

22 April 2021
153-21

Call for submissions – Application A1214

Nicotinamide riboside chloride as Vitamin B3 in FSMP

Food Standards Australia New Zealand (FSANZ) has assessed an application made by ChromaDex Inc. to amend the Code to permit the use of nicotinamide riboside chloride as a form of vitamin B3 in food for special medical purposes and has prepared a draft food regulatory measure. Pursuant to section 31 of the *Food Standards Australia New Zealand Act 1991* (FSANZ Act), FSANZ now calls for submissions to assist consideration of the draft food regulatory measure.

For information about making a submission, visit the FSANZ website at [information for submitters](#).

All submissions on applications and proposals will be published on our website. We will not publish material that we accept as confidential, but will record that such information is held. In-confidence submissions may be subject to release under the provisions of the *Freedom of Information Act 1991*. Submissions will be published as soon as possible after the end of the public comment period. Where large numbers of documents are involved, FSANZ will make these available on CD, rather than on the website.

Under section 114 of the FSANZ Act, some information provided to FSANZ cannot be disclosed. More information about the disclosure of confidential commercial information is available on the FSANZ website at [information for submitters](#).

Submissions should be made in writing; be marked clearly with the word 'Submission' and quote the correct project number and name. While FSANZ accepts submissions in hard copy to our offices, it is more convenient to receive submissions electronically through the FSANZ website via the link on [documents for public comment](#). You can also email your submission directly to submissions@foodstandards.gov.au.

There is no need to send a hard copy of your submission if you have submitted it by email or via the FSANZ website. FSANZ endeavours to formally acknowledge receipt of submissions within 3 business days.

DEADLINE FOR SUBMISSIONS: 6pm (Canberra time) 20 May 2021

Submissions received after this date will not be considered unless an extension had been given before the closing date. Extensions will only be granted due to extraordinary circumstances during the submission period. Any agreed extension will be notified on the FSANZ website and will apply to all submitters.

Questions about making submissions or the application process can be sent to standards.management@foodstandards.gov.au.

Hard copy submissions may be sent to one of the following addresses:

Food Standards Australia New Zealand
PO Box 5423
KINGSTON ACT 2604
AUSTRALIA
Tel +61 2 6271 2222

Food Standards Australia New Zealand
PO Box 10559
The Terrace WELLINGTON 6143
NEW ZEALAND
Tel +64 4 978 5630

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Supporting document

The following document which informed the assessment of this application are available on the FSANZ website:

- SD1 Risk Assessment: Nutrition, safety, food technology and dietary intake assessment report

Executive summary

ChromaDex Inc. lodged an application to amend the Australia New Zealand Food Standards Code (the Code) to permit the use of nicotinamide riboside chloride as a form of vitamin B3 in food for special medical purposes (FSMPs). FSMPs partially or totally replace the daily diet and are recommended for use under medical supervision.

Division 3 of Standard 2.9.5 of the Code permits substances that may be added to FSMPs, including vitamins and their permitted forms. Vitamin B3 compounds are referred to as 'niacin' in the Code.

Niacin functions as a source of nicotinamide adenine dinucleotide (NAD⁺) in the body which is required for a range of cellular functions. Niacin is an essential nutrient which must be obtained through dietary sources as the body cannot produce it on its own. Currently, nicotinic acid and niacinamide (nicotinamide) are permitted forms of niacin in FSMPs.

Based on the available evidence, FSANZ considers that nicotinamide riboside chloride is a precursor to NAD⁺ and therefore is a bioavailable form of niacin. FSANZ's risk assessment concludes there is no evidence of a public health and safety concern associated with the use of nicotinamide riboside chloride as a permitted form of niacin in FSMPs under the existing regulatory measures of Standard 2.9.5.

FSANZ has prepared a draft variation of the Code with the following proposed amendments:

- an amendment to the table to section S29—20 including nicotinamide riboside chloride in the list of permitted forms of niacin that may be added to FSMPs; and
- amendments to Schedule 3 related to including a specification for nicotinamide riboside chloride in that Schedule.

The draft variation, if approved, would permit the use of nicotinamide riboside chloride as a form of niacin in FSMPs in accordance with the Code.

The draft variation does not include any amendment to the existing mandatory compositional, labelling or other requirements for FSMPs.

1 Introduction

1.1 The Applicant

ChromaDex is a global company specialising in discovering, acquiring, developing, and commercialising patented and proprietary ingredients that address the dietary supplement, food, beverage, skin care and pharmaceutical markets.

1.2 The Application

The purpose of this application is to amend the Code to permit the use of nicotinamide riboside chloride (NRC) as a new form of vitamin B3 in Food for Special Medical Purposes (FSMPs). NRC is a precursor to nicotinamide adenine dinucleotide (NAD⁺) in the human body and is intended as a source of vitamin B3 in FSMPs that partially or totally replace the daily diet. FSMPs are recommended to be used under medical supervision.

The application states that NRC performs an equivalent nutritional function to the two forms currently being used in FSMPs. It is further purported that NRC intake has fewer adverse effects or identified safety issues.

This application refers to 'vitamin B3', however the Australia New Zealand Food Standards Code (the Code) refers to 'niacin' as the vitamin in its permissions, and herein the latter term will be referenced. Niacin is the generic descriptor commonly used for the closely related compounds nicotinic acid (pyridine-3-carboxylic acid) and nicotinamide (niacinamide or pyridine-3-carboxamide). These compounds are water soluble and naturally present in many foods.

This application does not propose any amendment to the existing mandatory compositional, labelling or other requirements for FSMPs.

1.3 The current standard

1.3.1 Australia and New Zealand

Australian and New Zealand food laws require food for sale to comply with the following requirements in the Code.

1.3.1.1 Permitted use

Standard 2.9.5 – Food for Special Medical Purposes regulates FSMPs and is applicable to products for use by adults and children under medical supervision. Infant formula products, including those formulated for special dietary use, are not considered to be FSMPs and therefore, Standard 2.9.5 does not apply to infant formula products. All infant formula products are regulated by Standard 2.9.1.

Subsection 2.9.5—6(1) of the Code permits the addition of the following substances to FSMPs:

- (a) a substance that is listed in Column 1 of the table to section S29—20 and that is in a corresponding form listed in Column 2 of that table;*
- (b) a substance that is listed in Column 1 of the table to section S29—7 and that is in a corresponding form listed in Column 2 of that table;*
- (c) any other substance, regardless of its form, that is permitted under this Code to be added to a food, if that substance is added in accordance with any applicable requirement of this Code.*

This application seeks to include NRC as a permitted form of niacin in the table to section S29—20, which may be added to FSMPs.

Section 2.9.5—7 includes compositional requirements for FSMPs that are represented as being suitable for use as a sole source of nutrition. This application does not seek to amend the minimum level or impose a maximum level for niacin set in the table to section S29—21.

1.3.1.2 Identity and purity

Section 1.1.1—15 requires that a substance used as a nutritive substance must comply with any relevant specification set out in Schedule 3. NRC is intended as a new ingredient in the Australian and New Zealand food supply, and since there are no specifications currently provided in the Code, a specification will be required in Schedule 3.

1.3.1.3 Labelling requirements

Paragraph 1.1.1—10(8) requires that food for sale must comply with all relevant labelling requirements in the Code for that food.

As stated above, paragraph 2.9.5—3(b) states that unless the contrary intention appears, Part 1.2 – Labelling and Other Information Requirements of the Code does not apply to FSMPs. However, Division 4 of Standard 2.9.5 sets out labelling requirements specific to FSMPs. This application does not seek to amend any labelling requirements for FSMPs.

1.3.2 International Standards

In developing food regulatory measures, FSANZ must have regard to the promotion of consistency between domestic and international food standards.

1.3.2.1 Codex Alimentarius (Codex)

Codex has not established compositional standards relating to foods which may be considered FSMPs internationally, except for foods for use in weight control diets (CXS 181—1991) and very low energy diets for weight reduction (CXS 203—1995)¹. In Australia and New Zealand, the definition of FSMPs in section 1.1.2—5 excludes foods which are formulated and represented for the dietary management of obesity or overweight. Irrespective of the current requirements of the Code, the abovementioned Codex standards do not specify permitted forms for nutrients, including niacin.

Codex has established a list of permitted forms for nutrients for FSMPs for infants and young children (CXS 72-1981; CXG 10-1979)². Permitted forms of niacin include nicotinic acid and nicotinamide.

1.3.2.2 United States (US)

The applicant's NRC has been determined as Generally Recognized as Safe (GRAS) in the US to be added to a number of foods (GRAS notice [GRN635](#)³) via the GRAS process system, with a US Food and Drug Administration (FDA) no questions letter.

¹ <http://www.fao.org/fao-who-codexalimentarius/codex-texts/list-standards/en/>

² <http://www.fao.org/fao-who-codexalimentarius/codex-texts/list-standards/en/>

³ <https://www.cfsanappsexternal.fda.gov/scripts/fdcc/index.cfm?set=GRASNotices&id=635>

1.3.2.3 European Union (EU)

NRC has been approved for use in the EU as a novel food when in [supplement form](#)⁴.

1.4 Reasons for accepting Application

The application was accepted for assessment because:

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

1.5 Procedure for assessment

The application is being assessed under the General Procedure.

2 Summary of Assessment

2.1 Risk assessment

FSANZ conducted a comprehensive assessment following the internationally recognised risk analysis framework based on a weight of evidence approach, combining information and scientific evidence provided by the applicant with independent sources. The risk assessment is included in Supporting Document 1 (SD1). This section provides a summary of these assessments.

To determine the bioavailability of NRC, FSANZ considered studies in humans and in laboratory animals on the effect of NRC supplementation on the concentration of nicotinamide adenine dinucleotide (NAD⁺) and metabolites in blood and/or urine. In human studies, NRC supplementation (100 to 2000 mg/day) in volunteers was associated with increases in blood concentrations of NAD⁺ and several NAD⁺ metabolites, relative to baseline values or placebo treatments showing that it is a bioavailable form of niacin. However, none of the studies included a comparator treatment group receiving nicotinic acid (NA) or nicotinamide (Nam) so it was not possible to establish bioequivalence to already permitted forms of niacin in the Code.

NRC has been shown to increase hepatic NAD⁺ levels in mice and increase plasma MeNam concentrations in other animal studies. A 90-day rat study showed that similar doses of NRC or Nam caused an elevation of plasma Nam and MeNam.

FSANZ concludes that based on the available evidence in laboratory animals and humans, NRC is a bioavailable form of niacin which at intakes ranging from 100 to 2000 mg/day in humans would be expected to support normal physiological function. In the absence of human studies to establish the bioavailability of NRC compared to already permitted forms of niacin, FSANZ cannot judge with certainty the extent to which lower NRC intakes which match adult recommended dietary intake levels for niacin (14 mg/day in women, 16 mg/day in men) would support essential requirements, when it is the only form of vitamin B3 in the diet.

The acute oral toxicity of NRC is low. No adverse effects were observed in rats gavaged with NRC at 300 mg/kg bw/day for 90 days, but statistically significant changes in some clinical pathology parameters were observed in rats dosed with 1000 mg/kg bw/day. In the same study, a number of adverse effects were observed in rats dosed with 3000 mg/kg bw/day, but the same adverse changes occurred in a positive control group of rats treated with an

⁴ <https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32020R0016&from=EN>

equimolar dose of Nam (1260 mg/kg bw/day). Additional animal studies also supported a no observed adverse effect level (NOAEL) of 300 mg/kg bw/day.

No chronic toxicity/carcinogenicity studies of NRC were submitted or located from other sources, but NRC was not genotoxic and no pre-neoplastic lesions were observed in the 90 day rat study. In a developmental study in rats, the fetal NOAEL was identified as 750 mg/kg bw/day on the basis of decreased fetal bodyweights at 1500 mg/kg bw/day, together with increases in the incidence of abnormalities commonly observed in association with maternal toxicity. In a one-generation reproductive study in rats, the NOAEL for fertility and reproductive performance was 12 000 ppm in the parental diet, the highest dose tested, equivalent to 675.2 mg/kg bw/day NRC in P generation males and 1088.4 mg/kg bw/day NRC in P generation females.

In human tolerance studies of up to 12 weeks in duration, NRC was well tolerated at doses up to 2000 mg/day. No case reports of allergy were found on literature search, and NRC would not be expected to be an allergen, on the basis of its rapid metabolism to Nam and low molecular weight.

Since NRC is metabolised to Nam it is important to consider NRC intakes relative to the upper level of intake (UL) for Nam. The maximum daily intake of NRC proposed in the application was 1000 mg/day, which assuming equimolar conversion, is equivalent to 420 mg Nam. This is less than half the UL for Nam in non-pregnant, non-lactating adults (900 mg), and is also below the UL for children aged 9-13 years (500 mg/day) and adolescents aged 14-18 years (750 mg/day). It is above the UL for children aged 1-3 years (150 mg/day) and 4-8 years (250 mg/day), however it is expected that FSMPs are prescribed by, and will be used under the supervision of medical practitioners and dietitians, at intakes that would not exceed the UL.

The margin of exposure (MOE) between the NOAEL of 750 mg/kg/day for fetal toxicity in a rat developmental study, and the maximum intake of 1000 mg/day NRC for a pregnant woman weighing 60 kg was 45. The corresponding MOE between the NOAEL in the one-generation reproductive toxicity in rats and proposed maximum human intake was approximately 66. On the basis of the low MOEs (<100) use at the maximum proposed NRC intake level in pregnant or lactating women is not supported. However, as for paediatric use, lower intakes approximating recommended intake levels of niacin, prescribed and supervised by medical practitioners and dietitians, do not represent a safety concern in pregnant or lactating women.

In conclusion, FSANZ considers that based on the best available evidence in laboratory animals and humans, NRC is a bioavailable form of niacin which at intakes ranging from 100 to 2000 mg/day would be expected to support normal physiological function. However it was not possible to establish bioequivalence to forms of niacin already permitted in the Code. On that basis it is not possible for FSANZ to establish with certainty whether lower NRC intakes which match adult recommended intake levels for niacin would support essential requirements, when it is the only form of vitamin B3 in the diet (assuming the FSMP is also low in protein).

NRC is not expected to represent a safety concern when prescribed and used under medical supervision at intakes below the UL for Nam, and for pregnant or lactating women, at levels of intake consistent with recommended intake levels for niacin.

2.2 Risk management

On the basis of the findings of the risk assessment, FSANZ considers the use of NRC for the proposed purpose is both safe and technologically justified. The risk management response to matters raised by the risk assessment are detailed below.

2.2.1 Background to overarching risk management strategies in Standard 2.9.5

Standard 2.9.5 regulates the sale, composition and labelling of foods specially formulated for the dietary management of individuals (including children) with certain diseases, disorders or medical conditions. FSMPs are required when the dietary management of individuals cannot be easily or completely achieved with other dietary modification including the use of other special purpose foods. FSMPs includes formulated dietary products that are intended for use as the sole source of nutrition, either consumed orally or through an enteral route (e.g. naso-gastric tube), as well as specialised supplementary formulated products. Food regulated by this Standard is intended to be used under medical supervision. Due to the specialised nature and purpose of these foods, this Standard also includes a restriction on the premises at which, and the persons by whom, FSMPs may be sold to consumers.

Nearly all FSMPs are imported from the EU or US, with the majority from EU. In order to limit the impost on manufacturers and therefore ensure continued supply of these products to Australia and New Zealand, the existing compositional (including permitted forms of nutrients) and labelling requirements in Standard 2.9.5 harmonise where possible with overseas regulations.

Standard 2.9.5 allows for manufacturers to vary the micronutrient composition of FSMPs from the specified limits for a specific medical purpose (including a particular medical condition, disease or disorder) but with an additional labelling requirement that indicates which nutrient levels have been varied. FSANZ's previous assessments in the development of Standard 2.9.5 considered the potential risk of inadequate and excessive nutrient intakes in both children and adults to be minimal as FSMPs are used under the supervision of medical practitioners and dietitians, and the nutritional status of the patient is closely monitored.

2.2.2 Required permission for substances that may be added to FSMPs

The addition of new permitted forms of particular substances for use in FSMPs requires an application to FSANZ to amend the Code. If permission to add a new form is sought, its bioavailability must be assessed and compared with the current permitted forms. Bioavailability in a nutritional context is the proportion of the ingested nutrient that is absorbed and utilised through normal metabolic pathways. For niacin, standard 'equivalence' factors are applied to allow for bioavailability and bioconversion. The equivalents are totalled and compared to appropriate Nutrient Reference Values (NRVs) expressed in units of equivalents i.e. niacin equivalents.

This application states the intended purpose is for NRC to be used as a permitted form of niacin in FSMPs for adults. FSANZ has considered the request within the existing regulatory arrangements which do not include any exceptions for children⁵.

FSANZ concludes that based on the best available evidence, NRC meets its stated purpose as a bioavailable form of niacin in FSMPs, which in humans would be expected to support normal physiological function. In the absence of controlled trials in humans demonstrating bioequivalence, from the available evidence and NRV standard equivalence factors⁶ for niacin, it is reasonable to anticipate that NRC would react similarly to nicotinamide in the body. As discussed above, the micronutrient composition of FSMPs can be varied from the specified limits, noting there is no prescribed maximum level for niacin equivalents.

FSANZ concludes there is no evidence of a public health and safety concern associated with the use of NRC as a permitted form of niacin in FSMPs under the existing regulatory

⁵ Infant formula products are not FSMPs and therefore are not regulated under Standard 2.9.5, but are regulated under Standard 2.9.1. It is not being proposed that NRC will be added to these products.

⁶ Nutrient Reference Values for Australia and New Zealand – Niacin: <https://www.nrv.gov.au/nutrients/niacin>.

measures of Standard 2.9.5. NRC was well tolerated at doses up to 2000 mg/day (equiv. 840 mg/day nicotinamide) which is less than the adult UL for nicotinamide of 900 mg/day. Given this, use of NRC within recommended intake levels of niacin is considered safe by adults, adolescents and children.

Similar to the inability to establish a UL for nicotinamide due to the lack of data on safety in pregnancy and lactation, it was not possible for FSANZ to reach a conclusion on the safety of NRC at high levels of intake for this subpopulation. However, it would be expected that the use of NRC within recommended intake levels of niacin, where prescribed and supervised by a medical practitioner or dietitian, will not represent a safety concern in pregnant or lactating women.

It must also be noted that NRVs are healthy population recommendations and individual requirements can vary from these population recommendations particularly in unwell or vulnerable groups. These factors are taken into consideration on an individual case by case basis when FSMPs are being supplied to patients. Standard 2.9.5 already requires manufacturers provide information regarding the total volume of their product that is required for nutritional adequacy when used as a sole source of nutrition (e.g. nutritionally complete in 1.5 litres) as well as the nutrient composition of a product. These are used to assess the nutritional adequacy of a product against disease specific requirements where known, or at least against cautious application of a specific NRV, where indicated for specific medical conditions. If it is known that any nutrients are not complete in a given volume over a long period of time, this would be monitored by the medical practitioner or dietitian. Micronutrient supplements or multivitamin preparations can also be used where required to account for any nutrient deficit and ensure nutritional adequacy.

The risk assessment concludes there is no evidence of a public health and safety concern associated with the use of NRC as a permitted form of niacin in FSMPs within recommended intake levels of niacin. This is further supported by the existing risk management strategies incorporated in Standard 2.9.5 including the intended use under medical supervision and restrictions relating to access and sale. Therefore, FSANZ has prepared a draft variation to permit the use of NRC as a form of niacin in FSMPs, with specifications for NRC drafted for inclusion in Schedule 3 of the Code.

2.2.3 Labelling requirements

The application does not seek to amend any labelling requirements for FSMPs. Section 2.9.5—9 of Standard 2.9.5 sets out the labelling information required for FSMPs. This includes:

- Paragraph 2.9.5—9(1)(e) requires the provision of information relating to ingredients. The use of NRC as an ingredient in FSMPs would require information to be provided in accordance with section 2.9.5—11.
- Paragraph 2.9.5—9(1)(h) requires the provision of nutrition information in accordance with section 2.9.5—13. This includes providing the minimum amount or average quantity of any substance listed in the table to section S29—20 that has been used as a nutritive substance in the food (see subparagraph 2.9.5—13(b)(iii)). This would apply to the use of NRC as a permitted form of niacin.

2.2.4 Risk management conclusion

Based on the risk assessment and consideration of the objectives of the FSANZ Act (see section 2.4) and relevant Ministerial Policy Guidelines (see section 2.4.3), the preferred approach is to prepare a draft variation that amends Schedule S29—20 to include NRC in the list of permitted forms of niacin that may be added to FSMPs; and amends Schedule 3 to include a specification for NRC in that Schedule.

The draft variation would permit the use of nicotinamide riboside chloride as a form of niacin in FSMPs in accordance with the Code.

2.3 Risk communication

2.3.1 Consultation

Consultation is a key part of FSANZ's standards development process. FSANZ developed and applied a standard communication strategy to this application. All calls for submissions are notified via the Food Standards Notification Circular, media release, FSANZ's social media tools and Food Standards News.

The process by which FSANZ considers standards' development matters is open, accountable, consultative and transparent. Public submissions are called to obtain the views of interested parties on issues raised by this application and the impacts of regulatory options.

The draft variation will be considered for approval by the FSANZ Board taking into account all submissions received from this call for submissions.

2.3.2 World Trade Organization (WTO)

As members of the World Trade Organization (WTO), Australia and New Zealand are obliged to notify WTO members 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.

There are no Codex standards concerning the use of NRC as a form of niacin in FSMPs. Other than GRAS status in the US to be added to a number of foods and EU approval as a novel food when in supplement form, there are currently no other relevant national food standards or regulations approving the use of NRC (see section 1.3.2). Amending the Code to permit a new form of niacin that may be added to FSMPs is unlikely to have a significant effect on international trade as this is a voluntary permission which would liberalise trade.

Therefore, a notification to the WTO under Australia's and New Zealand's obligations under the WTO Technical Barriers to Trade or application of Sanitary and Phytosanitary Measures Agreement was not considered necessary.

2.4 FSANZ Act assessment requirements

When assessing this application and the subsequent development of a food regulatory measure, FSANZ has had regard to the following matters in section 29 of the FSANZ Act:

2.4.1 Section 29

2.4.1.1 Consideration of costs and benefits

The Office of Best Practice Regulation (OBPR) granted FSANZ a standing exemption from the requirement to develop a Regulatory Impact Statement for the voluntary addition of a nutritive substance to food (OBPR correspondence dated 16 April 2013, reference 14943). This standing exemption was provided as permitting an additional nutritive substance to food is deregulatory as their use will be voluntary if the application is approved. This standing exemption relates to the introduction of a food to the food supply that has been determined to be safe.

FSANZ, however, has given consideration to the costs and benefits that may arise from the proposed measure for the purposes of meeting FSANZ Act considerations. The FSANZ Act requires FSANZ to have regard to whether costs that would arise from the proposed measure outweigh the direct and indirect benefits to the community, government or industry that would arise from the proposed measure (paragraph 29 (2)(a)).

The purpose of this consideration is to determine if the community, government, and industry as a whole is likely to benefit, on balance, from a move from the status quo (where status quo is rejecting the application). This analysis considers permitting the use of NRC as a form of niacin in FSMPs. FSANZ is of the view that no other realistic food regulatory measures exist, however information received may result in FSANZ arriving at a different outcome.

The consideration of the costs and benefits in this section is not intended to be an exhaustive, quantitative economic analysis of the proposed measures and, in fact, most of the effects that were considered cannot easily be assigned a dollar value. Rather, the assessment seeks to highlight the likely positives and negatives of moving away from the status quo by permitting the use of NRC as a form of niacin in FSMPs.

Costs and benefits of permitting the use of NRC as a form of niacin in FSMPs

Due to the voluntary nature of the permission, manufacturers would only use this form of niacin in the production of FSMPs, where they believe a net benefit exists for them. This could ultimately result in a better quality or lower cost product for consumers.

Permitting the use of NRC as proposed may result in a small cost to government in terms of adding the additional form of niacin to the current range of nutritive substances that are monitored for compliance. There may also be small and likely inconsequential costs of monitoring an extra food ingredient for regulators to ensure compliance with labelling requirements.

Conclusions from cost benefit considerations

FSANZ's assessment is that the direct and indirect benefits that would arise from permitting the use of NRC as a form of niacin in FSMPs most likely outweigh the associated costs.

2.4.1.2 Other measures

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

2.4.1.3 Any relevant New Zealand standards

The relevant standards apply in both Australia and New Zealand. There are no relevant New Zealand only standards.

2.4.1.4 Any other relevant matters

Other relevant matters are considered below.

2.4.2 Subsection 18(1)

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

2.4.2.1 Protection of public health and safety

FSANZ has undertaken a safety assessment (see SD1) and concluded there is no evidence

of a public health and safety concern associated with the use of NRC as a permitted form of niacin in FSMPs under the existing regulatory measures of Standard 2.9.5.

2.4.2.2 The provision of adequate information relating to food to enable consumers to make informed choices

Under Standard 2.9.5, FSMPs are to be used under medical supervision, ultimately allowing medical practitioners and dietitians to determine whether the FSMP is appropriate and safe for their patients' specific needs.

Existing labelling requirements for FSMPs would apply when NRC is added to FSMPs (see sections 1.3.1.3 and 2.2.3), which would provide information to assist medical practitioners and dietitians, and enable informed consumer choice.

2.4.2.3 The prevention of misleading or deceptive conduct

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

2.4.3 Subsection 18(2) considerations

FSANZ has also had regard to:

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

FSANZ has used the best available scientific evidence to assess this application. The applicant submitted a dossier of scientific studies as part of this application. FSANZ also had regard to other relevant information including scientific literature in assessing this application.

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

The proposed permission in the Code to use NRC as a form of niacin in FSMPs is consistent with similar permissions for NRC in other countries including America and Europe. Codex compositional standards relating to foods which may be considered FSMPs internationally do not specify permitted forms for nutrients, including niacin.

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

The proposed permission in the Code would allow for a competitive food industry in relation to FSMPs.

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

No issues were identified for this application relevant to this objective.

- **any written policy guidelines formulated by the Food Ministers' Meeting⁷**

The *Policy Guideline on the Intent of Part 2.9 of the Food Standards Code – Special Purpose Foods*⁸ states the composition of special purpose food should be consistent with the intended purpose. Based on our assessment, FSANZ considers that the Policy Guideline has been met.

⁷ Formerly referred to as *The Australian and New Zealand Ministerial Forum on Food Regulation*

⁸ <https://foodregulation.gov.au/internet/fr/publishing.nsf/Content/publication-Policy-Guideline-on-Intent-of-Part-2-9-of-the-Food-Standards-Code-Special-Purpose-Foods>

3 Draft variation

The draft variation to the Code is at Attachment A and is intended to take effect on gazettal.

A draft explanatory statement is at Attachment B. An explanatory statement is required to accompany an instrument if it is lodged on the Federal Register of Legislation.

4 References

EFSA Panel on Nutrition, Novel foods and Food allergens (NDA), Turck D, Castenmiller J, de Henauw S, Hirsch-Ernst KI, Kearney J, Maciuk A, Mangelsdorf I, McArdle HJ, Naska A, Pelaez C, Pentieva K, Siani A, Thies F, Tsabouri S, Vinceti M, Cubadda F, Engel KH, Frenzel T, Heinonen M, Marchelli R, Neuhäuser-Berthold M, Pöting A, Poulsen M, Sanz Y, Schlatter JR, van Loveren Agnès de Sesmaisons-Lecarré H, Germini A and Knutsen HK (2019) Safety of nicotinamide riboside chloride as a novel food pursuant to Regulation (EU) 2015/2283 and bioavailability of nicotinamide from this source, in the context of Directive 2002/46/EC. EFSA Journal 17(8):e05775.

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National Health and Medical Research Council (NHRMC), Australian Government Department of Health and Ageing, New Zealand Ministry of Health (2006). Nutrient Reference Values for Australia and New Zealand. Canberra: National Health and Medical Research Council.

US FDA (2016). GRAS Notices Inventory. Washington (DC): U.S. Food and Drug Administration (U.S FDA). Available at <https://www.cfsanappsexternal.fda.gov/scripts/fdcc/index.cfm?set=GRASNotices> Accessed 3 February 2021.

Attachments

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

Attachment A – Draft variation to the *Australia New Zealand Food Standards Code*



Food Standards (Application A1214 – Nicotinamide riboside chloride as Vitamin B3 in FSMP) Variation

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

Dated [To be completed by the Delegate]

[Insert name and title of Delegate]

Delegate of the Board of Food Standards Australia New Zealand

Note:

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

1 Name

This instrument is the *Food Standards (Application A1214 – Nicotinamide riboside chloride as Vitamin B3 in FSMP) Variation*.

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

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

3 Commencement

The variation commences on the date of gazettal.

Schedule

[1] **Schedule 3** is varied by

[1.1] inserting into the table to subsection S3—2(2), in alphabetical order

Nicotinamide riboside chloride section S3—44

[1.2] inserting after section S3—43

S3—44 Specification for Nicotinamide riboside chloride

(1) In this section,

Nicotinamide riboside chloride (CAS Number 23111-00-4) is the chemical with:

- (a) the chemical name Pyridinium, 3-(aminocarbonyl)-1-β-D-ribofuranosyl-, chloride (1:1);
- (b) the formula $C_{11}H_{15}N_2O_5 \cdot Cl$;
- (c) the formula weight 290.7 g/mol.

(2) For Nicotinamide riboside chloride, the specifications are the following:

- (a) description—a white to light brown powder;
- (b) solubility—freely soluble in water;
- (c) assay—not less than 90.0 w/w % and not more than 103 w/w %;
- (d) water—not more than 2.0 w/w %;
- (e) residual solvents:
 - (i) acetone—not more than 5000 ppm; and
 - (ii) methanol—not more than 1000 ppm; and
 - (iii) acetonitrile—not more than 50 ppm; and
 - (iv) methyl tert-butyl ether—not more than 500 ppm;
- (f) reaction by-products:
 - (i) methyl acetate—not more than 1000 ppm; and
 - (ii) acetamide—not more than 27 ppm; and
 - (iii) acetic acid—not more than 5000 ppm;
- (g) arsenic and heavy metals:
 - (i) arsenic—not more than 1 ppm; and
 - (ii) mercury—not more than 1 ppm; and
 - (iii) cadmium—not more than 1 ppm; and
 - (iv) lead—not more than 0.5 ppm;
- (h) microbial limits:
 - (i) standard plate count—maximum 1000 cfu/g; and
 - (ii) yeast and mould—maximum 100 cfu/g; and
 - (iii) *Escherichia coli*—absent in 10 g.

[2] **Schedule 29** is varied by omitting from the table to section S29—20

Niacin
substituting

Niacin

Nicotinic acid

Nicotinamide riboside chloride
Nicotinic acid

Attachment B – Draft Explanatory Statement

1. Authority

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

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

The Authority accepted Application A1214 which seeks to permit the use of nicotinamide riboside chloride as a form of niacin in food for special medical purposes (FSMPs). The Authority considered the application in accordance with Division 1 of Part 3 and has prepared a draft variation.

2. Purpose

The Authority has prepared a draft variation to the Code amending the table to section S29—20 to include ‘nicotinamide riboside chloride’ in the list of permitted forms of niacin that may be added to FSMPs. The draft variation also amends Schedule 3 to include a specification for nicotinamide riboside chloride in that Schedule.

The amendments in the draft variation would permit the use of nicotinamide riboside chloride as a form of niacin in FSMPs in accordance with the Code.

3. Documents incorporated by reference

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

4. Consultation

In accordance with the procedure in Division 1 of Part 3 of the FSANZ Act, the Authority’s consideration of Application A1214 will include one round of public consultation following an assessment and the preparation of a draft Standard and associated assessment summary.

The Office of Best Practice Regulation (OBPR) granted FSANZ a standing exemption from the requirement to develop a Regulatory Impact Statement for the voluntary addition of a nutritive substance to food (OBPR correspondence dated 16 April 2013, reference 14943). This standing exemption was provided as permitting an additional nutritive substance to food is deregulatory as their use will be voluntary if the application is approved. This standing exemption relates to the introduction of a food to the food supply that has been determined to be safe.

5. Statement of compatibility with human rights

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

6. Variation

Item [1] amends Schedule 3.

Sub item [1.1] inserts a reference to 'nicotinamide riboside chloride' and its relevant provision into the table to S3—2(2), in alphabetical order. The table to S3—2(2) lists certain substances and their 'relevant provisions' i.e. provisions indicating where specifications for the listed substances are located in Schedule 3.

Sub item [1.2] inserts new section S3—44 into Schedule 3, which contains the new specification for 'nicotinamide riboside chloride'.

Item [2] amends Schedule 29 by omitting the existing entry of 'Niacin' in the table to section S29—20 and substituting it with a new entry. The new entry for Niacin lists 'nicotinamide riboside chloride' as one of two permitted forms of Niacin that may be added to FSMPs. The effect of this amendment is that nicotinamide riboside chloride would be a permitted form of niacin that may be added to FSMPs in accordance with the Code.