of food derived from soybean DP-305423. On the basis of the available evidence, including detailed studies provided by the Applicant, food derived from high oleic acid soybean line DP-305423-1 is considered as safe and wholesome as food derived from other commercial soybean 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 high oleic acid soybean line DP-305423-1, 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 a novel protein is present in the seed.

In addition to this, however, is the consideration that soybean DP-305423-1 has been significantly changed with respect to its fatty acid profile, having intentionally elevated levels of oleic acid and reduced levels of linoleic acid. Clause 7(a) of Standard 1.5.2 states that labelling or other information requirements may be specified 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 considered this issue and is recommending that the label of refined oil derived from soybean line DP-305423-1 must only include a statement that the oil has been genetically modified. Specific labelling to indicate the changes in concentrations of oleic acid and linoleic acid are not considered to be informative for consumers as there is no significant change to the overall level of unsaturated fatty acids in the soybean oil. In this context, additional labelling for individual fatty acid changes is likely to be confusing and potentially misleading to consumers.

Impact of regulatory options

Following satisfactory completion of the safety assessment, two regulatory options were considered: (1) rejection of the Application; or (2) approval of food derived from soybean DP-305423-1.

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/Proposal

In assessing the Application/Proposal 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/Proposal 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

- 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
- any relevant New Zealand standards
- any other relevant matters.

Decision

Approve the variation to Standard 1.5.2 – Food produced using Gene Technology, to include food derived from high oleic acid soybean line DP-305423-1 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 high oleic acid soybean line DP-305423-1 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 high oleic acid soybean line DP-305423-1
- seed from high oleic acid soybean line DP-305423-1 contains elevated levels of oleic acid and reduced levels of linoleic acid, when compared to conventional soybean, but is equivalent to other commercially available soybean varieties in terms of its safety for human consumption and nutritional adequacy
- labelling of certain foods derived from high oleic acid soybean line DP-305423-1 will be required if novel DNA, novel protein and/or altered levels of oleic and linoleic acid are 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 relevant New Zealand standards
- 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 11 September and 23 October 2009. Comments were specifically requested on the scientific aspects of this Application, in particular, information relevant to the safety assessment of food derived from high oleic acid soybean line DP-305423-1. A total of 6 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.

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SUPPORTING DOCUMENTS

The following material, which was used in the preparation of this Assessment Report, is available on the FSANZ website at

<http://www.foodstandards.gov.au/standardsdevelopment/applications/applicationa1018food4091.cfm>

SD1: Safety Assessment Report: Application A1018 – Food Derived from High Oleic Acid Soybean Line DP-305423-1

INTRODUCTION

On 22 September 2008, Pioneer Hi-Bred International, Inc. (Pioneer), a DuPont Company, submitted an Application seeking approval for food derived from high oleic acid soybean line DP-305423-1 (also referred to as soybean 305423) under Standard 1.5.2 – Food produced using Gene Technology, in the *Australia New Zealand Food Standards Code* (the Code).

Soybean 305423 has been genetically modified (GM) with a partial gene sequence (fragment) designed to decrease the expression of the endogenous soybean fatty acid desaturase gene (*gm-fad2-1*). This leads to the production of seeds higher in oleic acid (C18:1) and correspondingly lower in linoleic acid (C18:2). Soybean 305423 also contains a modified version of a soybean acetolactate synthase (*als*) gene (*gm-hra*), conferring a degree of tolerance to the ALS-inhibiting class of herbicides (e.g. the sulfonylureas). This gene was used as a selectable marker to identify genetically modified plants during their initial development in the laboratory and commercial levels of herbicide tolerance have not been conferred on soybean 305423.

For cooking purposes, conventional soybean oil has undesirable thermal and oxidative stability due predominantly to the presence of linoleic acid. When heated such oil develops qualities that negatively influence flavour and cooking quality. Conventional chemical processing to reduce levels of linoleic acid, such as through partial hydrogenation, in which carbon double bonds are reduced, enables oxidative stability to be achieved but it also leads to the formation of undesirable *trans* fatty acids. Thus the conventional soybean oil is unsatisfactory both in the natural and hydrogenated forms. The Applicant claims that high oleic acid soybean oil may therefore be used for a number of food applications, including deep fat frying, while also potentially offering improved nutritional properties compared to conventional oil or partially hydrogenated oil.

FSANZ completed a full scientific evaluation of food derived from soybean 305423 according to FSANZ guidelines² to assess its safety for human consumption. The Assessment Report was released in September 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 / Problem

The Applicant has developed GM soybean 305423 whose seeds contain more oleic acid than conventional soybeans. The line also contains a gene conferring a degree of resistance to herbicides such as the sulfonylureas. Pre-market approval is necessary before this product may enter the Australian and New Zealand food supply. A variation to the Code granting approval to food derived from soybean 305423 must be approved by the FSANZ Board, and subsequently notified to the Australia and New Zealand Food Regulation Ministerial Council (Ministerial Council). A variation to the Code may only be gazetted once the Ministerial Council process has been finalised.

The Applicant has already obtained approval to grow soybean 305423 in several countries and is also seeking food approval for soybean 305423 in key trading markets for soybean, including Australia and New Zealand.

The Applicant has therefore sought the necessary variation to Standard 1.5.2 to include food derived from soybean line DP-305423-1 prior to any decision to commercialise this line.

² FSANZ (2007). Safety Assessment of Genetically Modified Foods – Guidance Document. http://www.foodstandards.gov.au/srcfiles/GM%20FINAL%20Sept%2007L%20_2_.pdf

The Application was assessed as a General Procedure.

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 soybean line DP-305423-1 have been made to the appropriate agencies for food, feed and environmental approvals in the United States (Food and Drug Administration, Department of Agriculture), Canada (Health Canada and the Canadian Food Inspection Agency), Japan (Ministry of Health, Labour and Welfare, Ministry of Agriculture, Forestry and Fisheries) and Korea (Rural Development Administration, Korea Food and Drug Administration). The U.S. Food and Drug Administration completed its regulatory review in January 2009³. Health Canada and the Canadian Food Inspection Agency⁴ approved Soybean DP-305423-1, for cultivation and food and feed use in Canada, in May 2009. Regulatory submissions for food import approvals have also been made in Mexico and the European Union⁵. The Applicant has advised that further submissions for import approvals in other key international markets will also be made.

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;

³ FDA (2009) *Biotechnology Consultation Note to the File BNF No. 000110*. Center for Food Safety and Applied Nutrition, U.S. Food and Drug Administration. <http://64.26.159.139/docroot/decdocs/09-052-002.pdf>. Accessed on 24 April 2009.

⁴ CFIA (2009) *Decision Document DD2009-76: Determination of the Safety of Pioneer Hi-Bred Production Ltd.'s Soybean (Glycine max (L.) Merr.) Event 305423*. Canadian Food Inspection Agency. <http://www.inspection.gc.ca/english/plaveg/bio/dd/dd0976e.shtml>. Accessed on 27 May 2009

⁵ Pioneer Hi-Bred International Inc. (2007) *Summary of the Application for Authorisation of Genetically Modified 305423 Soybean and Derived Food and Feed in Accordance with Regulation (EC) 1829/2003*. European Food Safety Authority. http://www.gmo-compass.org/pdf/regulation/soybean/305423_soybean_application_foo_feed.pdf. Accessed on 23 April 2009. COGEM (2007) *Import and Processing of Herbicide Tolerant Soybean 305423: COGEM Advice CGM/071219-03*. Commissie Genetische Modificatie, Netherlands. <http://www.cogem.net/ContentFiles/071219-03%20advies%20soja%20305423%20import2.pdf>. Accessed on 23 April 2009.

- the promotion of fair trading in food; and
- 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 soybean line DP-305423-1 comparable to food derived from conventional varieties of soybean in terms of its safety for human consumption?

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 high oleic acid soybean line DP-305423-1 has been evaluated according to the safety assessment guidelines prepared by FSANZ⁶ and is provided in **Supporting Document 1**. The summary and conclusions from the safety assessment 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 soybean 305423, a number of criteria have been addressed including: a characterisation of the transferred coding sequences, their origin, function and stability in the soybean 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 any newly expressed protein(s) to be either allergenic or toxic in humans.

The safety assessment applied to food from soybean 305423 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.

⁶ FSANZ (2007) Safety Assessment of Genetically Modified Foods – Guidance Document. http://www.foodstandards.gov.au/srcfiles/GM%20FINAL%20Sept%2007L%20_2_.pdf

5.2 Outcomes of the Safety Assessment

Soybean 356043 contains two introduced coding sequences (and associated regulatory elements), a *gm-fad2-1* partial sequence and a complete *gm-hra* gene. Detailed molecular analyses indicate that there are 4 insertion sites at a single genetic locus. These sites contain multiple copies, both intact and truncated, of the *gm-fad2-1* partial sequence and a single copy of the *gm-hra* gene. Breeding over three generations has confirmed stability of the introduced genetic elements and segregation data indicate their Mendelian inheritance. No antibiotic resistance marker genes are present in soybean 305423.

Since the introduced *gm-fad2-1* element is a partial sequence rather than a complete gene, a functional protein is not produced during its transcription in cells of soybean.305423. However, the effect of transcription of the partial sequence is to suppress expression of the endogenous *gm-fad2-1* gene which, in turn, leads to a reduction in formation of linoleic acid from oleic acid and a concomitant accumulation of oleic acid.

Soybean 305423 expresses one novel protein, GM-HRA. This protein is a modified version of the native ALS from soybean. The GM-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 GM-HRA protein is 656 amino acids in length with a predicted molecular weight of 71 kDa. Following transport into the chloroplast and cleavage of the transit peptide, the mature protein is 604 amino acids with a predicted molecular weight of 65 kDa. The GM-HRA protein is expressed at low levels in soybean 305423 seed, with a mean concentration of 2.5 ng/mg dry weight (range 0-4.9 ng/mg).

The GM-HRA protein conforms in size and amino acid sequence to that expected, does not exhibit any post-translational modification including glycosylation, and also demonstrates the predicted enzymatic activity.

Bioinformatic studies with the GM-HRA protein confirm the absence of any biologically significant amino acid sequence similarity to known protein toxins or allergens. Digestibility studies have demonstrated that the protein would be rapidly degraded following ingestion, similar to other dietary proteins, and a thermolability study has shown that the protein is inactivated after incubation for 15 minutes at 50°C and would therefore not survive standard cooking/processing procedures. An acute oral toxicity study in mice confirmed the absence of toxicity. Taken together, the evidence indicates that the GM-HRA protein is neither toxic nor likely to be allergenic in humans.

Compositional analyses were done to establish the nutritional adequacy of soybean 305423, and to compare it to a non-transgenic conventional soybean under typical cultivation conditions. The mean oleic acid (C18:1) content has been increased from 21.1% in the control soybean to 76.5% in soybean 305423. Since the level of oleic acid in soybean 305423 oil is comparable to that in a range of other commercially available vegetable oils, no safety concerns are raised. The linoleic acid (C18:2) and linolenic acid (C18:3) contents have been concomitantly decreased from a mean level of 52.5% to a mean level of 3.62% for linoleic acid and from 9.35% to 5.39% for linolenic acid. The level of C18:3 in soybean 305423, while significantly lower than that in the control is, nonetheless within the normal range found in soybeans while the level of C18:2 in soybean 305423 is outside the normal range. These changes are consistent with the intended outcome of inserting the *gm-fad2-1* partial sequence into soybean 305423.

An unintended result of the genetic modification is an increase in levels of heptadecanoic acid (C17:0) and heptadecanoic acid (C17:1) in soybean 305423. These two fatty acids together constitute around 2% of the total fatty acid content in soybean 305423, compared to 0.17% in the conventional counterpart.

A survey of dietary sources of these two acids shows that both are consumed in a normal human diet and are also readily metabolised. The increased levels of C17:0 and C17:1 therefore raise no safety concerns.

In terms of other analytes, seeds of soybean 305423 were found to be compositionally equivalent to those from the non-GM parent and other non-GM commercial soybean cultivars. Several minor differences in key nutrients and other constituents were found but the mean levels observed are within the range of values observed for the non-transgenic comparator and within the range of natural variation.

Soybean is one of the major allergenic foods. The potential allergenicity of soybean 305423 was compared to that of the parental soybean variety by assessing IgE binding responses using sera from known soybean allergic patients. These studies indicated that soybean 305423 does not have any greater potential to be allergenic than conventional soybean varieties.

Dietary exposure assessments of the fatty acids contained in soybean indicate that the substitution of soybean oil with oil from soybean 305423 would have minimal effect on the intake of dietary significant fatty acids. At most, if soybean oil was replaced with the oil derived from soybean 305423, there may be a marginal increase (up to 6%) in intake of oleic acid and a marginal decrease (up to 10%) in linoleic acid intake. In terms of both cooking quality and nutrition, the replacement of linoleic acid by oleic acid means that partial hydrogenation is not required to stabilise the fatty acids. This in turn, has the potential to reduce the intake of undesirable *trans* fats in the diet. Taken overall, it is concluded that use of oil from soybean 305423 would have minimal nutritional impact. This conclusion is consistent with that reached by FSANZ for a previous high oleic acid soybean Application (FSANZ, 2000)⁷.

Although not essential for establishing the safety of the food, two animal feeding studies with the high oleic acid soybeans were evaluated as additional supporting data. Such studies are not toxicity studies and are intended to address only whether food derived from the GM plant is able to sustain normal growth and well being. These studies demonstrated that the high oleic acid soybeans are equivalent to non-GM soybeans in their ability to support typical growth and well-being, thus confirming the nutritional adequacy of seeds from soybean 305423.

Based on the above findings, the introduction of high oleic acid soybean 305423 into the food supply would not be expected to have any adverse nutritional impact. This was supported by the results of two feeding studies with broiler chickens and rats, where no differences in health and growth performance were found between animals fed diets containing soybean 305423 meal and those fed conventional soybean meal diets.

5.3 Conclusion

No potential public health and safety concerns have been identified in the assessment of high oleic acid soybean 305423. On the basis of the data provided in the present Application, and other available information, food derived from soybean 305423 is considered as safe for human consumption as food derived from conventional soybean cultivars.

⁷ FSANZ (2000) Application A387: Food Derived from High Oleic Acid Soybean Lines G94-1, G94-19 and G168. Report prepared by Australia New Zealand Food Authority (now Food Standards Australia New Zealand). http://www.foodstandards.gov.au/srcfiles/A387_FAR.pdf.

RISK MANAGEMENT

6. Issues raised

6.1 Risk Management Strategy

If approved, food derived from high oleic acid soybean line DP-305423-1 will be required to be labelled as genetically modified if novel DNA and/or novel protein is present in the final food. 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. As the purpose of the genetic modification was to reduce the linoleic acid concentration of the oil and the change is significant, refined oil derived from soybean line DP-305423-1 will require labelling as genetically modified even though it will not contain any novel protein or DNA.

Soybeans and their products are allergenic substances that must always be declared when present in food (refer clause 4 of Standard 1.2.3 – Mandatory Warning and Advisory Statements and Declarations). Consequently, oil derived from soybean line DP-305423-1 will always need to be labelled as 'soybean oil', rather than the generic 'vegetable oil' as may be the case for some other oils. The requirement to label as 'genetically modified' is therefore also triggered in this particular case by Standard 2.4.1 – Edible Oils. Clause 3 of Standard 2.4.1 states that if the specific name of an oil is used, then the label must include a statement that describes the nature of any process that has been used to alter the fatty acid composition of the edible oil. In this case, oil derived from soybean line DP-305423-1 would require labelling as 'genetically modified'.

FSANZ has also considered whether imposing additional labelling requirements would be appropriate in this case. Labelling is intended to address the objective set out in subsection 18(1)(b) of the FSANZ Act; the provision of adequate information relating to food to enable consumers to make informed choices. Following a detailed consideration of how informative it would be to consumers to list changes in fatty acid profiles, FSANZ has concluded that any oil derived from soybean line DP-305423-1 does not require additional labelling.

For previously approved soybean lines G94-1, G94-19 and G168 which, like soybean line DP-305423-1, contain high levels of oleic acid (see Table to clause 2 in Standard 1.5.2) and are also the property of Pioneer Hi-Bred International Inc., the labelling statement is that the food has been genetically modified to contain high levels of oleic acid. The proposed labelling for soybean line DP-205423-1 is therefore different from that for these previously approved lines.

FSANZ acknowledges that the purpose of labelling foods is to provide meaningful nutritional information. Following public education campaigns consumers are now more likely to have a better understanding of the terms 'unsaturated' and 'saturated' with regard to fats, than to have an understanding of the differences between individual fatty acids. FSANZ now considers that it would be confusing for consumers if labelling addressed specific fatty acids and, given that the total concentration of unsaturated fatty acids in soybean line DP-305423-1 is essentially unaltered, considers that it is sufficient for the labelling to mention only that the product is genetically modified. Furthermore, the Applicant has advised that the previously approved soybean lines G94-1, G94-19 and G168 are no longer cultivated and therefore products derived from them are not available on the market. This removes the likelihood of products from these lines and from soybean line DP-305423-1 occurring side-by-side for retail sale and appearing to lack consistency in labelling.

Labelling to indicate minor changes in fatty acid compositions of heptadecanoic acid and heptadecanoic acid is not considered necessary based on their low abundance, lack of nutritional impact, and level of presence in other commonly consumed foods.

7. Options

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

7.1 Option 1 – Maintain the *status quo*

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 high oleic acid soybean line DP-305423-1, 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 soybean-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 soybean-containing food products
 - food retailers.
- Government:
 - enforcement agencies
 - national Governments, in terms of trade and World Trade Organization (WTO) obligations.

Soybean line DP-305423-1 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 soybean 305423 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 – Maintain the status quo

Consumers: Possible restriction in the availability of imported soybean products to those products that do not contain soybean line DP-305423-1.

No impact on consumers wishing to avoid GM foods, as food from soybean line DP-305423-1 is not currently permitted in the food supply.

Potential increase in price of imported soybean foods due to requirement for segregation of soybean line DP-305423-1.

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 soybean food products once soybean line DP-305423-1 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 food regulatory measure

Consumers: Broader availability of imported soybean products as there would be no restriction on imported foods containing soybean line DP-305423-1.

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

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

Government: Benefit that if soybean line DP-305423-1 was detected in soybean imports, approval would ensure compliance of those products with the Code. This would ensure no potential for trade disruption on regulatory grounds.

Approval of soybean line DP-305423-1 would ensure no conflict with WTO responsibilities.

This option could impact on enforcement resources, as certain foods derived from soybean line DP-305423-1 will be required to be labelled as genetically modified.

Industry: Importers of processed foods containing soybean derivatives would benefit as foods derived from soybean line DP-305423-1 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 soy products or imported foods manufactured using soybean derivatives.

Possible cost to food industry as some food ingredients derived from soybean line DP-305423-1 would be required to be labelled.

8.3 Comparison of Options

As food from high oleic acid soybean line DP-305423-1 has been found to be as safe as food from conventional varieties of soybean, 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 soybean line DP-305423-1 by other countries could limit the availability of imported soy products in the Australian and New Zealand markets. In addition, Option 1 would result in the requirement for segregation of any products containing soybean 305423 from those containing approved soybean lines which would be likely to increase the costs of imported soy foods. Even though soybean 305423 will be grown under identity preservation, certain products may inadvertently be co-mingled with those from other soybean lines. This means that costs could be incurred if approval for soybean 305423 were not given.

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 high oleic acid soybean line DP-305423-1 is therefore the preferred option.

COMMUNICATION AND CONSULTATION STRATEGY

9. Communication

FSANZ applied a basic communication strategy to this Application. Public comment on the Assessment was sought prior to preparation of this Approval Report. As normally applies to all GM food assessments, the Assessment and Approval Reports are available to the public on the FSANZ website.

The Applicant and individuals and organisations that made submissions on this Application will be notified at each stage of the assessment. The decision of the FSANZ Board to approve the draft variation to Standard 1.5.2 will be notified to the Ministerial Council. If the approval of food derived from high oleic acid soybean line DP-305423-1 is not subject to review, the Applicant and stakeholders, including the public, will 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 11 September and 23 October 2009. Comments were specifically requested on the scientific aspects of this Application, in particular, information relevant to the safety assessment of food derived from high oleic acid soybean line DP-305423-1. As this Application was assessed under a General Procedure, there was one round of public comment.

A total of six 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.

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, and the safety of food products derived from livestock fed GM feed, are available from the FSANZ website (see Table 1).

While the FSANZ assessment of GM foods is guided by concepts and principles developed through the work of the OECD, FAO, WHO and the Codex Alimentarius Commission, the FSANZ *Safety Assessment of Genetically Modified Foods* (see footnote 6) and the *Application Handbook*⁸ are the primary references relevant to GM food safety assessments in Australia and New Zealand.

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
Data used to inform the Safety Assessment	Food Matters <ul style="list-style-type: none"> • GM Foods 	http://www.foodstandards.gov.au/foodmatters/gmfoods/
Safety of food products derived from livestock fed GM feeds	Section 7.7: Safety Assessment of Genetically Modified Foods	http://www.foodstandards.gov.au/srcfiles/GM%20Foods_text_pp_final.pdf

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 Comment

One submitter suggests that food derived from soybean 305423 or any GMO may accelerate the ageing process in cells or have a degenerative effect on memory function.

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 soybean, has been implicated in cell ageing or loss of cognitive function.

⁸ Available online at <http://www.foodstandards.gov.au/standardsdevelopment/applicationshandbook.cfm>

10.1.2 Comment

The NSW Food Authority has concerns regarding some of the Compositional Analysis data generated by the Applicant, particularly the broadness of the tolerance intervals obtained for the isoflavones and the choice of the comparator. The Centre for Integrated Research in Biosafety (INBI) has similar concerns about the comparator.

10.1.2.1 Response

The tolerance intervals for each analyte were derived from the data from four non-GM commercial soybean cultivars grown at six field locations in soybean-growing areas of North America. These cultivars were planted, harvested, processed and analysed using the same methods as for soybean 305423 and the null-segregant control. Each tolerance interval was calculated to contain, with 95% confidence, 99% of the values contained in the commercial cultivar population. The broadness of the tolerance intervals for the isoflavones reflects the considerable variation that occurred between the four commercial cultivars and is therefore reflective of the natural variation. Section 5.3.7 of the Safety Assessment states *It is noted that for eight analytes the soybean 305423 mean has fallen outside the reported range for the particular analyte but within the tolerance interval determined for four non-GM commercial cultivars. This suggests that the literature is somewhat limited in providing a broad reflection of the natural diversity that occurs within soybean.*

Soybean line 305423 plants from which compositional data were generated were taken from a BC1F5 generation i.e. plants had been crossed to elite lines, backcrossed to the elite lines and then self fertilised four times (see Figure 2 in the Safety Assessment). The comparator used for all of the compositional analyses was a BC1F5 null (or negative) segregant. The FSANZ safety assessment guidelines recognise that negative segregants are often the only plant lines available that are close enough to the GM line to serve as a suitable control. However, as such comparators may be considered a product of gene technology, even though they themselves do not exhibit a detectable genetic modification, it is important to include additional conventional varieties that have an established history of safe use. In the case of soybean 305423 FSANZ determined that the null segregant is an appropriate comparator since genetically it is almost identical to the corresponding BC1F5 soybean 305423 generation except that it lacks the inserted novel genetic material. In addition, the Applicant included additional conventional varieties in the field trials to serve as further comparators, consistent with the requirements of the FSANZ safety assessment guidelines.

10.1.3 Comment

The New Zealand Food Safety Authority (NZFSA) asks that the data for vitamins and minerals be provided in the Compositional Analysis section of the Safety Assessment Report.

10.1.3.1 Response

Tables summarising the vitamin and minerals data have now been added to the Safety Assessment Report.

10.1.4 Comment

The NZFSA suggests that the Dietary Intake Assessment should have considered comparative information on the absolute amount of saturated, polyunsaturated and monounsaturated fats in the population diet. Queensland Health and INBI express concern about the level of data available to underpin the assumptions of the Dietary Intake Assessment.

Both Queensland Health and INBI also express concern about the implications for dietary intake if oil from soybean 305423 were available for retail sale rather than being confined to commercial use.

10.1.5.1 Response

Given the significant alteration to the levels of oleic and linoleic acid in oil derived from soybean 305423, the purpose of the Dietary Intake Assessment done by FSANZ was to gauge whether these changes would translate into differences in the mean intake of oleic and linoleic acids within the total diet of Australian and New Zealand populations. The scenario that 25% of all vegetable oils (excluding olive) would be replaced by oil from soybean 305423 was used although it is acknowledged that this is likely to be an overestimate of the actual market share of the soybean 305423 oil, especially as the oil would most likely be confined to commercial applications (i.e. the Dietary Intake considered all applications both commercial and 'household'). Despite this overestimate, the dietary modelling did not predict large changes to either oleic or linoleic acid intake, and for this reason FSANZ does not consider that a more comprehensive analysis is warranted.

Any dietary modelling is limited by the data available. The Dietary Intake Assessment was based on the best available data and clearly states the limitations and assumptions surrounding that data.

10.1.5 Comment

The NZFSA suggests that it would be appropriate to include a Food Technology Report as part of the Assessment Report, especially as this would better inform the dietary modelling.

10.1.5.1 Response

A Food Technology Report is typically associated with the risk assessment of food additives and processing aids, and its purpose is to consider the specifications/uses of the substance in question, particularly in relation to any claims made by the Applicant. The stated use of soybean 305423 (see Safety Assessment – Introduction) is for production of an identity preserved oil with a number of food applications, most prominently commercial frying. It is not possible to precisely define these food applications or to predict exactly which oils might be replaced by oil from soybean 305423. The Applicant has indicated that the broad purpose of the genetic modification is to provide a soybean oil with better oxidative stability and cooking properties. Whether or not this expectation is met in relation to oil derived from soybean 305423 is not a safety issue and therefore does not warrant consideration.

The discussion in response to comment 10.1.4 reiterates the intentional limiting of the Dietary Intake Assessment.

10.1.6 Comment

Two submitters make mention of the previous high oleic acid soybean lines approved by FSANZ and their relevance to the assessment of soybean line 305423. In particular, reference is made to the fact that the Applicant has indicated these previously approved lines are no longer cultivated. One submitter (INBI) suggests that this factor should be taken into account in the benefit/cost analysis and one submitter (NZFSA) is concerned that the proposed labelling for soybean 305423 is inconsistent with the labelling required for the previous high oleic acid soybean lines and may therefore cause legal ambiguity. NZFSA suggests that the previously approved high oleic acid soybean lines could be removed from the Code.

10.1.6.1 Response

FSANZ is aware that elite crop lines are under continuous development which means that, over time, a proportion of approved GM lines will be superseded. The reason why the previously approved lines are no longer used is not of relevance to the assessment of soybean 305423 unless a safety issue had been identified, which is not the case. An Applicant is under no obligation to commercialise an approved GM food, and the likely commercial viability of such a food is not a consideration in the assessment process. FSANZ is planning, in the near future, to provide an opportunity for redundant entries in the Table to clause 2 in Standard 1.5.2 to be removed. However, an Applicant may have a valid reason for maintaining an approved GM food in the Code even if that food is not currently under cultivation.

After careful consideration, FSANZ considers that the proposed labelling for oil derived from soybean 305423 is more meaningful to consumers than the labelling that was required for products derived from the previously approved high oleic soybean lines. As discussed in the Assessment Report, the fact that these previous lines are no longer grown, removes the likelihood of products from these lines and from soybean line 305423 occurring side-by-side for retail sale and appearing to lack consistency in labelling.

10.1.7 Comments from INBI

INBI made two submissions comprising a total of 28 recommendations. Of these, the authors identified nine main points. One of these main points is considered in 10.1.8. The remaining points are summarised and addressed below. As a general comment, in response to most of these points, and especially to those in which further studies are requested, it must be stated that the cumulative evidence from all the studies associated with soybean 305423, point to an absence of harm in foods derived from this GM plant. FSANZ considers the data supplied by the Applicant is sufficient to establish the safety of the food, and satisfies the requirements of the FSANZ *Application Handbook*. While it may be technically possible to generate data to answer an infinite number of interesting scientific questions, FSANZ only requests data that it deems necessary to draw a conclusion about the safety of a GM food. This particularly applies to points (iii), (vi) and (vii) below.

- (i) The charges applied by FSANZ to allow the public to access the scientific dossier of GM applications are prohibitive and should be eliminated.

Response: FSANZ charges an administrative fee, based on the number of files requested, for access to what is known as the Public Register, a dossier containing the full application (including scientific studies) provided by the Applicant together with any public submissions and other associated material. The charge may be partially or fully waived for academic institutions, private individuals, community, consumer or non-profit organisations. In most instances the Public Register for a GM application runs into tens of individual files. The hourly costs to FSANZ of the activities associated with preparing material to be released from the Public Register are, in most cases, considerably higher than the administrative fee that is charged. It is also worth noting that should the Applicant wish to see the Public Register (e.g. the public submissions), the same fee applies.

- (ii) Health and safety issues of changes in fatty acid levels. Elevated levels of oleic acid have been associated with respiratory distress (cites Matalon & Ji, 2005)⁹ and may cause lung irritation when inhaled in e.g. flour derived from soybean 305423. Concern is also expressed about the inhalation of heptadecanoic acid, the Material Safety Data Sheet (MSDS) of which states that this chemical is irritating to eyes, skin and the respiratory system. Concern is also expressed about the antibacterial/anti-viral property of oleic acid (cites Zheng et al 2005)¹⁰ leading to cross-resistance to clinical antibiotics and antiseptics. It is stated that FSANZ *makes repeated reference to the benefits of oleic acids*. It is suggested that FSANZ needs to consider the negative effects of cooking high oleic acid soybeans since the lysine will react to create potentially toxic compounds.

Response: The paper cited by INBI is a synopsis of a research paper (Vadasz et al 2005)¹¹ reported in the same journal issue. At no stage in either the Vadasz et al paper or in earlier research papers by other authors is any suggestion made that the ingestion or inhalation of oleic acid causes acute respiratory distress syndrome (ARDS). It is merely noted that an increase in the serum level of oleic acid is a predictor of the development of ARDS (a disease that occurs in approximately 75 out of 100,000 individuals). Experimentally, intravenous injection of oleic acid is often used as a means of modelling human lung injury in animals. Vadasz et al perfused oleic acid directly into isolated, ventilated rabbit lungs, a procedure that in no way relates to ingestion or inhalation of oleic acid in foodstuffs.

As the Dietary Intake Assessment for Application A1018 shows, oleic acid is ingested in a wide range of foods that are part of a normal diet. Addition of food derived from high oleic soybean line 305423 would not significantly alter that intake. There is no evidence that this ingestion has any effects related to respiratory distress.

The Safety Assessment provides data that show heptadecanoic acid is also a typical, albeit very minor, constituent of the human diet. To link the MSDS of a raw chemical with normal exposure to the same chemical in a food product is meaningless. For example, the MSDS for acetic acid, the main ingredient in vinegar, states that it is strongly corrosive, causes serious burns and is very harmful if swallowed. Similarly the sodium chloride MSDS states that it may cause eye irritation and the MSDS for linoleic acid states that it may act as an irritant.

Long chain unsaturated fatty acids (including palmitoleic [C16:1], oleic [C18:1], and linoleic [C18:2] acids) show antibacterial and antiviral activity when used at appropriate levels. Indeed, their presence in human breast milk has been linked to the protection of suckling infants from gastrointestinal infection (see Isaacs et al, 1991)¹². They are consumed as part of the normal daily diet and there is no evidence to suggest that this consumption is linked with cross-resistance to antibiotics.

⁹ Matalon, S. & Ji, H.-L. (2005). Oleic acid damages ion transport and promotes alveolar edema: the dark side of healthy living. *American Journal of Respiratory and Critical Care Medicine* 171: 424 – 425.

¹⁰ Zheng, C.J.; Yoo, J.-S.; Lee, T.-G.; Cho, H.-Y.; Kim, Y.-H.; Kim, W.-G. (2005). Fatty acid synthesis is a target for antibacterial activity of unsaturated fatty acids. *FEBS Letters* 579: 5157 – 5162.

¹¹ Vadasz, I.; Morty, R.E.; Kohstall, M.G.; Olschewski, A.; Grimminger, F.; Seeger, W.; Ghofrani, H.A. (2005). Oleic acid inhibits alveolar fluid reabsorption: a role in acute respiratory distress syndrome. *American Journal of Respiratory and Critical Care Medicine* 171: 469 – 479.

¹² Isaacs, C.E.; Thomar, H.; Kim, K.S.; Heird, W. (1991). Antiviral and antibacterial activity of fatty acids and monoglycerides. Patent 4997851, available online at <http://www.freepatentsonline.com/4997851.html>

Regarding the claim that FSANZ has overstated the benefits of oleic acid, FSANZ has reviewed the content of the safety assessment and does not agree with the submitter. There are two Sections in the Safety Assessment in which oleic (and linoleic acids) have been specifically discussed: In Section 5.3.2 in consideration of the significance of the compositional differences in soybean 305423 with respect to oleic and linoleic acid FSANZ has stated that *The consumption of high levels of oleic acid is not considered to pose any safety concerns*. In Section 6.3, in a nutritional consideration of the two fatty acids, FSANZ has stated that *In terms of both cooking quality and nutrition, the replacement of linoleic acid by oleic acid means that partial hydrogenation is not required to stabilise the fatty acids. This in turn, has the potential to reduce the intake of undesirable trans fats in the diet*. Neither instance represents any commentary on the benefits of high oleic acid *per se* and, in the context of the assessment, these neutral statements are made in order to indicate that FSANZ considers there are no health or safety concerns associated with increasing the level of oleic acid and decreasing the level of linoleic acid in soybean 305423.

It is not clear to FSANZ why INBI is relating lysine levels to soybean 305423, since fatty acid composition does not influence lysine levels. There are no differences between the lysine level of soybean 305423 and that of the near-isogenic 'Jack' and, in general, the high lysine content of soybean protein is regarded as a reason for the exceptional quality of the protein i.e. high lysine is expected in all soybean protein. In the animal feeding studies, toasted meal and hulls were a significant part of the diets and no adverse effects were noted in animals fed the soybean 305423 diet. FSANZ cannot identify any scientific reason why studies need to be done on the effects of high temperature on products derived from soybean 305423.

- (iii) FSANZ has not provided transcriptome or proteome profiling evidence to identify or analyse off-target effects of the novel dsRNA used in soybean DP-305423-1.

Response: Extensive molecular characterisation studies done by the Applicant, along with a selective breeding programme over six generations have not identified any undesirable genotypic or phenotypic effects resulting from the transformation event giving rise to soybean DP-305423-1. The molecular characterisation studies supplied by the Applicant satisfy all of the requirements of FSANZ for the *Safety Assessment of Genetically Modified Foods* (see footnote 6 for details of the reference). The FSANZ requirements are consistent with the *Codex Guideline for the Conduct of Food Safety Assessment of Foods Derived from Recombinant-DNA Plants*.

Transcriptome and proteome techniques are not yet fully developed and validated and have certain limitations that preclude Codex or FSANZ recommending them for safety assessments of GM foods. In particular the usefulness for the identification of unintended effects in GM crops depends largely on documented information about natural variations in gene expression levels in conventional crop plants, which is still lacking. While this baseline information is still unavailable, it would be irresponsible to place emphasis on data derived from these techniques in a safety assessment.

- (iv) FSANZ has not provided a convincing case for assuring those with concerns about allergenic effects. In particular, in the assessment of endogenous allergenic potential, the Applicant used sera from people sensitised to conventional soybean and this could not be relevant for demonstrating the safety of soybean 305423.

Response: With regard to the endogenous allergenicity study, it would not have been possible to use sera from individuals sensitised to soybean 305423 since this would have involved exposure of those individuals to an as yet unapproved GM food.

In any case, the purpose of the study was not to distinguish between the allergenic potentials of conventional soybean and line 305423 but to indicate whether the levels of endogenous allergens in the two are comparable. The fact that no differences were detected neither proves nor disproves the safety of soybean 305423 but does indicate that, with regard to allergenicity, soybean 305423 elicits a response similar to conventional soybean.

- (v) The inconsistent and inappropriate use of controls and test material throughout the studies makes correlation of data across the studies impossible. Data from field trials were pooled before analysis. Data from Chile and Argentina were not considered in the Safety Assessment although the data were used for assessment by the European Food Safety Authority¹³.

Response: The 'Jack' cultivar used originally for obtaining soybean line/event¹⁴ 305423 does not possess agronomic characteristics that may be as suitable as other commercial, elite, non-GM lines. For this reason, the Applicant made it clear that it would be necessary to transfer event 305423 into a number of existing commercial lines by conventional crossing/back crossing. Therefore in characterising line 305423 it is appropriate (and in some cases necessary e.g. generational data) to obtain data from the backcrossed lines since these represent the genetic product from which food derived from soybean line 305423 will ultimately come. Confirmation of the uniform genetic/phenotypic behaviour of event 305423, using a mix of generations and breeding lines, actually strengthens the argument for the inherent stability and safety of the event.

FSANZ is grateful to INBI for pointing out a discrepancy in Table 6 regarding the comparator. Cultivar 'Jack' was mistakenly referred to as the control line in this table and this mistake has now been corrected. As stated in Section 5.2 of the Safety Assessment Report, the comparator for the compositional analyses was the BC1F5 null segregant. See Response to 10.1.2 for discussion about use of the BC1F5 comparator.

It should be noted that, as far as statistical consideration goes, an across-locations analysis and individual location analyses were performed for each analyte and that the Applicant supplied the full raw data. However, for convenience, the analyte data presented in the Compositional Analysis tables show only the means averaged across all locations but provide the lowest and highest individual values (tolerance range) obtained across all locations. See also discussion in Response to 10.1.2.

The Applicant did not supply any data from field trials carried out in Chile and Argentina although such data (regarding the environmental impact – plant reproduction, dissemination and survivability) of soybean line 305423 were supplied to the European Food Safety Authority. The reason that the data were not supplied to FSANZ is that FSANZ does not consider such environmental data in its assessment of food safety and therefore does not require that such data be submitted.

¹³ Summary of the Application for Authorisation of Genetically Modified 305423 Soybean and Derived Food and Feed in Accordance with Regulation (EC) 1829/2003, available online at http://www.gmo-compass.org/pdf/regulation/soybean/305423_soybean_application_foo_feed.pdf

¹⁴ Standard 1.5.2 of the Code defines 'line' as a plant (and any of its descendents resulting from conventional breeding of that plant) the genetic material of which includes a transformation event or events.

- (vi) ORF analysis is not sufficient to rule out safety concerns.

Response: The Applicant used sequence analysis software to screen for the presence of novel ORFs in the four insertion regions (including the 5' and 3' genomic border sequences). Two putative ORFs were identified in this analysis, however there is no evidence to suggest that either would be expressed. Nevertheless, the Applicant undertook bioinformatic analysis of the proteins that could potentially be produced and no significant amino acid similarity with known toxins or allergens were identified.

- (vii) Evidence of non-expression of the introduced partial *fad2-1* sequence needs to be provided in order to prove the absence of harm from any potential translation of the sequence.

Response: The *fad2-1* sequence is identical to that found in non-GM soybean and represents about 40% of the middle region of a complete endogenous *fad2-1* gene. It would be unable to code for a complete FAD2-1 protein. Whether or not the partial *fad2-1* sequence is translated, there is no indication from the compositional analyses, feeding studies or from the agronomic observations that were used by the Applicant to select and breed soybean 305423 that there are any health and safety issues.

- (viii) The mouse anti-GM-HRA antiserum used to detect GM-HRA should have been raised to protein isolated from seeds of soybean 305423, otherwise novel GM-HRA isoforms produced in soybean 305423 could go undetected.

Response: The GM-HRA protein is not produced in sufficient quantity in soybean 305423 to isolate sufficient quantities for the requisite toxicological and biochemical studies required for the Safety Assessment. A standard procedure to overcome this type of problem is to overproduce the protein in a bacterial system and, if this protein shows equivalence to the *in planta*-produced protein, to then use the bacterially-produced protein for the toxicological and biochemical studies. The polyclonal nature of the antiserum used for detection ensures that any GM-HRA isoforms will be readily detected. Results from several techniques are used to provide a weight-of-evidence assessment of the equivalence of the proteins from the two sources. FSANZ is satisfied from the results of the studies supplied that the proteins are equivalent.

10.1.8 Comment

Both Queensland Health and INBI request more quantitative detail to support the conclusions of the Benefit Cost Analysis in the Assessment Report.

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) or intangible costs such as the time consumers spend reading labels.

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 draft variation to the Code would have a trade enabling effect as it would permit food derived from high oleic acid soybean DP 305423-1 to be imported into Australia and New Zealand and sold, where currently it is prohibited. For this reason it was determined there is 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

Approve the variation to Standard 1.5.2 – Food Produced Using Gene Technology, to include food derived from high oleic acid soybean line DP-305423-1 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 high oleic acid soybean line DP-305423-1 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 high oleic acid soybean line DP-305423-1
- seed from high oleic acid soybean line DP-305423-1 contains elevated levels of oleic acid and reduced levels of linoleic acid but is equivalent to other commercially available soybean varieties in terms of its safety for human consumption and nutritional adequacy
- labelling of certain foods derived from high oleic acid soybean line DP-305423-1 will be required in the ingredients list if novel DNA, novel protein or altered levels of oleic and linoleic acid are 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 relevant New Zealand standards
- 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 sunseting

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 high oleic acid soybean line DP-305423-1	
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Attachment 2

Summary of Public Submissions on Assessment Report

Submitter	Option	Comments
Paul Elwell-Sutton (Private)	1	<ul style="list-style-type: none"> Strongly opposes the approval of food derived from soybean line DP-305423-1 on the grounds that there is no evidence to demonstrate that such food would not accelerate the ageing process in cells or have a degenerative effect on memory function.
Food Technology Association of Australia	2	<ul style="list-style-type: none"> FTA Australia endorses the comments of its Technical Sub Committee: The committee agreed with Option 2.
NSW Food Authority	-	<ul style="list-style-type: none"> Does not object to the Application. Suggests that the tolerance intervals for the isoflavones reported in Table 10 of the Safety Assessment Report are generally too broad to be informative. In addition, some of the isoflavone levels in the control are higher than the levels indicated in the combined literature range; this creates some doubt about whether the control is appropriate.
New Zealand Food Safety Authority	-	<ul style="list-style-type: none"> Does not object to the application. Suggests that complete compositional data for vitamins and minerals be provided in the Safety Assessment Report. Suggests that the Dietary Intake Assessment should provide comparative information on the absolute amount of saturated, polyunsaturated and monounsaturated fats in the population diet following substitution with soybean 305423, as well as the percent contribution of these fatty acid categories to dietary energy. Does not believe that the proposed legal drafting is adequate re the labelling intent. There needs to be consistency between the labelling of soybean 305423 oil and the labelling currently in place for oil derived from other high oleic acid soybean lines already listed in the table to clause 2 in Standard 1.5.2. Suggests that if previously approved high oleic acid soybean lines are no longer used to derive food products, then the approval associated with these lines needs to be removed from Standard 1.5.2. Suggests that the inclusion of a Food Technology Report in the Assessment Report would provide useful information on the current uses of unmodified soybean oil which, in turn, would better inform the dietary modelling.

Submitter	Option	Comments
Centre for Integrated Research in Biosafety (Part 1)	1	<ul style="list-style-type: none"> • The submitter outlined 15 recommendations as follows: <ol style="list-style-type: none"> 1. The charges to the public wishing to access the scientific dossiers of the public record should be eliminated. 2. FSANZ should be able to indicate the value of additional benefit from introducing what appears to be another product with the same primary trait as those approved in 2000, and which have a history of being a commercialisation failure. FSANZ should include the cost of the application evaluation procedure and submitters time in considering this application as part of the ongoing public costs in their cost/benefit analysis. 3. FSANZ should address the impact of Option 2 (accepting the application) on New Zealanders who may encounter this food unlabelled in restaurants or regard the use of high oleic acid soybeans as an animal feed as a GM ingredient in their food and therefore may not be able to avoid this product even with labelling. 4. FSANZ should rigorously incorporate into the cost/benefit analysis the operational reality that GM high oleic acid soybeans will contaminate conventional soya supplies, thus reducing options for, and increasing costs to, the significant number of consumers who are avoiding all exposure to this product, not just detectable quantities. 5. FSANZ should provide quantitative estimates of the hidden costs to the public to exercise their legitimate option to source GM-free food using labelling, and demonstrate that such costs are lower than the costs of rejecting this application. 6. FSANZ should rigorously pursue its right to request experimental data from the Applicant to answer the questions outlined in the INBI submissions, before concluding that a rejection would not be justified on the basis of safety. 7. FSANZ should request a full chemical compositional description of whole foods prepared under a range of normal cooking and processing conditions using oil derived from DP-305423-1 and compared to oil from the proper conventional comparator line. This should be followed by animal feeding studies using whole foods produced using these two sources of oil. 8. FSANZ should request information from the Applicant on the effects of oleic acid on environmental flora that may flow through to human food and the dietary effects on human flora, particularly the ability of increased exposure to select for resistance and cross-resistance to clinical antibiotics and antiseptics. 9. FSANZ should show how it was demonstrated that unintended or unanticipated dsRNAs—which may still be unknown—produced in the DP-305423-1 soybean or secondarily in human cells had no adverse effects. 10. FSANZ should require the developer to determine the cause of reduced <i>fad2-2</i> transcript levels rather than assume that <i>gm-fad2-1</i> is the cause. 11. FSANZ should request information from the Applicant on all RNA molecules unique to DP-305423-1, or at unique concentrations in DP-305423-1, all off-target changes to gene expression in DP-305423-1, and the potential for the novel molecules (or molecules at novel concentrations), and possible derivatives that may be made in human cells, to cause effects on human cells. Moreover, that information should be informed by appropriate high throughput sequencing methodologies. 12. FSANZ should indicate how they or the Developer will monitor ongoing nucleotide-level changes in the transgene and subsequent changes to the off-target effects of the dsRNA. In the absence of such monitoring, approval should be conditional and limited to a period of no more than three years. 13. FSANZ should restrict its evaluation of compositional differences to those of significance between the proper, isogenic and conventional comparator grown under identical conditions and at the same time as DP-305423-1, in multiple environments and over several years, and not “water down” their significance by including uncontrolled comparisons. FSANZ should consider the risks of the whole food rather than each significant difference in isolation. 14. FSANZ should require data from proper immunostimulation and allergenicity testing of DP-305423-1 including tests from diet and inhalation exposures. (Comparisons using immune sera from subjects sensitised to conventional soy are not capable of detecting immune responses unique to DP-305423-1.) 15. FSANZ should request information from the Applicant on the effects of DP-305423-1 inhalation in animals that are used as models of acute respiratory syndrome, compared with inhalation of the proper conventional comparator. This should include an analysis of allergenicity and toxicity.

Submitter	Option	Comments
Centre for Integrated Research in Biosafety (Part 2)		<ul style="list-style-type: none"> • The submitter outlined 13 recommendations as follows: <ol style="list-style-type: none"> 1. FSANZ should require the Applicant to submit all safety studies using the appropriate, closely related non-GM parent 'Jack' as comparator with the <i>most closely related GM test variety</i>. 2. FSANZ should require the Applicant to submit all safety data using material from the 'T series' plants (progeny derived by selfing of the original transformed plant) as test material rather than the 'BC1F series' which are too distantly related to a conventional parent for proper comparisons to be made. 3. FSANZ should require the Applicant to provide full genotypes and breeding histories of the 'elite cultivars' used in crosses and backcrosses with T plants, which were then used as test material in several studies. 4. We recommend that FSANZ incorporate the South America field data into the Assessment Report. 5. FSANZ should require the Applicant to provide experimental data demonstrating that each statistically significant difference between soybean DP-305423-1 and 'Jack' in the analysis of key components and in respect to the broad range of values obtained for GM-HRA expression in different environments raises no safety concerns. 6. FSANZ should require the Applicant to submit data on the potential immunostimulatory effects of potential novel peptides that could be produced from the two identified new open reading frames. These data should comply with FAO/WHO guidelines. 7. FSANZ should require the Applicant to demonstrate that the two identified new ORFs are indeed not expressed to a specified level of expression or, if expressed, create no new safety risk. 8. FSANZ should require the Applicant to describe the experiments and the limits of detection in which potential unintended effects resulting from the disruption of endogenous genes were identified. 9. FSANZ should require the Applicant to submit data to verify the absence of additional new ORFs arising by the insertion of the rDNA within or outside the four insertion loci. 10. FSANZ should require the Applicant to demonstrate that the transformation process did not result in changes to expression or sequence of endogenous genes surrounding the four insertions. 11. FSANZ should require the Applicant to submit proof that no peptides are translated from any species of RNA that arises from transcription over the transgenic <i>gm-fad2-1</i> gene. 12. FSANZ should confirm that the source of GM-HRA used to produce the anti-HRA antiserum used in several assays originated from seeds of DP-305423-1. If this cannot be established, FSANZ should require the Applicant to resubmit data using an appropriate antiserum. 13. FSANZ should require the Applicant to perform the relevant experiments to confirm that there are no unprocessed or partly processed isoforms of GM-HRA in cells. If that assurance is not possible, FSANZ should require the Applicant to verify that these isoforms raise no safety concerns
Queensland Health (whole of Queensland government response)	-	<ul style="list-style-type: none"> • Does not object to the application. • Expresses concern that the level of data available to underpin the assumptions for the Dietary Intake Assessment may not be sufficient. • Asks whether any independent, long-term studies (i.e. in addition to studies submitted by the Applicant) are available for consideration in the Safety Assessment Report. • Asks whether the availability of PLENISH™ high oleic acid soybean oil for residential/household use would alter the outcome of the Dietary Intake Assessment. • Requests that more (quantitative) detail be provided in the Benefit Cost Analysis to support the conclusion reached.