

**3-07**  
**23 May 2007**

## **FIRST REVIEW REPORT**

### **APPLICATION A549**

### **FOOD DERIVED FROM HIGH LYSINE CORN LY038**

For information on matters relating to this Assessment Report or the assessment process generally, please refer to <http://www.foodstandards.gov.au/standardsdevelopment/>

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## **1. Introduction**

On 12 February 2007, the Ministerial Council requested a first Review of Application A549, which seeks approval of food derived from high lysine corn line LY038. Approval of this Application involves a variation to Standard 1.5.2 – Food produced using Gene Technology, of the *Australia New Zealand Food Standards Code* (the Code).

Following a request for a formal review, FSANZ has three months to prepare a response, in this instance, FSANZ is required to review the decision by 12 May 2007.

## **2. Objectives of Review**

The objective of this Review is to reconsider the draft variation to Standard 1.5.2 in light of the Ministerial Council's concerns as outlined in Section 3.

## **3. Grounds for the review requested by the Ministerial Council**

A First Review was requested on the grounds that approval of the Application:

- does not protect public health and safety; and
- does not promote consistency between domestic and international food standards where these are at variance.

The Ministerial Council provided additional information concerning the grounds on which the request for First Review is based, which have been summarised by FSANZ as follows:

- the safety assessment of LY038 was based on comparison with a negative segregant corn line, LY038(-), which is not considered to be an appropriate comparator as it is a product of gene technology and has no history of safe use as a food;
- the FSANZ Guidelines for the Safety Assessment of Genetically Modified Foods are not clear on the selection or use of an appropriate comparator to serve as a conventional counterpart food and ought to be revised to elaborate on this, taking into consideration the Codex Guideline for the Conduct of Food Safety Assessment of Food Derived from Recombinant-DNA Plants (CAC/GL 45-2003).

## **4. Background**

An Application was received from Monsanto Australia Limited to amend the Code to approve food derived from a genetically modified (GM) high lysine corn, corn line LY038. Standard 1.5.2 – Food produced using Gene Technology, requires that GM foods undergo a pre-market safety assessment before they may be sold in Australia and New Zealand.

Corn line LY038 has been genetically modified to have higher than usual levels of the amino acid lysine. It contains the *cordapA* gene from *Corynebacterium glutamicum*, which results in the accumulation of lysine in the corn grain. Corn line LY038 is intended specifically for animal feed, however it is possible it may also enter the human food supply. For this reason FSANZ has conducted a safety assessment on food derived from high lysine corn LY038.

High lysine corn LY038 is intended strictly for use as field corn for animal feed. Identity preservation methods will be used to segregate the product from other commercial corn grain and it will not be used in conventional breeding programs for other types of maize such as sweet corn, used predominantly as human food. Given the nature of the genetic modification, FSANZ considers there would be no sound agronomic reasons to use high lysine corn in significant amounts in grain destined for human consumption. FSANZ has assessed high lysine corn as if it was intended for human consumption because of the possibility that it could enter the food supply inadvertently, through co-mingling of commercial grains. This is consistent with the policy adopted by FSANZ following the Starlink corn incident.

FSANZ completed a comprehensive pre-market safety assessment of food derived from corn line LY038 as required under Standard 1.5.2 of the Code. The assessment included consideration of: (i) the genetic modification to the plant; (ii) the potential toxicity and allergenicity of any new proteins; and (iii) the composition and nutritional adequacy of the food, including whether there had been any unintended changes. The potential nutritional impact of increased lysine was also assessed.

FSANZ received a comprehensive package of information on high lysine corn and is satisfied that the level of evidence provided by the Applicant is sufficient to demonstrate the safety of the food. The conclusion at Final Assessment was that, on the basis of all the available evidence, food derived from corn line LY038 is as safe as food derived from other corn varieties.

Food from corn line LY038 may enter Australia and New Zealand in imported products.

## **5. Conclusions from the Final Assessment Report**

The Executive Summary and Statement of Reasons for this Application, which was approved by the FSANZ Board in December 2006, are in this report at **Attachment 2**.

The Board agreed to the recommendation at Final Assessment to approve food from high lysine corn line LY038 in view of the findings of the safety assessment report that food derived from high lysine corn is as safe and wholesome as food derived from other corn varieties.

## **6. Issues addressed in First Review**

### **6.1 Use of the negative segregant corn line LY038(-) as a comparator in the safety assessment of high lysine corn line LY038.**

FSANZ has reviewed the suggestion of the Ministerial Council that the Applicant be required to undertake additional comparative studies using a comparator or comparators that clearly satisfy current, relevant definitions, prior to any decision to approve LY038.

FSANZ restates the position taken at Draft and Final Assessment, that LY038(-) is an appropriate comparator for LY038. FSANZ did not rely on comparison with the negative segregant in order to make a judgement about safety of food derived from high lysine corn line LY038. Rather, the negative segregant was used to aid in the identification of any differences, which were then further evaluated by comparison with conventional corn varieties with a history of safe use.

This approach is consistent with both the FSANZ and Codex guidelines (CAC/GL45-2003), and in keeping with the principle that the safety of food derived from GM plants is assessed relative to a conventional counterpart having a history of safety use.

FSANZ does not support the suggestion that the Applicant be required to undertake additional comparative studies with additional comparator corn varieties. The FSANZ guidelines state that the comparator used to detect unintended effects on composition should ideally be the near isogenic parental line grown under identical conditions. Where this is not feasible, a line as close as possible should be chosen.

In the case of LY038, a series of conventional breeding steps have occurred between the original transformed H99 cells and LY038, so that H99 is no longer considered the most appropriate comparator as it is not a near isogenic line. LY038 and LY038(-) have the same parental plant and are therefore more closely related to each other than to the distant parental line H99. Therefore, from a scientific perspective, LY038(-) is in fact the only closely related line that could have been used for the purpose of identifying unintended effects. As the Ministerial Council acknowledges, the closer the comparator is in genetic background to LY038, the more sensitive the comparison will be in detecting unintended effects directly related to the introduced novel traits.

The purpose of a safety assessment is to identify new or altered hazards relative to a conventional counterpart having a history of safe use. If a new or altered hazard is indeed identified, then the risk associated with it should be characterised to determine its relevance to human health. This is typically done using a two-step process, with a number of different comparators being used. For the compositional analysis, it is important to use a line as closely related as possible to the modified line. Where differences are identified, comparison to conventional plant varieties already in the food supply (and with a history of safe use) is used to determine if those differences lie outside normal biological variation, and therefore whether they may raise nutritional or other safety concerns.

The process used for LY038 adhered to this approach and is entirely consistent with both the Codex and FSANZ guidelines. In addition to the negative segregant, a number of conventional corn varieties, with a history of safety use, were also used as comparators in both the molecular characterisation and the compositional analysis. This comparison was described at Draft and Final Assessment, and allowed the conclusion to be drawn that other than the intended increase in lysine, LY038 is not significantly different from conventional corn varieties. Additional comparators (e.g. conventional foods with similar high levels of lysine) were then subsequently used to further assess the increased lysine levels.

This approach is supported by the independent scientists who have reviewed the FSANZ safety assessment of high lysine corn, and is also consistent with decisions taken by other regulatory agencies, most notably Health Canada, which also concluded LY038 (-) to be an appropriate comparator.

## **6.2 Lack of clarity and inconsistency of definitions between FSANZ Guidelines and Codex Guidelines**

FSANZ assesses the safety of GM foods in accordance with the Codex General Principles for the Risk Analysis of Foods Derived from Biotechnology developed by the Codex *Ad Hoc* Inter-Governmental Task Force on Foods Derived from Biotechnology.

To assist in the consistent application of a safety assessment framework for GM foods, FSANZ developed the *Guidelines for the Safety Assessment of Genetically Modified Foods*<sup>1</sup>, which rely heavily on the work of the Codex *Ad Hoc* Inter-Governmental Task Force on Foods Derived from Biotechnology, as well as previous OECD and FAO/WHO consultations on GM foods. The FSANZ safety assessment guidelines are broadly consistent with the Codex Guideline for the Conduct of Food Safety Assessment of Foods Derived from Recombinant-DNA Plants.

All FSANZ Guidelines are updated from time to time in line with international developments in the area of risk assessment. In addition to this *ad hoc* review of guidelines, FSANZ will complete a review of all application guidelines, including the Guidelines for the Safety Assessment of Genetically Modified Foods over the coming months, in line with proposed changes to the FSANZ Act and the subsequent development of the Application Handbook. The current version of the FSANZ guidelines was developed in 2001, prior to the finalisation and publication of the Codex Guidelines, and although individual sections have been updated more recently, it is timely to conduct a thorough review.

As part of the review of the guidelines, the current FSANZ approach to the safety assessment of new GM foods will be considered, as will any inconsistencies between the FSANZ GM Guidelines and the relevant Codex Guidelines.

The rationale for choice of comparator/s in GM foods has already received special emphasis as part of the revised Application Handbook and FSANZ will pay particular attention to this part of the safety assessment guidelines during their review. Specifically, FSANZ intends to re-draft this particular section of the guidelines to provide clearer guidance in relation to the selection and use of comparators, particularly where there is no closely related non-GM line, or where the modification is intended to significantly alter some compositional parameters.

## **7. Review Options**

There are three options proposed for consideration under this Review:

1. re-affirm approval of the draft variation to Standard 1.5.2 of the Code as notified to the Council; or
2. re-affirm approval of the draft variation to Standard 1.5.2 of the Code subject to any amendments FSANZ considers necessary; or
3. withdraw approval of the draft variation to Standard 1.5.2 of the Code as notified to the Council.

## **8. Decision**

FSANZ has considered the issues raised by the Ministerial Council in relation to Application A549 – Food derived from High Lysine Corn LY038.

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<sup>1</sup> Available at <http://www.foodstandards.gov.au/srcfiles/GM%20Guidelines%20Nov%2005.doc> (accessed 23 February 2007).

The First Review concludes that the preferred review option is Option 1. This re-affirms the approval for the use and sale of food derived from high lysine corn line LY038 according to the draft variation to Standard 1.5.2 of the Code, as detailed in **Attachment 1**.

The recommended option is Option 1.

#### **Decision**

**FSANZ re-affirms the approval of the draft variation to Standard 1.5.2 of the Code to give permit the sale of food derived from high lysine corn line LY038.**

### **9. Implementation and review**

The draft variation to Standard 1.5.2 of the Code will come into effect on the date of gazettal.

#### **Attachments**

1. Draft variation to the *Australia New Zealand Food Standards Code*.
2. Executive Summary and Statement of Reasons from the Final Assessment Report

**DRAFT VARIATION TO THE AUSTRALIA NEW ZEALAND FOOD STANDARDS  
CODE**

**To commence: on gazettal**

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

Food derived from high lysine corn line LY038	Unless the protein content has been removed as part of a refining process, the label on or attached to a package of a food derived from high lysine corn line LY038 must include a statement to the effect that the food has been genetically modified to contain increased levels of lysine.
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### **Executive Summary and Statement of Reasons from the Final Assessment Report**

An Application has been received from Monsanto Australia Limited to amend the *Australia New Zealand Food Standards Code* (the Code) to approve food derived from a genetically modified (GM) high lysine corn, corn line LY038. Standard 1.5.2 – Food produced using Gene Technology, requires that GM foods undergo a pre-market safety assessment before they may be sold in Australia and New Zealand.

Corn line LY038 has been genetically modified to have higher than usual levels of the amino acid lysine. It contains the *cordapA* gene from *Corynebacterium glutamicum*, which results in the accumulation of lysine in the corn grain. Corn line LY038 is intended specifically for animal feed, however it is possible it may also enter the human food supply. For this reason FSANZ has conducted a safety assessment on food derived from high lysine corn LY038.

Food from corn line LY038 may enter Australia and New Zealand as imported products.

#### **Safety assessment**

FSANZ has completed a comprehensive pre-market safety assessment of food derived from corn line LY038 as required under Standard 1.5.2 of the Code. The assessment included consideration of: (i) the genetic modification to the plant; (ii) the potential toxicity and allergenicity of any new proteins; and (iii) the composition and nutritional adequacy of the food, including whether there had been any unintended changes. The potential impact of increased lysine was also assessed.

Although corn line LY038 is primarily intended for use as animal feed, the safety assessment conducted by FSANZ assumed the GM corn was intended for human food use and therefore was no different to the rigorous scientific assessment for any GM food.

No potential public health and safety concerns were identified and on the basis of all the available evidence, including detailed studies provided by the Applicant, it has been concluded that food derived from corn line LY038 is as safe and wholesome as food derived from other corn varieties.

#### **Labelling**

Food derived from corn line LY038 will be required to be labelled as genetically modified where novel DNA and/or protein are present in the final food. In addition to this, foods containing LY038 that have not been refined to remove the protein component (and hence lysine) will be required to be labelled with a statement informing consumers of the altered nutritional profile, that is, it contains increased lysine compared to other corn varieties.

Labelling addresses the requirement of section 10(1)(b) of the FSANZ Act; provision of adequate information relating to food to enable consumers to make informed choices.

## **Impact of regulatory options**

Two regulatory options were considered in the assessment: either (1) no approval; or (2) approval of food derived from corn line LY038 based on the conclusions of the safety assessment.

Following a cost and benefit analysis of the potential impact of each of the options on the affected parties (consumers, the food industry and government), Option 2 is the preferred option as food from LY038 has been found to be as safe as food from other varieties of corn.

## **Consultation**

A total of 214 submissions were received in response to the invitation to comment on the Initial and Draft Assessment Reports (200 on the Initial Assessment and 14 on the Draft Assessment). Issues raised in these submissions were considered in the Final Assessment.

A particularly significant submission was received in response to the Draft Assessment Report from the Centre for Integrated Research in Biosafety (INBI). This submission asserted that the assessment of high lysine corn has been inadequate, and raises a number of scientific points that in INBI's view should be considered in the assessment. FSANZ carefully considered each point raised and reiterates the conclusion of the safety assessment report that food derived from LY038 corn is as safe as foods from other varieties of corn.

External review was sought on the safety assessment report following the Draft Assessment. As this Application involves a novel gene and protein that FSANZ has not assessed before, it is standard practice for FSANZ to seek the opinion of external scientific experts. In general, the reviewers agreed with the conclusions of the safety assessment of LY038. Specific comments have been addressed in the safety assessment report or in this report.

## **FSANZ Decision**

**FSANZ agrees to amend Standard 1.5.2 of the Code to approve the sale and use of food derived from corn line LY038 in Australia and New Zealand.**

## **Statement of Reasons**

An amendment to Standard 1.5.2 of the Code to give approval to the sale and use of food derived from corn line LY038 in Australia and New Zealand is agreed 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 corn line LY038;
- in terms of its safety for human consumption and nutritional adequacy, food derived from corn line LY038 is equivalent to food from other commercially available corn varieties. The only difference is the increase in lysine;
- labelling of certain food fractions derived from corn line LY038 will be required if novel DNA, novel protein and/or increased levels of lysine, are present in the final food;

- a regulation impact assessment process has been undertaken that also fulfils the requirement in New Zealand for an assessment of compliance costs. The assessment concluded that the amendment to the Code is of net benefit to both food producers and consumers; and
- the proposed draft variation to Standard 1.5.2 of the Code is consistent with the section 10 objectives of the FSANZ Act and the regulatory impact assessment.

The variation will come into effect on the date of gazettal.