12 August 2021
167-21

Approval report – 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 Australia New Zealand Food Standards Code to permit the use of nicotinamide riboside chloride as a form of vitamin B3 (niacin) in food for special medical purposes.

On 22 April 2021, FSANZ sought submissions on a draft variation and published an associated report. FSANZ received three submissions.

FSANZ approved the draft variation on 4 August 2021. The Food Ministers' Meeting[1] was notified of FSANZ's decision on 12 August 2021.

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

[1] Formerly referred to as the Australia and New Zealand Ministerial Forum on Food Regulation.

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Supporting document

The following document which informed the assessment of this Application is available on the FSANZ website:

SD1 Risk Assessment: Nutrition, safety, food technology and dietary intake assessment report (at Approval)

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, Food Standards Australia New Zealand (FSANZ) concluded that nicotinamide riboside chloride is metabolised to nicotinamide and is a bioavailable form of niacin. There was 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 in accordance with the Code.

Following assessment and the preparation of a draft variation, FSANZ called for submissions regarding the draft variation from 22 April 2021 to 20 May 2021. Three submissions were received, all of which FSANZ had regard to (see Section 2.1 of this report for details of submissions made).

Based on the information above and on other relevant considerations set out in this report, FSANZ has approved the draft variation proposed following assessment without change. The approved draft variation will permit the use of nicotinamide riboside chloride as a form of niacin in FSMPs in accordance with the Code. The approved draft variation will amend:

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

The approved 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 application sought to amend the Australia New Zealand Food Standards Code (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 (i.e. *used as a nutritive substance*). FSMPs are recommended to be used under medical supervision.

The application stated that NRC performs an equivalent nutritional function to the two forms currently being used in FSMPs i.e. nicotinic acid and nicotinamide. It was further purported that NRC intake has fewer adverse effects or identified safety issues.

The application referred to 'vitamin B3', however 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.

The application did 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 relevant requirements in the Code. The requirements in the Code relevant to this application are summarised below.

1.3.1.1 Permitted use

Standard 2.9.5 – Food for Special Medical Purposes sets out requirements related to the sale, composition and labelling of 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. Standard 2.9.1 applies to infant formula products.

Subsection 2.9.5—6(1) 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 sought 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 did 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 was required in Schedule 3.

1.3.1.3 Labelling requirements

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

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

1.3.2 International Standards

In developing food regulatory measures, Food Standards Australia New Zealand (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). 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.

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

1.3.2.2 United States (US)

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

1.3.2.3 European Union (EU)

NRC has been approved for use in the EU as a novel food when in supplement form.

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 *Food Standards Australia New Zealand Act 1991* (the FSANZ Act)
- it related to a matter that warranted the variation of a food regulatory measure.

1.5 Procedure for assessment

The application was assessed under the General Procedure.

1.6 Decision

The draft variation as proposed following assessment was approved without change. The variation takes effect on Gazettal. The approved draft variation is at Attachment A.

The related 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.

2 Summary of the findings

2.1 Summary of issues raised in submissions

FSANZ called for submissions on a draft variation to the Code from 22 April 2021 to 20 May 2021. Three submissions were received, two from government agencies and one from an industry body (Nestlé). Nestlé fully supports the application and draft variation. The government agencies support the variation provided additional explanatory information was included in this report and the supporting document (SD1). The issues raised in submissions and how they have been addressed are provided in Table 1.

Table 1: Summary of issues

Issue	Raised by	FSANZ response
More information is requested on how NRC intake equates to nicotinamide intake in relation to meeting dietary requirements (i.e. demonstrate intended purpose).	New Zealand Ministry for Primary Industries Victorian Department of Health and the Victorian Department of Jobs, Precincts and Regions	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 NRC is a bioavailable form of niacin (i.e. nicotinamide, nicotinic acid). FSANZ notes that Standard 2.9.5 allows for manufacturers to vary the micronutrient composition of FSMPs for a specific medical purpose (including a particular medical condition, disease or disorder). FSANZ considers the potential risk of inadequate and excessive niacin 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. FSANZ has clarified this issue under section 2.3 of this report.
More information is requested on the evidence used by the applicant to support the stability of NRC, including the appropriate conditions for use.	Victorian Department of Health and the Victorian Department of Jobs, Precincts and Regions	It is the view of FSANZ that the applicant has provided sufficient stability data to support the use of NRC in FSMPs, noting much of the information provided is confidential commercial information (CCI) and cannot be discussed in detail publicly. Given this is a relatively new substance, FSANZ considered the supplied evidence on comparable products (supplemented foods/dietary supplements) in determining stability in food matrices. This included both powdered and liquid preparations. FSANZ has clarified this issue under section 2.3 of this report, and in SD1.

2.2 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.

A ***nutritional assessment*** determined that nicotinamide riboside chloride (NRC) can be metabolised to nicotinamide adenine dinucleotide (NAD+). To assess the bioavailability of NRC, FSANZ considered studies in humans and in laboratory animals on the effect of NRC supplementation on the concentration of 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. It was not possible to establish bioequivalence to currently permitted forms of niacin in the Code due to insufficient evidence.

A ***safety assessment*** concluded that 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 equimolar dose of nicotinamide (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 available, but NRC was not genotoxic and no pre-neoplastic lesions were observed in the 90 day rat study. Therefore carcinogenicity studies are not required.

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.

At the maximum proposed intake levels of 1000 mg/day proposed in the Application, the margins of exposure (MOE) for developmental and reproductive toxicity for pregnant and lactating women are less than 100 and of possible health concern. Acceptable MOEs would be achieved at levels approximating physiological requirements for niacin, and at those intake levels, under the supervision of medical practitioners and dietitians, do not represent a safety concern in pregnant or lactating women.

In human tolerance studies of up to 12 weeks in duration, NRC was well tolerated at doses up to 2000 mg/day.

Since NRC is metabolised to nicotinamide, FSANZ considered NRC intakes relative to the Upper Level of Intake (UL) for nicotinamide. The maximum daily intake of NRC proposed in the application was 1000 mg/day, which assuming equimolar conversion (on a conservative basis), is equivalent to 420 mg nicotinamide. This is less than half the UL for nicotinamide 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 FSMPs are used under the supervision of medical practitioners and dietitians, and it is expected that children under the age of 9 would be prescribed a lower quantity of FSMPs to align with their nutritional requirements.

FSANZ did not consider it necessary to estimate ***dietary intake*** of NRC as niacin is already permitted to be added to FSMPs, and there was no request to change the permitted level of addition. Furthermore, the hazard assessment did not identify any non-nutrient chemicals or compounds of a public health and safety concern associated with the addition of NRC to FSMP for which a ***dietary exposure*** assessment was warranted.

NRC would not be expected to be an allergen, on the basis of its metabolism to nicotinamide and low molecular weight.

FSANZ's ***technical assessment*** concluded that the NRC manufactured by the applicant is of appropriate chemical composition, purity and stability to fulfil the stated technological function. FSANZ developed specifications based on information provided by the applicant.

In summary, based on the best available scientific evidence, FSANZ considered that NRC is a bioavailable form of niacin. FSANZ is unable to reach a conclusion on whether NRC is bioequivalent to permitted forms of niacin in the Code due to insufficient evidence. NRC is not expected to represent a safety concern when prescribed and used in FSMPs under medical supervision at intakes below the UL for nicotinamide for the general population, and at levels of intake consistent with physiological requirements for niacin for pregnant or lactating women.

2.3 Risk management

On the basis of the findings of the risk assessment (section 2.2 and SD1), FSANZ considered the use of NRC as a permitted form of niacin in FSMPs raised no public health and safety concerns. The risk management response to matters raised by the risk assessment are detailed below.

2.3.1 Overarching risk management strategies in Standard 2.9.5

Standard 2.9.5 sets out requirements for 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. FSMPs are 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.

Standard 2.9.5 allows for manufacturers to vary the micronutrient composition of FSMPs that are represented as being suitable for use as sole source of nutrition from the specified limits for a specific medical purpose (including a particular medical condition, disease or disorder); but with an additional labelling requirement indicating:

- which nutrient levels have been varied; and
- unless provided in other documentation about the food—a statement indicating whether each modified nutrient has been increased, decreased, or eliminated from

the food, as appropriate (see subsection 2.9.5—7(2) and subparagraph 2.9.5—10(1)(g)(ii)).

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.

Nearly all FSMPs are imported from the EU or US, with the majority from the 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 with overseas regulations where possible.

2.3.2 Considering substances that may be added to FSMPs

There are currently many forms of vitamins that can be added to food in Australia and New Zealand. The addition of new permitted forms of vitamins (i.e. nutritive substances) for use in FSMPs requires an application to FSANZ to amend the Code (see subsection 2.9.5—6(1)). 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 available to be utilised through normal metabolic pathways. For niacin, standard equivalence factors are applied to allow for bioavailability and bioconversion (1 niacin equivalent as 1 mg niacin or 60 mg of the amino acid tryptophan). The equivalents are totalled and compared to appropriate Nutrient Reference Values (NRV) expressed in units of niacin equivalents[2].

This application stated the intended purpose was for NRC to be used as a permitted form of niacin in FSMPs for adults. FSANZ considered the request within the existing provisions in the Code relating to FSMPs which do not include any exceptions for children. Infant formula products are not FSMPs and therefore Standard 2.9.5 does not apply to these products (Standard 2.9.1 applies to infant formula products). It is not proposed that NRC will be added to infant formula products.

The available data assessed by FSANZ included NRC intake amounts primarily ranging between 100 mg/day and 2000 mg/day to demonstrate both bioavailability as a form of niacin and safety at high levels of intake. NRC supplementation 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. NRC at high doses was well tolerated and FSANZ did not identify any evidence of a public health and safety concern associated with the use of NRC as a permitted form of niacin in FSMPs in accordance with the Code.

Niacin bioavailability, like many nutrients, varies according to the form of niacin and the food matrix. The nutrient status of an individual can also affect the response to dietary or supplemental niacin intake. It was not possible for FSANZ to establish the bioequivalence of NRC to currently permitted forms of niacin in the Code due to insufficient evidence. As described earlier, standard equivalence factors provide an internationally recognised approach for addressing this issue. Therefore the evidence demonstrating NRC as a bioavailable form of niacin sufficiently upholds the principle of nutritional equivalence.

[2] https://www.nrv.gov.au/nutrients/niacin

Equivalence Factors*

1 mg nicotinamide = 1 mg niacin equivalent = 1mg niacin

1 mg nicotinamide riboside chloride (NRC) = 0.42 mg nicotinamide

1 mg niacin equivalent = 2.36 mg nicotinamide riboside chloride (NRC)

** Approximate equimolar equivalents demonstrating relative dietary nicotinamide contributions (noting individual response to micronutrient intake varies)*

With regards to meeting dietary requirements, FSANZ noted that NRVs are healthy population recommendations and individual requirements can vary from these, 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. As discussed previously, the micronutrient composition of FSMPs can be varied from the specified limits, noting there is no prescribed maximum amount for niacin equivalents. Manufacturers are required to provide information regarding the total volume of their product that is needed 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. This information can be used by medical practitioners and dietitians in considering 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 medically indicated to account for any nutrient deficiency and ensure nutritional adequacy.

FSANZ acknowledged that NRC is a relatively new substance and yet to be widely incorporated into available food products. As is standard practice, data sheets and technical information would be available to manufacturers of FSMPs regarding the appropriate use of NRC. This would specify any limitations around suitable product formulations, shelf life and delivery of niacin.

2.3.3 Labelling requirements

The application did not seek to amend any labelling requirements for FSMPs. Section 2.9.5—9 sets out the labelling information required for FSMPs. Specifically, the relevant Code requirements are:

- Paragraph 2.9.5—9(1)(e) requires the provision of information relating to ingredients. If used as an ingredient in FSMPs, NRC must be declared 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 per given amount of the food (see subparagraph 2.9.5—13(b)(iii)). Niacin is listed as a ‘substance’ in the table to section S29—20, with NRC as a permitted form of niacin in the approved draft variation.

Therefore, when NRC is added to an FSMP, under existing labelling requirements, a declaration of the niacin content of the FSMP would be required in the nutrition information and not the NRC content (see paragraph 2.9.5—13(b)).

2.3.4 Risk management conclusion

Overall, FSANZ concluded that NRC met its stated purpose as a safe and bioavailable form of niacin for use in FSMPs. This was further supported by the existing requirements in the Code, including the intended use under medical supervision and restrictions relating to access and sale.

Having considered the submissions and weighed all aspects of the assessment against the statutory requirements including the Ministerial Policy Guidelines, FSANZ approved a draft variation to the Code to permit the use of NRC as a form of niacin in FSMPs, with specifications for NRC included in Schedule 3 of the Code.

2.4 Risk communication

2.4.1 Consultation

Consultation is a key part of FSANZ's standards development process. FSANZ developed and applied a standard communication strategy to this application. Subscribers and interested parties were notified about the public consultation period via the Food Standards Notification Circular. A media release, FSANZ's social media tools and Food Standards News were also used to raise awareness in the community regarding the opportunity for comment.

A public consultation paper called for submissions from 22 April 2021 to 20 May 2021. Three submissions were received.

FSANZ had regard to all submissions received for this application.

FSANZ acknowledges the time taken by individuals and organisations to make submissions on this application. Every submission was considered by the FSANZ Board. All comments are valued and contribute to the rigour of our assessment.

2.5 FSANZ Act assessment requirements

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

2.5.1 Section 29

2.5.1.1 Consideration of costs and benefits

The Office of Best Practice Regulation (OBPR) granted FSANZ a standing exemption from the requirement to develop a Regulatory Impact Statement for the 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 once the application had been approved. This standing exemption related to the introduction of a food to the food supply that has been determined to be safe.

FSANZ, however, had 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 was to determine if the community, government, and industry as a whole is likely to benefit, on balance, from a move from the status quo (i.e. rejecting the application). This analysis considered permitting the use of NRC as a form of niacin in FSMPs.

The consideration of the costs and benefits in this section was not intended to be an exhaustive, quantitative economic analysis of the proposed measures and, in fact, most of the effects that were considered could not easily be assigned a dollar value. Rather, the assessment sought 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 at the call for submissions was 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. No further information was received during the consultation process that changed the findings from the analysis of costs and benefits in the call for submissions.

2.5.1.2 Other measures

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

2.5.1.3 Any relevant New Zealand standards

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

2.5.1.4 Any other relevant matters

Other relevant matters are considered below.

2.5.2 Subsection 18(1)

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

2.5.2.1 Protection of public health and safety

FSANZ had undertaken a safety assessment (see SD1) and concluded there were no public health and safety concerns with permitting NRC as a form of niacin in FSMPs in accordance with the Code.

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

Under the Code, FSMPs are intended 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 apply when NRC is added to FSMPs (see sections 1.3.1.3 and 2.3.3), which would provide information to assist medical practitioners and dietitians, and enable informed consumer choice.

2.5.2.3 The prevention of misleading or deceptive conduct

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

2.5.3 Subsection 18(2) considerations

FSANZ has also had regard to:

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

FSANZ 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 permission provided by the approved draft variation for the use of 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 permission provided by the approved draft variation 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' Meeting[3]**

The *Policy Guideline on the Intent of Part 2.9 of the Food Standards Code – Special Purpose Foods*[4] states the composition of special purpose food should be consistent with the intended purpose (Ministerial Council 2009). FSANZ considered that the Policy Guideline was met.

[3] Formerly the Australia and New Zealand Ministerial Forum on Food Regulation (the Forum). The Forum name change took effect on 21 February 2021 following a decision by Ministers.
[4] 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

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Attachments

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

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

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

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

Dated [To be completed by the Delegate]

[Insert name and title of the 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	Nicotinic acid

substituting

Niacin	Nicotinamide riboside chloride
	Nicotinic acid

Attachment B – Explanatory Statement

1. Authority

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

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

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 approved a draft variation.

Following consideration by the Food Ministers' Meeting[5], section 92 of the FSANZ Act stipulates that the Authority must publish a notice about the standard or draft variation of a standard.

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

2. Purpose

The Authority has approved a draft variation amending the table to section S29—20 of the Code 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 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 variation in this instrument does not incorporate any documents by reference.

However, the instrument will vary Schedule 3 of the Code which does incorporate documents by reference. Section 1.1.1—15 of the Code requires certain substances (such as nutritive substances) to comply with any relevant identity and purity specifications listed in Schedule 3. Schedule 3 incorporates documents by reference to set specifications for various substances in the circumstances specified in that Schedule. The documents incorporated include: the Joint FAO/WHO Expert Committee on Food Additives (JECFA) Compendium of Food Additive Specifications (FAO/WHO 2017); the United States Pharmacopeial Convention (2018) Food Chemicals Codex (11th edition); and the Commission Regulation (EU) No 231/2012.

[5] Formerly the Australia and New Zealand Ministerial Forum on Food Regulation (the Forum). The Forum name change took effect on 21 February 2021 following a decision by Ministers.

4. Consultation

In accordance with the procedure in Division 1 of Part 3 of the FSANZ Act, the Authority's consideration of Application A1214 included one round of public consultation following an assessment and the preparation of a draft variation and associated assessment summary. Submissions were called for on 22 April 2021 for a four week consultation period.

The Office of Best Practice Regulation (OBPR) granted the Authority 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 will be a permitted form of niacin that may be added to FSMPs in accordance with the Code.