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

8-04
20 October 2004

INITIAL ASSESSMENT REPORT

APPLICATION A542

NATAMYCIN - EXTENSION OF USE AS A FOOD ADDITIVE

DEADLINE FOR PUBLIC SUBMISSIONS to FSANZ in relation to this matter:
1 December 2004
(See 'Invitation for Public Submissions' for details)

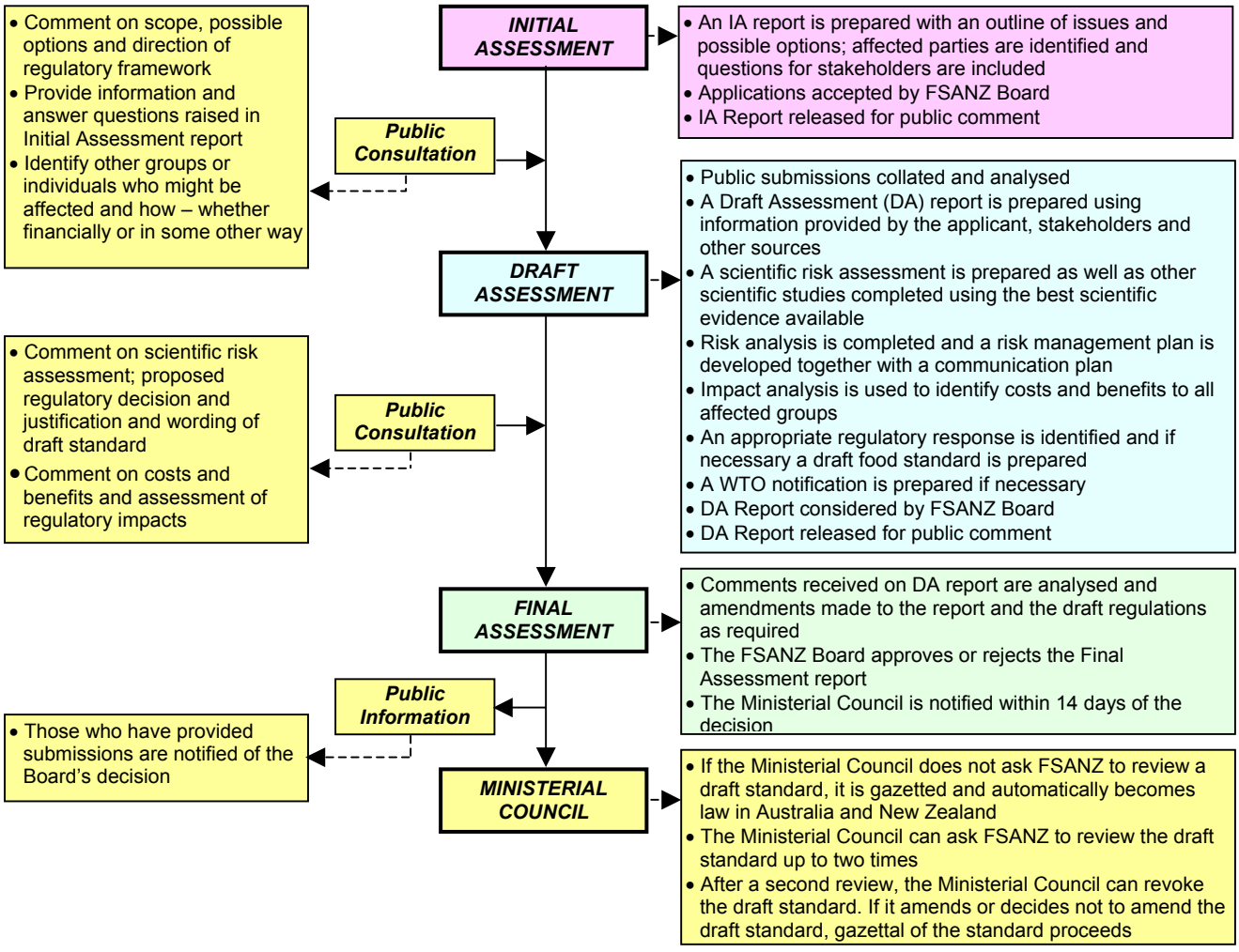
FOOD STANDARDS AUSTRALIA NEW ZEALAND (FSANZ)

FSANZ's role is to protect the health and safety of people in Australia and New Zealand through the maintenance of a safe food supply. FSANZ is a partnership between ten Governments: the Commonwealth; Australian States and Territories; and New Zealand. It is a statutory authority under Commonwealth law and is an independent, expert body.

FSANZ is responsible for developing, varying and reviewing standards and for developing codes of conduct with industry for food available in Australia and New Zealand covering labelling, composition and contaminants. In Australia, FSANZ also develops food standards for food safety, maximum residue limits, primary production and processing and a range of other functions including the coordination of national food surveillance and recall systems, conducting research and assessing policies about imported food.

The FSANZ Board approves new standards or variations to food standards in accordance with policy guidelines set by the Australia and New Zealand Food Regulation Ministerial Council (Ministerial Council) made up of Commonwealth, State and Territory and New Zealand Health Ministers as lead Ministers, with representation from other portfolios. Approved standards are then notified to the Ministerial Council. The Ministerial Council may then request that FSANZ review a proposed or existing standard. If the Ministerial Council does not request that FSANZ review the draft standard, or amends a draft standard, the standard is adopted by reference under the food laws of the Commonwealth, States, Territories and New Zealand. The Ministerial Council can, independently of a notification from FSANZ, request that FSANZ review a standard.

The process for amending the *Australia New Zealand Food Standards Code* is prescribed in the *Food Standards Australia New Zealand Act 1991* (FSANZ Act). The diagram below represents the different stages in the process including when periods of public consultation occur. This process varies for matters that are urgent or minor in significance or complexity.



INVITATION FOR PUBLIC SUBMISSIONS

FSANZ has prepared an Initial Assessment Report of Application A542, which includes the identification and discussion of the key issues.

FSANZ invites public comment on this Initial Assessment Report for the purpose of preparing an amendment to the Code for approval by the FSANZ Board.

Written submissions are invited from interested individuals and organisations to assist FSANZ in preparing the Draft Assessment for this Application. Submissions should, where possible, address the objectives of FSANZ as set out in section 10 of the FSANZ Act. Information providing details of potential costs and benefits of the proposed change to the Code from stakeholders is highly desirable. Claims made in submissions should be supported wherever possible by referencing or including relevant studies, research findings, trials, surveys etc. Technical information should be in sufficient detail to allow independent scientific assessment.

The processes of FSANZ are open to public scrutiny, and any submissions received will ordinarily be placed on the public register of FSANZ and made available for inspection. If you wish any information contained in a submission to remain confidential to FSANZ, you should clearly identify the sensitive information and provide justification for treating it as commercial-in-confidence. Section 39 of the FSANZ Act requires FSANZ to treat in-confidence, trade secrets relating to food and any other information relating to food, the commercial value of which would be, or could reasonably be expected to be, destroyed or diminished by disclosure.

Submissions must be made in writing and should clearly be marked with the word 'Submission' and quote the correct project number and name. Submissions may be sent to one of the following addresses:

Food Standards Australia New Zealand
PO Box 7186
Canberra BC ACT 2610
AUSTRALIA
Tel (02) 6271 2222
www.foodstandards.gov.au

Food Standards Australia New Zealand
PO Box 10559
The Terrace WELLINGTON 6036
NEW ZEALAND
Tel (04) 473 9942
www.foodstandards.govt.nz

Submissions should be received by FSANZ **by 1 December 2004**.

Submissions received after this date may not be considered, unless the Project Manager has given prior agreement for an extension.

While FSANZ accepts submissions in hard copy to our offices, it is more convenient and quicker to receive submissions electronically through the FSANZ website using the Standards Development tab and then through Documents for Public Comment. Questions relating to making submissions or the application process can be directed to the Standards Liaison Officer at the above address or by emailing slo@foodstandards.gov.au.

Assessment reports are available for viewing and downloading from the FSANZ website. Alternatively, requests for paper copies of reports or other general inquiries can be directed to FSANZ's Information Officer at either of the above addresses or by emailing info@foodstandards.gov.au.

CONTENTS

Executive Summary

FSANZ received an Application (A542) on 21 June 2004 from Danisco Australia Pty Ltd, submitted by Axiome Pty Ltd, seeking to amend Standard 1.3.1 – Food Additives, of the *Australia New Zealand Food Standards Code* (the Code), to approve the extended use of natamycin (pimaricin) as a food additive to a maximum level of 15 mg/kg in each of the following food categories:

- breads and bakery products;
- fruit and vegetable preparations, including pulp;
- dairy and fat based desserts, dips and snacks; and
- sauces and toppings (including mayonnaises and salad dressings).

This Application is a Group 3 (cost-recovered) Application.

Natamycin (INS 235) is a naturally occurring antimicrobial agent produced by the bacterium *Streptomyces natalensis* and related species. The Applicant wishes to broaden the use of natamycin as a preservative, which is a technological function listed in Schedule 5 to Standard 1.3.1.

This Initial Assessment Report is not a detailed assessment of the merits of the Application but rather an assessment of whether the Application should undergo further consideration according to criteria laid down in the *Food Standards Australia New Zealand Act 1991* (the FSANZ Act).

This Application has been assessed against the requirements of section 13 of the FSANZ Act and accepted for the following reasons:

- The Application seeks approval for extensions of use for natamycin, a permitted food additive.

- Preservative permissions are provided by Schedule 1 of Standard 1.3.1. Therefore, the Application relates to a matter that warrants a variation to Standard 1.3.1, if further assessment supports such a variation.

- This Application is not so similar to any previous application that it ought not be accepted.

- There are no other measures than a variation to the Code available to permit the extensions of use of this preservative.

This Initial Assessment Report includes a summary of information supplied in the Application with relevant issues identified so that interested parties can make submissions to assist in the assessment.

The Code currently permits 15 mg/kg of natamycin on cheese surfaces and 1.2 mg/dm^2 on uncooked fermented manufactured meats in Australia and New Zealand.

Evaluation of a broader use of natamycin will involve consideration of recent toxicological reviews, estimated dietary exposures based on the proposed new uses and the potential for development of antimicrobial resistance. Natamycin is permitted as an antimicrobial preservative in more than 70 countries, mainly for processed meat products, cheese and other dairy products. South Africa permits the widest range of uses, including cheese and cheese products, yoghurts, processed meat products, fish products, wine and fruit wine, fruit juices, fruit pulp and some canned foods. Natamycin is permitted in the USA in cheese, some dairy foods, non-standardised salad dressings and soft tortillas.

The Codex Alimentarius General Standard for Food Additives (Codex Stan 192-1995, Rev. 4 – 2003) includes pimaricin (syn. natamycin) in categories 08.2.1.2 Cured (including salted) and dried non-heat treated processed meat, poultry and game products in whole pieces or cuts to 6 mg/kg, and 08.3.1.2 Cured (including salted) and dried non-heat treated processed meat, poultry and game to 20 mg/kg.

The Application fulfils the requirements for an Initial Assessment and therefore FSANZ has decided to accept the Application. Submissions are now invited to assist in assessing the Application at Draft Assessment.

1. Introduction

FSANZ received an Application (A542) on 21 June 2004 from Danisco Australia Pty Ltd, submitted by Axiome Pty Ltd, seeking amendments to Standard 1.3.1 – Food Additives, of the Code to approve the use of natamycin (pimaricin) as a food additive to a maximum level of 15 mg/kg in each of the food categories:

- breads and bakery products;
- fruit and vegetable preparations, including pulp;
- dairy and fat based desserts, dips and snacks; and
- sauces and toppings (including mayonnaises and salad dressings).

The Applicant wishes to use natamycin (pimaricin) as a preservative, which is a technological function listed in Schedule 5 to Standard 1.3.1. Natamycin (INS 235) is a naturally occurring antimicrobial agent produced by the bacterium *Streptomyces natalensis* and related species.

The primary aim, as stated by the Applicant, is to provide natamycin as an alternative antimicrobial preservative to sorbates, benzoates, propionates and sulphites, and thereby provide many advantages and benefits compared to these compounds.

Work on this Group 3 (cost-recovered) Application commenced on 21 June 2004.

2. Regulatory Problem

Food additives, including preservatives, are required to undergo a pre-market safety assessment before approval for use in Australia and New Zealand.

Food additives are regulated by Standard 1.3.1. Natamycin is currently permitted in Schedule 1 of Standard 1.3.1 as a preservative for use on cheese surfaces to a maximum level of 15 mg/kg and fermented, uncooked processed comminuted meat products to a maximum level of 1.2 mg/dm^2 in a surface sample. This Application is to broaden the use of natamycin and therefore a safety assessment considering these proposed new uses will be required.

Natamycin is an effective antimicrobial preservative against yeasts and moulds, exhibiting a wide spectrum of activity and effectiveness at very low concentrations. Natamycin has strong cidal activity towards susceptible microorganisms and is particularly effective against fungi, which may produce mycotoxins.

In the food categories where the extension of use is requested, other preservatives are currently permitted, but all are claimed by the Applicant to have limitations. The other preservatives are generally only inhibitory in their action, limited in the range of microorganisms affected and often used at their maximum permitted levels. Even at maximum permitted levels, spoilage problems commonly occur and adverse flavours can result due to high usage levels. The Applicant claims that natamycin offers many advantages over these preservatives, including a much wider spectrum of activity, very low use levels, no adverse flavour effects, and generally, vastly superior effectiveness and improved product shelf-life.

3. Objective

The objective of this assessment is to determine whether it is appropriate to amend the Code to permit the extension of use of natamycin as a preservative in a wider variety of foods in Australia and New Zealand.

In developing or varying a food standard, FSANZ is required by its legislation to meet three primary objectives, which are set out in section 10 of the FSANZ Act. These are:

- the protection of public health and safety;
- 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;
- the promotion of fair trading in food; and
- any written policy guidelines formulated by the Ministerial Council.

4. Background

4.1 Overview

The contamination of foods by spoilage microorganisms and opportunistic pathogens have always created significant problems for the food industry. The growth in popularity of processed, convenience foods, urbanisation and globalisation have also contributed to increased awareness of potentially serious consequences resulting from microbial contamination. Food spoilage and food poisoning outbreaks cause economic losses and raise public health and safety concerns.

Various processing, formulation and packaging techniques, in combination with Good Manufacturing Practices and food safety programs are employed to control microbial contamination of food. Some foods are more susceptible to microbial contamination due to their inherent nature or composition, processing requirements or usage. For these foods antimicrobial preservatives are widely permitted and used.

Natamycin is an effective antimicrobial preservative against yeasts and moulds, exhibiting a wide spectrum of activity and effectiveness at low concentrations. Natamycin has been used for over 30 years as an antimicrobial food preservative and is currently approved in more than 70 countries.

Natamycin was re-evaluated by the Joint FAO/WHO Expert Committee on Food Additives (JECFA) in 2001 and confirmed as safe for its intended use and use levels with respect to cheese and processed meats proposed in the draft Codex Alimentarius General Standard for Food Additives (GSFA) in 2001. JECFA reconfirmed the existing Acceptable Daily Intake (ADI) of 0-0.3 mg/kg/bw.

The Applicant contends that the use of natamycin in the food categories requested in this Application would not lead to intakes in excess of the JECFA ADI. Furthermore the use of natamycin in these foods would provide improved protection against microbial spoilage, benefiting both consumers and manufacturers by reducing product losses, extending shelf-life and protecting public health and safety. An indirect benefit could be reduced use of other antimicrobial preservatives.

4.2 Work Plan Classification

This Application had been provisionally rated as Category of Assessment 3 (level of complexity) and placed in Group 3 (cost-recovered) on the FSANZ standards development Work Plan. This Initial Assessment confirms these ratings. Further details about the Work Plan and its classification system are given in *Information for Applicants* at www.foodstandards.gov.au.

5. Relevant Issues

5.1 Identity and Purity of Natamycin

Natamycin, also known as pimaricin, has;

INS Number: 235

Chemical Abstract (CAS) Number; 7681-93-8; and

JECFA specification in Food and Nutrition Paper series 52 Addendum 9 (2001).

Natamycin is a naturally occurring antimicrobial agent produced by the bacterium *Streptomyces natalensis* and related species. Natamycin acts by disrupting cell membranes of yeasts and moulds, causing leakage and eventual lysis. Natamycin therefore tends to be cidal rather than inhibitory in action to yeasts and moulds. It is active at low concentrations against a wide spectrum of yeasts and moulds, including mycotoxin-producing fungi. Natamycin is not active against bacteria.

5.2 Proposed New Food Uses

The Application states that they wish to use natamycin as a food additive to a maximum level of 15 mg/kg in each of the food categories:

- breads and bakery products;
- fruit and vegetable preparations, including pulp;
- dairy and fat based desserts, dips and snacks; and
- sauces and toppings (including mayonnaises and salad dressings).

The Applicant contends there will be no adverse dietary implications for the use of natamycin in the food categories requested. As part of the re-evaluation by JECFA in 2001, dietary intake of natamycin was reviewed from data supplied by a number of countries, including Australia. The intakes estimated were significantly lower than the JECFA ADI.
The dietary intake in Australia and New Zealand for the requested extensions of use for natamycin will be investigated at Draft Assessment.

5.3 Safety Assessment

5.3.1 Toxicological Assessment

The recent JECFA evaluation in WHO Food Additive Series: 48: "Safety Evaluation of Certain Food Additives and Contaminants – Natamycin (Pimaricin)" is available.

JECFA confirmed the previously established ADI of 0-0.3 mg/kg bw for natamycin, which was based on observations of gastrointestinal effects in humans.

The safety of the extended use of natamycin will be assessed in the context of the proposed new food uses at Draft Assessment.

5.3.2 Dietary Exposure Assessment

JECFA noted that the estimated intake of natamycin based on maximum levels of use in cheese and processed meats proposed in the draft Codex GSFA does not exceed the ADI.

Further dietary modelling will be required in the Draft Assessment Report for the product categories in which natamycin is requested for use in this Application.

5.3.3 Antimicrobial Properties

Natamycin is an antimicrobial agent produced by the bacterium *Streptomyces natalensis*. It belongs to the group of polyene macrolide antimycotics. Natamycin acts by complexing with sterols present in the cell membranes of yeasts and moulds and disrupting the membrane. Permeability of the membrane is increased, causing leakage from the cell and eventual lysis. Natamycin tends to be cidal in action rather than inhibitory to yeast and mould growth. Natamycin is active against a wide range of yeasts and moulds, including mycotoxin-producing fungi and strains pathogenic to humans, however it is reportedly not active against bacteria.

In addition to food applications, it has also been used therapeutically (via topical application) to treat several types of fungal infections of the eye. The emergence of antimicrobial resistance, particularly through misuse of antibiotics, has been a major human health issue in recent years. The World Health Organization recently developed a 'WHO Global Strategy for Containment of Antimicrobial Resistance' to address this issue. The use of antimicrobial agents in foods, such as natamycin, therefore, will need to be examined in light of any potential for antimicrobial resistance.

The Applicant claims that there is no development of antimicrobial resistance through the use of natamycin and that this is supported by the JECFA evaluation report. This issue will be further evaluated for Draft Assessment, including consultations with the National Health and Medical Research Council (NHMRC) External Advisory Group on Antibiotic Resistance.

5.4 Other International Regulatory Approvals

The Applicant supplied a detailed list of natamycin regulatory approvals and states that natamycin is permitted as an antimicrobial preservative in more than 70 countries, mainly for processed meat products, cheese and other dairy products. South Africa permits the widest range of uses, including cheese and cheese products, yoghurts, processed meat products, fish products, wine and fruit wine, fruit juices, fruit pulp and some canned foods. Natamycin is permitted in the USA in cheese, some other dairy foods, non-standardised salad dressings and soft tortillas.

FSANZ has also undertaken a preliminary search of various international regulations and standards and will review the permissions around the world at Draft Assessment.

The Codex GSFA (revision 4 -2004) includes pimaricin (syn. natamycin) in categories; 08.2.1.2 Cured (including salted) and dried non-heat treated processed meat, poultry and game products in whole pieces or cuts to 6 mg/kg; and 08.3.1.2 Cured (including salted) and dried non-heat treated processed meat, poultry and game to 20mg/kg. The Notes (3 and 81) associated with the Codex GSFA permissions are for surface treatment and equivalent to 1 mg/dm2 surface application to a maximum depth of 5 mm respectively. A previous draft of the GSFA (2001) provided a listing for natamycin to 40 mg/kg in category 01.6 for cheese.

6. Regulatory Options

FSANZ is required to consider the impact of various regulatory (and non-regulatory) options on all sectors of the community, which includes consumers, food industries and governments in Australia and New Zealand. The benefits and costs associated with the proposed amendment to the Code will be analysed using regulatory impact principles at Draft Assessment.

There are no options other than a variation to the Code for this Application. Therefore the two regulatory options available for this Application are:

Option 1. Not approve the extended use of natamycin in a wider range of foods.

Option 2. Approve the extended use of natamycin in a wider range of foods.

7. Impact Analysis

7.1 Affected Parties

The affected parties to this Application include the following:

1. those sectors of the food industry wishing to produce and market food;

2. consumers; and

3. Australian, State, Territory and New Zealand Government agencies that enforce food regulations.

7.2 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. 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.

The regulatory impact of the proposed change will be assessed at Draft Assessment.

8. Consultation

8.1 Public consultation

The Initial Assessment Report is not a detailed assessment of this Application but rather an assessment of whether the Application should undergo further consideration. FSANZ is seeking public comment in order to assist in assessing this Application at Draft Assessment. A further round of public comment will occur after the Draft Assessment Report is completed to assist in the Final Assessment.

FSANZ is seeking public comment to assist in assessing the Application. Comments on, but not limited to, the following would be useful:

- technological justification for extending the use of natamycin;
- if there are any safety considerations with its proposed use;
- likely costs and benefits of extending the use of natamycin; and
- affected parties to this Application.

8.2 World Trade Organization (WTO)

As members of the World Trade Organization (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.

This issue will be fully considered at Draft Assessment and, if necessary, notification will be recommended to the agencies responsible in accordance with Australia's and New Zealand's obligations under the WTO Technical Barrier to Trade (TBT) or Sanitary and Phytosanitary Measure (SPS) Agreements. This will enable other WTO member countries to comment on proposed changes to standards where they may have a significant impact on them.

9. Conclusion and Recommendation

This Application has been assessed against the requirements of section 13 of the FSANZ Act and accepted for the following reasons:

- The Application seeks approval for extensions of use for natamycin, a permitted food additive.

- Preservative permissions are provided by Schedule 1 of Standard 1.3.1 – Food additives. Therefore, the Application relates to a matter that warrants a variation to Standard 1.3.1, if further assessment supports such a variation.

- This Application is not so similar to any previous application that it ought not be accepted.

- There are no other measures than a variation to the Code available to permit the extensions of use of this preservative.

- No other relevant matters are apparent at this stage.

It is recommended that this Application now be progressed to Draft Assessment.