



**14 August 2018**  
**[56–18]**

Approval report – Application A1146

Thermolysin (protease) as a processing aid (enzyme)

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Food Standards Australia New Zealand (FSANZ) has assessed an application made by Amano Enzyme Inc., to permit the use of thermolysin from *Anoxybacillus caldiproteolyticus* strain TP-7 as a processing aid in the manufacture or processing of foods such as dairy, egg, meat, fish, yeast, protein products and flavourings.

On 12 April, FSANZ sought submissions on a draft variation and published an associated report. FSANZ received three submissions.

FSANZ approved the draft variation on 8 August 2018. The Australia and New Zealand Ministerial Forum on Food Regulation was notified of FSANZ's decision on 13 August 2018.

This report is provided pursuant to paragraph 33(1)(b) of the *Food Standards Australia New Zealand Act 1991* (the FSANZ Act).

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## Table of contents

<b>EXECUTIVE SUMMARY</b> .....	<b>3</b>
<b>1 INTRODUCTION</b> .....	<b>4</b>
1.1 THE APPLICANT.....	4
1.2 THE APPLICATION.....	4
1.3 THE CURRENT STANDARD.....	4
1.4 REASONS FOR ACCEPTING APPLICATION.....	4
1.5 PROCEDURE FOR ASSESSMENT .....	4
1.6 DECISION .....	5
<b>2 SUMMARY OF THE FINDINGS</b> .....	<b>5</b>
2.1 SUMMARY OF ISSUES RAISED IN SUBMISSIONS .....	5
2.2 RISK ASSESSMENT .....	6
2.3 RISK MANAGEMENT .....	6
2.3.1 <i>Levels of addition</i> .....	7
2.3.2 <i>Specifications</i> .....	7
2.3.3 <i>Labelling</i> .....	7
2.4 RISK COMMUNICATION.....	7
2.4.1 <i>Consultation</i> .....	7
2.5 FSANZ ACT ASSESSMENT REQUIREMENTS .....	8
2.5.1 <i>Section 29</i> .....	8
2.5.2 <i>Subsection 18(1)</i> .....	9
2.5.3 <i>Subsection 18(2) considerations</i> .....	9
<b>3 REFERENCES</b> .....	<b>10</b>
<b>ATTACHMENTS</b> .....	<b>10</b>
ATTACHMENT A – APPROVED DRAFT VARIATION TO THE AUSTRALIA NEW ZEALAND FOOD STANDARDS CODE.....	11
ATTACHMENT B – EXPLANATORY STATEMENT .....	13

### Supporting document 1

The [following documents](#) which informed the assessment of this application are available on the FSANZ website:

SD1 Risk and technical assessment

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## Executive summary

Amano Enzyme Inc. (Amano), applied to amend Schedule 18 of the Australia New Zealand Food Standards Code (the Code) to permit the use of a new enzyme, thermolysin (EC 3.4.24.27), sourced from *Anoxybacillus caldiproteolyticus* strain TP-7, as a processing aid.

The enzyme will be used to manufacture and process foods such as dairy, egg, meat, fish, yeast, protein products and flavourings. Thermolysin converts proteins and peptides in various foods, resulting in the improvement of functional properties (foaming ability, emulsifying ability, heat stability and viscosity) and organoleptic properties (taste and flavour).

Based on toxicological data, FSANZ concluded that in the absence of any identifiable hazard to the general population, an Acceptable Daily Intake (ADI) 'not specified' was appropriate, negating the need for a dietary exposure assessment.

FSANZ has determined that tuna protein from the culture medium may be present in thermolysin-treated foods at low levels. As there is no established threshold for allergenic responses to fish proteins, dietary exposure to even low amounts of tuna protein is potentially hazardous to individuals with an allergy to that food. On this basis, labelling is required to protect consumers with fish allergies. Where fish is present in a food for sale, including when present as a processing aid or an ingredient or component of a processing aid, it is required to be declared under section 1.2.3—4 of Standard 1.2.3.

FSANZ concluded that using thermolysin as a processing aid as specified in the application is technologically justified and that it performs a technological purpose during the manufacture and/or processing of food only. Therefore, it is appropriately categorised as a processing aid rather than a food additive.

Thermolysin also complies with the internationally accepted Joint Expert Committee on Food Additives (JECFA) specifications for chemical and microbiological purity. Enzymes used to produce and manufacture food are considered processing aids. Permitted processing aids are listed in Standard 1.3.3 and Schedule 18 of the Code.

FSANZ has therefore prepared a draft variation to the table to subsection S18—9(3) in Schedule 18 of the Code to permit the use of thermolysin as a processing aid for a specific technological purpose in certain foods, at a maximum permitted level in accordance with GMP.

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# 1 Introduction

## 1.1 The applicant

The applicant is Amano Enzyme Inc. (Amano), who produce specialty enzymes for use by the food industry, in the production of pharmaceuticals and in diagnostic medicines.

## 1.2 The application

The applicant requested an amendment Schedule 18 of the Australia New Zealand Food Standards Code (the Code) to permit the use of a new enzyme, thermolysin (protease - EC 3.4.24.27) sourced from *Anoxybacillus caldiproteolyticus* (*A. caldiproteolyticus*) as a processing aid. The processing aid is intended for use in the manufacture and/or processing of dairy, egg, meat, fish, yeast, protein products and in the flavouring production industry.

Thermolysin converts the substrate proteins and peptides in various proteinaceous foods, resulting in the improvement of functional properties (foaming ability, emulsifying ability, heat stability, viscosity) and organoleptic properties (taste and flavour).

## 1.3 The current standard

Enzymes used to process and manufacture food are considered processing aids as although they may be present in the final food, they are no longer providing a technological purpose in that final food.

Paragraph 1.1.1—10(6)(c) of the Code provides that a food for sale must not have, as an ingredient or a component, a substance that is used as a processing aid, unless expressly permitted.

Standard 1.3.3 and Schedule 18 of the Code list the permitted processing aids. Enzymes of microbial origin permitted to be used as processing aids are listed in the table to subsection S18—4(5) or in the table to subsection S18—9(3). The table to subsection S18—4(5) lists enzymes that may be used as a processing aid to perform *any* technological purpose. The table to subsection S18—9(3) lists those substances, including enzymes, that are only permitted to be used as processing aids for *specific* technological purposes.

There are no current permissions in Schedule 18 for thermolysin sourced from *A. caldiproteolyticus* strain TP-7.

## 1.4 Reasons for accepting application

The application was accepted for assessment because:

- it complied with the procedural requirements under subsection 22(2) of the FSANZ Act; and
- it related to a matter that warranted the variation of a food regulatory measure.

## 1.5 Procedure for assessment

The application was assessed under the general procedure.

## 1.6 Decision

The draft variation as proposed following assessment was approved without amendment.

Thermolysin (EC 3.4.24.27) produced by *A. caldiproteolyticus* strain TP-7 will be listed in the table to subsection S18—9(3), permitting its use for the specific technological purpose stated below with the condition that the amount used must be consistent with good manufacturing practice (GMP).

The specific technological purpose is to catalyse the hydrolysis of peptide bonds during the manufacture and/or processing of the following types of food: dairy, egg, meat, fish, protein, yeast and flavourings.

The approved draft variation is at Attachment A. The variation takes effect on the date of gazettal.

The related explanatory statement is at Attachment B, which is required to accompany an instrument that is lodged on the Federal Register of Legislation.

## 2 Summary of the findings

### 2.1 Summary of issues raised in submissions

FSANZ called for submissions on a proposed draft variation to Schedule 18 on 12 April 2018. Three submissions were received. The Victorian Departments of Health and Human Services, and Economic Development, Jobs, Transport and Resources and the Ministry for Primary Industries supported the application. The New Zealand Food and Grocery Council (NZFGC) supported the application, however noted the conservative position FSANZ took in relation to labelling for allergens. The issues raised by the NZFGC and FSANZ's responses are detailed in Table 1.

**Table 1: Summary of issues**

Issue	Raised by	FSANZ response
<p>NZFGC considered that FSANZ has taken a conservative approach to the possible presence of fish protein in the food for final sale and the consequent requirement for labelling. In particular, NZFGC highlighted that:</p> <ul style="list-style-type: none"> <li>- data supplied by Amano Enzymes Inc. showed that any residue from the fish used in the process to manufacture this enzyme (in the fermentation media) was below the limit of detection</li> <li>- that the heating of the enzyme most likely denatured any residual protein from the</li> </ul>	<p>New Zealand Food and Grocery Council</p>	<p>The applicant estimated that the use of thermolysin powder at 0.24% w/w would lead to a maximum of 7.2 mg fish extract/kg food ingredient.</p> <p>The statement in the Call for Submissions; "that fish must be declared where present in the final food" reflects the existing requirement in the Code. This requirement applies irrespective of the amount of the allergen present. FSANZ stated in its risk assessment that exposure to even low amounts of fish protein is potentially hazardous to individuals with an allergy to</p>

Issue	Raised by	FSANZ response
fish - when used in the very small amounts in the processing of foods in which it might be used there would be a very minuscule prospect of fish residue; and Noting there were no health and safety concerns identified by FSANZ.		that food. Requirements in the Code enable food suppliers to determine whether a declaration of fish is required for each individual food depending on the specific circumstances for that food. Therefore FSANZ did not consider it appropriate to state categorically whether food manufactured or processed using thermolysin would require labelling for the presence of fish.

## 2.2 Risk assessment

FSANZ conducted a risk assessment on the proposed use of the enzyme [see supporting document 1 (SD1)].

FSANZ concluded that thermolysin was not genotoxic *in vitro* or *in vivo* and did not cause adverse effects in a subchronic toxicity study in rats. In the absence of any identifiable hazard an acceptable daily intake (ADI) 'not specified' is appropriate for the general population. A dietary exposure assessment was therefore not required.

Tuna protein from the culture medium may be present in thermolysin-treated foods at low levels. There is no established threshold for allergenic responses to fish proteins. This means exposure to even low amounts of tuna protein in thermolysin-treated foods is potentially hazardous to individuals with an allergy to that food.

## 2.3 Risk management

The risk assessment concluded there were no public health and safety concerns associated with using this enzyme as intended for the general population although the potential for an allergic response to traces of fish protein in the final food was identified. The food technology assessment concluded that the enzyme met its stated technological purpose for use as a processing aid, rather than that of a food additive.

The main risk management options available to FSANZ were to approve or reject the request to amend the Code, imposing any appropriate conditions. Other risk management issues for this application were related to labelling, which are discussed below in section 2.3.3. The consideration of costs and benefits summarised in section 2.5.1.1 takes account of the safety of the enzyme preparation.

During the reaction between thermolysin and proteinaceous foods, low molecular weight peptides and some free amino acids are generated. These reactions help to improve taste and flavour but do not generate monosodium glutamate (MSG). Furthermore, Amano confirms that enzymes such as thermolysin from bacteria do not have peptidase activity and therefore rarely produce amino acids. FSANZ concluded that thermolysin does not increase the amount of free glutamates (including MSG) when used as a processing aid (see SD1, section 2.1).

Permission for the enzyme will be listed in subsection S18—9(3), limiting its technological purpose to catalysing the hydrolysis of peptide bonds during the manufacture and/or processing of the following types of food: dairy, egg, meat, fish, protein, yeast and flavouring.

### **2.3.1 Levels of addition**

In the absence of any public health or safety concerns identified in FSANZ's risk assessment, there was no reason to limit the levels of addition apart from the requirement to use in accordance with GMP.

### **2.3.2 Specifications**

The Codex Alimentarius does not establish standards for processing aids or for enzymes, however there are internationally recognised specifications for enzymes. These enzyme specifications are established by JECFA (2006) and the Food Chemicals Codex (2014).

Individual countries regulate the use of enzymes differently to the Code. The enzyme preparation has been approved for use in food production in France.

### **2.3.3 Labelling**

As a general rule, processing aids are exempt from the requirement to be declared in the statement of ingredients in accordance with paragraphs 1.2.4—3(2)(d) and (e) of Standard 1.2.4. In accordance with this exemption, thermolysin will not need to be declared in the statement of ingredients of foods manufactured or processed with this processing aid.

However the risk assessment concluded there may be a risk to individuals with an allergy to fish proteins from foods that have been manufactured or processed with thermolysin, as fish (tuna) products are used in the fermentation media and may be carried over into the final food albeit at trace levels. The Code requires the mandatory declaration of certain known allergens. Where fish is present in a food for sale, including when present as a processing aid or an ingredient or component of a processing aid, it is required to be declared under section 1.2.3—4 of Standard 1.2.3.

## **2.4 Risk communication**

### **2.4.1 Consultation**

Consultation is a key part of FSANZ's standards development process. Public submissions on a proposed draft variation to Schedule 18 were called on 12 April 2018 and closed on 24 May 2018.

The call for submissions was notified through a media release, Food Standards News and FSANZ's social media channels. Three submissions were received from various stakeholders and considered by the FSANZ Board. FSANZ noted that the NZFGC raised two issues and FSANZ has subsequently communicated directly with them.

FSANZ acknowledges the valuable contribution by these organisations to the rigour of our assessment of A1146.

## **2.5 FSANZ Act assessment requirements**

### **2.5.1 Section 29**

#### **2.5.1.1 Consideration of costs and benefits**

The Office of Best Practice Regulation (OBPR) granted FSANZ a standing exemption from the requirement to develop a Regulatory Impact Statement for the approval of additional processing aids (OBPR correspondence dated 24 November 2010, reference 12065). This standing exemption was provided as permitting additional processing aids is a minor, deregulatory change and their use is voluntary. This standing exemption relates to the introduction of a food to the food supply that has been determined to be safe.

However, notwithstanding that exemption, the FSANZ Act requires FSANZ to have regard to whether costs that would arise from the proposed measure outweigh the direct and indirect benefits to the community, government or industry that would arise from the proposed measure.

FSANZ's assessment is that the direct and indirect benefits that would arise from permitting the use of thermolysin as a processing aid outweigh the costs arising from that permission being granted.

The use of thermolysin as a processing aid in the manner proposed will not pose a health or safety risk for the general population (section 2.2 above). Consumers may benefit from: foods having improved functional properties (foaming ability, emulsifying ability, heat stability, viscosity) and organoleptic properties (taste and flavour). Further, there may be benefits from the choice of an additional range of food products that become available due to the use of enzyme by Australian and New Zealand manufacturers and access to products manufactured overseas.

Thermolysin's use by industry is voluntary, therefore it will only be used where industry believe a net benefit exists over existing manufacturing processes. The enzyme is already permitted for use in France, therefore permitting the enzyme may provide Australia and New Zealand manufacturers additional international trade opportunities.

Approval of the draft variation may result in a small cost to government in terms of adding the enzyme to the current range of enzymes that are monitored for compliance.

#### **2.5.1.2 Other measures**

There are no other measures (whether available to FSANZ or not) that would be more cost-effective than a food regulatory measure developed or varied as a result of the Application.

#### **2.5.1.3 Any relevant New Zealand standards**

Standards 1.1.1, 1.1.2 and 1.3.3 and Schedule 18 apply in both Australia and New Zealand. There are no relevant New Zealand only standards.

#### **2.5.1.4 Any other relevant matters**

Other relevant matters are considered below.

## **2.5.2 Subsection 18(1)**

FSANZ has also had regard to the three objectives in subsection 18(1) of the FSANZ Act during the assessment.

### **2.5.2.1 Protection of public health and safety**

FSANZ undertook a safety assessment (SD1), summarised in section 2.3.3. The conclusion was that there are no public health and safety concerns for the general population relating to permitting thermolysin, sourced from *A. caldiproteolyticus* strain TP-7, as an enzyme processing aid for the purposes stated in the draft variation. However, there may be a risk to a small proportion of consumers sensitive to fish proteins to foods that have been manufactured or processed with thermolysin as there is the potential that fish protein from the fermentation media may remain in the final product. The labelling requirements in the Code to manage this risk are outlined in section 2.3.3.

### **2.5.2.2 The provision of adequate information relating to food to enable consumers to make informed choices**

The existing labelling requirements in the Code, including the mandatory declaration of certain allergens when present as a processing aid or an ingredient or component of a processing aid, are considered to be appropriate for the permitted use of thermolysin in foods (refer to section 2.3).

### **2.5.2.3 The prevention of misleading or deceptive conduct**

There are no issues identified with this application relevant to this objective.

## **2.5.3 Subsection 18(2) considerations**

FSANZ has also had regard to:

- **the need for standards to be based on risk analysis using the best available scientific evidence**

FSANZ has used the best available scientific evidence to conduct the risk analysis, which is provided in SD1. The applicant submitted a dossier of scientific studies as part of its application. Other technical information, including scientific literature, was also sourced and used by FSANZ to assess the application.

- **the promotion of consistency between domestic and international food standards**

There are no Codex Alimentarius Standards for enzymes. However, thermolysin is permitted for use in France. It also meets international specifications for enzyme preparations, being the JECFA Compendium of Food Additive Specifications and the Food Chemicals Codex.

- **the desirability of an efficient and internationally competitive food industry**

Granting permission for thermolysin provides food manufacturers with an improvement in functionality when processing proteinaceous foods.

- **the promotion of fair trading in food**

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FSANZ did not identify any relevant issues relating to this consideration.

- **any written policy guidelines formulated by the Forum on Food Regulation**

FSANZ had regard to the [Policy Guideline for the Addition to Food of Substances other than Vitamins and Minerals](#),<sup>1</sup> which includes specific order policy principles for substances added to achieve a solely technological function, such as processing aids. These specific order policy principles state that permission should be granted where:

- the purpose for adding the substance can be articulated clearly by the manufacturer as achieving a solely technological function (i.e. the 'stated purpose')
- the addition of the substance to food is safe for human consumption
- the amounts added are consistent with achieving the technological function
- the substance is added in a quantity and a form which is consistent with delivering the stated purpose
- no nutrition, health or related claims are to be made in regard to the substance.

FSANZ is satisfied that the decision to approve the draft variation is consistent with the policy guideline.

### 3 References

[Food Chemicals Codex 9<sup>th</sup> Edition \(2014\)](#), The United States Pharmacopeia, United States Pharmacopeial Convention, Rockville, MD.

JECFA (2006) [General specifications and considerations for enzyme preparations used in food processing](#).

### Attachments

- A. Approved draft variation to the *Australia New Zealand Food Standards Code*
- B. Explanatory Statement

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<sup>1</sup> [Policy Guidelines](#)

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## Attachment A – Approved draft variation to the Australia New Zealand Food Standards Code



### Food Standards (Application A1146 – Thermolysin (Protease) as a Processing Aid (Enzyme) Variation)

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The Board of Food Standards Australia New Zealand gives notice of the making of this variation under section 92 of the *Food Standards Australia New Zealand Act 1991*. The variation commences on the date specified in clause 3 of this variation.

Dated [to be completed by Delegate]

Glen Neal  
General Manager, Risk Management & Intelligence  
Delegate of the Board of Food Standards Australia New Zealand

**Note:**

This variation will be published in the Commonwealth of Australia Gazette No. FSC XX on XX Month 20XX. This means that this date is the gazettal date for the purposes of clause 3 of the variation.

**1 Name**

This instrument is the *Food Standards (Application A1146 - Thermolysin (Protease) as a Processing Aid (Enzyme)) Variation*.

**2 Variation to a standard in the *Australia New Zealand Food Standards Code***

The Schedule varies a Standard in the *Australia New Zealand Food Standards Code*.

**3 Commencement**

The variation commences on the date of gazettal.

**Schedule**

**[1] Schedule 18** is varied by inserting in the table to subsection S18—9(3), in alphabetical order

Thermolysin (EC 3.4.24.27) sourced from <i>Anoxybacillus caldiproteolyticus</i> strain TP-7	To catalyse the hydrolysis of peptide bonds during the manufacture and/or processing of the following types of food: (a) dairy; (b) egg; (c) meat; (d) fish; (e) protein; (f) yeast; and (g) flavouring	GMP
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## Attachment B – Explanatory Statement

### 1. Authority

Section 13 of the *Food Standards Australia New Zealand Act 1991* (the FSANZ Act) provides that the functions of Food Standards Australia New Zealand (the Authority) include the development of standards and variations of standards for inclusion in the *Australia New Zealand Food Standards Code* (the Code).

Division 1 of Part 3 of the FSANZ Act specifies that the Authority may accept applications for the development or variation of food regulatory measures, including standards. This Division also stipulates the procedure for considering an application for the development or variation of food regulatory measures.

FSANZ accepted Application A1146, which sought an amendment to the Code to permit the use of thermolysin from *Anoxybacillus caldiproteolyticus* (*A. caldiproteolyticus*) strain TP-7 as a processing aid in protein, dairy, egg, meat and fish processing and flavour production. The Authority considered the Application in accordance with Division 1 of Part 3 and has prepared a draft variation to the Code.

Following consideration by the Australia and New Zealand Ministerial Forum on Food Regulation, section 92 of the FSANZ Act stipulates that the Authority must publish a notice about the draft variation of a standard.

Section 94 of the FSANZ Act specifies that a variation of a standard, in relation to which a notice is published under section 92 is a legislative instrument, but is not subject to parliamentary disallowance or sunseting under the *Legislation Act 2003*.

### 2. Purpose

The purpose of this legislative instrument is to amend the Code to permit the use of the enzyme, thermolysin (EC 3.4.24.27) sourced from *A. caldiproteolyticus* strain TP-7 as a processing aid to catalyse the hydrolysis of peptide bonds during the manufacture and/or processing of foods such as: dairy, egg, meat, fish, protein, yeast, and flavouring. This requires an addition to the table to subsection S18—9(3) in Schedule 18.

### 3. Documents incorporated by reference

The variations to food regulatory measures do not incorporate any documents by reference.

### 4. Consultation

In accordance with the procedure in Division 1 of Part 3 of the FSANZ Act, the Authority's consideration of Application A1146 included one round of public consultation followed by an assessment and the preparation of a draft variation and associated assessment summary.

The Office of Best Practice Regulation (OBPR) granted FSANZ a standing exemption from needing to develop a Regulatory Impact Statement for the approval of additional processing aids, in a letter dated 24 November 2010 (reference 12065). This standing exemption was provided as permitting additional processing aids is a minor, deregulatory change and their use is voluntary. This standing exemption relates to the introduction of a food to the food supply that has been determined to be safe.

**5. Statement of compatibility with human rights**

This instrument is exempt from the requirements for a statement of compatibility with human rights as it is a non-disallowable instrument under section 94 of the FSANZ Act.

**6. Variation**

Item [1] of the variation inserts a new entry into the table to subsection S18—9(3) in Schedule 18.

The new entry will, in effect, permit the enzyme, thermolysin (EC number 3.4.24.27), sourced from *A. caldiproteolyticus* strain TP-7, to be used as a processing aid in food for the particular technological purpose of catalysing the hydrolysis of peptide bonds during the manufacture and/or processing of the following types of food, with the condition that the amount that may be used must be consistent with good manufacturing practice:

- (a) dairy
- (b) egg
- (c) meat
- (d) fish
- (e) protein
- (f) yeast, and
- (g) flavouring.