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

APPLICATION A1015
ETHYL LAUROYL ARGINATE AS A FOOD ADDITIVE
EXPLANATORY STATEMENT

Executive Summary

Purpose

Food Standards Australia New Zealand (FSANZ) received an Application from Laboratarios Miret SA (LAMIRSA) on 28 August 2008. This Application seeks to amend Standard 1.3.1 – Food Additives of the *Australia New Zealand Food Standards Code* (the Code) to include a new food preservative, ethyl lauroyl arginate.

Ethyl lauroyl arginate is a synthetically produced cationic surfactant[1] that is intended to be used to protect food against microbial growth and thus spoilage. Cationic surfactants such as ethyl-N^{α}-lauroyl-L-arginate·HCl (active ingredient), can be used as food preservatives because they are able to disrupt the integrity of cell membranes in a broad spectrum of bacteria, yeasts and moulds. It is proposed to be used in a wide range of food groups.

Ethyl lauroyl arginate has been evaluated by other international agencies in recent years. In 2005, the US Food and Drug Administration (FDA) issued a Letter of No Objection regarding a submission that ethyl lauroyl arginate is Generally Recognised as Safe (GRAS, Notice No. GRN 000164) for use as an antimicrobial at levels up to 200 mg ethyl-N^{α}-lauroyl-L-arginate·HCl /kg in a wide range of foods. In April 2007, the European Food Safety Authority (EFSA) issued the opinion of the Scientific Committee on ethyl lauroyl arginate as a new food preservative for use in a range of food categories. An Acceptable Daily Intake (ADI) of 0-0.5 mg/kg body weight (bw) was established by EFSA. Most recently, in June 2008, the Joint FAO/WHO Expert Committee on Food Additives (JECFA) considered ethyl lauroyl arginate as a food additive and allocated an ADI of 0-4 mg/kg bw for the active ingredient, ethyl-N^{α}-lauroyl-L-arginate·HCl. The large difference in the ADIs established by EFSA and JECFA is due to a difference in the interpretation of haematology data obtained in animal toxicity studies.

Based on the availability of an adequate range of suitable studies, FSANZ has independently completed a safety assessment for ethyl lauroyl arginate and established an ADI of 0-5 mg/kg bw, equivalent to the ADI set by JECFA for the active ingredient. The safety assessment reports that only minimal amounts of unchanged ethyl lauroyl arginate enter the bloodstream because the compound is rapidly metabolised by enzymes in the upper intestine before substantial absorption can occur.

[1] Surfactants are wetting agents that lower the surface tension of a liquid, allowing easier spreading, and lower the interfacial tension between two liquids.

In the intestine, ethyl lauroyl arginate is rapidly degraded to compounds normally present in the diet such as the amino acid L-arginine and the fatty acid lauric acid.

In animal toxicity studies of up to one year duration, ethyl lauroyl arginate was well tolerated even at high concentrations in the diet. Ethyl lauroyl arginate and its major metabolites showed no evidence of genotoxic activity. In reproductive and developmental toxicity studies, the only notable and consistent finding was delayed onset of puberty in female rats. The ADI for ethyl lauroyl arginate established by FSANZ derived from this study was 0-5 mg/kg bw.

The ADI of 0-4 mg/kg bw published by JECFA was derived from this same study, however JECFA applied a correction factor for the content of active ingredient in the batch used in the study (88%) to arrive at an ADI expressed as the active ingredient, ethyl-N^{α}-lauroyl-L-arginate·HCl.

The dietary exposure assessment assumed the addition of ethyl lauroyl arginate at the proposed maximum use level for all food types proposed by the Applicant, i.e. assuming 100% uptake by food manufacturers. This scenario is highly protective of consumers as such complete uptake of ethyl lauroyl arginate is considered unlikely and actual use levels may be lower than maximum permitted levels. All estimated dietary exposures to ethyl lauroyl arginate for the population groups assessed were within the range of the ADI.

Estimated dietary exposure for high consumers of ethyl lauroyl arginate (90^{th} percentile) for Australian children aged 2-6 years approached 80% of the ADI, 90^{th} percentile dietary exposure for the whole population of Australians aged 2+ years was 30% of the ADI and for New Zealanders aged 15+ years 20% of the ADI. The major contributor to mean ethyl lauroyl arginate dietary exposure for Australians aged 2+ years and for New Zealanders aged 15+ years would be comminuted meat products and whole pieces of processed meat, assuming use in all requested food groups. For Australian children aged 2-6 years, the major contributor would be cordials.

Non-dietary sources of exposure to ethyl lauroyl arginate were evaluated as part of the Approval report. Systemic exposure arising from the dermal application and inhalation of cosmetic and personal care products was considered to be negligible because of its poor absorption through biological membranes. Non-food oral exposure from lipstick, toothpaste and mouthwash was estimated based on worst-case scenarios that assumed partial ingestion for adults and complete ingestion of toothpaste only in children. The oral exposure from dietary sources was below 2 mg/kg bw/day for the Australian population and non-dietary sources for adults was less than 1 mg/kg bw/day. For Australian children, the total estimated oral exposure combining exposure from food at the 90^{th} percentile and personal care use was estimated to be below the ADI. Therefore, the additional oral exposure from the use of cosmetics and personal care products is unlikely to exceed the ADI for any population group.

The unpublished data provided by the Applicant and supplemented with published scientific journal reports indicate that ethyl lauroyl arginate is an effective food preservative in the food categories proposed. This new antimicrobial agent is stable during storage in a range of food matrices and provides protection against microbial spoilage in these foods to extend their shelf life. Use of ethyl lauroyl arginate as a preservative in the specified food categories and at the maximum permitted level is technologically justified and it could be potentially a useful component of food preservation systems.

Based on the conservative assumptions in the dietary exposure calculations, FSANZ concludes that there are no public health and safety concerns for ethyl lauroyl arginate when used as a food additive at the maximum levels proposed by the Applicant.

Assessing the Application

The Application is being assessed under the General Procedure.

In assessing the Application and the subsequent development of a food regulatory measure, FSANZ has had regard to the following matters as prescribed in section 29 of the *Food Standards Australia New Zealand Act 1991* (FSANZ Act):

- Whether costs that would arise from the amendments of the Code to permit the use of the antimicrobial agent, ethyl lauroyl arginate, as a food additive would outweigh the direct and indirect benefits to the community, Government or industry.
- There are no other measures that would be more cost-effective than a variation to Standard 1.3.1 that could achieve the same end.
- There are no relevant New Zealand standards.
- There are no other relevant matters.

Decision

FSANZ approves the proposed draft variations to Standard 1.3.1, Schedule 1 – Food Additives, to include permissions for ethyl lauroyl arginate in the food types at the specified maximum limits for the active ingredient, ethyl-N$^{\alpha}$-lauroyl-L-arginate·HCl, in the list of intended uses of ethyl lauroyl arginate.

List of intended uses of ethyl lauroyl arginate

Food types*		Ethyl lauroyl arginate** (mg/kg; maximum)
0.1	Preparations of food additives	200
1.6	Cheese - soft/cream/processed and mozzarella	400 except for mozzarella at 200
1.6	Cheese – Hard/Semi-hard	1 mg/cm^2 of surface area of cheese (taken to a depth of 3 mm and not more than 5 mm)
4.1.3	Peeled and/or cut fruits and vegetables	200
4.3.8	Processed fruits and vegetables—rehydrated legumes only	200
6.3	Processed cereal and meal products- cooked rice only	200
6.4	Flour products (including noodles and pasta) – cooked pasta and noodles only	200
8.2	Processed meat, poultry and meat products in whole cuts or pieces	200
8.3	Processed comminuted meat and poultry products	315
9.3	Semi preserved fish and fish products	400

Food types*		Ethyl lauroyl arginate** (mg/kg; maximum)
14.1.2	Fruit and vegetable juices and fruit and vegetable juice products	50
14.1.3	Water based flavoured drinks	50
20.2	Savoury toppings or fillings - essentially sauces such as tomato paste used in ready to eat pizzas, etc.	200
20.2	Dairy and fat based desserts, dips and snacks	400

*the code number and food types are as listed in the Code, Standard 1.3.1, Schedule 1.
** Ethyl lauroyl arginate shall be calculated as ethyl-N^{α}-lauroyl-L-arginate·HCl.

Reasons for Preferred Approach

Amendments to the Code to include ethyl lauroyl arginate as a food preservative in Australia and New Zealand is proposed on the basis of the available scientific evidence for the following reasons:

- A detailed safety assessment has concluded the permission for the use of ethyl lauroyl arginate does not raise any public health and safety concerns, including considering development of antimicrobial resistance.

- Use of ethyl lauroyl arginate as a preservative in the specified food categories up to the maximum permitted level is technologically justified and it could potentially be a useful component of food preservation systems. Based on data provided by the Applicant, ethyl lauroyl arginate could possibly replace some approved food grade preservatives such as benzoates, sulphites and sorbates, which have some inherent limitations.

- The regulatory impact assessment concluded that the benefits of the potential use of ethyl lauroyl arginate in the specified food categories outweigh any costs associated with its use.

- The proposed variation to the Code is consistent with the section 18 objectives of the FSANZ Act.

Consultation

This Application is being assessed under the General Procedure and the Assessment Report was released for public comment from 6 May to 17 June 2009. Three submissions were received; they were all from government agencies. Two of these submitters support FSANZ's preferred option of including ethyl lauroyl arginate as a food additive in the food types at the specified maximum limits as stated in Table 1 of the Assessment Report, with one of these requesting further information and clarification. The third submitter reflected mixed opinions from different agencies within a jurisdiction on FSANZ's preferred approach. Issues raised by the submitters are summarised (Attachment 2) and have been taken into account in preparing the Approval Report for this Application. The issues raised in the submissions are addressed in Section 9.1.

Amendments to the Draft Variation after Consultation

The draft variation in the Assessment Report circulated for public comment excluded apple juice as a food type permitted to have ethyl lauroyl arginate as a food additive. Following consideration of submitters' comments and further assessment as described below, it was decided to allow the addition of ethyl lauroyl arginate to apple juice. Therefore 'not apple juice' was removed from the proposed variation [2.12].

Apple juice had been excluded from the list of intended uses in the Assessment Report because the Applicant believed it had the potential for ethyl lauroyl arginate exposure to exceed the ADI for children (2-6 years old). However, there is no technological reason for not using ethyl lauroyl arginate in apple juice.

Further dietary modelling has shown that the addition of ethyl lauroyl arginate in apple juice does not lead to a significant increase in the total exposure of ethyl lauroyl arginate in the Australian population, New Zealanders 15 years and above and Australians 2-6 years old (Supporting Document 2).

If the initial draft had been approved, it could lead to practical and regulatory complexity of monitoring its use in fruit juice blends that may contain up to 90% apple juice. Therefore, FSANZ has now permitted apple juice in the list of intended uses.

CONTENTS

SUPPORTING DOCUMENTS

The following materials, which were used in the preparation of this Approval Report, are available on the FSANZ website at http://www.foodstandards.gov.au/standardsdevelopment/applications/applicationa1015ethy4049.cfm

SD1: Hazard Assessment
SD2: Dietary Exposure Assessment
SD3: Food Technology Report
SD4: Antimicrobial Resistance Assessment Report

INTRODUCTION

Food Standards Australia New Zealand (FSANZ) received an Application from Laboratarios Miret SA on 28 August 2008. The Application seeks to amend Standard 1.3.1 – Food Additives of the *Australia New Zealand Food Standards Code* (the Code) to include ethyl lauroyl arginate as a preservative for a wide range of food categories at specified maximum levels.

Ethyl lauroyl arginate is a new synthetically produced chemical preservative. The Applicant claims that because of the effectiveness of ethyl lauroyl arginate in a wide range of food matrices and over a broad antimicrobial spectrum, some sectors of the food industry might prefer the use of ethyl lauroyl arginate over the other commonly used and approved antimicrobials. The Applicant has provided experimental data to demonstrate the relative effectiveness of ethyl lauroyl arginate.

In the original dossier submitted by the Applicant, their product is referred to as lauric arginate. However, FSANZ has referred to the product as ethyl lauroyl arginate throughout this assessment, in order to be consistent with international naming. Codex has proposed the name of the product as ethyl lauroyl arginate (INS 243). The abbreviation, ELA, will be used in Tables in this Approval Report because of spacing limitations.

1. The Issue / Problem

Food additives, including preservatives, are required to undergo a pre-market safety assessment before they are included in Standard 1.3.1. There is currently no permission for ethyl lauroyl arginate in the Code. Maximum limits for ethyl lauroyl arginate have to be established for all food types considered. The limits are established through consideration of:

- the safety assessment for ethyl lauroyl arginate
- the technological justification for and effectiveness of ethyl lauroyl arginate in the range of food groups requested.

2. Background

2.1 Current Standard

A food additive, as stated in the Purpose clause of Standard 1.3.1, 'is any substance not normally consumed as a food in itself and not normally used as an ingredient of food, but which is intentionally added to a food to achieve one or more of the technological functions as specified in Schedule 5. Preservation is one of the functions specified in Schedule 5 and a preservative is defined as an additive that 'retards or prevents the deterioration of a food by micro organisms'. Sub-classes of preservative are anti-microbial preservative, anti-mycotic agent, bacteriophage control agent, chemosterilant and disinfection agent.

This Standard regulates the use of food additives in the production and processing of food. A food additive may only be added to food where expressly permitted in this Standard. Additives may only be added to food in order to achieve an identified technological function according to Good Manufacturing Practice.

Currently, Standard 1.3.1, Schedule 1 permits one or more of the following preservatives for use in the food types, with the exception of precooked rice, in which the Applicant has proposed to use ethyl lauroyl arginate: sorbates, benzoates, parabens, sulphites, nisin, pimaricin, nitrates, nitrites, dimethyl dicarbonate and propionates. No preservative is permitted in precooked rice.

2.2 Technological Purpose

The active component of ethyl lauroyl arginate, ethyl-N^{α}-lauroyl-L-arginate·HCl, is a cationic surfactant with a broad spectrum of activity against bacteria, yeasts and moulds. Ethyl lauroyl arginate is stable in relatively acidic product formulations (for example, pH 4). It is effective as an antimicrobial in a wide range of food categories at the proposed usage limits and thus provides the food industry with a flexible tool to control shelf life of foods. However, ethyl lauroyl arginate binds to proteins and therefore a higher limit of usage is proposed in protein-based foods.

The Applicant has provided information to demonstrate ethyl lauroyl arginate could be used as a potential alternative to the currently approved preservatives, which have some inherent limitations. For example, sulphite consumption exceeds the ADI for some high-level consumers in Australia[2] .

2.3 International Regulatory Status

The WHO Joint Expert Committee on Food Additives (JECFA) first considered ethyl lauroyl arginate at its 69th meeting in June 2008 (FAO/WHO 2008). The Committee established an ADI of 0–4 mg/kg bw for ethyl lauroyl arginate, expressed as the active ingredient ethyl-N^{α}-lauroyl-L-arginate·HCl.

The specification for ethyl lauroyl arginate was revised at JECFA's 71st meeting in July 2009. There is no change in the main product specification. The revision is in the analysis of two impurities (L-arginine·HCl and Ethyl arginate·2HCl), where quantification procedures were modified.

The European Food Safety Authority (EFSA) published its opinion on ethyl lauroyl arginate in April 2007 and established an ADI for ethyl lauroyl arginate of 0-0.5 mg/kg bw[3]. EFSA has listed ethyl lauroyl arginate in their Working Document for discussion in July 2009.

The US Food and Drug Administration has issued a Letter of No Objection regarding the submission that ethyl lauroyl arginate is Generally Recognised as Safe (GRAS) for use as an antimicrobial at levels up to 225 mg/kg of ethyl lauroyl arginate in the food categories specified (USFDA 2005).

3. Objectives

The objective of this assessment is to determine whether it is appropriate to amend the Code to include ethyl lauroyl arginate in the specified food categories and to establish maximum allowable limits. In developing or varying a food standard, FSANZ is required by its legislation to meet three primary objectives which are set out in section 18 of the FSANZ Act. These are:

[2] FSANZ 2005, 21st Australian Total Diet Study: a total diet study of sulphites, benzoates and sorbates.
[3] Reason for discrepancy between JECFA and EFSA is given in Supporting Document 1.

- the protection of public health and safety; and
- the provision of adequate information relating to food to enable consumers to make informed choices; and
- the prevention of misleading or deceptive conduct.

In developing and varying standards, FSANZ must also have regard to:

- the need for standards to be based on risk analysis using the best available scientific evidence;
- the promotion of consistency between domestic and international food standards;
- the desirability of an efficient and internationally competitive food industry;
- the promotion of fair trading in food; and
- any written policy guidelines formulated by the Ministerial Council[4].

4. Questions to be answered

For this Application, FSANZ has considered the following key questions:

- What would the potential dietary exposure to ethyl lauroyl arginate be for mean and high consumers of foods containing the preservative?
- Are there any public health and safety issues as a consequence of approving the use of ethyl lauroyl arginate at the levels proposed in the range of food types applied for?
- Are the requested levels of ethyl lauroyl arginate technologically justified in the food categories applied for?

RISK ASSESSMENT

5. Risk Assessment Summary

5.1 Hazard Assessment

FSANZ has assessed the submitted evidence on the safety of ethyl lauroyl arginate including studies on absorption, metabolism, acute toxicity, repeat-dose toxicity, genotoxicity and reproductive toxicity. The submitted data were considered suitable for hazard assessment and assignment of an ADI for ethyl lauroyl arginate. For the full Hazard Assessment Report see Supporting Document 1.

JECFA first assessed the toxicity of ethyl lauroyl arginate in 2008 and established an ADI of 0-4 mg/kg bodyweight expressed as the active ingredient.

[4] In May 2008, the Australia and New Zealand Food Regulation Ministerial Council endorsed the Policy Guideline on Addition to Food of Substances other than Vitamins and Minerals. This includes policy principles in regard to substances added for technological purposes such as food additives and processing aids.

The ADI was based on the No Observed Adverse Effect Level (NOAEL) of 502 mg/kg bw/day (expressed as ethyl lauroyl arginate) established in a reproductive toxicity study. This NOAEL was corrected for the active ingredient content (88% w/w) to give a NOAEL for the active ingredient of 442 mg/kg bw/day. The ADI of 0-4 mg/kg bodyweight for the active ingredient was derived by applying a 100-fold safety factor (10-fold for inter-species differences and 10-fold to account for differences between individuals).

After assessing all of the available data, FSANZ has used the same NOAEL of 502 mg/kg bw/day obtained in the reproductive toxicity study and applied a 100-fold safety factor to establish an ADI of 0-5 mg/kg bodyweight for ethyl lauroyl arginate. Thus, the only difference between the ADIs derived by JECFA and FSANZ was the correction for active ingredient content by JECFA. FSANZ did not correct for active ingredient content because the batch used in the relevant study conformed to the approved JECFA specifications for ethyl lauroyl arginate.

In the submitted studies, systemic exposure to orally administered ethyl lauroyl arginate was low because most of the compound is rapidly metabolised in the intestines before absorption occurs. Ethyl lauroyl arginate is rapidly degraded to endogenous compounds and compounds normally present in the diet such as the amino acid L-arginine and the fatty acid lauric acid. In animal toxicity studies of up to one year duration, ethyl lauroyl arginate was well tolerated even at relatively high doses. Ethyl lauroyl arginate had a slight local irritant effect on the rat forestomach probably due to its surfactant activity. However, the rodent forestomach is not protected by mucus and has no anatomical equivalent in humans. The forestomach findings were therefore not considered to be relevant for a risk assessment in humans.

Ethyl lauroyl arginate and its major metabolite showed no evidence of genotoxic activity. In reproductive and developmental toxicity studies the only notable and consistent finding was delayed onset of puberty in female rats. There was no information to indicate that this effect may not be relevant to humans. The finding was therefore considered suitable for deriving an ADI. Because of uncertainties regarding the mechanism of delayed puberty in female rats and the relevant exposure period for the effect, a conservative dose was chosen on which to base the ADI as discussed in the Hazard Assessment Report (Supporting Document 1). No other effects on reproduction or development attributable to ethyl lauroyl arginate were observed.

Ethyl lauroyl arginate has been approved for use and commercialised in the USA since 2005 with no published reports of intolerance associated with consumption. Ethyl lauroyl arginate is rapidly metabolised to compounds which have not been associated with intolerance reactions.

5.2 Dietary Exposure

FSANZ conducted a dietary exposure assessment for the food additive ethyl lauroyl arginate based on the information provided by the Applicant. For the full Dietary Exposure Assessment Report see Supporting Document 2.

Food consumption data from the 1995 Australian and 1997 New Zealand National Nutrition Surveys were used for the exposure assessments. The population groups assessed were the Australian population (2 years and above), the New Zealand population (15 years and above) and children (2 to 6 years for Australia only).

The Applicant provided FSANZ with information on proposed levels of use for ethyl lauroyl arginate for specific food groups and the expected foods within each food group that may contain it.

Based on this information, dietary exposure was estimated assuming that ethyl lauroyl arginate was present in foods at the maximum permitted level suggested by the applicant, expressed as ethyl lauroyl arginate. This scenario is highly protective of consumers.

Estimated mean exposures for consumers of ethyl lauroyl arginate for all population groups assessed were 38 mg/day (0.7 mg/kg bw/day) for the Australian population 2 years and above; 38 mg/day (2.1 mg/kg bw/day) for Australian children 2-6 years; and 32 mg/day (0.4 mg/kg bw/day) for the New Zealand population aged 15 years and above. Estimated 90th percentile exposures for consumers of ethyl lauroyl arginate were 83 mg/day (1.6 mg/kg bw/day) for the Australian population 2 years and above; 73 mg/day (4.0 mg/kg bw/day) for Australian children 2-6 years; and 76 mg/day (1.0 mg/kg bw/day) for the New Zealand population aged 15 years and above.

Based on the food groups proposed by the Applicant, the major contributor to the estimated ethyl lauroyl arginate dietary exposure for Australians aged 2 years and above and for New Zealanders aged 15 years and above would be comminuted meat products and whole pieces of processed meat. For Australian children aged 2-6 years, the major contributor would be cordials.

5.3 Risk Characterisation

Comparisons of the dietary exposure to ethyl lauroyl arginate with the ADI of 0-5 mg/kg bw indicated that for all groups of Australian and New Zealand consumers assessed (including children), estimated dietary exposures were below this safe level of exposure. The estimated mean dietary exposures for consumers of ethyl lauroyl arginate correspond to 15% of the ADI for Australians aged 2 years and above, 40% of the ADI for Australian children aged 2-6 years, and 10% of the ADI for New Zealanders aged 15 years and above. The estimated 90th percentile dietary exposures for consumers of ethyl lauroyl arginate correspond to 30% of the ADI for Australians aged 2 years and above, 80% of the ADI for Australian children aged 2-6 years, and 21% of the ADI for New Zealanders aged 15 years and above. These comparisons raise no public health and safety concerns for the addition of ethyl lauroyl arginate at the proposed levels of use.

Non-dietary sources of oral exposure may occur if ethyl lauroyl arginate is used as a preservative in lipsticks, toothpaste and mouthwash. The additional oral exposure arising from the use of such products is unlikely to result in the ADI being exceeded for any population group.

5.4 Antimicrobial Resistance

While there is a potential for resistance of microorganisms to antimicrobial agents, such as ethyl lauroyl arginate and other preservatives used in food production, this can be minimised through proper management and monitoring of their use. These measures include the setting of appropriate maximum limits and following the principles of GMP i.e. the quantity of additive added to food shall be limited to the lowest possible level necessary to accomplish its desired effect.

While there is an absence of data in the peer-reviewed literature on the selection and/or development of microorganisms resistant to ethyl lauroyl arginate, resistance to other cationic surfactants, such as quaternary ammonium compounds, has been reported. Unpublished laboratory data provided by the Applicant showed that when test organisms were exposed to sub-lethal concentrations of ethyl lauroyl arginate, an increased resistance to the antimicrobial was observed over time. This adaption was temporary, however, as resistant cultures quickly became susceptible following growth in ethyl lauroyl arginate-free media. See Supporting Document 4 for the full review of antimicrobial resistance by FSANZ.

5.5 Food Technology Assessment

FSANZ conducted a review of the technological justification of ethyl lauroyl arginate as a preservative based on the information provided by the Applicant and on published information. For the full Food Technology Assessment Report see Supporting Document 3.

The Application requested ethyl lauroyl arginate as a preservative in a wide range of food groups as listed below:

- food additive preparations
- cheeses – soft, cream, processed, mozzarella, hard and semi hard
- peeled and/or cut fruit and vegetables – rehydrated legumes
- cereal products – cooked rice, noodles and pasta
- semi-processed fish and fish products – salted fish and roe
- processed meat, poultry and meat products in whole or cut pieces or comminuted products
- non-alcoholic beverages – fruit and vegetable juices and juice products, water based flavoured drinks and high energy drinks and soft drinks
- savoury toppings or fillings, dairy based desserts, dips and snacks

Within these foods, the Applicant proposed ethyl lauroyl arginate, expressed as the active ingredient ethyl-N^{α}-lauroyl-L-arginate·HCl, be used in levels ranging between 50 mg/kg (e.g. beverages) and 400 mg/kg (in protein based foods, e.g. cheese and fish products).

The Applicant provided 36 experimental studies to support their claims that ethyl lauroyl arginate effectively suppresses a broad spectrum of microorganisms in a wide range of food matrices. The Applicant provided information to demonstrate ethyl lauroyl arginate may be a potential alternative for some of the currently approved preservatives such as sulphites, benzoates and sorbates, which have some inherent limitations.

The data provided by the Applicant supplemented with published scientific journal information indicate that ethyl lauroyl arginate is an effective food preservative to extend shelf life of foods in the food groups proposed above and that it also reduces the levels of certain pathogenic bacteria. This new antimicrobial agent is stable in storage and processing of a range of food groups.

Use of ethyl lauroyl arginate as a preservative in the specified food types up to the maximum requested level is technologically justified based on consideration of stability and effectiveness. Along with good manufacturing practice, ethyl lauroyl arginate could be a useful component of food preservation systems.

RISK MANAGEMENT

6. Regulatory Options

There are no non-regulatory options for this Application. Two regulatory options have been identified for this Application:

Option 1 Reject the Application, thus maintaining the *status quo.*

Option 2 Amend Schedule 1 of Standard 1.3.1 to permit maximum limits for ethyl lauroyl arginate as a food additive in the range of food types specified in Table 1.

Ethyl lauroyl arginate will be added to the list of food additive code numbers in Standard 1.2.4 – Labelling of Ingredients. As ethyl lauroyl arginate complies with Monograph 5 published in the FAO Combined Compendium of Food Additive Specifications (Monograph 5) (JECFA, 2008), Monograph 5 will be a primary source of specification, as required in Clause 2 of Standard 1.3.4.

Table 1: Intended uses of ethyl lauroyl arginate

Food types*		Ethyl lauroyl arginate** (mg/kg; maximum)
0.1	Preparations of food additives	200
1.6	Cheese - soft/cream/processed and mozzarella	400 except for mozzarella at 200
1.6	Cheese – Hard/Semi-hard	1 mg/cm^2 of surface area of cheese (taken to a depth of 3 mm and not more than 5 mm)
4.1.3	Peeled and/or cut fruits and vegetables	200
4.3.8	Processed fruits and vegetables— rehydrated legumes only	200
6.3	Processed cereal and meal products- cooked rice only	200
6.4	Flour products (including noodles and pasta) – cooked pasta and noodles only	200
8.2	Processed meat, poultry and meat products in whole cuts or pieces	200
8.3	Processed comminuted meat and poultry products	315
9.3	Semi preserved fish and fish products	400
14.1.2	Fruit and vegetable juices and fruit and vegetable juice products	50
14.1.3	Water based flavoured drinks	50
20.2	Savoury toppings or fillings - essentially sauces such as tomato paste used in ready to eat pizzas, etc.	200
20.2	Dairy and fat based desserts, dips and snacks	400

* the code number and food types are as listed in the Code, Standard 1.3.1, Schedule 1.
**Ethyl lauroyl arginate shall be calculated as ethyl-N$^{\alpha}$-lauroyl-L-arginate·HCl.

7. Impact Analysis

FSANZ is required to consider the impact of various regulatory and non-regulatory options on all sectors of the community, especially relevant stakeholders who may be affected by this Application. The benefits and costs associated with the proposed amendment to the Code have been analysed using regulatory impact principles.

In accordance with the Best Practice Regulation Guidelines the preliminary assessment for this application indicated low or negligible impacts. The Office of Best Practice Regulation has advised that the analysis is adequate and approved the preliminary assessment (RIS ID 10222).

7.1 Affected Parties

The affected parties may include the following:

1. Those sectors of the food industry wishing to use this new food preservative.

2. Consumers who may be affected, either negatively or positively, as a result of a new preservative becoming available in processed foods.

3. Government agencies with responsibility for compliance and enforcement of the Code.

7.2 Benefit Cost Analysis

7.2.1 Option 1 – Reject Application

- Food industries may be disadvantaged as they would be unable to capture the potential benefits of the new food preservative. Some sectors of the food industry are under pressure to reduce their levels of benzoates and sulphites. These sectors face increasing costs if alternatives are not permitted.

- There is no perceived impact on consumers.

- There is no perceived impact on government agencies.

7.2.2 Option 2 – Permit maximum limits for ethyl lauroyl arginate as a food additive in the range of foods specified in Table 1

- Food industries may benefit as they may be able to include ethyl lauroyl arginate in their products as part of their food preservation systems with consequent market advantages from reduced spoilage losses and extended shelf life. However, the food industries would incur the cost of labelling changes if they chose to use the new preservative.

- Consumers may benefit from foods containing ethyl lauroyl arginate through reduction in losses associated with food spoilage and potential for lowered consumption of some of the currently approved preservatives. However, some consumers may object to having a new chemical preservative added to foods.

- Government agencies may incur an increase in the cost of monitoring compliance, but this is expected to be minor as the method of analysis is published and uses typical laboratory apparatus.

7.3 Comparison of Options

Option 1 appears to provide no apparent benefits to industry, consumers or government. Option 1 denies industry access to a flexible preservative in a wide range of food products.

Option 2 does not appear to impose any significant costs on industry, consumers or government. Option 2 provides benefits to industry in terms of product innovation and potential benefits for industry and consumers in reducing the losses associated with food spoilage and to reduce the level of usage of some of the current approved preservatives.

An assessment of the costs and benefits of Option 1 and 2 indicates that there would be a net benefit in permitting the use of ethyl lauroyl arginate in the food categories listed in Table 1 at the specified maximum level of usage. Therefore Option 2 is the preferred option.

8. Other considerations

8.1 Non-food use

Based on use information provided by the National Industrial Chemicals Notification and Assessment Scheme (NICNAS) for cosmetics and personal care products likely to contain ethyl lauroyl arginate, FSANZ has estimated the additional exposure arising from these products. The calculations for the exposure of cosmetics and personal care products including mean dietary exposure for the Australian population and Australian children are shown in Table 2 and discussed in Section 9.1.1.

8.2 Policy Guidance on Addition of Substances other than Vitamins and Minerals

In developing or reviewing food regulatory measures and variations of food regulatory measures FSANZ must have regard to any relevant written policy guidelines formulated by the Australia and New Zealand Food Regulation Ministerial Council (Ministerial Council).

The *Policy Guideline on the Addition to Food of Substances other than Vitamins and Minerals* (the Guideline) provides guidance on the addition to food of substances other than vitamins and minerals. This includes substances intentionally added solely for a technological purpose, such as food additives and processing aids.

The Guideline states that the addition of substances other than vitamins and minerals to food where the purpose of the addition is to achieve a solely technological function should be permitted where the substance meets a number of safety and technological objectives.

Having given due regard to the Guideline, FSANZ concluded that the addition of ELA should be permitted as proposed for the following reasons:

- the purpose for adding ELA to food is as a preservative. This has been articulated clearly by the manufacturer (see Section 2.2 and Supporting Document 3)
- the proposed addition of ELA to food is safe for human consumption (see Sections 5.1, 5.2 and 5.3; Supporting Documents 1 and 2)
- the proposed amounts of ELA added are consistent with achieving the technological function (see Section 5.5 and Supporting Document 3)
- ELA would be added in a quantity and a form which is consistent with delivering the stated purpose (see Section 5.5 and Supporting Document 3)
- no nutrition, health or related claims are to be made in regard to ELA.

COMMUNICATION AND CONSULTATION STRATEGY

9. Communication and Consultation

FSANZ has developed a communication strategy for Application A1015 that involved advertising the availability of the assessment report for public comment in the national press and placing the reports on the FSANZ website. In addition, FSANZ will issue a media release drawing journalists' attention to the matter.

The aim of the communication strategy is to inform the food industry and consumers about the issues raised in the Application and to communicate with health professionals about the proposed change to the standard and provide them with information for their clients if this should become necessary.

The process by which FSANZ considers standard matters is open, accountable, consultative and transparent. The purpose of inviting public submissions is to obtain the views of interested parties on the issues raised by the application and the impacts of regulatory options. The issues raised in the public submissions are evaluated and addressed in FSANZ assessment reports.

The Applicant, individuals and organisations that make submissions on this Application will be notified at each stage of the Application. The FSANZ Board's decision to approve the draft variation to the Code has been notified to the Ministerial Council. The Applicant and stakeholders, including the public, will be notified of the notification to the Ministerial Council as well as any gazettal of amendments to the Code in the national press and on the website.

9.1 Consultation

This Application is being assessed under a general procedure and was published for a round of public comment from 6 May to 17 June 2009. Three submissions were received; they were all from government agencies. Two of these submitters support FSANZ's preferred option of including ethyl lauroyl arginate as a food additive in the food types at the specified maximum limits as stated in Table 1 of the Assessment Report, with one of these requesting further information and clarification. The third submitter reflected mixed opinions from different agencies within a jurisdiction on FSANZ's preferred approach. Issues raised by the submitters are summarised (Attachment 2) and have been taken into account in preparing the Approval Report of this Application. The issues raised in the submissions are addressed in this Section.

9.1.1 Consider potential exposure from non-food sources

Two submitters commented that it is appropriate to consider the contribution of cosmetics and personal care products to total exposure for different age groups.

9.1.1.1 FSANZ response

An application for ethyl lauroyl arginate as a preservative to be used in cosmetics and personal care products is currently under consideration by NICNAS. Information provided by NICNAS has allowed FSANZ to consider additional exposure to ethyl lauroyl arginate from the use of cosmetics and personal care products. Routes of exposure from such products include dermal (for example, from deodorant, body lotion, soap, shampoo and shaving cream), inhalation (from deodorant sprays and hairsprays), and oral (from lipstick, toothpaste and mouthwash).

Experimental data to estimate dermal exposure indicate that systemic exposure to ethyl lauroyl arginate is likely to be negligible. An *in vitro* study using pig skin resulted in only 3.9% penetration of the applied ethyl lauroyl arginate dose into the epidermis, 1.5% into the dermis and undetectable transfer into the receptor solution (SCCP, 2008)[5]. Pig skin is generally a good model for human skin permeability (see for example Barbero & Frasch, 2009[6]). It is therefore likely that the systemic bioavailability of dermally applied ethyl lauroyl arginate in humans will be negligible or zero.

[5] SCCP (Scientific Committee on Consumer Products, 2008). Opinion on ethyl lauroyl arginate HCl.
[6] Barbero AM & Frasch HF (2009). Pig and guinea pig skin as surrogates for human *in vitro* penetration studies: a quantitative review. *Toxicol In Vitro*. **23**, 1-13.

Inhalation exposure from the use of cosmetic and personal care products that form aerosols, such as anti-perspirant /deodorant sprays and hairsprays was considered by FSANZ, even though the use of ethyl lauroyl arginate in such products is not recommended by NICNAS. The inhalation bioavailability of ethyl lauroyl arginate in aerosol form is not known but is also likely to be negligible because only a small percentage of such aerosol droplets are respirable. However, even assuming an inhalation bioavailability of 10% the upper estimate of inhalation systemic exposure is only several micrograms/kg bw/day. Inhalation can also lead to oral exposure, however this contribution is also expected to be minimal. The dermal and inhalation routes of exposure to ethyl lauroyl arginate are therefore considered to contribute negligibly to overall exposure and are not considered further.

Non-food oral exposure to ethyl lauroyl arginate from cosmetic and personal care products may also occur by inadvertent ingestion of products such as toothpaste, mouthwash and lipstick. The estimated oral exposure to ethyl lauroyl arginate from non-food and dietary sources for the Australian population and Australian children is shown in Table 2 below.

For non-food oral exposure in adults it was assumed that mouthwash (10 mL) is used three times daily with 10% swallowed each time, that toothpaste (1 g) is used twice daily with 17% swallowed and that lipstick (10 mg) is applied 4 times daily with 100% swallowed. The only source of non-food oral exposure for children was from the use of toothpaste (twice daily) with the worst case assumption that 100% is swallowed. The concentrations of ethyl lauroyl arginate proposed for lipstick, toothpaste and mouthwash are 0.4%, 0.8% and 0.8%, respectively. For children, a toothpaste amount of 0.5 g per brushing was assumed, the same amount used to calculate the amount of fluoride consumed by children for Application 588: Fluoride in packaged water. This results in an estimated intake of 0.9 mg/kg bw/day for non-food oral exposure in 18 month old children. While the level of consumption of 0.5 g was assumed based on the recommendation for young children to use a “pea sized” amount of toothpaste, recent studies indicate this amount is what is actually used by young children (Institute of Medicine, 1997; Table 8-4)[7]. The recommended level of toothpaste used is the same for all ages 18 months to 6 years, therefore the dietary exposure for children older than 18 months would be lower than that estimated for 18 month olds given their higher body weights. The Australian Dental Association (ADA, 2007)[8] recommends that children under the age of 18 months do not need to use toothpaste. Therefore non-food oral exposure does not need to be considered for this age group.

Table 2: Estimated oral exposure (non-food and dietary) to ethyl lauroyl arginate by population group.

	Exposure Source (mg/kg bw/day)		
	Oral	**Dietary**	
Population Group	**(non-food)**	**Mean**	**90th Percentile**
Australian Adults	0.4**		
Australian population 2+ years	-	0.7	1.6
Australian children (2 – 6 years)	0.4*	2.1	4.0
Children (18 months)	0.9*	-	-

* Calculation based on the assumptions of concentration of 0.8% ethyl lauroyl arginate, 0.5 g of toothpaste, 2 brushings/day and 9 kg bodyweight (18 months old) or 19 kg (2-6 years).
** Provided by the National Industrial Chemicals Notification and Assessment Scheme (NICNAS).

[7] Institute of Medicine (1997). Dietary Reference Intakes for Calcium, Phosphorus, Magnesium, Vitamin D, and Fluoride. Washington DC.
[8] Australian Dental Association (2007). Policy Statement 1.2.1, Community Oral Health Promotion Fluoride Use.

The oral exposure from dietary sources is less than 2 mg/kg bw/day for the Australian population 2 years and above and exposure from non-dietary sources for adults is less than 1 mg/kg bw/day. For Australian children, the total estimated oral exposure would not exceed the ADI of 0-5 mg/kg bw, based on dietary exposure at the 90th percentile.

A separate analysis was not done for the New Zealand population – it was assumed that similar exposure levels would apply.

9.1.2 Current International approval for use of ethyl lauroyl arginate

A submitter questioned the number of countries that have given the approval for ethyl lauroyl arginate and if the ADI proposed by EFSA in 2007 has changed.

9.1.2.1 FSANZ response

In September 2005, FDA issued a GRAS notice recognising the safety of ethyl lauroyl arginate when used as an antimicrobial ingredient in a wide range of food types at a maximum level of 200 ppm ethyl-N$^{\alpha}$-lauroyl-L-arginate·HCl. This determination was based on an ADI of 9 mg/kg bw of ethyl lauroyl arginate. The intended uses of ethyl lauroyl arginate in foods are listed in Appendix 1 of the Food Technology Report (Supporting Document 3).

The Ministry of Health of Mexico published in its Official Journal on 17 July 2006 a list of substances allowed as additives or processing aids in food, beverages and food supplements and ethyl lauroyl arginate is included. No maximum level was specified.

The 69th Joint Expert Committee on Food Additives (JECFA) held in June 2008 considered information available on ethyl lauroyl arginate. The Committee noted that EFSA had established an ADI of 0-0.5 mg/kg bw in 2007 and acknowledged that new information not available to EFSA enabled JECFA to conclude that the effects of ethyl lauroyl arginate on some white blood cell parameters in rodents were not relevant for a human risk assessment. Based on their evaluation, JECFA established an ADI of 0 – 4 mg/kg bw expressed as the active ingredient. JECFA has published a proposed use level for ethyl lauroyl arginate in a wide range of foods (except carbonated drinks) at 200 ppm (Appendix 2 of Supporting Document 2).

EFSA has not yet amended their ADI but has listed ethyl lauroyl arginate for consideration in July 2009.

In the EU, the Working Group of government experts on additives recently adopted the Working Document that will amend the EU Directive 95/2/EC by the end of 2009. This Working Document includes the statement “list of uses of ethyl lauroyl arginate should be restricted in order to bring the estimated intake within the limit of the ADI. Ethyl lauroyl arginate can under certain conditions be used as an efficient alternative to the currently authorised preservatives. It is therefore appropriate to permit these uses at Community level and to assign E243 as E number for ethyl lauroyl arginate”. (The Working Group’s list is included in Appendix 3 in the Food Technology Report – Supporting Document 3)

9.1.3 Levels of ethyl lauroyl arginate and food types

A submitter asked why the levels of ethyl lauroyl arginate appear higher and more food types are proposed in this application compared to the US and Europe.

9.1.3.1 FSANZ response

The proposed levels of ethyl lauroyl arginate in different countries reflect the ADI and food consumption pattern adopted by individual countries. Each country provides permissions in certain food types to ensure that sufficient ethyl lauroyl arginate level is used to justify its technological function while not exceeding their ADI.

The lists of intended uses of ethyl lauroyl arginate reported by the US FDA and JECFA (Appendices 1 and 2 in Food Technology Report – Supporting Document 3) have adopted a standard usage level of 200 ppm ethyl-N^{α}-lauroyl-L-arginate·HCl in a wide range of food types, with limited exceptions. On the other hand, the proposed applications of ethyl lauroyl arginate by the EC (Appendix 3 in Food Technology Report – Supporting Document 3) and FSANZ suggest specific usage levels depending on the type of food, e.g. 50 ppm ethyl-N^{α}-lauroyl-L-arginate·HCl in juices and drinks. A higher level, 400 mg ethyl-N^{α}-lauroyl-L-arginate·HCl, is proposed by FSANZ in certain foods such as fish and dairy based products. This is because ethyl lauroyl arginate reacts with protein-based foods and the higher amount of ethyl lauroyl arginate is required for effective preservation of the products.

9.1.4 Exclusion of apple juice

Submitters asked why apple juice was being excluded in this application and raised queries over the impact this would have on juice blends containing apple juice.

9.1.4.1 FSANZ response

Apple juice had been excluded from the list of intended uses initially because the Applicant believed it had the potential for ethyl lauroyl arginate exposure to exceed the ADI for children. There is no technological reason for not using ethyl lauroyl arginate in apple juice.

Additional dietary modelling has shown that the addition of ethyl lauroyl arginate to apple juice does not lead to a significant increase in the total exposure of ethyl lauroyl arginate in the Australian population, New Zealanders 15 years and above and Australians 2-6 years old (Supporting Document 2).

Therefore, FSANZ has now included apple juice in the list of intended uses. This will result in a simpler regulatory outcome.

9.1.5 Dietary exposure

A request was made to include the use of survey data from both New Zealand's 2002 National Children's Nutrition Survey and Australia's 2007 Children's Nutrition and Physical Activity Survey, which were not available during the assessment of A1015.

9.1.5.1 FSANZ response

The current situation with both of the children's surveys is that only the consumption data is uploaded into FSANZ's modelling program DIAMOND and available for use. For food additive modelling additional data sets need to be uploaded. These data sets are nearing completion, but some work still remains to incorporate the data into DIAMOND before it is ready for use. Therefore, the estimates of ethyl lauroyl arginate exposure will not be able to be conducted with the Australian and New Zealand children's survey data within the statutory time frame for this Application.

As the 2007 Australian consumption data are available, it was possible to estimate 2007 consumption of the major contributors as food groups identified in the Assessment Report for Application 1015 for the population group Australians 2 to 6 years. These consumption figures can be compared to the consumption figures extracted for the same population group from the 1995 Australian National Nutrition Survey. These data are presented in Table 3.

It should be noted that the comparison of consumption figures can only give an indication of differences between the surveys or changes in consumption patterns, due to differences in survey methodology.

Table 3: Consumption data from the 1995 National Nutrition Survey and the 2007* Australian Children's Nutrition and Physical Activity Survey for Australians 2 to 6 years.

Children 2 - 6 years				
Food Group	**Survey**	**No. of consumers**	**No. of consumers as % of all respondents**	**Mean** g/day
Comminuted meat products	1995	231	23.4	56
	2007	395	21.9	54
Fruit and vegetables juice and fruit drinks	1995	447	45.2	320
	2007	834	46.6	251
Cordials 'made up'	1995*	264	26.7	472
	2007	7	0.4	143
Cordial bases	1995	176	17.8	66
	2007**	350	19.5	49

*Both 1995 & 2007 data are unweighted
** The majority of cordial consumption is recorded under cordial bases for the 2007 NNS and cordials 'made-up' for the 1995 NNS.

The consumption data for the major contributors to ethyl lauroyl arginate exposure from the 1995 and 2007 nutrition surveys indicate potential for estimated dietary exposures of ethyl lauroyl arginate to be somewhat lower based on more recent consumption data. The exposures would need to be estimated using data for all foods and beverages consumed in the 2007 survey before this could be confirmed. However, from the conservative calculation using 1995 data there is limited evidence for potential overexposure.

9.1.6 Limited published literature supporting the effectiveness of ethyl lauroyl arginate

A submitter requested further evidence to be provided with respect to the effectiveness of ethyl lauroyl arginate and suggested that the internal studies provided by the Applicant be reviewed by one or two independent food microbiologists.

9.1.6.1 FSANZ response

FSANZ has required that the Applicant produce data for at least one representative food in each of the food types assessed in this Application.

The Applicant provided data from an independent laboratory study that demonstrated the activity of ethyl lauroyl arginate against a broad range of Gram-negative and Gram-positive bacteria, yeasts and moulds, with reported minimal inhibitory concentrations of 4-128 µg/mL.

There have been limited published scientific journal reports describing the use of ethyl lauroyl arginate in food products, due largely to the novelty and originality of the food preservative. However, the Applicant submitted 35 internal laboratory studies gathered using standardised techniques to demonstrate the activity of ethyl lauroyl arginate in a wide range of food products.

FSANZ microbiology experts reviewed all the data provided and in some cases, further information and clarification was sought.

FSANZ confirmed ethyl lauroyl arginate performed its stated technological function (i.e. retard or prevent the deterioration of foods by microorganisms) when applied to specific foods at the required concentration and stored under test conditions. As for any preservative, the extent of inhibition will vary depending on the physical and chemical nature of the food, type of microorganism, and the conditions of application, including the environment (e.g. temperature of storage).

FSANZ does not believe further review is required.

9.2 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.

Amending the Code to include ethyl lauroyl arginate as a food additive is unlikely to have a significant effect on trade. The ethyl lauroyl arginate preparation is consistent with the international specifications for ethyl lauroyl arginate. For these reasons FSANZ did not notify the WTO under either the Technical Barriers to Trade or Sanitary and Phytosanitary Measures Agreements.

CONCLUSION

10. Conclusion and Preferred Option

The Applicant has sought to amend Schedule 1 of Standard 1.3.1 – Food Additives, of the Code to permit maximum limits for the use of ethyl lauroyl arginate as a preservative in food types as listed in Table 3.

Decision

FSANZ approves the proposed draft variations to Standard 1.3.1, Schedule 1 – Food Additives, to include ethyl lauroyl arginate in the food types at the specified maximum limits as listed in Table 1 with subsequent amendments to Standard 1.2.4 – Labelling of Ingredients and Standard 1.3.4 – Identity and Purity.

10.1 Reasons for Preferred Approach

Amendments to the Code to include ethyl lauroyl arginate as a food preservative in Australia and New Zealand is proposed on the basis of the available scientific evidence for the following reasons:

- A detailed safety assessment has concluded the permission for the use of ethyl lauroyl arginate does not raise any public health and safety concerns, including considering development of antimicrobial resistance and exposure from cosmetics and personal care products. The relevant assessments are based on the best available scientific evidence.

- Use of ethyl lauroyl arginate as a preservative in the specified food categories and at the maximum permitted level is technologically justified and it could potentially be a useful component of food preservation systems. Based on data provided by the Applicant, ethyl lauroyl arginate could potentially replace some approved food grade preservatives, such as benzoates, sulphites and sorbates.

- The regulatory impact assessment concluded that the benefits of the potential use of ethyl lauroyl arginate in the specified food categories outweigh any costs associated with its use.

- The proposed variation to the Code is consistent with the section 18 objectives of the FSANZ Act.

11. Implementation and Review

The FSANZ Board's decision on this Approval Report has been notified to the Ministerial Council. Following notification, the proposed draft variation to the Code is expected to come into effect on gazettal, subject to any request from the Ministerial Council for a review of FSANZ's decision.

ATTACHMENTS

1A. Draft variation to the *Australia New Zealand Food Standards Code* (at Approval)
1B. Draft variations to the *Australia New Zealand Food Standards Code* (Indicating Changes from Drafting at Assessment)
1C. Draft variations to the *Australia New Zealand Food Standards Code* (at Assessment)
2. Summary of issues from Assessment Submissions

Attachment 1A

Draft variations to the *Australia New Zealand Food Standards Code* (at Approval)

Section 87(8) of the FSANZ Act provides that standards or variations to standards are legislative instruments, but are not subject to disallowance or sunsetting

To commence on gazettal:

[1] ***Standard 1.2.4*** *of the Australia New Zealand Food Standards Code is varied by –*

[1.1] *inserting in* Part 1 *of* Schedule 2 –

Ethyl lauroyl arginate	243

[1.2] *inserting in* Part 2 *of* Schedule 2 –

Ethyl lauroyl arginate	243

[2] ***Standard 1.3.1*** *of the Australia New Zealand Food Standards Code is varied by –*

[2.1] *inserting in subclause 5(2) –*

ethyl lauroyl arginate shall be calculated as ethyl-N^{α}-lauroyl-L-arginate·HCl

[2.2] *inserting in* Schedule 1, *under item* 0.1 Preparations of food additives –

243	Ethyl lauroyl arginate	200	mg/kg	

[2.3] *inserting in* Schedule 1*, under item* 1.6 Cheese and cheese products, *immediately following the last additive entry –*

1.6.1 Soft cheese, cream cheese and processed cheese

243	Ethyl lauroyl arginate	400	mg/kg	

Mozzarella cheese

243	Ethyl lauroyl arginate	200	mg/kg	

1.6.2 Hard cheese and semi-hard cheese

243	Ethyl lauroyl arginate	1	mg/cm^2	applied to the surface of food; maximum level determined in a surface sample taken to a depth of not less than 3 mm and not more than 5 mm.

[2.4] *inserting in* Schedule 1*, under item* 4.1.3 Peeled and/or cut fruits and vegetables –

243	Ethyl lauroyl arginate	200	mg/kg	

[2.5] *inserting in* Schedule 1*, under item* 4.3.8 Other fruit and vegetable based products* –

Rehydrated legumes

243	Ethyl lauroyl arginate	200	mg/kg	

[2.6] *inserting in* Schedule 1*, under item* 6.3 Processed cereal and meal products, *immediately following the last additive entry* –

6.3.1 Cooked rice

243	Ethyl lauroyl arginate	200	mg/kg	

[2.7] *inserting in* Schedule 1*, under item* 6.4 Flour products (including noodles and pasta)* –

243	Ethyl lauroyl arginate	200	mg/kg	cooked pasta and noodles only

[2.8] *inserting in* Schedule 1*, under item* 8.2 Processed meat, poultry and meat products in whole cuts or pieces –

243	Ethyl lauroyl arginate	200	mg/kg	

[2.9] *inserting in* Schedule 1*, under item* 8.3 Processed comminuted meat, poultry and game products –

243	Ethyl lauroyl arginate	315	mg/kg	

[2.10] *inserting in* Schedule 1*, under item* 9.3 Semi preserved fish and fish products –

243	Ethyl lauroyl arginate	400	mg/kg	

[2.11] *inserting in* Schedule 1*, under item* 14.1.2 Fruit and vegetable juices and fruit and vegetable juice products* –

243	Ethyl lauroyl arginate	50	mg/kg	

[2.12] *inserting in* Schedule 1*, under item* 14.1.3 Water based flavoured drinks* –

243	Ethyl lauroyl arginate	50	mg/kg	

[2.13] *inserting in* Schedule 1*, under item* 20.2 Food other than beverages*, *sub-item* dairy and fat based desserts, dips and snacks –

243	Ethyl lauroyl arginate	400	mg/kg	

[2.14] *inserting in* Schedule 1*, under item* 20.2 Food other than beverages*, *sub-item* sauces and toppings (including mayonnaises and salad dressings) –

243	Ethyl lauroyl arginate	200	mg/kg	

Attachment 1B

Draft variations to the *Australia New Zealand Food Standards Code* (Indicating Changes from Drafting at Assessment)

1. Item [2.11]

1.1 At Assessment

[2.11] *inserting in* Schedule 1*, under item* 14.1.2 Fruit and vegetable juices and fruit and vegetable juice products* –

243	Ethyl lauroyl arginate	50	mg/kg	not apple juice

1.2 At Approval

[2.11] *inserting in* Schedule 1*, under item* 14.1.2 Fruit and vegetable juices and fruit and vegetable juice products* –

243	Ethyl lauroyl arginate	50	mg/kg

Attachment 1C

Draft variations to the *Australia New Zealand Food Standards Code* (At Assessment)

Section 87(8) of the FSANZ Act provides that standards or variations to standards are legislative instruments, but are not subject to disallowance or sunsetting

To commence on gazettal:

[1] ***Standard 1.2.4*** *of the Australia New Zealand Food Standards Code is varied by –*

[1.1] *inserting in* Part 1 *of* Schedule 2 –

Ethyl lauroyl arginate	243

[1.2] *inserting in* Part 2 *of* Schedule 2 –

Ethyl lauroyl arginate	243

[2] ***Standard 1.3.1*** *of the Australia New Zealand Food Standards Code is varied by –*

[2.1] *inserting in subclause 5(2) –*

ethyl lauroyl arginate shall be calculated as ethyl-N^{α}-lauroyl-L-arginate·HCl

[2.2] *inserting in* Schedule 1, *under item* 0.1 Preparations of food additives –

243	Ethyl lauroyl arginate	200	mg/kg	

[2.3] *inserting in* Schedule 1*, under item* 1.6 Cheese and cheese products, *immediately following the last additive entry –*

1.6.1 Soft cheese, cream cheese and processed cheese

243	Ethyl lauroyl arginate	400	mg/kg	

Mozzarella cheese

243	Ethyl lauroyl arginate	200	mg/kg	

1.6.2 Hard cheese and semi-hard cheese

243	Ethyl lauroyl arginate	1	mg/ cm2	applied to the surface of food; maximum level determined in a surface sample taken to a depth of not less than 3 mm and not more than 5 mm.

[2.4] *inserting in* Schedule 1*, under item* 4.1.3 Peeled and/or cut fruits and vegetables –

243	Ethyl lauroyl arginate	200	mg/kg

[2.5] *inserting in* Schedule 1*, under item* 4.3.8 Other fruit and vegetable based products* –

Rehydrated legumes

243	Ethyl lauroyl arginate	200	mg/kg	

[2.6] *inserting in* Schedule 1*, under item* 6.3 Processed cereal and meal products, *immediately following the last additive entry* –

6.3.1 Cooked rice

243	Ethyl lauroyl arginate	200	mg/kg	

[2.7] *inserting in* Schedule 1*, under item* 6.4 Flour products (including noodles and pasta)* –

243	Ethyl lauroyl arginate	200	mg/kg	cooked pasta and noodles only

[2.8] *inserting in* Schedule 1*, under item* 8.2 Processed meat, poultry and meat products in whole cuts or pieces –

243	Ethyl lauroyl arginate	200	mg/kg

[2.9] *inserting in* Schedule 1*, under item* 8.3 Processed comminuted meat, poultry and game products –

243	Ethyl lauroyl arginate	315	mg/kg

[2.10] *inserting in* Schedule 1*, under item* 9.3 Semi preserved fish and fish products –

243	Ethyl lauroyl arginate	400	mg/kg

[2.11] *inserting in* Schedule 1*, under item* 14.1.2 Fruit and vegetable juices and fruit and vegetable juice products* –

243	Ethyl lauroyl arginate	50	mg/kg	not apple juice

[2.12] *inserting in* Schedule 1*, under item* 14.1.3 Water based flavoured drinks* –

243	Ethyl lauroyl arginate	50	mg/kg

[2.13] *inserting in* Schedule 1*, under item* 20.2 Food other than beverages*, *sub-item* dairy and fat based desserts*,* dips and snacks –

243	Ethyl lauroyl arginate	400	mg/kg

[2.14] *inserting in* Schedule 1*, under item* 20.2 Food other than beverages*, *sub-item* sauces and toppings (including mayonnaises and salad dressings) –

243	Ethyl lauroyl arginate	200	mg/kg

[3] ***Standard 1.3.4*** *of the Australia New Zealand Food Standards Code is varied by omitting paragraph 2(a), substituting –*

(a) Combined Compendium of Food Additive Specifications, FAO JECFA Monograph 1 (2005) as superseded by specifications published in FAO JECFA Monographs 3 (2006) and FAO JECFA Monographs 4 (2007) and FAO JECFA Monographs 5 (2008), Food and Agriculture Organisation of the United Nations, Rome; or

Attachment 2

Summary of issues in Assessment submissions

ISSUES	PROPOSED ACTION/INFORMATION REQUIRED
New Zealand Food Safety Authority	Support Option 2
New South Wales Food Authority	Satisfied with the justification of the use of ELA. Support progression of this Application
Need clarification on why the levels proposed by this Application are higher than levels allowed by US FDA	The higher levels are required only in foods that contain protein, for effective use of ELA. As this does not result in the exceedance of the ADI for any consumer groups, it does not cause public health concern.
Potential exposure through non-food source such as cosmetics	With advice from NICNAS regarding personal care products likely to contain ELA, FSANZ has estimated the potential dermal, inhalation and oral exposure arising from the use of such products. The potential additional exposure to ELA from cosmetics and personal care products is so low that it is unlikely to be of concern.
Queensland Government	
- Heath Department	Does not support either option
- Department of Employment, Economic Development and Innovation	Indication of supporting Option 2
Has EFSA revised its position on the ADI?	EFSA has not yet amended its ADI but has listed ethyl lauroyl arginate for consideration in July 2009
Should dietary modelling with data from 2002 NZ and 2007 Australia's children survey be included since they have now become available?	The estimates of ethyl lauroyl arginate exposure will not be able to be conducted with the Australian and New Zealand children's survey data within the statutory time frame for this Application. Work still remains to incorporate the additional datasets into DIAMOND before food additive modelling can be conducted. However, food consumption data is available to be used. The consumption data for the major contributors to ethyl lauroyl arginate exposure for Australian children aged 2 to 6 years from the 1995 and 2007 nutrition surveys may indicate a potential for estimated dietary exposures to be lower based on more recent consumption data.
Application in cosmetics - additional potential exposure in non-foods	See response to NSWFA above.
Status of international permissions for use of ELA	No change since the Assessment Report was published in May 2009

ISSUES	PROPOSED ACTION/INFORMATION REQUIRED
Requested further and more convincing evidence be provided for microbial effectiveness and that these results be reviewed by independent food microbiologists.	The Food Technology Report has been expanded to provide more information on the conditions of the studies. FSANZ has reviewed the data again and concluded that no further review by external microbiologists is required.
Why was ELA excluded for its use in apple juice? Regulatory clarification needed for juice blends that may contain apple juice.	There was no technological reason for excluding the use in apple juice. It was the Applicant's initial view that inclusion of apple juice may potentially exceed the ADI. Since the apple juice makes a minor difference in the dietary exposure in the high consumption group (2-6 year olds), it does not change the risk assessment conclusion. FSANZ acknowledges that this exclusion could lead to practical and regulatory complexity. FSANZ has now recommended to remove 'NOT apple juice' from Food type 14.1.2. in Standard 1.3.1.

ATTACHMENT 3

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

APPLICATION A1015
ETHYL LAUROYL ARGINATE AS A FOOD ADDITIVE
1st REVIEW REPORT

Executive Summary

On 30 October 2009, the Australia and New Zealand Food Regulation Ministerial Council (Ministerial Council) requested a First Review of Application A1015. This Application seeks to amend Standard 1.3.1 – Food Additives of the *Australia New Zealand Food Standards Code* (the Code) to include a new food preservative, Ethyl Lauroyl Arginate (ELA). FSANZ was required to review the decision by 30 January 2010.

The grounds for the review were that the draft Standard –

- did not protect public health and safety
- placed an unreasonable cost burden on industry or consumers
- was difficult to enforce or comply with in both practical or resource terms.

Within these grounds, the key issues addressed by FSANZ were:

- Chemical safety issues. Toxicological relevance of adverse findings in the rat forestomach and delayed onset of puberty in rat pups. Effects on rat forestomach are usually not considered to be toxicologically relevant for a hazard assessment because there is no equivalent organ in humans. Delayed onset of puberty in rat pups was considered relevant and the ADI was based on this effect.

- Side effects of arginine in humans. Arginine, being an integral part of the human diet, is unlikely to elicit an adverse response at the levels likely to be consumed through the use of ELA as a food preservative.

- Consumption data based on 1995 National Nutrition Survey (NNS). At the time the Approval Report was prepared, dietary modelling based on 1995 or 1997 NNS food consumption data provided the best estimate of dietary exposure to ELA. FSANZ believes that use of the older intake data does not invalidate the safety assessment, but in fact provides a more conservative estimation of intake. The dietary exposure assessment incorporated key findings of the 2007 Children's Nutrition and Physical Activity Survey. The data indicated that dietary exposures to ELA estimated using the 2007 food consumption data may be somewhat lower than that estimated using the 1995 food consumption data.

- The relationship between the levels proposed in the Code and the general permitted levels in the USA. The proposed levels in the Code vary with different food types and are based on technological needs. This approach resulted in lower levels being proposed in some food types and higher levels in others, depending on the technical need that was demonstrated for the individual food types.

- Use of unpublished scientific data for pre-market approval of ELA. It is conventional practice by all regulatory agencies around the world to consider and evaluate all available scientific data for pre-market approval of drugs, pesticides, food additives and processing aids. Relevant published and unpublished data which considered the safety of ELA has been evaluated in the FSANZ risk assessment.

- Limited cost-benefit analysis. The cost-benefit analysis did not identify medium to significant additional competitive impacts or compliance costs and therefore a detailed, quantitative cost-benefit analysis was not required under the Regulatory Impact Statement requirements. The analysis therefore met the requirements of the Office of Best Practice Regulation, who confirmed that permission to use the proposed additive appeared to be of a minor nature.

- Absence of suitable ELA analysis method. While it is agreed that there is no published method, an effective method was provided by the Applicant and should be within the capability of most accredited laboratories. The method is available upon request from FSANZ.

FSANZ has considered the grounds raised by the Ministerial Council in relation to Application A1015 – Ethyl Lauroyl Arginate as a Food Additive. The preferred option is to re-affirm the approval of the draft variations to Standard 1.3.1 and Standard 1.2.4 as notified to the Ministerial Council.

Decision

To re-affirm the variations to Standard 1.3.1, Schedule 1 – Food Additives and Standard 1.2.4, to include permissions for ethyl lauroyl arginate in the specified food types at the specified maximum limits for the active ingredient, ethyl-N^{α}-lauroyl-L-arginate·HCl.

Reasons for Decision

- The questions posed by the Ministerial Council in relation to the risk assessment of ELA did not yield any specific public health and safety concerns.

- The regulatory impact assessment indicates that there are no significant additional costs associated with this Application (as this is a voluntary permission). The use of ELA as a preservative could have potential benefits to industry and consumers by increasing choice and the shelf life of products.

- FSANZ considers the method of analysis provided by the Applicant and available for the enforcement of the new standard is practical and the procedure for the extraction in the different food types provided by the Applicant should be within the capabilities of most accredited analytical laboratories.

CONTENTS

1. Introduction

On 30 October 2009, the Australian and New Zealand Food Regulation Ministerial Council (Ministerial Council) requested a First Review of Application A1015. This Application seeks to amend Standard 1.3.1 – Food Additives of the *Australia New Zealand Food Standards Code* (the Code) to include a new food preservative, Ethyl Lauroyl Arginate (ELA).

FSANZ approved the addition of this preservative to the food types at specified maximum permitted levels (MPL) of the active ingredient in a range of food types.

FSANZ was required to review the decision by 30 January 2010.

2. Objectives of Review

The objective of this Review is to reconsider the draft variation to Standards 1.3.1 and 1.2.4 in light of the Ministerial Council's grounds for review as outlined in Section 3 below.

3. Grounds for Review requested by the Ministerial Council

The Ministerial Council requested that FSANZ review the decision to approve the draft variations for Application A1015, for a range of food types, on the grounds that the draft standard –

- did not protect public health and safety
- placed an unreasonable cost burden on industry or consumers
- was difficult to enforce or comply with in both practical or resource terms.

4. Background

FSANZ received an Application from Laboratarios Miret SA (LAMIRSA) on 28 August 2008. This Application seeks to amend Standard 1.3.1 – Food Additives of the *Australia New Zealand Food Standards Code* (the Code) to include a new food preservative, ELA.

ELA is a new synthetic chemical preservative that is currently not permitted as a food additive in Standard 1.3.1 or Standard 1.2.4. Its active component, ethyl-N^{α}-lauroyl-L-arginate·HCl, is a cationic surfactant[9], which is able to disrupt the integrity of cell membranes of a broad spectrum of bacteria, yeast and moulds. The active ingredient is typically present at a concentration between 85% and 95%. ELA is intended to be used to protect food against microbial growth and thus spoilage and it is proposed to be used in a wide range of food groups.

Based on a comprehensive risk assessment, FSANZ concluded that there was no public health and safety concern for ELA when used as a food additive at the maximum levels proposed by the Applicant (see Section 5.3 in the Approval Report). ELA has been shown to be an effective preservative against a broad range of micro-organisms in the food types proposed and it is stable during storage (see Section 5.5 in the Approval Report).

[9] Surfactants are wetting agents that lower the surface tension of a liquid, allowing easier spreading, and lower the interfacial tension between two liquids.

ELA has Generally Recognised As Safe (GRAS) status in the USA (2005). In April 2007, the European Food Safety Authority (EFSA) issued the opinion of the Scientific Committee on ELA as a new food preservative for use in a range of food categories. An Acceptable Daily Intake (ADI) of 0-0.5 mg/kg body weight (bw) based on the ELA preparation was established by EFSA. Most recently, in June 2008, the Joint FAO/WHO Expert Committee on Food Additives (JECFA) considered ELA as a food additive and allocated an ADI of 0-4 mg/kg bw for the active ingredient, ethyl-N^{α}-lauroyl-L-arginate·HCl. The large difference in the ADIs established by EFSA and JECFA is due to a difference in the interpretation of haematology data obtained in animal toxicity studies.

Based on the availability of an adequate range of suitable studies, FSANZ independently completed a safety assessment for ELA and established an ADI of 0-5 mg/kg bw[10], equivalent to the ADI set by JECFA for the active ingredient. The safety assessment reported that only minimal amounts of unchanged ELA enter the bloodstream because the compound is rapidly metabolised by enzymes in the upper intestine before substantial absorption can occur. In the intestine, ELA is rapidly degraded to compounds normally present in the diet such as the amino acid L-arginine and the fatty acid lauric acid.

Based on the conservative assumptions in the dietary exposure calculations, FSANZ concluded that there are no public health and safety concerns for ELA when used as a food additive at the maximum levels proposed by the Applicant.

5. Conclusion from the Approval Report

The FSANZ Board approved the proposed draft variations to Standards 1.2.4 and 1.3.1 to include permissions for ethyl lauroyl arginate in the food types at the specified maximum limits for the active ingredient, ethyl-N^{α}-lauroyl-L-arginate·HCl, as summarised in Table 1 of this Review Report.

6. Issues addressed in the First Review[11]

6.1 Public Health and Safety

6.1.1 Chemical safety issues

6.1.1.1 Risk assessment of rodent forestomach study

Ministerial Council statement: 'It is noted *ELA had a slight local irritant effect on the rat forestomach probably due to its surfactant activity. However, the rodent forestomach is not protected by mucus and has no anatomical equivalent in humans. The forestomach findings were therefore not considered to be relevant for a risk assessment in humans (page 5 of the Approval Report).* It is considered that more evidence is needed rather than making an assumption'.

Response: FSANZ acknowledges that the mechanism of forestomach irritation due to ELA has not been specifically investigated. However, establishing the mechanism of the local irritant effect of ELA on the rat forestomach is not considered necessary for safety assessment.

[10] The ADI of 0-4 mg/kg bw published by JECFA was derived from the same study as assessed by FSANZ, however JECFA applied a correction factor for the content of active ingredient in the batch used in the study (88%) to arrive at an ADI expressed as the active ingredient, ethyl-N^{α}-lauroyl-L-arginate·HCl. On the other hand, FSANZ established an ADI of 0-5 mg/kg bw expressed as ELA.

[11] The quotations used in this section are quotes of statements from the Request for Review Report while the italics within the quotation marks are quotes by the Ministerial Councils from the Approval Report.

The relevant points are: (i) humans do not possess a forestomach; (ii) the human stomach is lined by a protective layer of mucus; (iii) the rat stomach, which is also protected by mucus, did not show signs of irritation by ELA, and (iv) organs histologically similar to the forestomach, but with contact periods comparable to analogous human tissues such as the oral cavity, pharynx and oesophagus also did not show irritation in the rat studies. This can be explained by the short contact time with these organs relative to the much longer residence time applicable for the forestomach. There is no evidence of irritation of tissues analogous to human GI tract tissues where residence time is also analogous. Consequently, in view of the point made above and taking a weight of evidence approach, the finding of slight local irritation of the rat forestomach in isolation is not relevant for a human health and safety assessment and does not represent a risk to humans. This approach represents the usual practice which would be followed by the other (international) food regulatory agencies.

Mode of action studies may be justified in some cases, for example when a chemical exhibits carcinogenic activity in animal studies. Indeed, the relevance of chemically induced forestomach tumours to human safety assessment has been recently reviewed with a focus on the unique aspects of the rodent forestomach and the use of information on mode of action (Proctor et al., 2007). The review concluded that forestomach tumours associated with chronic irritation of the forestomach epithelium, particularly those induced by repeated oral gavage dosing, should not form the basis for carcinogenic classification or quantitative cancer potency estimates for humans. This highlights that even a severe adverse finding in animal studies may be of limited relevance to human safety assessment when other relevant information is considered.

6.1.1.2 Research on the reproductive and developmental toxicity studies

Ministerial Council statement: *'*It is also noted *In reproductive and developmental toxicity studies the only notable and consistent finding was delayed onset of puberty in female rats. There was no information to indicate that this effect may not be relevant to humans* (page 5 of the Approval Report). Accordingly it would appear further research needs to be initiated on this issue'.

Response: As FSANZ was unable to conclude that the delayed onset of puberty observed in female rat pups was not relevant for a human risk assessment this endpoint was used as a conservative basis to derive a human health standard. The ADI, which in turn was used to derive the limits on levels of ELA permitted in food. If the resulting health standard was too low to permit ELA to be used in a range of human foods then it would be the responsibility of the sponsor to provide additional data to demonstrate that this endpoint observed in rats was not relevant for a human risk assessment. Dietary exposure estimates for ELA in a wide range of foods indicates that this health standard (ADI) will not be exceeded when ELA is used at levels specified in the code.

6.1.1.3 Arginine, the metabolites and breakdown products of ELA

Ministerial Council statements: 'It is noted that ethyl lauroyl arginate can rapidly metabolise to N^{α}-lauroyl-L-arginine (LAS) and arginine. It is also the case that arginine can pose serious side effects.' and 'Drugs containing arginine have been found to cause adverse reactions in diabetes and kidney disease sufferers and stomach irritation in other persons. The FSANZ risk assessment has not addressed these matters sufficiently.'

Response: Arginine is present in food predominantly as a component of proteins and also as the free amino acid and is therefore a normal component of the human diet. The typical dietary intake of arginine for an individual is several grams per day.

Arginine plays an essential role in human physiology and metabolism and there is extensive published scientific literature on the potential therapeutic benefits of arginine supplementation (recently reviewed by Wu *et al.*, 2009). Very large oral doses of supplementary arginine administered in clinical trials to test for adverse effects have sometimes been shown to be associated with adverse effects such as nausea, vomiting and diarrhoea (Grimble, 2007). Most side effects of arginine occurred at single doses greater than 9 g in adults often when part of a regime of 30 g per day. Adverse effects seemed dependent on the dosage regime and disappeared if divided doses were ingested. A more recent analysis of published clinical trial data suggests that a safe level for arginine supplementation is up to 20 g per day (Shao and Hathcock, 2008).

The estimated additional exposure to arginine resulting from consumption of ELA at 5 mg/kg bw (the upper limit of the ADI) is approximately 100 mg for a 60 kg person. This additional exposure is very small relative to the amount of arginine consumed from eating a typical diet and raises no health or safety concerns.

6.1.1.4 Dietary intake in view of cumulative impact from a variety of foods

Ministerial Council statement: *Further dietary modelling work is required in view of the wide range of foods for which the use of ELA would be permitted. The cumulative impact of ELA intake from a variety of foods could mean that some people will consume a dose that is much higher than their acceptable daily intake.*

Response: The dietary exposure assessment that was conducted for the Approval Report incorporated all food types for which the Applicant requested ELA permissions and at the Maximum Permitted Level requested. This assessment included where a food containing ELA was consumed on its own (e.g. cheese eaten as a piece of cheese) and where a food containing ELA was consumed as an ingredient in another food (e.g. cheese on a pizza, the cheese in cheese sauce). Therefore, the dietary exposure assessment already considers the cumulative impact of exposure from a variety of foods using very conservative assumptions.

When conducting a dietary exposure assessment using NNS food consumption data, each individual's exposure to ELA is calculated using his or her individual food records from the NNS. The modelling is based on the total amount of ELA from all foods consumed summed for each individual. Population statistics (mean and 90th percentile consumer exposures) are then derived from the individuals' ranked dietary exposures.

FSANZ considers that the 90th percentile of dietary exposure is the best estimate of long term high exposure to a food chemical when only a single day of food consumption data is available for individuals. The 90th percentile dietary exposure to ELA is estimated to be well below the ADI for all population groups assessed. FSANZ considers that actual dietary exposure to ELA would be even lower as it is unlikely that all foods permitted to contain ELA would in fact contain it, or that all food manufacturers would use the Maximum Permitted Level of this preservative. FSANZ considers it is highly unlikely that individuals would have regular dietary exposure to ELA at a level higher than the ADI.

Therefore FSANZ concluded that further dietary modelling is not required.

6.1.1.5 Consumption data

Ministerial Council statement: 'The Approval Report continues to rely heavily on out-of date data where approximately 14 years has elapsed since the 1995 Australian National Nutrition Survey (NNS) and the assumptions may not represent current nutritional intakes. It is noted that the Approval Report states *it should be noted that limitations exist within the NNS data.*

These limitations relate to the age of the data and the changes in eating patterns that may have occurred since the data were collected '

Response: At the time the Approval Report was written, dietary modelling based on 1995 or 1997 NNS food consumption data provided the best estimate of actual consumption of a food and the resulting estimated dietary exposure to a food additive for the population or sub-groups of the population. There were no other more recent data sets that detailed food consumption data on an individual basis in the required format in FSANZ's dietary modelling computer program (DIAMOND). Although the consumption data for Australia's 2007 Children's Nutrition and Physical Activity Survey had been uploaded into DIAMOND at the time of the Approval Report, additional data sets needed to be developed for food additive dietary exposure assessments to be conducted.

The Approval Report examined the issue of possible changes in consumption by Australian children of major ELA-contributing foods (fruit and vegetable juices, cordials and comminuted meat products) between 1995 and 2007. This indicated that potential dietary exposures estimated using the 2007 food consumption data may be somewhat lower than that estimated using the 1995 food consumption data. The dietary modelling was done on highly conservative assumptions that all foods with this permission would contain it at the maximum level.

Therefore FSANZ believes that use of the older intake data does not invalidate the safety assessment, but in fact provides a more conservative estimation of intake.

6.1.1.6 UK dietary modelling results

Ministerial Council statement: 'Dietary modelling for ELA in the UK indicated that some children had up to 170% of the acceptable daily intake for ELA. There may be valid reasons why these results would not be replicated in Australia. However, this issue is not canvassed in the FSANZ report.'

Response: Dietary exposure assessments conducted by FSANZ are specific for the Australian and New Zealand populations, using food consumption data for our two countries and the proposed food additive use levels that are the subject of the application or proposal under consideration.

The major reason why estimated mean dietary exposures to ELA are much higher for UK children as a percentage of the ADI is that the UK exposure assessment used an ADI (0.5 mg/kg bw/day) that is one tenth of that used by FSANZ (5 mg/kg bw/day). The reasons for the different ADIs derived by EFSA and JECFA/FSANZ are considered in 6.1.3.1.

6.1.2 Efficacy and stability

6.1.2.1 Efficacy and stability of the different physical forms of ELA

Ministerial Council statement*: '*There are references in the Approval Report to ELA as a powdered substance as well as in an aqueous solution. As the report appears to mainly refer to ELA in the powder form, there are questions as to its suitability and efficacy in an aqueous solution*.'* and *'*Nearly all the scientific data relied upon is taken from studies of ELA as a compound rather than in the various solution forms. It is not clear whether conclusions drawn from the compound studies are applicable to the solution form of ELA.'

Response: ELA is effective in either solid or liquid form, depending on its application on the product.

ELA is a white solid powder after its synthesis and purification. According to the Applicant, the application of this substance in its solid form presents technical difficulties due to the need to apply ELA homogenously and it being used at a low dosage in food products. The food industry prefers liquid product over solids. Therefore most of the ELA commercial products are sold in solution, in which ELA is dissolved in appropriate food-grade solvents such as water, propylene glycol, glycerine or ethanol. Examples of these commercial products with their respective solvents (in brackets) are: Mirenat-N (propylene glycol), Mirenat-G (glycerine) and Mirenat-ET (ethanol and water). A few of the ELA products are sold in solid form mixed with maltodextrin or salt.

The Applicant tested the stability and efficacy of ELA in the media appropriate for each food product to ensure that the stated amount of active ingredient is present through the stated shelf life of the product. The level of the active ingredient of ELA, ethyl-N^{α}-lauroyl-L-arginate·HCl, stated in the studies, is the actual amount of the compound required for preserving the food product over the desired length of storage irrespective of its physical forms. For example, ELA dissolved in propylene glycol (10% w/w) added to refrigerated soups at 200 mg/kg inhibited growth of aerobic mesophiles for at least 31 days. Another example showed that ELA dissolved in glycerine (20% w/w) used at 200 mg/kg suppressed growth of aerobic and enteric bacteria in a ready-to-eat salad for at least 30 days.

6.1.2.2 Evidence on the stability and efficacy of ELA in the various solutions and in specific food types stored under different environmental conditions

Ministerial Council statement: 'It is noted *While the data submitted by the Applicant demonstrates the inhibition of specific micro-organisms in a wide variety of food types, empirical laboratory data would need to be gathered to confirm efficacy in specific food products and under different environmental conditions.'* and 'There is insufficient evidence in the FSANZ report or in the literature on the stability of ELA in the various solutions to perform effectively as an antimicrobial in foods. Some foods may cause ELA to break down and thus render it ineffective as a preservative. This could potentially lead to food borne illness in consumers.'

Response: As it is not feasible to test the efficacy of ELA in every food product, FSANZ required the Applicant to demonstrate the efficacy of ELA in a food representative of each food type including storage under appropriate conditions.

Food types in the initial list of intended uses provided by the Applicant were removed from the initial list if no evidence of efficacy and stability was given in relevant storage studies. Examples of food types from the initial list removed as a result of the FSANZ assessment were: chewing gum, oil emulsions, ice confection, low joule jam, bakery products, tabletop sweeteners, liquid egg products, vegetable protein products, infant formula, formulated supplementary sports drinks, alcoholic beverages, tea, herbal infusions and beverages in mixed food types.

Thirty five laboratory reports were provided by the Applicant that demonstrated the inhibition of specific microorganisms in the approved food types over the desired shelf life. Many of these tests were done in collaboration with the Applicant's potential customers, i.e. food manufacturers.

FSANZ confirmed ELA performed its stated technological function (i.e. retard or prevent the deterioration of foods by microorganisms) when applied to foods at the required concentrations and stored under test conditions. As was noted by the Ministerial Council, approval for use of ELA in any food types not listed in the current list would need to be assessed for its efficacy in the specific food types and under appropriate environmental conditions prior to its use. This would require a new application and assessment.

6.1.2.3 Proposed ELA limits compared to the USA proposed levels

Ministerial Council statement: 'We also noted in the Approval Report that ELA is being proposed to be added to some foods well in excess of the 200mg/kg (e.g. up to 400 mg/kg in semi preserved fish and fish products and dairy and fat based desserts, dips and snacks).'

Response: Different levels of ELA are set out in the regulations of different countries for certain food types, to ensure that sufficient ELA is used to perform its technological function in those particular foods, without resulting in dietary exposures exceeding the ADI. Each country sets limits that reflect the ADI and the food consumption patterns of their countries.

A general level of 200 mg ethyl-Nα-lauroyl-L-arginate.HCl/kg in the permitted range of food types has been permitted by some countries.

However, FSANZ proposes specific usage levels depending on the type of food, e.g. 50 mg/kg for juices and drinks. A higher level, 400 mg/kg, is proposed in certain foods such as fish and dairy based products because ELA interacts with proteins and therefore these high protein foods require a higher level for effective preservation.

6.1.2.4 Review by independent microbiologist

Ministerial Council statement: 'The Approval Report does not adequately address the issue of a review by independent food microbiologists relative to the microbial effectiveness of ELA.'

Response: The usual practice in FSANZ is to obtain independent expert reviews where an issue is particularly complex – or contentious. In this case the microbiological aspects of the risk assessment were relatively routine and therefore there was no need for an independent review.

Laboratory studies provided by the Applicant were reviewed by food technologists and microbiologists in FSANZ to confirm that ELA performed its stated technological function (i.e. to retard or prevent the deterioration of foods by micro-organisms) when applied to specific food types. In a number of cases, further information and/or clarification on particular studies was sought from the Applicant. This included providing further details on the properties of the food to which ELA was being applied, as well as justification of the study duration with respect to the expected shelf-life of the product.

As with any preservative, the extent of inhibition will vary depending on the physical and chemical nature of the food, type of micro-organism, and the conditions of application including the environment (e.g. temperature of storage). Only food types with studies that demonstrated satisfactory results were included in the proposed intended uses of ELA.

6.1.3 Other aspects

6.1.3.1 The reason for the differing ADIs derived by EFSA and JECFA/FSANZ

Discussion of the differing ADIs derived by EFSA (0.5 mg/kg bw/day) and JECFA/FSANZ (5 mg/kg bw/day) was provided in the Assessment Report and the Approval Report. Since completion of the FSANZ Approval Report, EFSA has considered the opinions of three experts on white blood cell data obtained in a series of animal toxicity studies with ELA (EFSA 2009). These expert opinions were considered as part of the FSANZ (and JECFA) assessments. EFSA stated that each of these experts concluded that the haematological findings are toxicologically not significant.

However, EFSA concluded that scientific evidence of a plausible mechanism for the alterations in white blood cell counts has not been provided and that their original concerns and uncertainties have therefore not been addressed by these expert opinions. The original ADI derived by EFSA therefore remains unchanged.

Although FSANZ acknowledges that EFSA has used a more conservative toxicological endpoint, usual international best practice is to take a weight of evidence approach. In this case such a conservative endpoint would not be considered to conform with agreed practice – which is reflected in the different end point agreed by JECFA. FSANZ's conclusions are consistent with those of both the EU Scientific Committee on Cosmetic Products Intended for Consumers (SCCP) and of JECFA.

FSANZ is of the opinion that the haematological findings are unlikely to be toxicologically significant and therefore not an appropriate end-point for defining the ADI. As discussed in the Assessment Report, the white blood cell findings did not show a clear dose-effect relationship, varied depending on the rat strain and sex, and were inconsistent both within and between studies. In addition, there were no effects on normal myeloid cell production, bone marrow, lymphoid tissues or any other adverse histology findings.

Professor Brian Priestly was requested to review the toxicological assessment and concluded that on balance the totality of the information available is more consistent with the conclusions of JECFA and FSANZ than with those of EFSA. Therefore FSANZ reiterates its decision to base its risk characterisation on an ADI of 5 mg/kg bw/day.

6.1.3.2 Unpublished technical data

Ministerial Council statement: *'*The FSANZ review acknowledges throughout the document that the available data set is suboptimal. This is evidenced by *Unpublished laboratory data...';* and *'*Under *References* shown in Supporting Document 1 – Hazard Assessment Report there are 41 referred to publications – 35 have the words *Unpublished report* beside them.'

Response: FSANZ does not acknowledge that the available data set is suboptimal. While the available data on ELA consists primarily of unpublished reports, FSANZ is not of the opinion that this constitutes a suboptimal data set.

Applications to amend the Code were and must be supported by the provision of an adequate and robust data package which is frequently a combination of published journal articles and unpublished studies. All food regulators and other regulatory agencies, e.g. pharmaceutical regulators consider both published and unpublished student in their risk assessments. While there is a perception that a peer-reviewed article in a scientific journal has greater authority for a safety assessment, published journal articles also have some limitations. Published articles are often limited in length and this has the inevitable consequence of data being presented almost exclusively in summary or minimal form. Many of the important technical details or supporting observations are not included and the 'pathway' to the conclusions is not always transparent. In some instances, the paucity of important technical detail can prevent validation of the conclusions.

The peer review process which selects the articles appropriate for publication is usually based on whether the material is worthy of dissemination to other scientists. For example, it describes significant advances in the understanding of a biological process, proposes and tests or refutes hypotheses, or describes potentially useful new test methods or materials. These articles also provide a very valuable forum for the discussion of the findings in relation to other publications.

Consequently investigations, such as safety studies, which may reveal no adverse findings, are frequently not submitted for publication because they fail to meet the selection criteria for publication.

A limitation of unpublished studies can be that the results are usually discussed only within the context of that particular study and do not refer to other companion studies. The nature of these studies also sometimes necessitates that they are evaluated as 'commercial-in-confidence' but this does not devalue the quality of the data.

In undertaking a risk assessment, FSANZ evaluators consider all available data. The strength or weighting of individual studies (published or unpublished) depends on whether the evaluator has access to all the data or only an abridged summary from which to make an independent evaluation and interpretation. The same issues exist for the evaluation of drugs for human or veterinary use or the use of agricultural chemicals in Australia, Europe, North America and Japan.

Both published and unpublished studies have perceived limitations and benefits but all such studies are essential in establishing standards to protect public health. FSANZ needs to be able to consider the scientific merit of all available data in order to base its decisions on 'the best available evidence'. FSANZ was assured by its review of the studies that the data set was sufficient to substantiate the safety of the ELA.

6.1.3.3 US Food and Drug Administration (FDA) GRAS statement

The Ministerial Council stated that the Approval Report contained conflicting statements regarding the GRAS notices in which maximum levels were quoted as 200 mg ethyl-N^{α}-lauroyl-L-arginate·HCl /kg and 225 mg ELA/kg.

Response: There is no conflict in these levels because 200 mg/kg of the active ingredient (ethyl-N^{α}-lauroyl-L-arginate·HCl) corresponds to 225 mg/kg of ELA commercial product containing the active ingredient at a concentration of approximately 90% w/w (i.e. the middle of the range of 85-95% as listed in the JECFA specifications). FSANZ accepts there would have been less confusion if the same units and only one of either the active form or the commercial preparation of ELA had been used in the report.

6.1.3.4 Cosmetic use studies by the Scientific Committee on Cosmetic Products Intended for Consumers (SCCP)

M**inisterial Council statement***:* 'It is noted *the SCCP considered that ELA was considered safe for consumers, when used up to a maximum concentration of 0.4% as a preservative in cosmetic products but excluding products for the lips, oral hygiene products and spray products.* There is no explanation given why products for the lips, oral hygiene products and spray products were excluded*.'* and 'It is also noted *The SCCP opinion was based on the use of ELA in the specified cosmetic products only and took no account of other sources of exposure.'*

Response: FSANZ agrees that the SCCP report does not state the reason(s) for excluding products for the lips, oral hygiene products and spray products. The SCCP was considering a permission for the addition of 4000 mg/kg of cosmetic product compared to the proposed food use of 200 mg/kg of food. As irritation is a concentration and contact time dependent effect, a conclusion that irritation of mucous membranes is a potential risk at a level of 4000 mg/kg in a cosmetic or oral care product, is not inconsistent with a conclusion that a level of 200 mg/kg in a food does not present such a risk. The latter conclusion is entirely consistent with the results of the rat oral study which demonstrated no irritation in rat tissues relevant for human risk assessment.

The lack of explanatory detail in the SCCP report does not compromise the validity of the FSANZ safety assessment which also considered the potential additional oral exposure to ELA from the use of cosmetics and personal care products, in addition to dietary exposure.

6.2 Cost burden on industry or consumers

Ministerial Council statement: 'The cost-benefit analysis provides so little detail that it is impossible to know how the conclusion was reached by FSANZ', and 'FSANZ is requested to provide advice on how costs associated with the enforcement by jurisdictions were determined and how these costs were agreed upon in regard to this Application'.

Response: According to the FSANZ Act and the Council of Australian Government (COAG) guidelines, FSANZ's Regulatory Impact Statement (including cost-benefit analyses) considers the impact of various options on all sectors of the community, including consumers, the food industry and governments in Australia and New Zealand.

The Regulatory Impact Statement relies on input from stakeholders where relevant and is subject to clearance from the Office of Best Practice Regulation (OBPR), which promotes the Government's objective of improving the effectiveness and efficiency of regulation.

The OBPR Best Practice Regulation guidelines suggest that for proposals with no or low compliance costs, no further analysis is required12.

Where medium to significant competitive impacts or compliance costs are likely, FSANZ consults further with stakeholders and OBPR to estimate compliance costs of regulation. The level of analysis is commensurate to the issue and the regulatory impacts of the application or proposal.

In relation to this Application, a Best Practice Regulation Preliminary assessment did not identify any significant additional costs or issues for affected parties. This was approved by OBPR (OBPR Ref 10222), and they confirmed that the permission to use the proposed additive would appear to be of a minor or machinery of government nature and to not substantially alter existing regulatory arrangements. Therefore detailed or quantitative estimates of costs and benefits were not required and this Application did not seek input from stakeholders. However, although quantification of costs was not required, if this information had been provided voluntarily by submitters it would have been included in the Approval Report.

No further quantitative estimates, including additional enforcement costs from any jurisdictions, were provided by way of submission during the consultation period. Any costs incurred by manufacturers would be voluntary and determined by market forces rather than regulatory pressures.

As there were no public health and safety issues identified, and use of this preservative would be voluntary thereby increasing choice and potentially the shelf life of products, FSANZ's Cost Benefit Analysis concluded that there could be a net benefit from this Application.

[12] Best Practice Regulation Handbook, Pg 18.
http://www.finance.gov.au/obpr/docs/handbook.pdf

6.3 Enforcement and compliance issues

6.3.1 Analytical methods

6.3.1.1 Analytical methods for a range of foods

Ministerial Council statement: 'From a laboratory perspective, it is an on-going concern that FSANZ continues to develop standards where there are no or few analytical procedures to enable jurisdictions to monitor industry compliance with the new standards.' and 'There does not appear to be any peer reviewed or published analytical method that can reliably extract and determine the levels of ELA added to the range of foods proposed by the applicant. As a result, it will not be possible to enforce the new standard.'

Response: As was noted in the Approval Report, ELA is a novel food additive and therefore there are limited published methods for the use of this new preservative.

The analytical method suggested by the Applicant for quantifying the content of the active compound is reverse-phase high performance liquid chromatography (RP-HPLC). Despite the range of foods to be analysed being broad, the equipment, reagents and chromatographic conditions would be the same for the different food types; they differ only in method of extraction of the active ingredient from each sample.

The Applicant's proposed extraction method involves the use of slightly different but routine sample preparation techniques, depending on the type of food matrix to be analysed. Two of the techniques are suitable for solid and semi-solid food matrices and a third technique is suitable for liquid food matrices. The Application provided examples of different food matrices from which the ELA has been successfully extracted.

These methods are routine laboratory procedures, with slight variations on the RP-HPLC running conditions (e.g. temperatures, solutions and rates of elution). They are available in the Application A1015 Public Register file or from FSANZ by request if the enforcement agencies wish to consider these methods.

6.3.1.2 Methods for determining arginine and lauric acid

Ministerial Council statement: 'It should be noted that the extraction and determination of ELA is especially difficult in foods with high protein and fat levels, such as meat and cheeses as these naturally contain arginine and lauric acid, the metabolites of ELA.'

Response: The proposed method measures the active ingredient of ELA, ethyl-N^{α}-lauroyl-L-arginate·HCl. The presence of arginate and lauric acid does not interfere with the analysis.

6.3.1.3 Number of submitted internal studies

Ministerial Council noted a discrepancy regarding the number of studies submitted by the Applicant.

Response: There were 35 internal laboratory reports submitted by the Applicant (as stated on page 16 of the Approval Report). However, Experiment #33 was split into Part A and Part B. As a result, it was correctly reported as 36 studies being submitted (on page 7 of the Approval Report).

6.3.2 Drafting clarity

6.3.2.1 Propylene glycol is proposed as a solvent for ELA but it is not permitted to be used in fresh cut fruits and vegetables

Ministerial Council statement: *'*Under a different part of the Code, propylene glycol is not permitted to be added to certain foods such as cut fresh fruit and vegetables, fruit and vegetable juices and certain kinds of preserved fish. However, the proposed new standard would appear to permit the use of ELA soluble in propylene glycol as a preservative in these foods. It is not clear whether this general permission is intended to override the prohibition on the use of propylene glycol in certain foods elsewhere in the Code.' and 'It is noted that the product is to be sold in a solution form with ELA dissolved in appropriate carriers such as water, propylene glycol, glycerine or ethanol. The draft standard is not clear on this issue.'

Response: Propylene glycol, water, glycerin and ethanol are generally permitted processing aids in clause 3 of Standard 1.3.3. The use of these substances as carriers, solvents or diluents for ELA would therefore be permitted.

Additives in Schedule 2 of Standard 1.3.1, including propylene glycol, are permitted in a range of foods including peeled and/cut fruit and vegetables, and semi-preserved fish and fish products (food type 4.1.3 and food type 9.3, respectively, in Schedule 1 of Standard 1.3.1).

7. Review Options

There are three options proposed for consideration under this Review:

1. re-affirm approval of the draft variations to Standard 1.3.1 and Standard 1.2.4 of the Code as notified to the Ministerial Council; or

2. re-affirm approval of the draft variations to Standard 1.3.1 and Standard 1.2.4 subject to any amendments FSANZ considers necessary; or

3. withdraw approval of the draft variations to Standard 1.3.1 and Standard 1.2.4 as notified to the Council.

8. Decision

Decision

To re-affirm the variations to Standard 1.3.1, Schedule 1 – Food Additives and Standard 1.2.4, to include permissions for ethyl lauroyl arginate in the specified food types at the specified maximum limits for the active ingredient, ethyl-N$^{\alpha}$-lauroyl-L-arginate·HCl.

The specified maximum limits for the active ingredient, ethyl-N$^{\alpha}$-lauroyl-L-arginate·HCl, in the permitted food types are listed in Table 1.

Table 1: Intended uses of ethyl lauroyl arginate

Food types		Ethyl lauroyl arginate* (mg/kg; maximum)
0.1	Preparations of food additives	200
1.6	Cheese - soft/cream/processed and mozzarella	400 except for mozzarella at 200

Food types		Ethyl lauroyl arginate* (mg/kg; maximum)
1.6	Cheese – Hard/Semi-hard	1 mg/cm^2 of surface area of cheese (taken to a depth of 3 mm and not more than 5 mm)
4.1.3	Peeled and/or cut fruits and vegetables	200
4.3.8	Processed fruits and vegetables—rehydrated legumes only	200
6.3	Processed cereal and meal products-cooked rice only	200
6.4	Flour products (including noodles and pasta) – cooked pasta and noodles only	200
8.2	Processed meat, poultry and meat products in whole cuts or pieces	200
8.3	Processed comminuted meat and poultry products	315
9.3	Semi preserved fish and fish products	400
14.1.2	Fruit and vegetable juices and fruit and vegetable juice products	50
14.1.3	Water based flavoured drinks	50
20.2	Savoury toppings or fillings - essentially sauces such as tomato paste used in ready to eat pizzas, etc.	200
20.2	Dairy and fat based desserts, dips and snacks	400

* Ethyl lauroyl arginate is the name given to the commercially available product which contains 85-95% w/w of the active ingredient ethyl-N$^{\alpha}$-lauroyl-L-arginate·HCl, as indicated in the JECFA specifications. The values in Table 1 are the maximum permitted levels of the active ingredient.

8.1 Reasons for Decision

- The questions posed by the Ministerial Council in relation to the risk assessment of ELA did not yield any specific public health and safety concerns.

- The regulatory impact assessment indicates that there are no significant additional costs associated with this Application (as this is a voluntary permission). The use of ELA as a preservative could have potential benefits to industry and consumers by increasing choice and the shelf life of products.

- FSANZ considers the method of analysis provided by the Applicant and available for the enforcement of the new standard is practical and the procedure for the extraction in the different food types provided by the Applicant should be within the capabilities of most accredited analytical laboratories.

9. Implementation and Review

The draft variations to Standards 1.3.1 and 1.2.4 will come into effect on the date of gazettal.

10. References

European Food Safety Authority (EFSA). (2007) Opinion of the Scientific Panel on Food Additives, Flavourings, Processing Aids and Materials in Contact with Food on a request from the Commission related to an application on the use of ethyl lauroyl arginate as a food additive; Question number EFSA-Q-2006-035. The EFSA Journal, 511:1-27.

European Food Safety Authority EFSA) (2009) Statement on the evaluation of the new information provided on the food additive ethyl lauroyl arginate. The EFSA Journal, 7(10):1333. http://www.efsa.europa.eu/en/scdocs/doc/ans_ej1333_Ethyl_lauroyl_arginate_st_en.pdf

Grimble GK (2007) Adverse gastrointestinal effects of arginine and related amino acids. *J. Nutr.*, 137(6 Suppl 2):1693S-1701S.

Proctor DM, Gatto NM, Hong SJ, Allamneni KP (2007) Mode-of-action framework for evaluating the relevance of rodent forestomach tumors in cancer risk assessment.*Toxicol. Sci.*, 98(2):313-326.

Shao A, Hathcock JN (2008) Risk assessment for the amino acids taurine, L-glutamine and L-arginine. *Regul Toxicol Pharmacol.*, 50(3):376-399.

Wu G, Bazer FW, Davis TA, Kim SW, Li P, Marc Rhoads J, Carey Satterfield M, Smith SB, Spencer TE, Yin Y (2009) Arginine metabolism and nutrition in growth, health and disease. *Amino Acids*, 37(1):153-168.

ATTACHMENT

Draft variations to the *Australia New Zealand Food Standards Code*

Attachment 1

Draft Variations to the *Australia New Zealand Food Standards Code*

Section 87(8) of the FSANZ Act provides that standards or variations to standards are legislative instruments, but are not subject to disallowance or sunsetting

To commence on gazettal:

[1] ***Standard 1.2.4*** *of the Australia New Zealand Food Standards Code is varied by –*

[1.1] *inserting in* Part 1 *of* Schedule 2 –

Ethyl lauroyl arginate	243

[1.2] *inserting in* Part 2 *of* Schedule 2 –

Ethyl lauroyl arginate	243

[2] ***Standard 1.3.1*** *of the Australia New Zealand Food Standards Code is varied by –*

[2.1] *inserting in subclause 5(2) –*

ethyl lauroyl arginate shall be calculated as ethyl-N^{α}-lauroyl-L-arginate·HCl

[2.2] *inserting in* Schedule 1, *under item* 0.1 Preparations of food additives –

243	Ethyl lauroyl arginate	200	mg/kg	

[2.3] *inserting in* Schedule 1*, under item* 1.6 Cheese and cheese products, *immediately following the last additive entry –*

1.6.1 Soft cheese, cream cheese and processed cheese

243	Ethyl lauroyl arginate	400	mg/kg	

Mozzarella cheese

243	Ethyl lauroyl arginate	200	mg/kg	

1.6.2 Hard cheese and semi-hard cheese

243	Ethyl lauroyl arginate	1	mg/cm^2	applied to the surface of food; maximum level determined in a surface sample taken to a depth of not less than 3 mm and not more than 5 mm.

[2.4] *inserting in* Schedule 1*, under item* 4.1.3 Peeled and/or cut fruits and vegetables –

243	Ethyl lauroyl arginate	200	mg/kg

[2.5] *inserting in* Schedule 1*, under item* 4.3.8 Other fruit and vegetable based products* –

Rehydrated legumes

243	Ethyl lauroyl arginate	200	mg/kg	

[2.6] *inserting in* Schedule 1*, under item* 6.3 Processed cereal and meal products, *immediately following the last additive entry* –

6.3.1 Cooked rice

243	Ethyl lauroyl arginate	200	mg/kg	

[2.7] *inserting in* Schedule 1*, under item* 6.4 Flour products (including noodles and pasta)* –

243	Ethyl lauroyl arginate	200	mg/kg	cooked pasta and noodles only

[2.8] *inserting in* Schedule 1*, under item* 8.2 Processed meat, poultry and meat products in whole cuts or pieces –

243	Ethyl lauroyl arginate	200	mg/kg	

[2.9] *inserting in* Schedule 1*, under item* 8.3 Processed comminuted meat, poultry and game products –

243	Ethyl lauroyl arginate	315	mg/kg	

[2.10] *inserting in* Schedule 1*, under item* 9.3 Semi preserved fish and fish products –

243	Ethyl lauroyl arginate	400	mg/kg	

[2.11] *inserting in* Schedule 1*, under item* 14.1.2 Fruit and vegetable juices and fruit and vegetable juice products* –

243	Ethyl lauroyl arginate	50	mg/kg	

[2.12] *inserting in* Schedule 1*, under item* 14.1.3 Water based flavoured drinks* –

243	Ethyl lauroyl arginate	50	mg/kg	

[2.13] *inserting in* Schedule 1*, under item* 20.2 Food other than beverages*, *sub-item* dairy and fat based desserts, dips and snacks –

243	Ethyl lauroyl arginate	400	mg/kg	

[2.14] *inserting in* Schedule 1*, under item* 20.2 Food other than beverages*, *sub-item* sauces and toppings (including mayonnaises and salad dressings) –

243	Ethyl lauroyl arginate	200	mg/kg	