FINAL RISK ANALYSIS REPORT

APPLICATION A373

Pectinesterase as a processing aid

Note: This report is the "Inquiry" as referred to in Section 16 of the *Australia New Zealand Food Authority Act (1991)* and sets out the reasons for making a recommendation to the Australia New Zealand Food Standards Council under Section 18 of the Act.

EXECUTIVE SUMMARY

- No changes to the Full Assessment or Regulatory Impact Statement are proposed. The Inquiry Report includes drafting for the joint Australia New Zealand Food Standards Code.

- The approval of the use of pectinesterase from a new source organism is technologically justified and poses no additional risk to public health and safety.

- The draft variation should come into force on gazettal.

Executive Summary from the Full Assessment Report

- The Australia New Zealand Food Authority (ANZFA) received an application on 1 March 1999, from Novo Nordisk for the approval of the enzyme, pectinesterase (EC 3.1.1.11), for use as a processing aid for fruit and vegetable processing. The variation would constitute an addition of an enzyme obtained from a genetically modified strain of *Aspergillus oryzae*, carrying the gene coding for pectinesterase isolated from *Aspergillus aculeatus*. The commercial name for the enzyme product is Rheozyme.

- Eleven submissions were received in response to the section 14 gazette notice. Four submitters supported the application. The Office of Regulation Review submitted comments pertaining to the Regulatory Impact Assessment. One submitter did not express any support or objection. Four submitters did not support the use of an enzyme derived from a genetically modified source organism, and on this basis did not support the application.

- The main issues raised by submissions were the labelling of processing aids obtained from genetically modified organisms (GMOs); and, the importance of safety assessment for the new organism and the enzyme product.

- The scientific evaluations concluded that the use of pectinesterase, produced by *Aspergillus oryzae,* from a pectinesterase gene isolated from *Aspergillus aculeatus,* is technologically justified and poses no additional risk to public health and safety. No significant concerns were raised in the public comment regarding the actual use or approval of the processing aid. Concerns were raised in regard to approval of foods produced from GMOs. ANZFA's section 10 objectives are not compromised by the proposed change to Standard A16. It is recommended that the draft variation should come into effect on the date of gazettal.

- The Regulatory Impact Statement concluded that the amendment to Standard A16 of the *Food Standards Code* to permit pectinesterase from the new source organism *Aspergillus oryzae* carrying the donor gene from *Aspergillus aculeatus,* is necessary, cost effective and of benefit to both producers and consumers.

- A consequential amendment to Standard 1.3.3 - Processing Aids, in the joint Australia New Zealand Food Standards Code will be required to include the enzyme in the joint Code.

Previous Authority consideration

- The Authority undertook a Full Assessment of A373 in November 2000. A call for public submissions for the purpose of Inquiry was gazetted on 8 November 2000 and submissions closed on 20 December 2000.

ISSUES RAISED IN PUBLIC SUBMISSIONS AT INQUIRY

Four submissions were received at Inquiry from the New Zealand Ministry of Health, Australian Food and Grocery Council, Food Technology Association of Victoria Inc and the National Council of Women of Australia (NCWA).

Submitter	Position	Comments
National Council for Women of Australia	Opposes	• Decisions should err on the side of Public health and safety, not on innovation for industry or trade matters. • Codex Inventory of processing aids is not intended to be a complete or positive list of processing aids. • Supports maintaining the status quo i.e. do not provide permission. • Concerned with labelling of genetically engineered foods. NCWA refer to genetically engineered tryptophan. Concerned with toxicology of gm food. The NWCA refer concerns on the number of "aberrations" noted in the 13 week toxicity study in rats. • The NWCA are concerned that foods had not been subjected to long term testing. • Enzyme approval will be an additional cost to consumers
Australian Food and Grocery Council	Supports	• Support ANZFA assessment that the use of enzyme poses no additional risk to public health and safety and that its use is technologically justified. • Labelling of GMO products including processing aids has been decided as a separate issue to this Application and is subject to Standard A18- Food Produced Using Gene Technology. The proposed drafting will need to be amended to Standard 1.3.1.

Submitter	Position	Comments
Food Technology Association of Victoria Inc	Supports without further comment	Accepts the application
New Zealand Ministry of Health		• Need to explain the benefits of the new source organism for pectinesterase. • There does not seem to be a suitable Food Chemicals Codex specification for the enzyme. A specific specification for Pectinesterase [EC 3.1.1.11]. source *A. niger*.

ASSESSMENT OF ISSUES RAISED IN PUBLIC SUBMISSIONS AT INQUIRY

Genetically engineered tryptophan

NCWA refer to genetically engineered tryptophan.

Response

In 1989, more than 1500 people, mainly in the United States, were afflicted with the disease eosinophilia myalgia syndrome. The disease resulted in at least thirty-seven deaths and was linked to the consumption of an L-tryptophan dietary supplement manufactured by a Japanese company that had introduced genetically modified bacteria into their production system.

The tryptophan case is frequently cited as evidence that genetically modified foods may be potentially hazardous. However, these arguments are false and misleading as the specific batches of the dietary supplement implicated could not be linked in the ensuing investigation to the use of genetically modified bacteria in the production process.

At the time of the outbreak of the disease, it was acknowledged that significant manufacturing changes had occurred in the production of batches of tryptophan by the Japanese company, including reduction of a particular purification step.

The investigations which took place after the outbreak of the disease clearly showed that the occurrence of the disease resulted from impurities in the tryptophan preparation. The occurrence of the contaminant does not arise from the use of genetically modified bacteria but appeared during the subsequent purification steps.

The same impurities have been detected at low levels in commercial preparations of tryptophan sold in health and nutrition stores, even in brands derived from seed extracts which have been described as natural source extracts. In light of the available evidence, there is no justification for relating these events to gene technology.

13 week toxicity study

The NWCA refer concerns on the number of "aberrations" noted in the 13 week toxicity study in rats.

Response

Firstly it should be pointed out that it was necessary in the opinion of the scientists conducting the experiments to kill several of the animals ahead of scheduled sacrifice – one control, one at 1 mg/kg/day and three at 5 mg/kg/day. The reason was that blood sampling from the orbital sinus of the eye had caused irreparable damage to the eyes of these animals and the animals had to be killed for ethical reasons. It is standard practice in animal research to end an experiment where the protocol has caused pain and suffering to the animals. The effect on the eyes of the animals was not due to treatment with the pectinesterase, since there were no symptoms produced when the enzyme was administered. The eye damage was clearly associated with the blood sampling technique.

In relation to the other so-called "aberrations" mentioned by NCWA, the small number of effects that were noted in some animals was not attributed to the pectinesterase because these occurred randomly across all groups, that is, they also occurred in animals that had not been dosed with any of the enzyme. Some effects that were noted in the test groups were not consistent across the animals in the group. Since the deaths and adverse effects were not concluded to be a result of the administration of pectinesterase, no additional studies were considered necessary.

Long term/chronic toxicity studies

The NWCA are concerned that foods had not been subjected to long term testing.

Response

The safety of pectinesterase from the source organism Aspergillus oryzae was assessed against several criteria, including:

- The safety of the host organism and the source organism; and
- The presence of contaminants in the enzyme preparation.

If good manufacturing practice is followed, contamination can only come from the enzyme source organism itself. If the source organism is non-toxic and non-pathogenic, then it is likely that an enzyme preparation obtained from that source will be safe for use in food processing.

The non GM source of this enzyme is already permitted in the *Food Standards Code*. Data supporting the safety of pectinesterase (short-term toxicity study and mutagenicity study) from the GM source were provided by the applicant in their submission.

The extent of toxicological testing of substances added to food is considered on a case-by-case basis and depends on a number of factors such as the nature of the substance, the likely route of metabolism and the potential for human exposure. Food enzymes are considered inherently non-toxic since they are inactivated and hydrolysed during digestion of the food. Toxicity studies are conducted on enzyme preparations largely to examine the potential toxicity of possible contaminants. For this purpose, mutagenicity tests and a short-term toxicity study are normally considered adequate. Long-term toxicity studies are not normally required for enzymes whether they are from a genetically-modified source or non-genetically modified source.

Labelling of Genetically Modified Food

Response

Labelling of Genetically Modified Food including processing aids has been decided as a separate issue to this Application and is subject to Standard A18- Food Produced Using Gene Technology and Standard 1.5.2 Food Produced Using Gene Technology.

The labelling of genetically modified food has been the subject of much recent discussion. Contrary to the claim made by NCWA, ANZFA is not violating its "Objective" to provide consumers the information they require to make informed choices about the food they eat. On 28 July 2000 Health Ministers approved a standard for GM labelling. The standard is considered by the Ministerial council and most stakeholders to be a satisfactory compromise between consumers desire for full labelling and the necessity to avoid undue impost on industry. In doing so, Health Ministers have publicly stated that labelling of genetically modified food is about consumers making informed choices about the food they eat and is not a safety issue – safety is addressed at world best practice level through the safety assessment work of ANZFA. ANZFA has been given the responsibility by the Ministerial Council to establish appropriate processes to ensure the smooth transition of the new standard for GM food labelling. The new standard will come into effect on 7 December 2001, twelve months after gazettal. A guideline for compliance with the amended standard on genetically modified food labelling was released for public consultation on 7 December in conjunction with gazettal of the standard. This consultation period is due to end on 26 February 2001.

Division 1 of Standard A18 addresses health and safety requirements, regulating the sale of foods produced using gene technology. Additives and processing aids produced using gene technology are not regulated in Division 1 of this Standard. Other Standards in the *Food Standards Code* regulate health and safety requirements of additives and processing aids and require pre-market approval for these substances. Division 2 of Standard A18 specifies labelling and other information requirements for foods, including food additives and processing aids, produced using gene technology.

The new food standard will require the labelling of food and food ingredients where novel DNA and/or protein is present in the final food and has altered characteristics.

Exempt from these requirements are:

- highly refined food, where the effect of the refining process is to remove novel genetic material and/or protein;

- processing aids and food additives, except where novel genetic material and/or protein is present in the final food;
- flavours which are present in a concentration less than or equal to 0.1 per cent in the final food; and
- food prepared at point of sale (e.g. restaurants, takeaways).

The new standard allows an ingredient to contain up to 1 per cent of unintended presence of genetically modified product.

- **Benefits of the new source organism**

New Zealand Ministry of Health queried the benefits of the new source organism for this enzyme.

Response

The benefits of the enzyme produced from a new source organism require assessment rather than the source organism. The benefits of the enzyme include improved specificity and efficacy. As stated in the full assessment report, the possibility to clone and express selected enzymes has facilitated a shift from enzyme mixtures towards utilisation of mono-component enzymes or of specifically boosted enzyme complexes. Pectinesterase is an example of such a mono-component enzyme, substantially free from interfering depolymerising activities such as polygalacturonases.

The enzyme may either be used as an efficient booster in combination with traditional multi-component pectinase products for clarification of fruit juice or wine, or alone with the aim of modifying the viscosity of fruit and vegetable based products, thus eliminating the need for adding exogenous pectin or other thickeners.

- **Specification**

An issue was raised by New Zealand Ministry of Health about the suitability of the enzyme specification.

Response

Historically, enzymes used in food processing have been found to be non-toxic, and the main toxicological consideration is in relation to possible contaminants. The production organism in this case is non-toxic and non-pathogenic and, as long as good manufacturing practice is followed, the enzyme produced should be safe.

The enzyme complies with the recommended purity specifications for food grade enzymes issued by the Joint FAO/WHO Expert Committee on Food Additives (JECFA) and the Food Chemicals Codex (FCC, 1996). The general issue of enzyme specification suitability is not specific to this application and will be considered internationally by JECFA.

Cost to consumer

The issue of an additional cost being imposed on the consumer if the enzyme was approved, was raised by National Council for Women of Australia.

Response

Insufficient information to support this claim was provided in the submission. It appears that the any additional cost may relate to the use of genetically modified organisms in general and is not specific to this application.

CHANGES TO FULL ASSESSMENT/RIS RESULTING FROM INQUIRY

No changes to the full assessment or Regulatory Impact Statement are proposed. The Inquiry Report includes drafting for the joint Australia New Zealand Food Standards Code.

CONCLUSIONS

The approval of the use of pectinesterase from a new source organism is technologically justified and poses no additional risk to public health and safety.

The draft variation should come into force on gazettal.

Attachments:

1. Proposed Draft Variations
2. Statement of Reasons

ATTACHMENT 1

DRAFT VARIATIONS VOLUME 1 AND VOLUME 2
OF THE *FOOD STANDARDS CODE*

To commence: On gazettal

The *Food Standards Code* is varied by -

[1] *inserting in columns 1 and 2 respectively of the Table in the Schedule in Standard A11 of Volume 1, after the entry for* Pectinesterase (Aspergillus niger) -

Pectinesterase	FCC p107 (enzyme preparations)

[2] *inserting in columns 1 and 2 respectively of the Table IV, Group III of the Schedule in Standard A16 of Volume 1, after the entry for* Pectinase multicomponent enzyme

Pectinesterase [EC 3.1.1.11]	*Aspergillus oryzae*[13]

[3] *inserting in the footnotes to Table IV, Group III of the Schedule in Standard A16 of Volume 1, after footnote 12 –*

[13] Pectinesterase may be produced from a genetically manipulated strain of *Aspergillus oryzae* containing the gene for pectinesterase isolated from *Aspergillus aculeatus*.

[4] *omitting the entry for* pectin methylesterase or Pectinesterase [3.1.1.11] *in the Table to clause 17 in Standard 1.3.3 of Volume 2 and the corresponding entry in the column headed* Source *and substituting –*

Pectin methylesterase or Pectinesterase [EC 3.1.1.11]	*Aspergillus niger* *Aspergillus oryzae* containing the gene for pectinesterase isolated from *Aspergillus aculeatus*

ATTACHMENT 2

STATEMENT OF REASONS

APPLICATION A373 - FOR RECOMMENDING A VARIATION TO MAKE AN AMENDMENT TO VOLUMES 1 AND 2 OF THE *FOOD STANDARDS CODE* TO PERMIT PECTINESTERASE FROM A NEW SOURCE ORGANISM.

The new source organism is *Aspergillus oryzae* carrying the donor gene from *Aspergillus aculeatus,* is necessary, cost effective and of benefit to both producers and consumers.

The Australia New Zealand Food Authority has before it application A373 received on 1 March 1999, from Novo Nordisk for approval of the enzyme, pectinesterase (EC 3.1.1.11), for use as a processing aid during fruit and vegetable processing, when produced in *Aspergillus oryzae* from a pectinesterase gene isolated from *Aspergillus aculeatus*. The commercial name for the enzyme product is Rheozyme. ANZFA has completed an inquiry of the application and has prepared draft variations to Volumes 1 and 2 of the *Food Standards Code*.

ANZFA recommends the adoption of the draft variation for the following reasons:

The scientific evaluations have concluded that the use of pectinesterase produced in *Aspergillus oryzae,* from a pectinesterase gene isolated from *Aspergillus aculeatus,* is technologically justified and poses no additional risk to public health and safety. No significant concerns were raised in the public comment regarding the actual use or approval of the processing aid. None of the ANZFA's section 10 objectives are compromised by the proposed changes.

It is recommended that the draft variation should come into effect on the date of gazettal.

REGULATION IMPACT

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

WORLD TRADE ORGANIZATION (WTO) NOTIFICATION

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

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

This matter was not notified to the WTO because the proposed variations to the Code constitutes a minor change to the Code and is not expected to impact on trade issues for either technical or sanitary or phytosanitary reasons.