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

8 July 2021
161-21

Consultation paper 2 – Nutrient Composition

Proposal P1028 – Infant Formula

Executive summary

Food Standards Australia New Zealand (FSANZ) is reviewing regulatory requirements for infant formula under Proposal P1028 – *Infant formula*.

The protection of public health and safety is a primary objective for FSANZ. Infant formula must be safe for formula-fed infants to consume, and its nutrient composition must support normal growth and development when infant formula is used as the sole or principal source of nutrition up to 12 months of age.

Infant formula is currently regulated under Standard 2.9.1 – Infant formula products and Schedule 29 – Special purpose foods in the Australia New Zealand Food Standards Code (the Code). Other standards also contain provisions related to definitions, calculations and nutrition information, such as Standard 1.1.2 – Definitions used throughout the Code, Standard 1.2.8 – Nutrition information requirements and Schedule 11 – Calculation of values for nutrition information panel.

This paper is one of a series of consultation papers that discusses regulatory options for Standard 2.9.1 and Schedule 29. The consultation papers will inform the 1st Call for Submissions (CFS) which will summarise the entirety of considerations and outline the proposed regulatory approach.

The focus of this paper is nutrient composition for macronutrients and energy, vitamins and minerals, permitted forms and other nutritive substances. Where relevant, the prescribed minimum and maximum type and value for the nutrient is discussed, as well as related information such as calculations. This paper follows previous consultations undertaken in 2012, 2016 and 2017 which considered these topics.

Based on the assessment to date, including consideration of stakeholder views from previous consultations, FSANZ proposes a number of regulatory/risk management approaches within this paper. Proposed approaches are made with consideration to the objectives of the proposal, the requirements of the *Food Standards Australia New Zealand Act 1991* (the FSANZ Act) and relevant risk management principles. One supporting document providing further details on the nutrition risk assessment accompanies this Consultation paper.

The 2016 Consultation paper concluded that some nutrients would not be reviewed again as no issues were identified and all criteria for nutritional safety were met. These nutrients included vitamin K, thiamine, riboflavin, pantothenic acid, vitamin B_{12}, biotin, sodium, chloride and magnesium (further details can be found in Table 13 and 15 in the 2016 SD1 Attachment A1.1 – Nutrition Assessment). However, since then, new European regulations for nutrient

composition were introduced and therefore some further assessment has been undertaken in this report.

We are seeking stakeholder comment on key issues and proposed approaches. Key questions for stakeholders are listed in the final section to the paper.

Table of Contents

SUPPORTING DOCUMENT:

SD 1: Nutrition Risk Assessment

Abbreviations and glossary

25OHD	25-hydroxyvitamin D—a biomarker of serum vitamin D status
AA	Arachidonic acid C20:4, n-6
AAA	Aromatic amino acids (tyrosine and phenylalanine)
AI	Adequate intake—the average daily nutrient intake level based on observed or experimentally-determined approximations or estimates of nutrient intake by a group (or groups) of apparently healthy people that are assumed to be adequate.
Amino acids	In this paper, refers to L-amino acids which are the only forms that are biologically active/available.
ANZ	Australia and New Zealand
ANZFA	Australia New Zealand Food Authority, the former name for FSANZ
ATDS	Australian Total Diet Study
α-TE	Alpha-tocopherol equivalent
Breast milk	A general term for human milk provided from a mother's breast (described as mature milk to distinguish it from colostrum).
CAC	Codex Alimentarius Commission
CCNFSDU	Codex Committee on Nutrition and Foods for Special Dietary Uses
CLA	Conjugated linoleic acid
Codex	Refers to Codex Alimentarius
Complementary feeding	The gradual introduction of solid food and fluids along with the usual milk feed (breast milk or infant formula) to an infant's diet (Ministry of Health, 2008).
CRIS	Consultation regulatory impact statement
Crude protein	In this paper, based on all N-containing substances in breast milk, calculated from the total N content multiplied by a conversion factor. Crude protein thus captures amino acid protein and other N-containing substances that do not contribute to protein.
DFE	Dietary folate equivalents
DHA	Docosahexaenoic acid C22:6, n-3
DIAAS	Digestible indispensable amino acid score
DPA	Docosapentaenoic acid C22:5, n-3
DRV	Dietary reference value
EAR	Estimated average requirement
EC	European Commission

EC SCF	European Commission Scientific Committee on Food
EFSA	European Food Safety Authority
EPA	Eicosapentaenoic acid C20:5, n-3
ESPGHAN	European Society for Paediatric Gastroenterology, Hepatology and Nutrition
EU	European Union
EWG	Electronic working group
FAO	Food and Agriculture Organization of the United Nations
Follow-on formula (FOF)	An infant formula product that is represented as either a breast milk substitute or replacement for infant formula and is suitable to constitute the principal liquid source of nourishment in a progressively diversified diet for infants from the age of six months, as defined in Standard 1.1.1 of the Code.
Follow-up formula (FUF)	Under CODEX STAN 156-1987, this is a food intended for use as a liquid part of the weaning diet for infants and for young children (age 6-<36 months)
FSMP	Food for Special Medical Purposes
GL	Guideline level
GMP	Good manufacturing practice
GUL	Guidance upper level
IDA	Iron deficiency anaemia
IFPSDU	Infant formula products for special dietary use
Infant	A person under the age of 12 months, as defined in Standard 2.9.1
Infant formula (IF)	An infant formula product represented as a breast milk substitute for infants and which satisfies the nutritional requirements of infants aged up to four to six months, as defined in Standard 1.1.1 of the Code
Infant formula product (IFP)	A product based on milk or other edible food constituents of animal or plant origin which is nutritionally adequate to serve as the principal liquid source of nourishment for infants; as defined in Standard 1.1.1 of the Code
Infant formula products for special dietary use (IFPSDU)	An infant formula product listed in Division 4 of Standard 2.9.1
IOM	US Institute of Medicine
ISP	Isolated soy protein
IU	International units
JECFA	FAO/WHO Joint Expert Committee on Food Additives
JEMNU	Joint FAO/WHO Expert Meetings on Nutrition
LC-PUFA	Long chain polyunsaturated fatty acids
LSRO	Life Sciences Research Organization

Mature breast milk	Breast milk from four weeks post-partum
MCT	Medium chain triglycerides
ML	Maximum level
MoH	Ministry of Health (New Zealand)
NCF	Nitrogen conversion factor
NE	Niacin equivalents
NHMRC	National Health and Medical Research Council (Australia)
NMI	National Measurement Institute (Australia)
NPN	Non-protein nitrogen which consists mainly of free amino acids, peptides, and urea. Breast milk contains 20–25% total nitrogen as NPN.
NRV	Nutrient reference value established by NHMRC & MoH (2006)
N.S.	Not stated
PDCAAS	Protein digestibility-corrected amino acid score
PER	Protein efficiency rating
PL	Phospholipids
RE	Retinol equivalents
rNRV	Regulatory nutrient reference value
SAA	Sulphur Amino Acids (methionine and cysteine)
SD	Supporting document
Soy-based formula	An infant formula product in which soy protein isolate is the sole source of protein, as defined in Standard 2.9.1
TDS	Total Diet Survey/Study
TFA	Trans fatty acids
The Code	Australia New Zealand Food Standards Code
True protein	Is based on all N-containing substances minus NPN multiplied by an appropriate conversion factor (e.g. 6.38 for milk proteins). However, the calculation excludes nitrogen that may be metabolically available e.g. amino acids, small peptides, urea, amino sugars, nucleotides, carnitine and choline.
UL	Upper Level of intake
US	United States of America
US FDA	US Food and Drug Administration
WHO	World Health Organization
WTO	World Trade Organization

1 Introduction

Although breastfeeding is the recommended way to feed infants, a safe and nutritious substitute for breast milk is needed for infants who are not breastfed. Infant formula products are the only safe and suitable alternative to breast milk.

Infant formula is regulated within the Australia New Zealand Food Standards Code (the Code) through:

- Standard 2.9.1 – Infant formula products, and
- Schedule 29 – Special purpose foods.

While the standards in the Code that regulate infant formula are mostly working well, Proposal P1028 aims to ensure these standards are appropriate, clear and functional now and into the future. The overarching goal of Proposal P1028 is to ensure that infant formula remains safe, suitable and takes account of current science, market developments and the international regulatory context. As part of its assessment of the proposal, FSANZ will consider key stakeholder views, relevant Ministerial policy guidance and alignment with updated international regulations. Proposal P1028 is being prepared under section 113(6) of the *Food Standards Australia New Zealand Act 1991* (the FSANZ Act) and assessed under the Major Procedure.

The scope of Proposal P1028 includes all requirements for infant formula products in Standard 2.9.1 excluding follow-on formula (FOF). Infant formula products include general infant formula and infant formula for special dietary use (IFPSDU) for infants aged from 0–<12 months. Although some issues reviewed in the proposal may be relevant for FOF (for infants aged from 6–<12 months), these are not in scope for P1028. However, because of the overlap in age ranges for infant formula products and FOF, relevant information related to international regulations for FOF may be considered.

The protection of public health and safety is the primary objective for FSANZ. The nutrient composition of infant formula is appropriately prescriptive to ensure that infant formula provides sufficient energy and nutrients to promote normal growth and development of formula-fed infants, without posing a risk to infant health.

1.1 The proposal to date

Reviewing an entire standard which regulates food for a very vulnerable population is complex. Therefore, ample opportunity for stakeholders to provide input into the process and for their views to be considered is critical. To date, FSANZ has released two consultation papers[1] on this proposal:

- The 2016 Consultation paper focused on the regulation of infant formula. IFPSDU and FOF were excluded from scope (FSANZ 2016a).
- The 2017 Consultation paper focused on IFPSDU. Many submissions to the 2016 paper requested IFPSDU be included in the proposal's scope. This is because requirements for IFPSDU are founded on those for infant formula (FSANZ 2017).

These two papers and additional targeted consultation have enabled FSANZ to examine the available evidence, scope the regulatory issues and consider options to improve the current regulation.

[1] http://www.foodstandards.gov.au/code/proposals/Pages/P1028.aspx

The reasons for preparing the proposal and a description of the current standards for the regulations of infant formula is provided more fully in the 2016 Consultation paper.

1.2 Progressing the proposal

To progress the consideration of regulatory options for the 1st Call for Submission (CFS), FSANZ is releasing three consultation papers in 2021. These papers address grouped aspects of the regulation and topics, as indicated below.

- Consultation paper 1 – Safety and food technology (released 21 May 2021)
- Consultation paper 2 – Nutrition composition (this paper)
- Consultation paper 3 – Definitions and regulatory framework (tentative release August 2021)

Following these papers, the 1st CFS will include consideration of labelling requirements that relate to the provision of information, collated stakeholder views and consideration of the FSANZ Act objectives.

1.3 Consultation paper 2 – Nutrient composition

The document is organised into sections to cover:
- macronutrients and energy
- vitamins and minerals
- permitted forms, and
- other nutritive substances.

For each nutrient, the nutrient range (minimum and maximum) is discussed plus, where applicable, related information such as calculations, units of expression, ratios, definitions, sources and quality.

This paper addresses nutrient composition issues identified from a range of sources including:
- the 2016 Consultation paper on current requirements in the Code and comparison to Codex STAN 72-1981 (Codex 1981)
- stakeholder consultation (including, where relevant, submissions to the 2012 Consultation paper (which preceded the raising of Proposal P1028) (FSANZ 2012),
- other FSANZ projects, and
- regulatory and policy activities at a national and international level.

Discussion of the issues has considered:
- safety concerns about certain substances
- clarity and enforceability of the Code
- suitability for the Australian and New Zealand population
- international trade barriers created by existing regulations
- harmonisation with international regulations.

In particular, we have considered the European regulation on compositional requirements for infant formula (referred to in this paper as EU 2016/127) that was adopted after FSANZ's 2016 Consultation paper was released (European Commission 2016).

Label surveys were conducted in 2013–14 and 2021 to evaluate micronutrients amounts in infant formula products available on the market in Australia. Micronutrient amounts as reported in the Nutrient Information Panel were recorded from a sample of supermarket

products. Amounts reported were converted from units/100 mL to units/100 kJ using 2725 kJ/L as the energy content of breast milk (the midpoint of the Codex STAN 72-1981 energy range). Breast milk micronutrient concentrations were sourced from the Life Sciences Research Office Report (LSRO 1998). The ranges were then graphed against permitted ranges in international standards and regulations. The graphs enable direct comparison of the permitted range of micronutrients under the different regulations.

Within each section of this report, we have considered the above points and the need for additional risk management measures. A proposed approach and the rationale has been provided. The proposed approaches are not final decisions on whether amendments to the Code will be made. We are seeking comments from stakeholders to further inform the 1st CFS which will present an assessment for decision under section 59 of the FSANZ Act.

1.4 Background

1.4.1 Regulatory approach to developing or varying food standards

Section 18 of the FSANZ Act sets out the three primary objectives (in descending order of priority) that FSANZ is required to meet in developing or varying a food standard. These are:

(a) the protection of public health and safety
(b) the provision of adequate information relating to food to enable consumers to make informed choices, and
(c) the prevention of misleading or deceptive conduct.

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

(a) the need for standards to be based on risk analysis using the best available scientific evidence
(b) the promotion of consistency between domestic and international food standards
(c) the desirability of an efficient and internationally competitive food industry
(d) the promotion of fair trading in food, and
(e) any written policy guidelines formulated by the Australia and New Zealand Food Regulation Ministerial Council[2] (see section 1.5.3).

These objectives and principles are all relevant for the revision and clarification of standards. The first objective is paramount given the vulnerability of formula-fed infants, particularly those for which infant formula provides the sole source of nutrition during the first months of life.

1.4.2 The Code

Provisions for IFP and its three categories - IF, FOF and IFPSDU - are located in Standard 2.9.1 – Infant Formula Products and Schedule 29 – Special Purpose Foods. Other standards in the Code also contain specific provisions for IFP including IFPSDU:

- Standard 1.3.1 – Food additives and Schedule 15 – Substances that may be used as food additives which regulate the use of food additives in the production and processing of food.

[2] Now known as the Food Ministers' Meeting; previously called the Australia and New Zealand Ministerial Forum on Food Regulation (convening as the Australia and New Zealand Food Regulation Ministerial Council)

- Standard 1.4.1 – Contaminants and Natural Toxicants and Schedule 19 – Maximum levels of contaminants and natural toxicants which set out the maximum levels of specified metal and non-metal contaminants and natural toxicants in nominated foods.
- Standard 1.6.1 – Microbiological limits for food and Schedule 27 – Microbiological limits in food which list the maximum permissible levels of foodborne microorganisms that pose a risk to human health in nominated foods, or classes of foods.

1.4.3 International and overseas regulations

In developing or reviewing food standards, FSANZ must have regard to, among other things, the promotion of consistency between domestic and international food standards. As the developer of internationally recognised food standards, the approach of Codex Alimentarius (Codex) has been considered in assessing the issues discussed in this paper[3].

Codex Alimentarius

Codex STAN 72-1981 (Codex 1981) sets out the essential composition of infant formula including minimum and maximum nutrient amounts. This standard guides member countries when establishing the essential composition of infant formula, and takes account of safety, nutrient adequacy, promotion of growth and development, bioavailability, levels of naturally occurring nutrients, and the inherent variability of nutrients within ingredients and in water.

Codex STAN 72-1981 was revised in 2007 and amended in 2011 and 2015 to reflect more recent scientific understanding of nutritional needs of infants, and methods of infant formula production. The revision was completed by the Codex Committee on Nutrition and Foods for Special Dietary Uses (CCNFSDU), based on advice from international scientific experts in infant nutrition. Therefore, Codex STAN 72-1981 is based on a more recent review of the evidence than Standard 2.9.1.

The Codex *Advisory List of Nutrient Compounds for Use in Foods for Special Dietary Uses Intended for Infants and Young Children* (CAC/GL 10-1979) lists the forms of nutrients (and some optional ingredients) permitted for use in infant formula (last updated in 2008).

Where appropriate we have considered requirements under Codex STAN 156-1987 *Standard For Follow-Up Formula*. Follow-up formula (FUF) is defined within Codex regulations for infants aged 6-<36 months, which overlaps with the age range for infant formula products (0-<12 months). CODEX STAN 156-1987 is currently under review by the CCNFSDU and the draft essential composition requirements[4] have been published (FAO/WHO 2018).

Other Codex standards and guidelines relevant to issues discussed in this consultation paper are cited as applicable.

European Commission

The European Commission (EC) released new Regulations for infant formula and FSMP in early 2016. The Commission Delegated Regulation (EU) 2016/127 outlines the compositional and information requirements for infant formula and FOF and requirements relating to infant and young child feeding. The Commission Delegated Regulation (EU)

[3] https://www.foodstandards.gov.au/publications/riskanalysisfoodregulation/Pages/default.aspx
[4] Referred to as Codex Draft Standard for FUF in this paper.

2016/128 outlines the compositional and information requirements for FSMP for infants. The Commission Regulation (EU) No 1129/2011 amending Annex II to Regulation (EC) No 1333/2008 of the European Parliament and of the Council by establishing a Union list of food additives (Commission Regulation No 1129/2011) provides a list of EU food additive permissions for different food categories in Annex II, for which category 13.1.1 applies for infant formula.

United States

Infant formula is regulated under Section 412 of the Federal Food, Drug and Cosmetic Act (FFDCA) and the US Food and Drug Administration's (FDA) implementing regulations in Title 21 of the Code of Federal Regulations (21 CFR). Relevant parts of 21 CFR are:

- 106 – Infant formula requirements pertaining to current good manufacturing practice, quality control procedures, quality factors, records and reports, and notifications.
- 107 – Infant formula
- 170 – Food additives.

1.4.4 Ministerial policy guidelines

FSANZ must also have regard to Ministerial policy guidance in developing and varying standards in the Code. The relevant policy is the Ministerial Policy Guideline on the *Regulation of Infant Formula Products* (the Policy Guideline). The Policy Guideline contains *Specific Policy Principles* that address product composition, labelling and advertising. The Policy Guideline also refers to the regulation of infant formula "being consistent to the greatest extent possible" with relevant World Health Organization (WHO) and World Trade Organization (WTO) agreements, and Codex standards. The main policy principle relevant to this Consultation paper is:

d) The composition of infant formula products must be safe, suitable for the intended use and must strive to achieve as closely as possible the normal growth and development (as measured by appropriate physiological, biochemical and/or functional outcomes) of healthy full term exclusively breastfed infants when infant formula used as the sole source of nutrition up to six months of age.

2 Submitter comments to the 2016 Consultation paper: general composition issues

Table 2.1 lists general composition issues that were raised in the 2016 consultation, along with FSANZ's response. Submitter comments to specific issues are discussed within sections on the individual nutrients.

The 2016 Consultation paper also received several submitter comments regarding alignment with EU 2016/127 as this represented the most recent science-based assessment. EU 2016/127 is mostly based on the 2014 European Food Safety Authority (EFSA) recommendations (EFSA 2014b). FSANZ assessed the science underpinning the EFSA 2014 recommendations within the 2016 nutrition risk assessment and noted that the recommendations were generally not based on new science. EFSA (2014b) also did not evaluate the maximums for micronutrients. The panel noted that:

> *'specifications for the currently permitted maximum amounts of micronutrients in formulae were mostly calculated as three to five times the minimum amounts*

established at the time and took into account the established history of apparent safe use and were not based on scientific evidence for adverse effects owing to the lack of such evidence for most nutrients'.

FSANZ reiterates that the purpose of the proposal, in regard to harmonisation, is to align with international standards and not jurisdiction regulations. Where applicable, this Consultation paper considers EU 2016/127 and the EFSA (2014b) findings to inform proposed options for amending Standard 2.9.1.

Table 2.1 Submitter comments on general composition issues

Comment	Submitters	FSANZ response
Nutrients and substances should only be added to infant formula in amounts that serve a nutritional function or other benefit; and should not place a burden on the infant's metabolism or other physiological functions.	Government (1)	FSANZ agrees and has had regard to the Ministerial Policy Guideline in section 1.4.3. The 2016 Consultation paper provided principles that underpin the approach to ensure nutrients do not exceed an infant's requirements. (FSANZ 2016c, page 36-37)
Minimum levels of nutrients should be used as target values, as there is no need to provide values in excess of the target value.	Government (1)	FSANZ reiterates the EFSA (2014b) opinion that minimum amounts should be understood as target values which cover the nutritional needs of the majority of infants born at term for optimal growth and development.
Maximum levels should be regarded as upper limits as provision of excess nutrients may overload an infant's ability to excrete the nutrients i.e. excessive renal solute load.	Government (1)	FSANZ agrees and reiterates the EFSA (2014b) opinion that maximum amounts are driven by safety aspects while also taking into account technological considerations and should not be interpreted as target values but rather as upper limits of a range which should not be exceeded.
Technical calculation errors have been identified on nutrient composition specified in Codex STAN 72-1981 on a per 100 kcal basis which have not all been correctly converted to a per 100 kJ basis in this Codex standard. These errors have led to some values being applied in Standard 2.9.1 (intended to be aligned with Codex) being incorrectly stated. The inconsistencies that result from these incorrect conversion calculations create barriers to trade.	Industry (1)	FSANZ considered this issue in the nutrition risk assessment (SD1). It was found that multiplying micronutrient values expressed in kcal by the conversion factor specified in the Code (4.18) gives a maximum difference of 10% in the values expressed in kJ. The differences are due to rounding. Given that there is unlikely to be prolonged consumption of formula containing the highest or lowest concentrations of micronutrients, it is proposed that the inconsistencies can be rectified in Standard 2.9.1/Schedule 29 (i.e. align with the Codex minimum or maximum as stated in units/100 kJ).
Use of 4.18 to convert kcal to kJ (main implication is for protein minimum).	Industry (3)	FSANZ Application A1173 (2019a) assessed lowering the minimum protein in FOF. The application applied the 4.18 factor to convert kcal to kJ, however did not discuss any associated issues. Calculations throughout this proposal are based on 4.18. See section 5 and section 9 of the SD1 for further discussion.

3 Energy

3.1 Energy content

Current regulations

To ensure infant formula provides sufficient but not excess energy, Standard 2.9.1 prescribes the energy range of 2500–3150 kJ/L. This range was based on the evidence and alignment with the Codex provisions at the time of the previous review (ANZFA 1999b). Since then, the permitted range in Codex STAN 72-1981 has been narrowed to 2500–2950 kJ/L by lowering the maximum energy content.

Previous consideration

In 2016 FSANZ considered narrowing the energy content range to match Codex STAN 72-1981 as the nutrition assessment concluded it was unlikely to pose a risk to infant health.

Stakeholder views

Six submitters (two government, four industry) commented on the energy content in response to the 2016 Consultation paper. All supported lowering the maximum to align with Codex STAN 72-1981. FSANZ's label survey indicated that the average energy content, as labelled, was within the Codex permitted range.

Nutrition risk assessment

No further nutrition risk assessment was considered on this issue.

Options and discussion

Given that (1) the purpose of the proposal is to, where possible, align compositional requirements with Codex STAN 72-1981, (2) there were no potential adverse health risks identified in the nutrition risk assessment and (3) all submissions supported the alignment with the Codex standard, the only option considered by FSANZ was to align with Codex STAN 72-1981.

Proposed approach

FSANZ proposes to retain the current minimum energy content and lower the maximum energy content to 2950 kJ/L in line with Codex STAN 72-1981.

3.2 Calculation of energy content

Current regulations

Paragraph 2.9.1—4(2)(a) specifies that the energy of infant formula must be calculated in accordance with section S29—2. That is, using only the energy contributions from fat, protein and carbohydrate components, using the energy factors relevant energy factors set out in section S11—2. Codex STAN 72-1981 does not list energy factors or refer to the Codex *Guidelines on Nutrition Labelling* (CAC/GL 2-1985) which lists energy factors for labelling.

Previous consideration

During development of Standard 2.9.1, the energy factors previously listed in Standard 1.2.8 were considered appropriate for calculating the energy content of infant formula (ANZFA 2002). However, Standard 1.2.8 included a statement that it did not apply to Standard 2.9.1. The 2016 Consultation paper acknowledged the apparent conflict between the two standards in the Code and proposed that the Code's energy factors should be applied to infant formula.

Stakeholder views

Two submitters (both industry) commented on this issue. Both supported FSANZ's preliminary view that energy factors in Standard 1.2.8 be applied to infant formula.

Nutrition risk assessment

No further nutrition risk assessment was considered on this issue.

Options and discussion

The issue regarding energy factors used to calculate the energy content was resolved in Proposal P1025 – Code Revision. S29—2 now states that the energy content must be calculated using energy contributions from fat, protein, and carbohydrate with the relevant energy factors set out in S11—2.

4 Protein

Protein is important to support normal growth and development of the infant. Aspects of protein regulation discussed in the following sections include: calculation of protein content, the required range, protein source and quality, and amino acid requirements.

4.1 Calculation of protein content

Protein content is generally determined by measuring the nitrogen content then converting to the protein content using a nitrogen conversion factor (NCF). Different protein sources have variable nitrogen content and therefore different nitrogen-protein conversion factors. They range from 13 to 18% as nitrogen content varies due to greater content of glutamine and asparagine (which have a greater number of nitrogen atoms compared to other amino acids) or due to chemical side chains that reduce the nitrogen content of the protein. Other factors that can affect the estimation of protein content in a protein source include measurement conditions (e.g. pH), and levels of non-protein nitrogen (e.g. urea) which can lead to an overestimation of the true protein content. All of these factors have led to on-going debate about appropriate NCFs and/or whether different protein sources used in infant formula products should have a separate specified minimum protein amount.

Current regulations

Tables 4.1 and 4.2 summarise current regulations for NCF for infant formula based on cow's milk protein and soy protein, respectively. EU 2016/127 and the Codex Draft Standard for FUF are included as these have been subject to recent reviews and are not harmonised with Standard 2.9.1 or Codex. The minimum protein level is also shown since this has been used in some regulations to account for protein composition in different sources (and therefore nitrogen content in that protein).

Table 4.1 Standards and regulations for NCF: cow's milk protein

Standard or Regulation	NCF	Minimum protein (g/100 kJ)	Also specified in standard or regulation
Standard 2.9.1 and S29—3	6.38	0.45	Includes partial protein hydrolysates
Codex STAN 72-1981	6.25	0.45	6.38 generally established as NCF appropriate for milk products
EU 2016/127	6.25	0.43[1]	Includes protein hydrolysates
Draft Codex FUF (2018)	6.38	0.43[1]	Other NCF can be used if scientifically justified

[1] *Minimum specified as 1.8 g/kcal in these standards which is consistent with Codex STAN 72-1981. The lower minimum of 0.43 g/100 kJ results from the calculation to g/100 kJ using an energy conversion factor of 1 kcal = 4.18 kJ.*

Table 4.2 Standards and regulations for NCF: soy protein

Standard or Regulation	NCF	Minimum protein (g/100 kJ)	Also specified in standard or regulation
Standards 2.9.1 and S29—3	6.25	0.45	
Codex STAN 72-1981	6.25	0.5[1]	5.71 generally established as NCF appropriate for soy-based products
EU 2016/127	6.25	0.54[1]	
Draft Codex FUF (2018)	6.25	0.54[1]	Other NCF can be used if scientifically justified

[1] *Higher minimum protein to ensure adequate protein for soy-based products when NCF 6.25 is used.*

Previous consideration

In 2016 FSANZ's preliminary view proposed specifying two conversion factors: 6.25 for mammalian milk and 5.71 for soy protein.

Milk protein

The 6.25 NCF was derived from the average nitrogen content of mixed food proteins which is approximately 16%. Thus, 1 g of nitrogen is equivalent to about 6.25 g of crude protein. As reviewed by the EC SCF (2003), 6.25 was considered to be appropriate to calculate amounts of crude (or total) protein and amino acids in infant formula.

The 6.38 factor was derived from the amino acid sequence of casein protein component (6.36) and whey protein component (6.41) where regardless of the relative proportions of these protein components, the NCF remains about 6.38 (Maubois and Laurient 2015).

For the calculation of protein content, use of 6.25 for cow's milk protein sources when 6.38 is more appropriate underestimates protein content by about 2%. Given the relatively large variation in non-protein nitrogen (NPN) amounts in cow's milk, this underestimation can be considered minor for typical cow's milk-based infant formulas. If the protein source is processed and enriched with certain protein fractions, the percentage could be greater or less but there is no data published on such NCFs.

Soy protein

The nitrogen-protein factor for soy (5.71) is substantially lower than that for milk proteins. The composition of soy protein is different from milk proteins as it contains side chain glycosylation which reduces its nitrogen content. If 6.25 was used to calculate the protein

amount for soy protein, the calculated protein amount would be overestimated and potentially the true protein content would be insufficient to meet infant requirements.

Table 4.3 summarises the basis for the three NCFs of concern in this discussion, based on experimental analyses of samples and/or theoretical calculations based on amino acid data, noting experimental conditions may cause some variation.

Table 4.3 Basis for NCFs used for infant formula protein sources

Protein source	NCF	Basis
Soy	1 g N = 5.71 g protein	Experimentally determined, science-based NCF for soy protein sources (Maubois and Laurient 2015).
General	1 g N = 6.25 g protein	An approximated conversion factor for all protein sources based on average nitrogen content of mixed food proteins which is approximately 16%
Cow's milk	1 g N = 6.38 g protein	Experimentally determined, science-based NCF for dairy protein sources (Maubois and Laurient 2015).

Stakeholder views

Thirteen submitters (one government, 12 industry) commented on NCFs, with no clear agreement across the submissions (Table 4.4).

Table 4.4 Submitter comments on nitrogen protein conversion factors

View	Submissions	Submitter comments	FSANZ response
Supports 6.25 as appropriate NCF for all infant formula.	Industry (3)	Considers 5.71 to be derived from incorrect data	Codex has recently completed systematic review of data to derive NCF. See discussion section.
		Considers 6.25 to be consistent with Codex and EU legislation and with scientific literature.	Codex and EFSA (2014b) specify NCF 6.25 but Codex includes footnotes for 6.38 or 5.71. Note that both also set higher minimum protein for soy protein isolate to correct for over-estimation in soy-based infant formula.
		Change to 5.71 has implications for soy as a high quality protein source, and on economic and international trade factors (higher product cost, re-formulation, adaption of labelling)	FSANZ is aware of potential costs to industry (which are potentially passed on to consumers). See discussion section.
Supports 5.71, 6.25, or 6.38 depending on source; manufacturer to decide most appropriate.	Industry (6), Government (1)	Supports alignment with Codex which provides permission for all three factors: 5.71, 6.25 and 6.38	Although comments appear somewhat conflicting, these submitters basically support the most flexible option: NCF specified to allow industry to use most appropriate for their protein source. FSANZ also notes: - Codex use of footnotes to allow 6.38 or 5.71. EFSA 2014 specifies only NCF 6.25. Minimum protein for SPI is 0.54 g/100 kJ (EFSA 2014b) or 0.5 g/100 kJ (Codex)
		Supports alignment with Codex STAN 72-1981 and EFSA (2014b) with higher minimum for soy (0.5 g/100 kJ)	
		Either 6.25 or 6.38 is appropriate for dairy as there is only 2% difference	
		6.25 is not appropriate for soy-based infant formula as it	

		overestimates protein content by 9% If 6.25 is used, then need to increase protein minimum to 0.5 g/100 kJ to ensure appropriate protein amount Manufacturer to choose most appropriate NCF to the market of sale ensures flexibility is maintained	- From a scientific and technical perspective 6.25 is not appropriate for soy-based infant formula for reasons cited by submitters. See discussion section for other considerations.
Supports 5.71 for soy-based infant formula and 6.38 for dairy-based infant formula; does not support 6.25.	Industry (3)	Supports 5.71 for soy and 6.38 for dairy on scientific, nutritional, sustainability and economic basis; use of 6.25 not supported as it was selected based on arbitrary considerations.	FSANZ notes that 6.25 may be more appropriate NCF for whey-based protein. FSANZ also notes that adopting 6.25 as the NCF for all protein sources has been used in the most recent international regulations (EU 2016/127) and standards (2020 Codex Draft Standard for FUF).
Supports 5.71 for soy-based infant formula and 6.25 for all other infant formula.	Industry (1)	6.38 not supported as most infant formula products are now whey-dominant which have a lower NCF; increased minimum of 0.5 g/100kJ when considered together with a conversion factor of 5.71 for soy-based infant formula; support 0.5 g/100 kJ for soy and 0.43 g/100 kJ otherwise	Use of 6.25 for whey-based infant formula is consistent with science (Maubois and Lorient 2016) which reports NCF of 6.29-6.07. FSANZ understands approximately 85% of infant formula on the market is whey-based formula (60:40 or 70:30 whey:casein).

Nutrition risk assessment

No further nutrition risk assessment was considered on this issue.

Options and discussion

Issues with the current Standard 2.9.1 (Schedule 29) and Codex STAN 72-1981

S29—3 prescribes the NCF for soy-based protein is 6.25 and there is one minimum protein level for all protein sources (0.45 g/100 kJ) including soy based protein. Therefore, there is no correction for the lower nitrogen content of soy protein, for example by increasing minimum protein amount or applying 5.71 as the NCF.

The main issue with Codex STAN 72-1981 is that 5.71 is specified as the correct NCF for soy protein but also prescribes a higher minimum protein amount for soy-based formulas. Only one of these corrections is needed, not both.

Both standards allow the use of 6.38 for cow's milk protein although in S29—3 this is mandatory for these protein sources.

Recent reviews on NCF

There have been two recent reviews commissioned by Codex committees on the appropriate NCF to calculate protein content in infant formula.

The 37th session of Codex Committee on Methods of Analysis Sampling was presented with a position paper which considered 6.25 to be the appropriate NCF for soy protein (Codex

2016). This conclusion was supported by several scientific and regulatory experts and organisations. The paper purported that the 5.71 NCF for soy protein was based on outdated and inaccurate data originally reported in 1931 and that this value has been invalidated by improvements in analytical methodology, and by new information about protein composition and its impact on human health. The paper also contended that "soy is a high-quality protein that supports growth and maintenance when consumed as a sole source protein and 6.25 is used to calculate the protein content of diet". The paper argues that changing from the 6.25 to 5.71 conversion factor will result in an almost 10% reduction in the *calculated* protein content of "soy foods" without any change to the product itself.

In 2020, a systematic review of the scientific literature on nitrogen and protein content measurement and nitrogen to protein conversion factors for dairy and soy protein-based infant formulas was published by the Joint FAO/WHO Expert Meetings on Nutrition (JEMNU) (WHO/FAO 2019). The review included assessment of known NCFs and measurement methods as there are a number of factors (e.g. pH, amino acid determination, non-protein nitrogen, presence of side-chain groups) that can lead to variable NCFs for a particular protein source. The review also specifically addressed the most appropriate NCF for infant formula and FOF by including studies where the nitrogen content was determined directly in infant formula products. Based on a limited number of studies for both cow's milk- and soy-based formulas, the mean NCF of 6.08 was determined for cow's milk-based formula (moderate certainty of evidence) and a mean NCF of 5.71 was determined for soy-based formulas (very low certainty of evidence).

Based on these two recent reviews, there is apparently no consensus on the most appropriate NCF for infant formula products. For consumers of a mixed diet, 6.25 is a valid approximation to calculate the protein content. But because infant formula is the sole source of nutrition for some infants, scientifically accurate NCFs should be applied to avoid potential health effects associated with excess or deficient protein intakes. Given the approach used in the JEMNU review (i.e. determine NCF in infant formula product directly), the JEMNU findings provide the best scientific basis for the appropriate NCFs for infant formulas. However, the JEMNU conclusion of 6.08 as appropriate for cow's milk-based formulas does not align with any international regulations.

Economic factors

The amount of protein source needed to achieve the prescribed protein minimum depends on the NCF that is used. This is an important consideration for both cow's milk- and soy-based infant formulas. For soy-based formulas, approximately 9% more protein source is needed to meet the minimum protein amount if 5.71 is used instead of 6.25. Similarly for cow's milk-based formulas, 2% more protein source is needed to meet the minimum protein amount if 6.25 is used instead of 6.38. These differences represent significant business costs for manufacturers. (An example of this calculation is provided in Appendix 2).

Possible options

Two options are proposed that best meet submitters concerns, agree with the scientific evidence, and align with international regulations:

> ***Option 1:*** Adopt 6.25 as the NCF for all protein sources. Advantages of this approach are that it aligns with approaches that have been used in the most recent international regulations (EU 2016/127) and standards (Codex Draft Standard for FUF). It is considered to be a scientifically valid NCF for whey-based infant formula (which represents approximately 85% of the market). It is also valid to apply this NCF for soy-based protein as long as the minimum protein amount is increased to 0.54 g/100 kJ. The higher minimum will account for the lower protein content in soy (based on its

composition) that leads to over-estimation of the actual protein content in infant formula products. A higher minimum protein amount for soy-based infant formula products has also been adopted into EU 2016/127and the Codex Draft Standard for FUF.

Option 2: Adopt all three NCF (5.71, 6.25, 6.38). Advantages of this option are that it is science-based (albeit with some disagreement in recent expert reviews) and it enables the highest degree of flexibility for manufacturers to apply the most appropriate NCF for a particular protein source (e.g. 5.71 for soy, 6.25 for whey-based protein, and 6.38 for other dairy). Manufacturers would have the option to use 6.25 which is aligned with international regulations. If 6.25 is used for a soy-based protein, then a higher minimum protein amount (0.54 g/100 kJ) will apply.

Both options will require the NCF to be used to calculate protein content of the final product ready for consumption.

Proposed approach

Based on the arguments presented above, FSANZ proposes that Option 1 is the most practical option and should be adopted into Standard 2.9.1.

4.2 Protein range

4.2.1 Cow's milk-based

Current regulations

The Code and Codex STAN 72-1981 are already aligned for the protein permitted range for infant formula based on cow's milk protein (0.45 g/100 kJ minimum to 0.7 g/100 kJ maximum). This range is similar to EU 2016/127 range of 0.43 g/100 kJ minimum to 0.6 g/100 kJ maximum.

Previous consideration

Protein amounts have been specified as a range (0.45–0.70 g/100 kJ) in Standard 2.9.1 and Codex STAN 72-1981 to allow for differences in amino acid profile between breast milk and cow's milk.

Despite concerns that high protein amounts in infant formula may be associated with higher obesity risk in childhood (European Childhood Obesity Trial or ECOT (Koletzko et al. 2009)), the preliminary view in 2016 was to retain the current permitted range for protein. FSANZ considered that more evidence was required to demonstrate the benefits to infant health by decreasing infant protein intakes through a reduction in the protein minimum in infant formula.

The assessment also noted that although there is no protein UL, very high protein content (around 20% of total energy) causes increased urea production and impairs water balance (EFSA 2012). The EC SCF (2003) recommended that formula should not provide more than 12% of energy content as protein to ensure that the potential renal solute load is not unacceptably high.

Based on a review of current research, FSANZ concluded that the protein minimum and maximum should be retained at the current amounts (as per both Standard 2.9.1 and Codex STAN 72-1981) as use of these amounts is unlikely to pose a risk to infant health.

Stakeholder views

Eight submitters (two government, six industry) commented on this issue. Seven of these supported the preliminary view to retain the current minimum and maximum values. One submitter supported reducing the maximum to 0.6 g/100 kJ to align with EU 2016/127 and to ensure that the percentage of energy as protein does not exceed 12%.

In addition, three industry submitters requested a technical adjustment be made to the minimum and maximum amounts to correct what they consider is an error in converting kcal to kJ in Codex STAN 72-1981 (see section 2). These submitters support a protein range of 0.43 g to 0.72 g/100 kJ based on the equivalence factor of 1 kcal = 4.18 kJ.

Nutrition risk assessment

Additional nutrition risk assessment considered the scientific basis for the maximum of 0.6 g/100 kJ as prescribed in EU 2016/127. The lower EU 2016/127 maximum was based on EFSA (2014b) which cited the estimated upper bound of protein intakes for European infants and the observation that there is no evidence of a physiological need for protein intakes at ≥ 0.72 g/100 kJ in infancy.

The nutrition risk assessment also considered that the lowered maximum permitted protein levels in the EU 2016/127 are based on estimated upper bounds of the adequate range of protein intake. The EFSA (2014b) recommendations were based on the observation that there is no evidence of a physiological need for protein intakes at amounts of 3.0 g/100 kcal in infancy, which is the currently permitted maximum content in infant formula, and that protein intakes by infants in the EU are generally well above requirements.

The higher permitted maximum amounts in EU 2016/127 for formulas based on isolated soy proteins, compared with cow's milk- or goat's milk-based formulas, are to account for lower levels of some essential amino acids and lower digestibility of plant proteins compared to milk proteins due to the increased content of phytic acid and trypsin inhibitors. A rationale for the higher maximum level set for formula containing protein hydrolysates, compared with cow's milk- or goat's milk-based formulas, was not provided.

Options and discussion

Minimum protein

The minimum protein amount is set to ensure minimum amino acid requirements can be met for a given protein source. FSANZ's 2016 assessment reviewed the evidence linking high protein-containing formulas and obesity in older infants and concluded that the evidence was not sufficient to warrant a change in the permitted range for protein in IF. Submitters to the 2016 Consultation paper supported this approach.

In 2019, FSANZ approved a reduction in the minimum protein in FOF (i.e. for infants 6-12 months) to 0.38 g/100 kJ (FSANZ 2019a). This was based on an assessment that found that this minimum was consistent with human milk protein content, would support infant growth that was comparable to breast fed infants, and did not introduce risk of inadequate protein intakes (for infants aged 6-12 months this includes protein from complementary foods). In submissions to A1173, health professionals noted that obesity has complex causality and it is simplistic to attribute a lower rate of obesity to lower protein concentrations in FOF.

Since 2016, there has been continued debate on the possible link between high protein content in infant formula and risk of obesity in later life. However, most studies that examine low protein formulas utilise experimental formulas in which composition relies on a high

content of free amino acids (see for example Kouwenhoven et al 2020) in order to meet amino acid requirements. This is unlikely to be practical for infant formula manufacturers and may influence formula intakes as free amino acids may be unpalatable.

A recent systematic review on the link between protein intakes and obesity outcomes showed that total protein intakes from birth to 2 years was associated with higher body mass index in later childhood and adolescence (Stokes et al 2021). The study did not examine the association between obesity outcomes and infant formula of varying protein concentrations. Therefore it is not possible to derive a conclusion about a minimum protein concentration for infant formula from this study.

Based on the above discussion, FSANZ confirms the proposed approach from 2016 to retain the current minimum amount for protein. We note that the Codex draft revised standard for FUF has set a protein range of 0.43–0.72 g/100 kJ. The slight difference from Codex STAN 72-1981 and Standard 2.9.1 is due to a technical calculation issue which is discussed in section 2 of this report.

Maximum protein

EU 2016/127 specifies a protein maximum of 0.6 g/100 kJ if infant formula manufactured from cow's milk or goat's milk proteins and a maximum 0.67 g/100 kJ in infant formula manufactured from protein hydrolysates. Both are lower than the single maximum specified in Commission Directive 2006/141/EC (in effect prior to the 2016 regulation) and in Codex STAN 72-1981 (3.0 g/100 kcal (equivalent to 0.7 g/100 kJ). This change appears to be based on the conclusion from EFSA that "there is no evidence of a physiological need for protein intakes at 3.0 g/100 kcal in infancy" (EFSA 2014b). The EFSA Panel also acknowledged that "there are no scientific data available which allow the establishment of precise cut-off values for the maximum protein content in infant formula."

Proposed approach

Based on absence of evidence noting harm to infant health for this range, submitter comments to the 2016 Consultation paper, consistency with the EU 2016/127 regulations (minimum), FSANZ proposes to prescribe a permitted protein range of 0.43–0.7g/100 kJ for cow's milk-based infant formula. FSANZ also notes that the recently reviewed Codex Draft Standard for FUF (FAO/WHO 2018) is also aligned with this range.

4.2.2 Soy-based

Current regulations

A footnote in Codex STAN 72-1981 specifies a higher minimum protein content (0.5 g/100 kJ) for infant formula based on soy protein isolate to ensure that amino acid requirements can be met. Standard 2.9.1 does not differentiate between protein sources for the protein minimum.

Previous consideration

The Codex standard is based on the consideration that soy and other plant proteins have a different amino acid profile to cow's milk proteins and takes into account the lower nitrogen conversion factor used for soy (see section 4.1). FSANZ's 2016 nutrition assessment concluded that the current protein range was unlikely to adversely affect infant health and there were no indications that soy-based formulas formulated under either standard would not meet nutritional needs to support normal growth and development. However, we sought

further information from submitters on the need for a higher protein minimum for isolated soy protein of 0.5 g/100 kJ instead of 0.45 g/100 kJ.

Stakeholder views

Seven submitters (four government, three industry) commented on the minimum protein level for isolated soy protein. All supported a higher minimum to be applied for soy-based formulas, noting that this needs to be considered in conjunction with the appropriate NCF for the protein source.

Nutrition risk assessment

No further nutrition risk assessment was considered on this issue.

Options and discussion

There is unlikely to be infant health issues related to insufficient protein in ANZ. However, to get an accurate estimate of the amount of a protein source to be added to meet the minimum, an accurate NCF should be used.

Using 6.25 (which is not accurate for soy protein) will overestimate the true protein content. Therefore, if using 6.25 then the minimum protein content for soy-based formula must be increased by about 10%, or to 0.54 g/100 kJ as set in the Codex Draft Standard for FUF and EU 2016/127. Based on the arguments presented in section 4.1, FSANZ considers it appropriate set a higher minimum protein amount for soy-based formula only if 6.25 is used as the NCF.

Proposed approach

FSANZ proposes that the minimum protein amount for soy-based infant formula be 0.54 g/100 kJ. This is based on the use of 6.25 as the NCF. This is consistent with the regulations set under EU 2016/127 and with the Codex Draft Standard for FUF.

4.3 Protein source

Current regulations

Standard 2.9.1 and Codex STAN 72-1981 are aligned in that neither standard specifies protein sources. The definition of infant formula products under Standard 2.9.1 requires that the product must be based on “milk or other edible food constituents of animal or plant origin”. Similarly, Codex STAN 72-1981 defines infant formula as a product based on “milk of cows or other animals or mixture thereof and other ingredients proven to be suitable for infant feeding”.

Previous consideration

Both Standard 2.9.1 and Codex STAN 72-1981 set minimum requirements for protein content and essential amino acid amounts to align with the reference protein i.e. breast milk, regardless of protein source. Generally this has restricted the type of protein sources that can be used. It has also been considered that pre-assessment requirements of novel foods and novel sources of ingredients would manage any potential risks of new ingredients (i.e. new sources of proteins) in infant formula (ANZFA 2002). On this basis, FSANZ’s preliminary view in 2016 was that the current sources of protein are appropriate.

Stakeholder views

Six submitters (three government, three industry) commented on whether the protein source should be specified in Standard 2.9.1. Government submitters did not support FSANZ's preliminary view that protein source does not need to be regulated if the quantity and quality of protein is regulated. Industry, on the other hand, supported the view that no change to protein requirements in relation to source was required.

Several submitters commented on the related question regarding macronutrients that are added for other nutritive purposes (this topic will be discussed in the next Consultation paper).

Nutrition risk assessment

No further nutrition risk assessment was considered on this issue.

Options and discussion

Government submitters did not support the preliminary view on the basis that plant-based sources of protein may contain anti-nutrient factors that can interfere with nutrient absorption. In addition they considered that to be consistent with the *Ministerial Policy Guideline on the Regulation of Infant Formula Products*, the protein source needs to be clearly defined to remove ambiguity about what substances require pre-market assessment.

New plant-based proteins to be used in foods have been of considerable interest over the past several years. This interest has stemmed largely from sustainability arguments and extends across the food supply including infant formula products. Thus, the context around the issue of defining protein sources in Standard 2.9.1 has changed since the publication of the 2016 Consultation paper.

Definition of protein sources has been addressed in both EU 2016/127 and the Codex Draft Standard for FUF. EU 2016/127 specifies that infant formula must be manufactured from cow's milk or goat's milk proteins, soya protein isolates, alone or in a mixture with cow's milk or goat's milk proteins. The regulation was based on the recommendation of EFSA (2014b) which also stated that the use of other protein sources in infant formula and FOF required clinical evaluation and their safety and suitability should be established in the target population prior to their general use in infant formula and FOF. The Codex Draft Standard for FUF (2020) states *"Follow-up formula for older infants is a product based on milk of cows or other animals or a mixture thereof and/or other ingredients which have been proven to be safe and suitable for the feeding of older infants*".

Proposed approach

The recent focus on new proteins to be used in foods, and the potential safety issues associated with their use in infant formulas, has increased concerns about these sources if not approved through the pre-market assessment process. Therefore, FSANZ proposes that the protein source be specified to be cow's milk protein, goat's milk protein, protein hydrolysates of one or more proteins normally used in infant formula, and soy protein isolate.

4.4 Protein quality

Current regulations

Both Standard 2.9.1 and Codex STAN 72-1981 regulate the protein quality through mandating minimum amounts of the amino acids considered essential (and semi essential) for infants (see section 4.5).

Previous consideration

FSANZ's 2016 nutrition assessment supported the continued use of minimum amino acid amounts to ensure protein quality. The assessment discussed the protein digestibility-corrected amino acid score (PDCAAS) and digestible indispensable amino acid score (DIAAS) protein scoring systems, noting that very limited data currently using the DIAAS method exists. The assessment concluded that when data becomes available, it is unlikely to dramatically alter the quality protein scores for infant formula as the main ingredients are already high-quality protein.

It was FSANZ's preliminary view that the amino acid composition of breast milk should remain the reference for determining minimum amino acid requirements in infant formula. This approach aligns with Codex i.e. the minimum recommendations of Codex STAN 72-1981 are based on the average amount of amino acids present in breast milk, rather than a protein scoring system.

Stakeholder views

Four submitters (all industry) commented on the issue of the protein scoring methods to assess protein quality. All supported FSANZ's preliminary view but considered also that implementation of the DIAAS method to be appropriate once the supporting science was complete.

Nutrition risk assessment

Further nutrition risk assessment (SD1) considered whether the current evidence base for the DIAAS and PDCAAS methods of protein scoring still supports the current approach for ensuring protein quality. Based on the recommendation of the 2018 FAO Expert Working Group, the DIAAS and PDCAAS methods for protein quality assessment are ideal methods, however as the evidence base relevant for human infants is incomplete, the DIAAS and PDCAAS methods are not currently suitable for regulatory purposes. Therefore, using the amino acid composition of human milk as the reference for determining minimum amino acid requirements in infant formula is recommended.

Options and discussion

Protein quality in infant formula is ensured by setting minimum amounts of essential amino acids. In contrast, protein quality scoring systems (protein efficiency rating (PER) or PDCAAS) has been recommended in Codex for ensuring protein quality in FUF. In the recently reviewed Codex Draft Standard for FUF (FAO/WHO 2018), the CCNFSDU considered whether the new scoring system DIAAS should be used. The report from the 38th session of the CCNFSDU indicated that the DIAAS method was not considered to be ready for use. Therefore the Code Draft Standard for FUF (which does not use breast milk amino acid composition as the reference for protein quality) has adopted the PDCAAS as the preferred method to determine protein quality.

Proposed approach

Because current methods for measuring protein quality have yet to be established for regulatory purposes, FSANZ proposes to maintain the current requirements for protein quality by mandating minimum amino acid amounts (see section 4.5).

4.5 Amino acid content

Current regulations

Both Standard 2.9.1 and Codex STAN 72-1981 specify minimum amounts of 11 essential and semi-essential amino acids (Table 4.5). Both standards specify that isolated amino acids should be added to infant formula only to improve its nutritional quality.

Minimum amounts are largely aligned for histidine, isoleucine, leucine, lysine, threonine, tryptophan and valine. However Codex has a different approach to express amounts of the sulphur amino acids (SAA) methionine and cysteine, and the aromatic amino acids (AAA) tyrosine and phenylalanine. In Codex STAN 72-1981 methionine and cysteine each have a listed minimum value, with the following footnote: "The concentrations of methionine and cysteine may be added together if the ratio is less than 2:1; in the case that the ratio is between 2:1 and 3:1, the suitability of the formula has to be demonstrated by clinical testing". Section S29—6 specifies a minimum amount of cysteine and cysteine total (which would include the cystine form[5]), as well as a minimum summed value of cysteine, cystine and methionine. Similarly, for the AAA, section S29—6 specifies a minimum for phenylalanine and a minimum summed value for phenylalanine and tyrosine.

Table 4.5 Minimum amounts of amino acids

Amino acid	Standard 2.9.1 (S29—6) (mg/100 kJ)	Codex STAN 72-1981[1] (mg/100 kJ)
Sulphur amino acids		
Cysteine	-	9
Methionine	13 (amount by difference)[2]	6
Cysteine & cysteine total	6	-
Cysteine, cystine & methionine total	19	-
Aromatic amino acids		
Phenylalanine & tyrosine total	32	-
Phenylalanine	17	19
Tyrosine	15 (present by difference)[3]	18

[1] Values in Annex I of Codex STAN 72-1981, converted to mg/100 kJ using 4.18 and rounding.
[2] To enable comparison with the Codex level, this is the amount calculated by difference (cysteine, cystine & methionine total minus cysteine & cysteine total).
[3] To enable comparison with the Codex level, this is the amount calculated by difference (phenylalanine & tyrosine total minus tyrosine).

[5] Cysteine is the sulphydryl form, cystine is the disulphide form. The two forms are interconverted through a redox reaction, are nutritionally equivalent, and combined represent "cysteine total". Some older literature reports appear to use the terms interchangeably.

Previous consideration

The minimum amounts of amino acids in infant formula are mainly based on 'typical' amino acid profiles of breast milk. As noted in the nutrition assessment, infants may be unable to synthesise cysteine (or cystine) and tyrosine from their amino acid precursors (methionine and phenylalanine, respectively), thus these amino acids are considered to be semi-essential amino acids for infants and minimum amounts are also set for them.

In 2016 we proposed to align the minimum amounts of isoleucine, leucine, lysine, threonine, tryptophan and valine with Codex STAN 72-1981 as it was considered unlikely to pose a risk to infant health.

The current expression for SAA and AAA in specifying the minimum for cysteine (including both forms cysteine and cystine) and phenylalanine and the summed values of SAA and AAA was proposed to be retained on the basis that the expression is clear and not subject to possible misinterpretation. Accordingly, the current minimums for total SAA and AAA was also rposed to be retained.

Stakeholder views

Nine submitters (one government, eight industry) commented on amino acid minimum amounts. All agreed with FSANZ's preliminary view to align with Codex STAN 72-1981 for isoleucine, leucine, lysine, threonine, tryptophan and valine. However, all disagreed with the preliminary view to retain the current requirements for SAA and AAA as set in Standard 2.9.1 (S29—6) and instead supported the alignment with Codex STAN 72-1981 for SAA and AAA.

Nutrition risk assessment

No further nutrition risk assessment was considered for this issue.

Options and discussion

Summed amounts of SAA and AAA are specified in Standard 2.9.1 (S29—6) because at the time the standard was developed concentrations of these in human milk had not been measured individually. Minimum amino acids amounts in Codex STAN 72-1981 were based on the findings of the SCF 2003 where concentrations of methionine, cysteine, tyrosine and phenylalanine in human milk were determined individually rather than grouped as SAA and AAA. A recent systematic review reported amino acid concentrations in human milk that were consistent with the SCF 2003 findings (Zhang et al. 2013). On the basis of this review, EFSA (2014b) recommended amino acid concentrations that were closely correlated with Codex STAN 72-1981. These amounts were adopted into EU 2016/127.

Summed amounts of SAA and AAA may still be used by manufacturers. Therefore, Codex and EU 2016/127 also require (as a footnote) that the ratios of methionine to cysteine and tyrosine to phenylalanine must both be less than 2:1. This is to ensure that the amino acid composition remains closely aligned with human milk composition. FSANZ notes that the wording of the footnote in EU 2016/127 has been clarified to read:

> "*For an equal energy value, infant formula manufactured from cows' milk or goats' milk proteins must contain an available quantity of each indispensable and conditionally indispensable amino acid at least equal to that contained in the reference protein as set out in Section A of Annex III. Nevertheless, for calculation purposes, the concentration of methionine and cysteine may be added together if the methionine:cysteine ratio is not greater than 2, and the concentration of phenylalanine and tyrosine may be added together if the tyrosine:phenylalanine ratio is not greater than 2*."

EU 2016/127 strengthens the requirement the individual minimum amounts for each amino acid must be met. In addition, as pointed out by submitters, the Codex standard is aligned with the most recent research on human milk composition and that compliance with the S29—6 could lead to a ratio of methionine to cysteine that exceeds 2.[6]

Proposed approach

FSANZ proposes to align the minimum amounts of all amino acids with Codex STAN 72-1981. Regarding SAA and AAA, the added requirements to define ratios of methionine to cysteine and tyrosine to phenylalanine is proposed to be included in Schedule 29 as a condition (for example, see EU 2016/127 above).

5 Fat

Fat (or lipids) are the main energy source in infant formula.

Current compositional requirements of fat and fatty acids in infant formula and FOF are provided mainly in sections 9 and 11 in Standard 2.9.1 and section S29–8 in Schedule 29 of the Code, which set the following:

- mandatory minimum and maximum content requirements for fat and the essential fatty acids; linoleic acid (LA) and α-linolenic acid (ALA)
- maximum limits and certain ratios for long chain polyunsaturated fatty acids (LC-PUFA)
- limits on the presence of various other fatty acids.

Both Codex STAN 72-1981 and EU 2016/127 specify mandatory requirements for fat and the essential fatty acids, including specific requirements for certain fatty acids, limits on the presence of saturated fats and phospholipids. These requirements are, in general, similar to those currently provided in the Code.

The issues related to each aspect of the regulation of lipids and fatty acid are discussed in the following sections. This includes what was proposed in the 2016 Consultation paper, conclusions of the nutrition risk assessment and issues raised in submissions to the 2016 Consultation paper.

5.1 Fat content

Current regulations

Table 5.1 lists currents regulations for the minimum and maximum fat content under Standard 2.9.1, Codex STAN 72-1981, and EU 2016/127.

Table 5.1 Permitted range for total fat (g/100 kJ)

Micronutrient	Standard 2.9.1		Codex STAN 72-1981		EU 2016/127	
	Min	Max	Min	Max	Min	Max
Total Fat* (g/100 kJ)	1.05	1.5	1.05	1.4	1.1	1.4

**Referred to as Lipids in EU 2016/127*

[6] Using minimum amounts in Table 4.5: If cysteine + cysteine total = 6 and methionine + cysteine + cystine = 19 then methionine = 13 (by difference) and the ratio of Met:Cys = 2.2.

Previous consideration

In 2016 FSANZ considered it appropriate to retain the current minimum of 1.05 g/100 kJ and lower the maximum level from 1.5 g/100 kJ to align with Codex STAN 72-1981. This approach was supported by the conclusion of the nutritional safety assessment, which concluded that the amounts proposed were consistent with average fat content in human milk; and the estimated intakes of fat would be unlikely to pose a risk to infant health. It was also noted that the proposed levels were consistent with the EFSA (2014b) recommendations.

Stakeholder views

Six submitters (two government, four industry) commented on the permitted range for total fat. All submitters supported the proposal to retain the minimum fat content at 1.05 g/100 kJ and to slightly reduce the maximum from 1.5 to 1.4 g/100 kJ. One submitter commented that fat in infant formula should be aligned with levels found in human milk and established adequate intakes.

Nutrition risk assessment

No further nutrition risk assessment was considered on this issue.

Options and discussion

The 2016 nutrition risk assessment considered the permitted range for fat specified in Codex STAN 72-1981 compared to the fat content of human milk and whether the minimum fat amount would meet the ANZ adequate intake (AI). The fat content in both Standard 2.9.1 and Codex STAN 72-1981 is consistent with the amount of total fat reported in human milk. Based on the energy midpoint (2725 kJ/L) and the mean intake volume of 0.8 L/day for infants 0–<6 months, the estimated minimum intake is 23 g/day which is less than the ANZ AI (31 g/day). FSANZ did not consider that the difference would pose a health risk because the ANZ AI is calculated from reported concentration at the upper range of breast milk concentrations (40 g/L) rather than the average fat content of breast milk (NHMRC and MoH 2006). The estimated intake for infants 6–<12 months was found to meet 50% of the AI (16 g/day) where it was assumed that these infants would receive 50% of nutrient intake from infant formula and 50% of from complementary foods.

Proposed approach

Based on the conclusions of the 2016 nutrition risk assessment, alignment with Codex STAN 72-1981, EU 2016/127 and fat content levels found in human milk, FSANZ proposes to retain the current minimum level and lower the maximum to 1.4g/100 kJ.

5.2 Units of expression

Current regulations

Currently Standard 2.9.1 specifies fat content per 100 kJ and Schedule 29 sets the fatty acid limits as a percentage of total fatty acid content. This approach recognises the inter-related fats and the complexity of essential fatty acid metabolism (ANZFA 2002). The approach also recognises the challenges of setting a specific value per unit of energy where a range of fat content is permitted.

Previous consideration

FSANZ's preliminary view was to retain the requirement that amounts of particular fatty acids are expressed as a percentage of total fatty acids, as this expression refers to the overall fatty acid profile that is independent of the energy content of the formula. FSANZ used a calculation in the 2016 Consultation paper to compare Codex requirements for fat and fatty acids with Standard 2.9.1. The calculation converted the minimum fatty acid requirement in Standard 2.9.1 (e.g. LA = 9% of fatty acids) to units of mg/100 kJ using the prescribed range of fat content (minimum and maximum) and the assumption that the fats and oils are 95% fatty acids (Greenfield and Southgate 2003). This calculation was used for illustrative purposes only, i.e. to make the comparison between the two standards.

Stakeholder views

Three submitters (all from industry) commented on this issue and agreed with the view from 2016 Consultation paper that the primary unit of expression for essential fatty acids should be mg/100 kJ to align with other nutrients and with Codex STAN 72-1981. They also considered that a calculation and appropriate assumptions should be included in Standard 2.9.1 so that fatty acids acid be expressed as a percentage of total fatty acids. It was noted that expression on a fatty acid basis is useful in raw material specifications but having both units in the standard is unnecessary.

Nutrition risk assessment

No further nutrition risk assessment was considered on this issue.

Options and discussion

FSANZ notes that Codex STAN 72-1981 uses a mixed approach for units of expression of fatty acids. Total fat, LA and ALA requirements are specified per 100 kJ (and 100 kcal), while limits on specific fatty acids (docosahexaenoic acid (DHA), lauric acid, myristic acid, and erucic acid) are set as a percentage of total fatty acids (i.e. aligned with Standard 2.9.1). However, the Codex Draft Standard for FUF (2020) now sets DHA amounts in mg/100 kJ but still uses the percentage of fatty acids to set limits on lauric acid, myristic acid, and erucic acid. EU 2016/127 does not use percentage of fatty acids as a unit of expression.

Conversion of the percentage of fatty acids (e.g. 9 - 26% of fatty acids for LA) to units of mg/100 kJ is calculated using the prescribed total fat content. Because this is set as a minimum and maximum amount, the calculation can be done in two ways:

1) using the minimum fat content and the minimum fatty acid amount and the maximum fat content and the maximum fatty acid amount (gives the widest range of fatty acid content); or
2) using the midpoint of the fat content range with the minimum and maximum fatty acid amount.

Table 5.2 shows this calculation for LA acid. The calculation using the minimum and maximum total fat amount (i.e. not the midpoint) best aligns with the Codex range for LA acid (70 - 330 mg/100 kJ).

Table 5.2 Calculation of LA range in mg/100 kJ

Standard 2.9.1 (S29—8) LA amount (% of total fatty acids)	Total fat (g/100 kJ)		LA amount[1] (mg/100 kJ)
9	**1.05**	**(minimum)**	**90**
9	1.4	(maximum)	120
9	1.23	(midpoint)	105
26	1.05	(minimum)	260
26	**1.4**	**(maximum)**	**350**
26	1.23	(midpoint)	304

[1] *assumes 95% of fat is fatty acids (Greenfield and Southgate (2003). Note: Best alignment with Codex STAN 72-1981 shown in bold.*

During the development of Standard 2.9.1 in Proposal P93 (ANZFA 1999a), ANZFA considered whether the amount of fatty acids should be expressed as absolute values per 100 kJ of energy, or as a proportion of the total fatty acids. It was noted that most of the relevant scientific reports about infant fatty acid requirements at that time expressed them as a percentage of total fatty acids, rather than as absolute values or per 100 kJ. ANZFA considered it appropriate to use a proportional unit of expression for inter-related fats, in recognition of the complexity of essential fatty acid metabolism (ANZFA 2002). Additionally, setting a specific value per unit of energy was problematic where a range of fat content (1.05–1.5 g/100 kJ) in formula was established; this was further confounded by the interplay of protein and carbohydrate levels (ANZFA 2002).

However, given that international regulations have moved on from this position and that there appears to be support for the adoption of consistent units of expression for fatty acids, FSANZ considers that it is appropriate to align with Codex for this issue. Defining a calculation for converting fatty acid amounts from percentage of total fatty acids to mg/100 kJ is not needed as no safety issue has been identified and this approach would be inconsistent with the general view of manufacturers on minimum effective regulation.

Proposed approach

Based on alignment with Codex STAN 72-1981 and the Codex Draft Standard for FUF, FSANZ proposes to express the amounts of fatty acids in terms of mg/100 kJ. This applies to LA, ALA and DHA. Limits on lauric acid, myristic acid, and erucic acid will still be prescribed as a percentage of fatty acids.

5.3 Essential fatty acid composition: LA and ALA

LA and ALA are essential fatty acids because they cannot be synthesised endogenously. They are precursors of several n-6 and n-3 LC-PUFA such as arachidonic acid (AA), eicosapentaenoic acid (EPA) and DHA.

Current regulations

There are requirements for the essential omega 6 and omega 3 fatty acids, LA (18:2, n-6) and ALA (18:3, n-3) in both standards, although there are some differences (Table 5.3). Standard 2.9.1—11(1)(b) and Codex STAN 72-1981 are aligned for the LA:ALA ratio. To compare fatty acid composition to Codex, Standard 2.9.1 (S29—8) amounts converted to amounts in units of mg/100 kJ.

Table 5.3 Permitted ranges for LA and ALA

Fatty acid	Standard 2.9.1 and S29—8		Codex STAN 72-1981	EU 2016/127
	Min–Max % total fatty acids	Min–Max mg/100 kJ[1]	Min–Max mg/100 kJ	Min–Max mg/100 kJ
LA	9–26	90–371	70–330 (GUL)	120–300
ALA	1.1–4	11–57	12–NS	12–24
LA:ALA ratio	5:1–15:1	–	5:1–15:1	–

NS: not specified; GUL: Guidance upper levels
[1] Calculated in mg/100 kJ to compare with Codex amounts (see previous section).

Previous consideration

In 2016 FSANZ noted that there is no international consensus on the recommended amount of LA in infant formula. The nutrition assessment concluded that the evidence did not support the lower Codex minimum but was more consistent with the current Standard 2.9.1 (S29—8). Therefore, FSANZ proposed retaining the current minimum requirement for LA (9% total fatty acids) in infant formula and sought comments on this approach.

FSANZ also considered that use of ALA at the current levels within Standard 2.9.1 (S29—8) or at the levels prescribed by Codex STAN 72-1981 are unlikely to pose a risk to infant health. The maximum amount of ALA is controlled by the maximum ratio of LA to ALA of 15:1, which is same across the Code and Codex. The 2016 nutrition risk assessment suggested that adopting the Codex STAN 72-1981 guidance upper level (GUL) as a maximum for ALA was also unlikely to pose a risk to infant health. Further assessment of the maximum LA, ALA range and LA:ALA ratio is therefore not required.

Stakeholder views

Eight submitters (four government, three industry, one health professional) commented on the permitted range and ratio for LA and ALA in infant formula. All eight submitters commented on the minimum amount of LA without clear agreement of a preferred approach. Three industry submissions and one health professional considered that the minimum LA amount was too high and should be lowered to the Codex level (70 mg/100 kJ), with appropriate consideration of the LA:ALA ratio. Four government submitters supported aligning the minimum requirement with EU 2016/127 and 2014 EFSA Scientific opinion (Table 5.4).

Table 5.4 Submitter comments and FSANZ responses regarding fatty acids

Comment	Raised by	FSANZ response
The minimum requirement for LA (9% total fatty acids) in infant formula is high. The minimum level to prevent LA deficiency is <1% total fatty acids.	Health professional (1)	Converting amounts in order to compare between standards, the minimum amount of LA set in the Code (90 mg/100 kJ) is in between the minimum amount of LA in Codex STAN 72-1981 (70 mg/100 kJ) and EU 2016/127 (120 mg/100 kJ). These values are consistent with LA concentrations in breast milk that range from 8 to 17% of total fatty acids (LSRO 1998). However, an infant consuming infant formula containing the minimum LA amount according to Codex STAN 72-1981 would not meet the EFSA recommendation for the young infants but would be comparable to the recommended intake for the older infants.

		While giving regard to the ALA:LA ratio, the approach followed by FSANZ, as well as EFSA, considered providing the AI of n-6 PUFA through infant formula products. Standard 2.9.1 does not specify a minimum amount for n-6 LC-PUFA. Therefore, providing sufficient amounts of LA within the required ratio with ALA will ensure sufficient bioconversion into n-6 LC-PUFA.
LA levels in infant formula should be aligned with that in breast milk, established AIs and with the scientific opinion provided by the EFSA NDA panel and those set in EU 2016/127.	Government (3)	As noted in the 2016 Consultation paper there is no international consensus on the appropriate amounts of LA and ALA for infant formula. The current minimum value for LA in S29—8 is consistent with that in breast milk concentrations (8–17% of total fatty acids (LSRO 1998)). An infant consuming infant formula containing the minimum LA amount according to Codex STAN 72-1981 would not meet the EFSA recommendation for young infants but the amount consumed would be comparable to the recommended intake for older infants. FSANZ assessment has also given regard to the AI for n-6 PUFA. EFSA (2014b) used AI derived for LA and ALA that was based on breast milk concentration reported in 1992 (EFSA, 2013) to recommend the minimum amounts of LA in infant formula to be 120 mg/100 kJ, reiterating the 2003 EC SCF recommendations. EFSA (2014b) also recommended that preformed DHA be added to infant formula but did not recommend that a specific ratio of LA:ALA was needed. Therefore, the higher amount of LA recommended by EFSA was likely made to ensure appropriate balance between n-6 LC-PUFA and n-3 LC-PUFA, which is already regulated by Standard 2.9.1.
The minimum level of LA should not be too high to avoid limiting the ability to produce infant formula products with LA:ALA ratios at the lower end of the 5:1-15:1 range that is generally accepted as appropriate to maintain a proper balance between LA and ALA as well as the LC-PUFA.	Industry (1)	FSANZ 2021 label survey found that infant formula products that declared the LA levels on the label were within the minimum and maximum ranges of Codex STAN 72-1981, EU 2016/127 and Standard 2.9.1 (S29—8). Therefore, it is unlikely that the minimum level of LA will limit the capacity for compliant compositions and formulations of infant formula. The minimum and maximum amounts of LA and ALA in S29—8 are within the natural range of variation for LA and ALA in breast milk (converting percentages of total fatty acids in S29 to mg/100 kJ – see section 5.2)
Suggest establishing a GUL for LA	Government (1)	The upper bound of 300 mg/100 kJ for LA in EU 2016/127, based on EFSA's scientific opinion, is a maximum value not GUL. According to the nutrient reference value (NRV) for ANZ, no upper level of intake (UL) was set for LA because there is no known level at which adverse effects may occur and for infants 0–>12 months it is not possible to establish a UL.
Compositional requirements for LA and ALA are interlinked and as such all aspects should be considered together, particularly	Government (1)	There is no evidence that the LA:ALA ratio as currently specified in Standard 2.9.1 and Codex STAN 72-1981 is likely to pose a risk to infant health. The LA:ALA ratio in both Codex STAN 72-1981 and Standard 2.9.1 permit an appropriate balance of n-6 and n-3 PUFA.

with regard to the suitability of the LA:ALA ratio.		
Given the advantages of harmonisation with Codex, all requirements for LA and ALA in the revised Standard 2.9.1 are recommended to align with those in Codex STAN 72-1981.	Industry (3)	FSANZ considers that risk to infants is low if fatty acid requirements are aligned with Codex STAN 72-1981. However, the evidence supports maintaining a minimum amount for LA in S29—8 rather than aligning with Codex. The amount of LA and ALA in S29—8 is expressed as a proportion of total fatty acids. Codex STAN 72-1981 expresses the essential fatty acid requirements as an amount per unit energy. FSANZ proposes to continue to require that the amount of essential fatty acids be expressed as a proportion of total fatty acids.

Nutrition risk assessment

Based on the best available evidence specific to the ANZ population, the 2021 nutrition risk assessment concluded that use of a minimum amount of LA between 110 mg/100 kJ and 140 mg/100 kJ poses a low risk to infant health.

Options and discussion

The 2016 nutrition risk assessment evaluated the risk of adopting the Codex STAN 72-1981 requirements. The assessment considered that the minimum LA level did not align with breast milk composition of the ANZ population and had potential to pose risk to infant health. As mentioned in response to submitter comments, based on the nutrition risk assessment conclusions FSANZ does not find it appropriate to adopt the Codex STAN 72-1981 minimum level for LA.

Reported LA concentrations in human milk vary based on numerous factors, such as maternal diet, body fat stores and differences in research methodologies. For this reason the 2021 nutrition risk assessment evaluated evidence relevant to the ANZ population. The assessment found that for the ANZ population the minimum LA concentrations in breast milk were approximately 140mg/100 kJ. The nutrition risk assessment also noted that an LA level of 140/mg/100 kJ would meet the EFSA AI and allow the proposed minimum ALA concentration to be met (through the LA:ALA ratio).

The LA concentration in ANZ breast milk reported by the nutrition risk assessment (140mg/100 kJ) best aligns with EU 2016/127, which prescribes a minimum LA level of 120mg/100 kJ. This level is recommended by the EFSA (2014b) and the EC SCF (2003). EU 2016/127 also prescribes the mandatory addition of DHA to infant formula within the range of 12–24 mg/100 kJ.

Increasing the levels of LC-PUFAs can pose challenges to infant formula manufacturers (Mendonça et al. 2017, Daoud et al. 2020). LC-PUFAs, such as DHA, AL and ALA, are prone to oxidation which can alter the stability, palatability and nutritional value of the final product. The ESPGHAN (2005) noted that a maximum level of LA of 300 mg/100 kJ (1200 mg/100 kcal) is necessary as higher levels of LA can induce unwanted metabolic effects with respect to lipoprotein metabolism, immune function, eicosanoid balance and oxidative stress. Infant formula enriched with LC-PUFA have particularly evident oxidised flavours, described as ‘fishy’ and metallic’.

FSANZ 2021 label survey assessed LA content in products on the ANZ market (Figure 5.3). The survey found that LA content in infant formula products ranged between 146–267 mg/100 kJ, which meets the requirements of Standard 2.9.1, Codex STAN 72-1981 and EU

2016/127. The products with the lowest levels of LA also aligned with the ANZ breast milk levels noted in the 2021 nutrition risk assessment.

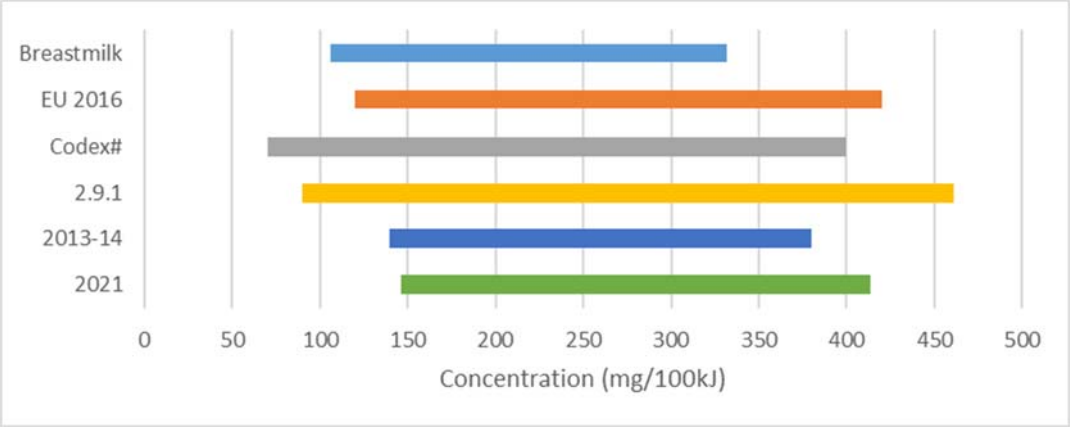


Figure 5.3 Comparison of the permitted ranges for LA across standards (Standard 2.9.1, Codex STAN 72-1981 and EU 2016/127), human milk concentration, and the FSANZ survey of the average content in products on the ANZ market.
 # Codex specifies a guidance upper level

Given the above discussion, FSANZ acknowledges that there is some evidence to support increasing the LA minimum requirement. However, further information is needed to address the issues surrounding the stability and palatability of infant formula when LA levels are increased. Moreover, adopting a higher minimum LA level may create some trade barriers as Codex STAN 72-1981 already sets a lower minimum LA requirement.

Two options are proposed to best meet submitters concerns, agree with the scientific evidence, and align with international regulations:

> ***Option 1:*** Adopt EU 2016/127 minimum LA level of 120 mg/100 kJ. This option supports alignment with the most recently updated regulation standards and alignment with the minimum LA levels noted within breast milk of the ANZ population.
>
> ***Option 2:*** Retain the current minimum LA level of 90 mg/100 kJ within Standard 2.9.1 (S29—8). This option migrates risks surrounding infant formula stability and palatability when LA levels are increased. It also represents the best available option for alignment with Codex and would mitigate risk of reformulation or trade implications.

Proposed approach

FSANZ proposes to align with Codex STAN 72-1981 on the following:
- the LA maximum (GUL) of 330 mg/100 kJ
- minimum amount for ALA (12 mg/100 kJ) with no prescribed maximum for ALA
- LA:ALA ratio range.

Based on the conclusions of the 2016 and 2021 nutrition risk assessments, the risk to infant health using these amounts is low.

Based on the stability and palatability concerns associated with higher LA levels, history of safe use at current levels and no emerging safety or adequacy concerns for infants, FSANZ proposes to retain the current minimum requirement for LA within Standard 2.9.1 (S29—8). However, we note the conclusions of the 2021 nutrition risk assessment. Therefore, we are seeking further information from health professionals on nutritional adequacy concerns related to the current LA minimum requirement in Standard 2.9.1 (S29—8). FSANZ is also seeking further information from industry professionals on the technological concerns in

meeting a higher level of LA within infant formula, such as how palatability and stability are affected by further addition of ALA and DHA.

5.4 Long chain polyunsaturated fatty acids and other LC-PUFA, ratios and sources

The 2016 Consultation paper covered a range of issues related to LC-PUFA. Only DHA generated numerous comments that did not support FSANZ preliminary view. Submissions for questions about the other LC-PUFA were either supportive with FSANZ's preliminary view or did not comment.

Current regulations

Table 5.5. summarises regulatory requirements for the permitted range of LC-PUFAs.

Table 5.5 Permitted range for LC-PUFAs

Standard	n-6 and n-3 LC-PUFA maximum			DHA, AA, EPA maximum			
	% total fatty acids		Ratio	*% total fatty acids*			Ratio
	n-6 LC-PUFA	3 LC-PUFA		AA	DHA	EPA	
Standard 2.9.1 (S29—8)	2%	1%	n-6 ≥ n-3	1%	NS	NS	DHA ≥ EPA
Codex STAN 72-1981	NS	NS	AA ≥ DHA DHA ≥ EPA	NS	0.5% (GUL)	NS	NS
EU 2016/127	2%		DHA ≥ EPA	1%	~0.5-1%	NS	NS

NS: Not stated

DHA

The addition of DHA is optional in both Standard 2.9.1 and Codex STAN 72-1981.

The main difference between the standards is Codex STAN 72-1981 lists a DHA maximum as a GUL of 0.5% fatty acids whereas Standard 2.9.1 (S29—8) limits DHA as a component of the maximum 1% of n-3 LC-PUFA.

AA

The table to section S29—8 prescribes a maximum proportion of AA when present at no more than 1% total fatty acids. Codex STAN 72-1981 requires AA content of infant formula to reach at least the same content as DHA.

DHA:AA

The total n-6:n-3 ratio is included in Standard 2.9.1 to manage any potential risk of imbalance between n-6 to n-3 LC-PUFA. Codex STAN 72-1981 does not include any maximum or ratios for total n-3 and n-6 content. Instead a minimum AA:DHA ratio is included to manage any potential n-6 and n-3 imbalance.

Previous consideration

DHA

DHA is a non-essential fatty acid as it is synthesised from the essential fatty acid ALA. The 2016 nutrition risk assessment considered that over recent years there has been considerable debate about whether a mandatory minimum of DHA should be set for infant formula. The assessment concluded that mandatory inclusion of a minimum amount of DHA was based on mixed and inconclusive studies on infant development.

The 2016 nutrition risk assessment considered that the current maximum proportion of 1% total n-3 LC-PUFA in Standard 2.9.1 consists of DHA and smaller proportions of EPA and other n-3 LC-PUFA. From a review of specifications for DHA oil in the Code (Standard 1.3.4 – Identity and Purity), it is possible that present formulations of infant formula contain slightly more DHA than the Codex GUL of 0.5% total fatty acids. However, FSANZ concluded that there was minor or no impact expected on current infant formula formulations if the maximum for all n-3 LC-PUFAs in the Code were replaced by a GUL for DHA (and other relevant ratios).

Therefore, FSANZ's preliminary view in 2016 was that a mandatory minimum DHA is not supported by the evidence and it is appropriate to control DHA when present with a guidance limit, by adopting the Codex GUL amount for DHA of 0.5% total fatty acids.

AA

In 2016 FSANZ concluded that it is appropriate to maintain the requirement for EPA content to be no more than DHA content as this is already aligned with Codex. FSANZ also concluded that it is appropriate to maintain a maximum proportion of no more than 1% total fatty acids when AA is present.

DHA:AA

FSANZ also proposed replacing the minimum ratio of total n-6 to total n-3 with the Codex minimum ratio of AA:DHA to avoid metabolic imbalance between the n-3 and n-6 LC-PUFA.

Stakeholder views

Eight submitters (three government, five industry) expressed varied views on the DHA addition to infant formula. Two industry submitters commented on issues pertaining to sources and ratios of other LC-PUFA (Table 5.6).

Table 5.6 Submitter comments on LC-PUFA, ratios and sources

Comment	Raised by	FSANZ Response
DHA		
Supports FSANZ considerations in 2016 Consultation paper (retain voluntary addition of DHA) citing lack of safety data for addition of DHA without AA and cost of AA compared to DHA.	Industry (2)	Refer to options and discussion section (below).
Align with EU 2016/127 for mandatory addition of DHA	Government (3) Industry (2)	In 2016, EU mandated that by February 2021, infant formula must contain DHA at levels of 20–50 mg/100 kcal (approximately 0.5–1% of total fatty acids or 4.8–12 mg/100 kJ). The legislation does

		not provide a requirement for addition of ARA. The decision to mandate DHA levels was based on a 2013 EFSA opinion paper.
Align with EU 2016/127 with minimum DHA level equal to or in excess of AA amount.	Industry (1)	Refer to options and discussion section (below).
LC-PUFA		
Sources of LC-PUFA	No comments	
EPA		
Support maintaining the current requirement for EPA content to be no more than DHA content, as this is already aligned with Codex.	Industry (1)	FSANZ agrees.
AA		
Support maintaining the current requirement that a maximum proportion of no more than 1% total fatty acids when AA is present.	Industry (1)	FSANZ agrees.
AA:DHA ratio		
Support the proposal to replace the minimum ratio of total n-6 to total n-3 with the Codex minimum ratio of AA:DHA.	Industry (1)	FSANZ agrees.

Nutrition risk assessment

No further nutrition risk assessment was considered on these issues.

However, FSANZ notes the key points made in a position paper published by the European Academy of Pediatrics and the Child Health Foundation (Koletzko et al. 2020):

- concerns about the safety of feeding infants high levels of DHA without providing adequate amounts of AA
- the safety of infant formula with relatively high concentration of DHA but without AA has not been evaluated in infants
- high DHA may lead to adverse effects such as reduced AA levels in brain tissue suboptimal neurodevelopment, poor growth and immune development
- minimal or optimal intake levels of AA in infancy have not been defined, and the optimal ratio of AA to DHA in the infant diet has not been determined.

The lack of evidence on the safety of infant formula with added DHA without concomitant AA amounts were noted in the 2016 Consultation paper nutrition risk assessment.

Options and discussion

Standard 2.9.1 and Codex STAN 72-1981 currently permit the optional addition of DHA provided the content of DHA does not exceed the AA amount. Based on submitter comments, the options to be considered for this issue are maintaining the current permission in Standard 2.9.1 or aligning with EU 2016/127 which has mandated a minimum level of DHA. Because Standard 2.9.1 currently permits voluntary DHA addition, infant formula that is manufactured overseas and includes DHA (and AA) would be permitted to be sold in ANZ.

Given the uncertainty in the safety of a mandatory minimum of DHA without equivalent AA addition and the lack of evidence on requirements for dietary AA in infants, FSANZ

considers that the Specific Policy Principals - Composition in the infant formula policy guideline[7] would not be met.

Since DHA and AA are not components of the essential nutrient composition for infant formula, a mandatory minimum amount of DHA would be best evaluated through the pre-market assessment process.

Proposed approach

Based on further alignment with Codex STAN 72-1981 and the conclusions of the 2016 nutrition risk assessment, FSANZ proposes to retain the current voluntary permission for DHA, provided the content of DHA does not exceed the AA amount. When DHA is present, the amount should be controlled with a GUL, by adopting the Codex GUL for DHA of 0.5% total fatty acids.

Based on submitter support and the conclusions of the 2016 nutrition risk assessment, the proposed options for source of LC-PUFA, EPA and AA and ratios of DHA, AA and LC-PUFA are unchanged from the previous consideration of these topics in the 2016 Consultation paper.

5.5 Fat source

Current regulations

Standard 2.9.1 does not specify or prohibit any particular sources of fat. Instead, specific requirements which restrict fat composition are listed in section 2.9.1—11 and section S29—8. Codex STAN 72-1981 generally takes a similar approach on the source of fat (as the macronutrient component) in infant formula in that no specific sources are specified. However, the footnote to Part 3.1(b) specifies that commercially hydrogenated oils and fats should not be used. DHA is specifically listed as a permitted optional ingredient.

Previous consideration

Submissions to the 2012 Consultation paper commented that as technology develops; more detail may be required in the standard to specify which ingredients are permitted to make up the essential fat composition and that there is no clear definition or differentiation between what is considered a lipid component versus a lipid ingredient incorporated for the macronutrient profile of the formula.

In 2016 FSANZ sought further information on whether submitters had any issues with the current approach to regulation of the source of fat in infant formula.

Stakeholder views

Nine submitters (two government, six industry, one health professional) commented on the regulation of sources of fat. Six submitters supported the current approach or did not convey a view. Two submitters considered that clarity was needed about fat sources that can or cannot be used to manufacture infant formula with respect to certain fats (Table 5.7).

---

[7] https://foodregulation.gov.au/internet/fr/publishing.nsf/Content/publication-Policy-Guideline-on-Infant-Formula-Products See Specific Policy Principal g) *Compositional requirements for infant formula and follow-on formula products should only be mandated in regulation where there is sufficient evidence to demonstrate that they are safe and essential for normal growth and development of infants.*

Table 5.7 Submitter comments on source of fat

Comment	Raised by	FSANZ response
Greater certainty around certain fat sources, for example β-palmitin which meets specific fatty acid requirements but may fall under the definition of a novel food or nutritive substance.	Government (1)	See Consultation paper 3 for discussion of the pre-market assessment requirements for macronutrient sources.
Novel, edible fats used in combination with other vegetable oils to achieve the desired fatty acid profile. The current standard does not identify when these fat sources require pre-assessment approval.	Industry (1)	See Consultation paper 3 for discussion of the pre-market assessment requirements for macronutrient sources.

Nutrition risk assessment

No further nutrition risk assessment has been considered.

Options and discussion

When certain fats or fatty acids were considered harmful, restrictions were put in place in the Code to protect infants from adverse health consequences. A similar approach is taken in Codex STAN 72-1981.

Two options are proposed to best meet submitters concerns, agree with the scientific evidence, and align with international regulations:

Option 1: Retain current approach which restricts specific fats and no further definition of fat source.

Option 2: Relax or remove restrictions on specific fats but introduce more definition about permitted sources of fat.

Proposed approach

FSANZ considers that retaining the current approach is appropriate based on the number of submissions which supported this view. This conclusion has been factored into consideration on restrictions of certain fats, discussed in following sections.

5.6 Restrictions on certain fats

Table 5.8 summarises the regulatory requirements for maximum amounts of certain fats.

Table 5.8 Maximum amounts of fatty acids

Fat	Unit	Standard 2.9.1 (S29—8)	Codex STAN 72-1981	EU 2016/127
Phospholipids (PL)	g/L	–	2*	2
Trans fatty acids	% total FA	4	3	3
Erucic acid	% total FA	1	1	1
Lauric acid + myristic acid	% total FA	–	20	–

** Codex STAN 72-1981 prescribes a maximum of 72 mg/100 kJ, which is equivalent to 2 g/L*

5.6.1 Medium chain triglycerides

Current regulations

Medium chain triglycerides (MCT) contain fatty acids of 6–12 carbon chains which include caprylic (C:8) and capric (C:10) acids. They occur naturally in many foods including dairy products, coconut and palm oils. Standard 2.9.11 permits MCT to be present only as a natural constituent of a milk-based ingredient of that formula; or as a component of a processing aid in the preparation of a permitted fat-soluble vitamin. Codex STAN 72-1981 and EU 2016/127 do not include any statement about MCT.

Previous consideration

In 2016 FSANZ considered that the current limitations on MCTs in Standard 2.9.1 remain appropriate as they do not pose a risk to infants and there is no apparent benefit from permitting MCTs in infant formula. Stakeholder feedback was requested to inform the future assessment.

Stakeholder views

Six submitters (three government, three industry) commented on the restriction on MCT, with government submitters supporting the existing restriction or recommending additional assessment be undertaken. Industry submitters supported removal of existing restrictions on MCT to align with Codex STAN 72-1981 and allow greater choice of fat sources to be used.

Nutrition risk assessment

No further nutrition risk assessment has been considered on this issue.

Options and discussion

The original prohibition on MCTs in Standard 2.9.1 was based on potential safety concerns. This prohibition was retained by FSANZ in Application A563 – Medium Chain Triglycerides in Infant Formula (FSANZ 2006). The prohibition of MCTs in Standard 2.9.1 was retained on the basis that (1) MCT fats are not normally present in significant amounts in breast milk; (2) the long term effects of infants consuming a relatively high amount of saturated fats are unknown; and (3) there is no convincing evidence that the inclusion of MCTs in infant formula has any benefit to infant health (ANZFA 1999a; LSRO 1998). More recently, the EC SCF (2003) noted that there was no nutritional need to add MCTs to infant formula on the basis of similar arguments and, accordingly, Codex STAN 72-1981 does not specify anything about MCTs. EFSA (2014b) reiterated this conclusion.

Industry submitters supported removal of the current MCT restrictions based on alignment with Codex STAN 72-1981, permission of a greater choice of fat sources that can be used and that considering that MCTs are permitted for IFPSDU (products based on protein substitutes only).

However, MCTs are used in specific IFPSDU as the addition has shown to be beneficial for some infants with severe fat malabsorption (Delplanque et al. 2015). This benefit does not apply to healthy infants and therefore does not justify addition of MCTs in infant formula. There are also some safety concerns associated with the use of MCTs for longer periods of time in infant diets, such as potential risk of deficiency of necessary unsaturated fatty acids and some fat-soluble vitamins.

Proposed approach

Based on the conclusions of the 2016 nutrition risk assessment, evidence that the inclusion of MCTs in infant formula does not provide any benefit to infant health, and that MCTs are not normally present in significant amounts in breast milk, FSANZ proposes to retain the current restrictions on MCTs.

5.6.2 Trans fatty acids

Current regulations

Section S29—8 restricts the total trans fatty acids (TFA) content of infant formula to a maximum of 4% of the total fatty acids. Codex STAN 72-1981 states that TFA, as endogenous components of milk fat, are allowed up to 3% while the use of commercially hydrogenated oils that may contain industrial TFA are not permitted in infant formula products. EU 2016/127 restricts trans fatty acid content of infant formula to a maximum of 3% of the total fat content.

Previous consideration

Regulatory definitions of TFA are not consistent around the world and therefore restrictions on their presence in food products, in general, can vary.

FSANZ has relied on an interpretation to support its view that the definition of TFA in the Code is consistent with Codex. TFA are defined in Standard 1.1.2 of the Code as the total of unsaturated fatty acids where one or more of the double bonds are in the *trans* configuration. Codex CAC/GL 2-1985 (Guidelines on Nutrition Labelling) has a similar definition for TFA as that in the Code, and includes all geometrical isomers of monounsaturated and polyunsaturated fatty acids having non-conjugated, interrupted by at least one methylene group, carbon-carbon double bonds in the *trans* configuration.

The reason for the non-zero specification in both the Code and Codex is to allow for TFA that are naturally present in the milk of ruminant animals. TFA occur naturally in foods, including milk and dairy products, and can be formed or added to foods during manufacturing or processing.

FSANZ's preliminary view was to either:

1) maintain the restriction on the total (i.e. naturally-occurring and added) TFA at a maximum of 4% of the total fatty acids, or
2) lower the maximum proportion of naturally-occurring TFA to 3% of the total fatty acids to align with Codex. This option will require further alignment with Codex by prohibiting the use of hydrogenated fats from any other source if they may contain TFA.

Stakeholder views

Six submitters (one government, five industry) commented on the issues around TFA. One government submitter supported the lowering the maximum TFA amount to 3% of total fatty acids. Industry submitters did not support this option due to the differences in definitions used by Codex and the Code and because the maximum of 3% of total fatty acids would limit the amounts of milk fats that could be used in manufacture.

Nutrition risk assessment

No further nutrition risk assessment was considered on this issue.

Options and discussion

The Codex definition for TFA excludes the classification of conjugated linoleic acid (CLA) as a TFA. CLA is a conjugated polyunsaturated fat that is a natural component of milk fat in dairy and human milk. Adoption of the Codex restriction of TFA at a maximum of 3% without also adopting the Codex definition for TFA would restrict the amount of milk fat that could be used as a fat source. Therefore, the existing restriction for the maximum amount of TFA at 4% of total fatty acids in the Code is appropriate.

Proposed approach

Aligning with Codex STAN 72-1981 for TFA would require a change in the definition of TFA in the Code. FSANZ considers this to be out of scope for this proposal. The proposed option is to retain the current restriction for TFA at 4% of total fatty acids.

5.6.3 Phospholipids

Current regulations

Standard 2.9.1 does not set a maximum amount for phospholipids (PL) in infant formula products, whereas Codex STAN 72-1981 states that the total content of phospholipids should not exceed 72 mg/100 kJ (equivalent to 2 g/L). EU 2016/127 specifies that the amount of PL shall not exceed 2 g/L.

Schedule 15 of the Code also permits the use of lecithin (which is a source of PL) as food additive emulsifier at 5 g/L in infant formula products. Codex STAN 72-1981 also permits use of lecithin as an emulsifier to at 5 g/L in all types of infant formula.

Previous consideration

PL are added as a source of LC-PUFA (i.e. as a nutritive substance). PL can also be present as a component of lecithin which is a processing aid or food additive emulsifier. Lecithin derived from soy contains PL at a range of 65-75%. Therefore, soy lecithin added to infant formula at 5 g/L (the Schedule 15 maximum) could add approximately 3.75 g/L of PL which would exceed the maximum PL amount in Codex STAN 72-1981 (2 g/L).

The 2016 nutrition assessment considered that given the potential bioactivity of PLs, the lack of adequate safety data, and unknown biological activity of certain types of PL in infants the amount of PL in infant formula should not exceed the amount that normally occurs in breast or cow's milk (i.e. approximately 0.25 g/L).

On this basis, the 2016 Consultation paper considered restricting the total amount of PL was appropriate but that more information was needed before a maximum could be established. Any final maximum amount needs to take account of PL amounts derived from lecithin in infant formula. Further input was sought from stakeholders.

Stakeholder views

Nine submitters (three government, six industry) commented on this issue (Table 5.9). Government stakeholders supported restriction of total PL and industry stakeholders supported the current approach of no maximum limit for PL. However, if a maximum is needed, some industry submitters supported alignment with Codex STAN 72-1981 and EU 2016/127.

Table 5.9 Submitter comments on the maximum amount of phospholipids

Comment	Raised by	FSANZ response
Do not support a specified maximum based on lack of evidence that there are safety concerns, and if maximum is applied, additional testing and compliance costs ultimately reflected in the price of formula products.	Industry (4)	See Options and discussion.
If specified maximum is needed, support alignment with Codex STAN 72-1981 and EU 2016/127 (2 g/L)	Industry (2)	See Options and discussion.
Questions whether a maximum limit will allow for composition of soy and canola based formulas which have intrinsically higher natural PL levels and would the maximum naturally occurring amounts.	Industry (1)	In line with international regulations, FSANZ considers that the maximum PL amount would include all sources of PL and would be applied to all IF products.
Support restriction on the amount of PL with further assessment to consider the appropriate maximum level. Noting that PL can be sources of other nutrients, (serine or choline), it is important that any permissions for PL are clear with regard to how contributions to other nutrient levels are calculated. Clarification on PL amounts depending on the source ingredient is also needed.	Government (1)	See Options and discussion.
Support alignment with Codex STAN 72-1981 but noted that PL should not exceed the amount that normally occurs in breast or cow's milk (0.1–0.2 g/L) due to their potential bioactivity, lack of safety data and insufficient evidence of their benefit.	Government (2)	See Options and discussion.

Nutrition risk assessment

No further nutrition risk assessment has been considered on this issue.

Options and discussion

International opinion, standards and regulations on maximum PL levels vary depending on whether PL is present as a nutritive substance or as the food additive/processing aid lecithin (Table 5.10). For PL as a nutritive substance, there is alignment across expert panel recommendations, Codex STAN 72-1982 and EU 2016/127, although the justification for this amount has not been clearly reported.

Regarding lecithin, FSANZ has not conducted nutrition risk assessment for the use of lecithin in infant formula or conducted a review to determine whether there is a history of safe use up to the permitted maximum level in Schedule 15 (5 g/L for all foods). EFSA re-evaluated the safety of lecithins as a food additive in foods for infants and concluded that lecithin up to a maximum permitted level of 1 g/L does not raise safety concerns (EFSA 2020).

Regulation (EC) No 1333/2008 sets a maximum of 1 g/L lecithin whereas the infant formula regulation (EU 2016/127) sets a maximum for PL of 2 g/L. If soy lecithin (which is reported to be 65-75% PL and higher compared to other sources of lecithin) was used at 1 g/L, the maximum amount of PL in infant formula would be expected to be in the range of 0.65-0.75 g/L, well below the maximum permitted level for PL under EU 2016/127.

We noted in the FSANZ 2016 assessment that that soy lecithin added at 5 g/L would add about 3.75 g/L of PL which exceeds the maximum PL amount in Codex STAN 72-1981 and EU 2016/127.

FSANZ notes that based on industry supplied data, the 2020 EFSA review reported the total phospholipid content in formula using soy lecithin and sunflower lecithin was 239.7 ± 216.7 202.3 ± 182.9 mg/L, respectively, which is comparable to that reported for mature human milk (248 ± 91 mg/L). This indicates that soy lecithin used in infant formulas manufactured in the European market is consistent with human milk PL content and is able to meet the EU 2016/127 restriction on PL amounts.

Table 5.10 Maximum permitted amounts of lecithin and PL

Standard, Regulation or Recommendation	Lecithin (i.e. food additive)	Phospholipids (i.e. nutritive substance)
EC SCF 2003	1 g/L[1]	
ESPGHAN 2005	N.A.	72 mg/100 kJ (2 g/L)
Codex STAN 72-1981	5 g/L	72 mg/100 kJ (2 g/L)
The Code – Standard 2.9.1	N.A.	No maximum defined
The Code – Schedule 15 (Substances that may be used as food additives)	5 g/L	N.A.
Regulation (EC) No 1333/2008 (food additive regulation)	1 g/L	N.A.
EU 2016/127	N.A.	2 g/L
EFSA 2020 (Re-evaluation of lecithins as a food additive)	1 g/L	N.A.

[1] *Applies whether addition is for technological or nutritional purpose. N.A. = not applicable.*

Three options would provide clarity on the maximum PL amount and align with international regulations and recommendations:
(1) Restrict the PL content to 2 g/L, or
(2) Restrict the lecithin content to 1 g/L for infant formula product, or
(3) Both (1) and (2)

Option 3 would provide the most clarity for the PL maximum. However, section 1.1.1—10(6) (*Requirements relating to food for sale*) includes the following notes in relation to substances added to foods:

> ***Note 2:***
> *There is an overlap between some of these categories. For example, some substances may be used as a food additive or as a nutritive substance. For such substances, there will be different provisions permitting use of the substance for different purposes.*
>
> ***Note 3:***
> *In some cases, a provision refers to the total amount of a substance added to a food. In these cases, the total amount applies irrespective of whether the substance was used as a food additive, used as a processing aid or used as a nutritive substance.*

If a specified maximum PL of 2 g/L is the most appropriate approach (Option 1), any inconsistency in the Code would also need to be addressed (e.g. a condition applied to the Schedule 15 permission for lecithin).

Phosphotidylcholine is a component of lecithin which when hydrolysed produces choline. The 2020 EFSA evaluation of lecithin as a food additive also considered the contribution of lecithin to choline intakes. The appropriate levels of choline in infant formula, including that derived from added lecithin is discussed in section 7.1.

Proposed approach

FSANZ proposes to set the maximum permitted amount of PL as 2 g/L (72 mg/100 kJ) and the maximum lecithin amount to 1 g/L (Option 3). This approach provides alignment with the most recently reviewed international regulations (EU 2016/127) and provides the most clarity for PL amounts in the Code. We request information (including quantitative evidence) about this approach, particularly from manufacturers that may be disproportionately impacted by these restrictions.

5.6.4 Other fatty acids: myristic, lauric and erucic acids

Current regulations

Section S29—8, Codex Stan 72-1981 and EU 2016/127 permit erucic acid at a maximum of 1% of total FA.

Myristic and lauric acid do not have permissions in Standard 2.9.1 or EU 2016/127. However, Codex STAN 72-1981 permits both fatty acids at a maximum of 20% of total FA content combined.

Previous consideration

Both section S29—8 and Codex specify that erucic acid (22:1n-9) should not be present at more than 1% of the total fatty acid content in infant formula. As the Code is currently aligned with Codex on this point, FSANZ's preliminary view in 2016 was to retain the limit on erucic acid. Feedback received through previous consultation has supported this option.

FSANZ also considered it appropriate to maintain no restriction on the levels of myristic (14:0) and lauric (12:0) acids in Standard 2.9.1. This view is in line with the recent expert opinion on the safety of these fatty acids in infant formula. Although this approach is inconsistent with Codex, it is less restrictive for innovation and trade. Feedback received through our previous consultations has supported this approach.

Stakeholder views

One industry submitter supported FSANZ's preliminary view to retain the current maximum for erucic acid.

Two industry submitters supported FSANZ's preliminary view to maintain no restriction on the levels of myristic and lauric acid.

Nutrition risk assessment

No further nutrition risk assessment has been considered on this issue.

Proposed approach

The proposed options for myristic, lauric and erucic acids are unchanged from the views on these topics in the 2016 Consultation paper. FSANZ proposes to retain the current restrictions in Standard 2.9.1 for these fatty acids.

6 Carbohydrate

Carbohydrate is a significant energy source in infant formula. Some carbohydrates have other physiological functions such as probiotic effects. Regulation of carbohydrate in infant formula requires consideration of definitions and calculations relevant to carbohydrate identity, dietary fibre, carbohydrate source, and the permitted range for total carbohydrate content.

6.1 Definitions and calculations relevant to carbohydrate identity

Current regulations

Identification of carbohydrate types, such as available and unavailable carbohydrate, are not defined in Standard 2.9.1 and Codex STAN 72-1981. Instead the Code sets out definitions for carbohydrates for foods (including in infant formula) in Standard 1.1.2. Similarly, Codex definitions are covered in the the *Codex Guidelines on Nutrition Labelling* (CAC/GL 2-1985). The Code and Codex carbohydrate definitions are set out in Table 6.1.

Table 6.1 Definitions for carbohydrates

Term	Code definition[1]	Codex definition[2]
Carbohydrate	Available carbohydrate or *available carbohydrate by difference	Not defined
Available carbohydrate	Available carbohydrate calculated in accordance with section S11—3 (See section 7.3)	Dietary carbohydrate excluding dietary fibre
Available carbohydrate by difference	Available carbohydrate by difference calculated in accordance with section S11—3.	Not defined
Dietary fibre	The fraction of the edible part of plants or their extracts, or synthetic analogues that is resistant to digestion and absorption in the small intestine, usually with complete or partial fermentation in the large intestine; and promotes one or more of the following beneficial physiological effects: laxation; reduction in blood cholesterol; modulation of blood glucose. It includes polysaccharides or oligosaccharides that have a degree of polymerisation greater than 2; and lignins.	Carbohydrate polymers with ten or more monomeric units , which are not hydrolysed by the endogenous enzymes in the small intestine of humans and belong to the following categories: – edible carbohydrate polymers naturally occurring in the food as consumed, – carbohydrate polymers, which have been obtained from food raw material by physical, enzymatic or chemical means and which have been shown to have a physiological effect of benefit to health as demonstrated by generally accepted scientific evidence to competent authorities, – synthetic carbohydrate polymers which have been shown to have a physiological effect of benefit to health as demonstrated by generally accepted scientific evidence to competent authorities.

[1] *Standard 1.1.2*
[2] *Codex Guidelines on Nutrition Labelling (CAC/GL 2-1985)*

Previously, several definitions relevant to Standard 2.9.1 were located across different standards in the Code. Standard 1.1.2 in the Code now sets out definitions for 'carbohydrate', 'available carbohydrate' and 'available carbohydrate by difference' which apply throughout the Code. This clarifies previous confusion about whether definitions located in other standards applied to Standard 2.9.1.

Schedule 11 sets out the calculation for energy content, available carbohydrate, and available carbohydrate by difference for the nutrition information panel. Energy factors for carbohydrate (excludes unavailable carbohydrate) and unavailable carbohydrate (includes dietary fibre) are prescribed as 17 kJ/g and 8 kJ/g, respectively. Codex STAN 72-1981 does not include energy factors and CAC/GL 2-1985 lists a carbohydrate energy factor (17 kJ/g).

Previous consideration

FSANZ's preliminary view was that definitions in the Code are appropriate for infant formula. FSANZ considered that the classification of carbohydrates as available or unavailable was best left to manufacturers. Energy factors were considered to be appropriate as specified in Schedule 11.

Stakeholder views

Three submitters (one government, two industry) commented on the definitions to the type of carbohydrates. All supported FSANZ's preliminary considerations.

Nutrition risk assessment

No further nutrition risk assessment has been considered on this issue.

Proposed approach

There are no proposed options as Standard 1.1.2 now sets out definitions for 'carbohydrate', 'available carbohydrate' and 'carbohydrate by difference' used throughout the Code.

6.2 Dietary fibre

Current regulations

Standard 2.9.1 does not include requirements for dietary fibre other than permissions for specific oligosaccharides (see below). Dietary fibre is defined in the Code in Standard 1.1.2. Codex STAN 72-1981 does not define dietary fibre but a definition is listed in the Codex Guidelines on Nutrition Labelling (Table 6.1). Mainly, dietary fibre includes polysaccharides and oligosaccharides that are *largely* undigested in the small intestine and undergo colonic fermentation by microorganisms to yield short chain fatty acids. According to this description, these oligosaccharides (and possibly other carbohydrates such as dried glucose syrup and maltodextrins) may comprise both unavailable and available carbohydrates.

Standard 2.9.1 permits optional addition of inulin-type fructans and galacto-oligosaccharides, with several other oligosaccharides currently being assessed for permissions as optional ingredients (FSANZ 2020). Codex STAN 72-1981 has no provisions for the addition of specific oligosaccharides but includes permissions for optional ingredients that can be added in order to provide substances ordinarily found in human milk and to ensure that the formulation is suitable as the sole source of nutrition for the infant or to provide other benefits that are similar to outcomes of populations of breastfed babies.

Previous consideration

FSANZ did not have a preliminary view on dietary fibre. We noted that inulin-type fructans are permitted in infant formula products. These substances have a prescribed method of analysis in Schedule 11 (section S11–4) when identified as a dietary fibre but these are not applicable to Standard 2.9.1. Whether the concept of dietary fibre or its prescribed methods of analysis are relevant to infant formula is an open question.

Stakeholder views

Four submitters (two government, two industry) commented on whether the concept of dietary fibre or its prescribed methods of analysis should be relevant to infant formula. Government submitters indicated that more information was required, and industry submitters either supported alignment with Codex (which is already the case) or supported extension of the concept of dietary fibre and its prescribed methods of analysis to infant formula.

Nutrition risk assessment

No further nutrition risk assessment has been considered on this issue.

Options and discussion

Dietary fibre as defined in Standard 1.1.2 includes polysaccharides and oligosaccharides that are plant-derived or synthetic analogues that perform one or more of the listed physiological effects (see Table 6.1) and some inulin-type fructans. Whereas, some oligosaccharides used in infant formula products do not meet part (a) of the dietary fibre definition because they are derived from animal sources or are synthetic analogues such as galacto-oligosaccharides and other GM-produced oligosaccharides subject to current applications to FSANZ. This definitional differentiation relates to the need to standardise calculation of the energy content of infant formula products and to be clear about the application of energy factors for animal derived oligosaccharides. Subsection S11—2(2) sets out the energy factors for carbohydrates: 17 kJ/g for carbohydrate (excludes unavailable carbohydrate) and 8 kJ/g for unavailable carbohydrate (includes dietary fibre).

Depending on their structure, oligosaccharides in infant formula products could be classified as either available or unavailable carbohydrates (including dietary fibre) or both. It is FSANZ's expectation that all companies will apply the energy factors for available and unavailable carbohydrates in subsection S11—2(2) to their products and to apply both factors in accordance with the proportion of oligosaccharides directly absorbed in the small intestine.

The ANZ NRV (2006) determined that as human milk contained no dietary fibre, no AI could be set. This conclusion predates the current situation where dietary fibre in the form of oligosaccharides is considered to be an important component of human milk.

Since the last review of the infant formula standard substances which fall within the definition of dietary fibre have been approved to be added to infant formula as optional ingredients. These substances include inulin-derived substances and galacto-oligosaccharides (P306) and short chain fructo-oligosaccharides (A1055), and most recently 2′-O-Fucosyllactose and lacto-N-neotetraose (A1155). In these cases, FSANZ considered that it was not appropriate to prescribe methods of analysis. This is consistent with other specifications in the Code (Schedule 3) where methods of analysis are not prescribed.

AOAC methods of analysis for some dietary fibre substances are published (Stephen et al 2017). For new permissions of dietary fibre substances added to infant formula products, applications provided to FSANZ include methodological information that the dietary fibre can be appropriately quantified. Prescribing these methods of analysis in the Code would limit future improvement of methods for detection and quantitative measurement (see submitter comments to A1155 1st CFS).

EU 2016/127, which permits addition of fructo-oligosaccharides and galacto-oligosaccharides to infant formula products, does not specify methods of analysis for these substances.

Proposed approach

The primary objective of the P1028 proposal is to align with international regulations unless safety or other concerns do not support alignment. FSANZ is unaware of safety issues associated with addition of permitted oligosaccharides to infant formula without a prescribed method of analysis for that substance. Currently the Code is aligned with Codex STAN 72-1981 and EU 2016/127 in not prescribing methods of analysis for dietary fibre. Therefore no change to the existing requirements is proposed.

6.3 Carbohydrate source

Current regulations

Standard 2.9.1 does not include any provisions relating to the source of carbohydrate in infant formula. Codex STAN 72-1981 includes guidance on carbohydrates to be used (Box 6.1), but this is not mandatory.

Box 6.1: Codex STAN 72-1981 guidance on carbohydrates in infant formula

Lactose and glucose polymers should be the preferred carbohydrates in formula based on cows' milk protein and hydrolysed protein. Only precooked and/or gelatinised starches gluten-free by nature may be added to Infant Formula up to 30% of total carbohydrates and up to 2 g/100 mL.

Sucrose, unless needed, and the addition of fructose as an ingredient should be avoided in infant formula, because of potential life-threatening symptoms in young infants with unrecognised hereditary fructose intolerance.

Previous consideration

Lactose is the main source of carbohydrate in breast milk. Lactose, maltose, glucose, dried glucose syrup, sucrose, malto-dextrins, and pre-cooked starch and gelatinised starch (gluten free) are the main carbohydrates used in infant formula. Their use in infant formula varies depending on the type of protein upon which the formula is based, although this is more relevant to formulas for specific dietary use. For example sucrose is used in formulas made from protein hydrolysates to mask the bitter taste.

The P93 assessment (ANZFA 1999a) considered the suitability of carbohydrate sources and determined that:

- maltodextrin could be permitted for use in all infant formula products
- sucrose could be permitted for use in formula except pre-term formula, in amounts up to 20%
- high fructose corn syrup should not be permitted in infant formula products
- glucose syrup and dried glucose syrup could be permitted in pre-term formula

- the origin of starch must be declared in the ingredient list.

Submitter comments at the time recommended that the source of carbohydrate in infant formula should be controlled and that lactose should be the preferred carbohydrate in formulas that are not for a special purpose. However at that time, the Codex standard and draft revised Codex standard did not specify carbohydrate sources. Therefore, FSANZ decided not to prescribe the source in Standard 2.9.1 on the basis that doing so may have created a trade barrier.

The nutrition assessment for the 2016 Consultation paper notes that Codex guidance for source of carbohydrate in infant formula is in line with current expert opinion.

The use of 'prebiotic' carbohydrates (non-digestible carbohydrates) is an area of current research. As mentioned above, inulin-type fructans and galacto-oligosaccharides are permitted in Standard 2.9.1 whereas Codex has no specific provisions for the addition of oligosaccharides other than through the permission for optional ingredients.

As evidence was not strong for mandatory restrictions on the source of carbohydrate in infant formula, FSANZ's preliminary view was to maintain the current provisions in Standard 2.9.1 which would not align with the Codex STAN 72-1981 guidance. The 2016 Consultation paper sought views from submitters on the source of carbohydrate.

Stakeholder views

Ten submitters (four government, six industry) commented on carbohydrate source with industry supporting FSANZ's preliminary view. Industry submissions cited the absence of safety concerns or adverse effects with the current approach, but also indicated that substances such as sucrose are not being used in infant formulas manufactured for the Australian New Zealand market. Government submitters supported consideration of the EFSA (2014b) opinion and alignment with Codex.

Nutrition risk assessment

No further nutrition risk assessment has been considered on this issue.

Options and discussion

Carbohydrate source refers to available carbohydrates that are a primary energy source in infant formula. The source of carbohydrate does not include permissions for oligosaccharides or other specific carbohydrates that may have physiological functions other than as an energy source for the infant. These types of substances do not make up the essential composition of infant formula and therefore require pre-market assessment for permission to be added to infant formula.

FSANZ proposes three options regarding provisions for the source of carbohydrate:

Option 1: Retain current Standard 2.9.1 (no restrictions on carbohydrate source)

Option 2: Adopt limits on sucrose and fructose that are aligned with Codex STAN 72-1981 guidance

Option 3: Adopt guidelines from EU 2016/127 and set a list of permitted carbohydrates

EU 2016/127[8] introduced restrictions on carbohydrates which apply from early 2020. Carbohydrates that can be used are lactose, maltose, sucrose, glucose, glucose syrup or dried glucose syrup, maltodextrins, pre-cooked starch, gelatinised starch. Sucrose and glucose are permitted to be added to infant formulas manufactured from protein hydrolysates and there are additional conditional details on the use of glucose syrup and dried glucose syrup. The EU requirements are based on the latest scientific advice of EFSA in its opinion on infant formula composition (EFSA 2014b). The EFSA opinion is consistent with FSANZ's conclusions reported in P93.

FSANZ's initial view was to retain the current conditions in Standard 2.9.1 and not prescribe the source as it would create a trade barrier. Because European requirements for carbohydrate source will change in 2020 this argument is less justified.

Proposed approach

FSANZ proposes to adopt limits on sucrose and fructose that are aligned with Codex STAN 72-1981. This option is supported by safety concerns cited by government submitters, by FSANZ's safety assessment conducted in 2002, and by international requirements that come into place in 2020 that are in line with Codex STAN 72-1981.

6.4 Permitted range for total carbohydrate content

Current regulations

Standard 2.9.1 does not directly specify a minimum or maximum level of carbohydrate for infant formula as it is indirectly controlled by the regulations on protein, fat and energy content. Codex STAN 72-1981 lists a carbohydrate range of 2.2–3.3 g/100 kJ.

Previous consideration

FSANZ's preliminary view was that it was appropriate to retain the current approach by not specifying a minimum and maximum amount for carbohydrate. The 2016 Consultation paper reported calculated carbohydrate amounts based on Standard 2.9.1 provisions for energy, fat, and protein content. This demonstrated that Standard 2.9.1 and Codex STAN 72-1981 are effectively aligned for minimum and maximum carbohydrate amounts.

Stakeholder views

Two submitters (both industry) commented on the permitted range for carbohydrate content. Both agreed to retain the current approach in Standard 2.9.1.

Nutrition risk assessment

No further nutrition risk assessment has been considered on this issue.

Proposed approach

Based on the conclusions from the 2016 Consultation paper, FSANZ proposes to retain the current approach in Standard 2.9.1.which does not specify a permitted range for carbohydrate content.

[8] https://ec.europa.eu/food/safety/labelling_nutrition/special_groups_food/children_en

7 Micronutrients

7.1 Guideline and maximum amounts

Current regulations

In Standard 2.9.1(S29) all nutrients have either a maximum amount or a recommended maximum (or guideline) amount. Absolute maximum amounts are only prescribed for those vitamins and minerals considered to pose a significant risk to infants if consumed in excess. Recommended maximum amounts (hereafter referred to as GULs - guidance upper level) are listed for 14 micronutrients as the risk posed by the nutrient was “not of significance on the basis of current scientific knowledge” (ANZFA 1999a). These GULs are not binding and serve as guidance for industry in deriving formulations.

Codex STAN 72-1981 uses a similar approach, with principles for setting maximum and minimum values set out in Annex II of the Codex standard. GULs are assigned to 20 of the micronutrients in the Standard. GULs have been assigned where there was insufficient information about adverse effects from excessive intakes for a science-based risk assessment to set a mandatory limit.

Previous consideration

The reasons for the use of guideline maximums in the Codex standard and Schedule 29, and how they are derived, were provided in the 2016 Consultation paper. FSANZ’s view in 2016 was that retaining the GUL in Standard 2.9.1 (S29) or some nutrients was appropriate, and for others the prescribed maximum should be amended to a GUL to align with Codex (Table 7.1). We sought further information from submitters on folate, selenium, and phosphorus (considered in section 7.2.2, 7.3.11, and 7.4.1, respectively).

Table 7.1 Guideline versus mandatory maximums

Micronutrient	Standard 2.9.1 (Schedule 29)	Codex	Preliminary view FSANZ 2016	Proposed approach (this CP)
Vitamins				
Vitamin A	Max	Max	Retain Max	Retain Max
Vitamin D	Max	Max	Retain Max	Retain Max
Vitamin E	Max	GUL	Change Max to a GUL	Change Max to a GUL
Vitamin K	GUL	GUL	Retain GUL	Retain GUL
Vitamin C	GUL	GUL	Retain GUL	Retain GUL
Niacin	GUL	GUL	Retain GUL	Retain GUL
Thiamin	GUL	GUL	Retain GUL	Retain GUL
Riboflavin	GUL	GUL	Retain GUL	Retain GUL
Vitamin B6	Max	GUL	Change Max to a GUL	Change Max to a GUL
Folate	GUL	GUL	Further information sought	Align with Codex GUL
Pantothenic acid	GUL	GUL	Retain GUL	Retain GUL
Vitamin B12	GUL	GUL	Retain GUL	Retain GUL
Biotin	GUL	GUL	Retain GUL	Retain GUL

Minerals				
Chloride	Max	Max	Retain Max	Retain Max
Sodium	Max	Max	Retain Max	Retain Max
Potassium	Max	Max	Retain Max	Retain Max
Calcium	GUL	GUL	Retain GUL	Retain GUL
Phosphorus	Max	GUL	Further information sought	Change Max to GUL
Magnesium	Max	GUL	Change Max to a GUL	Change Max to a GUL
Iron	Max	ns[1]	Change Max to a GUL	Retain Max
Iodine	Max	GUL	Change Max to a GUL	Retain Max
Copper	Max	GUL	Change Max to a GUL	Change Max to a GUL
Zinc	Max	GUL	Change Max to a GUL	Change Max to a GUL
Manganese	Max	GUL	Change Max to a GUL	Change Max to a GUL
Selenium	Max	GUL	Further information sought	Retain Max
Chromium	GUL	ns	Retain GUL	Retain GUL
Molybdenum	GUL	ns	Retain GUL	Retain GUL

[1] ns = not specified

Stakeholder views

Eleven submitters (eight industry, three government) commented on this issue (Table 7.2). All industry submissions supported the FSANZ position from the 2016 Consultation paper. In general, government submitters did not support the use of GULs and suggested that industry information could be collected to determine how frequently GULs are exceeded. It was also noted that despite the lack of a UL for infants aged 0-12 months, ULs may be set for other age groups, indicating that excessive intakes should be avoided. Submitter comments on specific nutrients are summarised below.

Table 7.2 Submitter comments for selected micronutrients

Issue	Raised by	Comment and FSANZ response
Vitamin C	Government (1)	Submitter reserves position on suitability of use of a GUL. Submitter provided published evidence (including Pehrsson et al discussed below) indicating that commercial infant formula products do not exceed the existing Codex GUL. Significant losses of vitamin C over the shelf life of the product were acknowledged in notes from the electronic working group EWG on the review of the Codex Draft Standard for FUF. **On this basis, the proposed approach is to retain the GUL for vitamin C.**
Iodine	Government (1)	Submitters oppose change from regulatory maximum to a GUL. Comments included: (1) A UL was not established for the 0-12 month age group but has been set for 1-3 years old based on evidence that excess iodine has a critical effect on thyroid function. (2) FAO/WHO have established safe upper limits for iodine (indicates that there is a level of iodine intake that should not be exceeded) (3) need to ensure no safety concerns for export market (4) despite variability of iodine in cow's milk, there is evidence that industry can technically meet the current regulatory maximum. **The proposed approach is to retain the regulatory maximum for iodine.**

Phosphorus	Government (3), Industry (3)	Industry submitters consider a GUL to be appropriate as it has not been possible to establish a UL based on a lack of evidence in this age group. However, submitters opposing the use of a GUL commented that ULs have been derived for young children indicating excessive intakes should be avoided, and expressed concerns about hypocalcaemia. FSANZ reiterates the conclusions of the 2016 nutrition risk assessment, noting there is no recent contradictory literature to suggest otherwise, that the incidence of hypocalcaemia in neonates fed infant formula is associated with vitamin D deficiency, and aligning with the Codex STAN 72-1981 voluntary maximum is unlikely to pose a risk to infant health. For further details see section 7.4.1. **On this basis the proposed approach is to adjust the current phosphorus maximum (25 mg/100 kJ) in Schedule 29 to a GUL of 24 mg/100 kJ.**
Selenium	Government (3)	Submitters oppose or reserve position on use of a GUL. Submitters commented that a selenium UL was established by the NHMRC for infants 0-12 months of age indicating that excess intakes should be avoided. **On this basis the proposed approach is to retain the regulatory maximum.**
Folate	Government (1)	Submitter reserves position on suitability of use of a GUL. Comments provided include: (1) A UL is not established for the 0-12 month age group but has been set for 1-3 years old (2) excess folic acid can lead to the presence of un-metabolised folic acid in the blood although the consequence of this is uncertain. FSANZ reiterates the findings of the 2016 nutrition risk assessment, noting that the ANZ UL applies only to folic acid from fortified food or supplemental intake. No folic acid UL is listed for infants for which it states "not possible to establish for supplemental folic acid. Source of intake should be milk, formula and food only" (NHMRC and MoH 2006). Moreover, excessive folate intakes can mask vitamin B12 deficiency particularly in the elderly but this is not considered to be a problem in formula-fed infants (MacLean et al. 2010). The Schedule 29 and Codex STAN 72-1981 maximum amounts (which are effectively aligned) have been in place since 2002 and FSANZ is not aware of new evidence (i.e. published since the last reviews of the two standards) indicating infants are at risk of excessive folate intakes. Therefore, use of the Codex STAN 72-1981 GUL for folate is unlikely to pose a risk to infant health. **On this basis the proposed approach is to align Schedule 29 with the Codex GUL.**

Nutrition risk assessment

No further nutrition risk assessment was considered on this issue.

Options and discussion

Submitters proposed that FSANZ acquire information from manufacturers on Australian and New Zealand infant formula products that exceed GUL micronutrient levels, however FSANZ cannot acquire this information. Instead, we examined the published scientific literature to assess the potential proportion of products on the market that exceed Codex GULs. To be included, studies needed to report results for vitamins or minerals in appropriate units (e.g. mg/100 kcal) so that they could be compared with the Codex GUL. Six studies published since 2010 were identified (including MacLean et al. (2010) which was discussed in the 2016 Consultation paper). Only a subset of micronutrients were covered across the different studies, and no studies covered the ANZ market specifically. Overall, the studies show that

the proportion of products on the market with micronutrient concentrations that exceed the GUL is likely to be low (Table 7.3).

Table 7.3 Studies on micronutrient amounts in commercial infant formula samples

Study	Nutrients analysed	Results
MacLean et al. 2010	Vitamin A, Vitamin K, Thiamin, Riboflavin, Niacin, Vitamin B12, Folic acid, Vitamin C, Biotin, Potassium, Manganese, Iodine, Copper	715 - 27,920 infant formula products sampled and reported as a range of the mean for each micronutrient. Exceedance of the Codex GUL was noted for niacin and copper; all others were below the Codex GUL.
Da Silva 2013	Sodium, Potassium, Calcium, Magnesium, Copper, Zinc, Manganese	Five infant formula products sampled. Concentrations reported individually for each micronutrient. None exceeded the Codex GUL.
Pehrsson 2013	Vitamin C, Thiamin, Vitamin D, Vitamin K, Vitamin A, Vitamin E, Calcium	15 infant formula products sampled. Concentrations reported individually for each micronutrient. A small proportion for vitamin A (2/15), vitamin E (1/15), thiamin (1/15), and calcium (1/5) exceeded the Codex GUL.
Ahmed 2017	Calcium, Magnesium, Potassium, Sodium, Chromium, Copper, Manganese, Selenium, Zinc	15 infant formula products sampled. Measured concentrations were within 10% of the label claim.
Papachristodoulo 2018	Potassium, Calcium, Zinc	28 infant formula products sampled and results reported as a range for each micronutrient. None exceeded the maximums for these nutrients.

We also consider that there is unlikely to be incentives for manufacturers to consistently add more than what is reported on the Nutrition Information Panel. Industry food quality assurance systems and food safety management systems would be implemented to ensure infant formula meets the compositional requirements set under the Code. We also note the comments by MacLean et al. (2010) that there will invariably be batches with one nutrient at the higher or lower end of the range but there is unlikely to be prolonged consumption of the highest or lowest levels by individual infants. Even when formula is purchased by the case, infants would consume different batches of infant formula during the first six months of life.

FSANZ notes the results of the 22nd Australian Total Diet Study which assessed intakes of iodine, selenium, molybdenum, and chromium in a number of population groups. The estimated dietary intake of each nutrient was compared to the Upper Level of Intake (UL) (NHMRC, 2006). Estimated intakes for 9 month old infants did not approach the UL and there were no concerns of excessive intakes for these minerals.

EU 2016/127 prescribes maximums for all vitamins and minerals. EFSA's 2014 review did not come to a conclusion on recommended maximum amounts (guideline or mandatory) but the Panel noted that specifications for the current maximum amounts (e.g. under Codex) should be considered to be upper limits of a range which should not be exceeded.

Proposed option

FSANZ's proposed option for each micronutrient is listed in Table 7.1. Based on the arguments presented above, the preliminary view from 2016 was confirmed with the exception of iodine and selenium which were reconsidered in light of submitter comments. FSANZ proposes that existing Schedule 29 maximums be retained for these two micronutrients.

7.2 Vitamin equivalents and conversion factors

Most vitamins consist of several chemically-related compounds that can differ in physiological utilisation when consumed in food. For some vitamins there are different ways of determining and reporting the vitamin activity, sometimes termed as vitamin equivalents. Vitamin equivalents are used to express the amounts of vitamins A and E, niacin and folate in infant formula requirements.

7.2.1 Vitamin A, β-carotene, and calculation of retinol equivalents

Vitamin A refers to a group of compounds that includes retinal, retinoic acid, retinyl esters, and provitamin A carotenoids that are dietary precursors to retinol. Dietary sources of vitamin A are either preformed vitamin A (retinal, retinoic acid, retinyl esters, retinol) obtained from animal sources or provitamin A carotenoids (β-carotene) obtained from plant sources.

Three units of expression have been used to report the vitamin A activity in food: international units (IU), retinol equivalents (RE) and retinol activity equivalents. RE are generally used to report vitamin A intakes or requirements where one RE is defined as the biological activity associated with 1 µg of all-trans retinol (NHMRC and NZ MOH 2006).

Current regulations

Section S29—7 lists four retinol forms (retinol, retinyl acetate, retinyl palmitate, and retinyl propionate) as permitted forms of vitamin A as well as β-carotene as a provitamin A form.

Section S29—14 sets vitamin A requirements for infant formula in µg/100 kJ without reference RE or applicable conversion factors[9]. However, the Code also sets out in Standard 1.1.2 *Definitions used throughout the Code* (paragraph 1.1.2—14(3)(a)) that vitamin A should be calculated in terms of RE (for all foods including infant formula) and, for provitamin A forms, calculated using the RE conversion factors in section S1—4. Thus, if β-carotene is added, regardless of whether it is for colouring or nutritional purposes, the Code requires that β-carotene should be counted as contributing to the vitamin A content of infant formula.

Codex lists the permitted forms of vitamin A in Codex CAC GL 10-1979 and it includes β-carotene as a provitamin A form used for nutritional purposes. Codex STAN 72-1981 lists the vitamin A amounts as µg RE/100 kJ but also includes a footnote which states “retinol contents shall be provided by preformed retinol whereas any carotenoid content should not be included in the calculation and declaration of Vitamin A activity”. The following conversion factors are listed in the footnote:

1 µg RE = 3.33 IU Vitamin A = 1 µg all-trans retinol

US regulations (21CFR184.1245) permit β-carotene to be added as a vitamin A source. However, β-carotene is not a permitted form of vitamin A for infant formula products under EU legislation (Regulation (EU) 609/2013).

Previous consideration

FSANZ’s 2016 nutrition risk assessment considered whether it was appropriate to restrict permitted forms of vitamin A to preformed vitamin A and exclude β-carotene. The

[9] The vitamin A requirements were expressed as RE in the previous infant formula standards in the Code (Standard R7, transitional Standard 1.1A.1) however, it is not clear why RE was removed in Standard 2.9.1 (S29).

assessment noted that the β-carotene bioavailability from infant formula is less certain than from breast milk. It also noted that the NRV for vitamin A relates to preformed vitamin A only and does not include β-carotene (NHMRC and MoH 2006). Recent reviews (e.g. EFSA 2014) continue to exclude carotenoid forms from total vitamin content on the basis of a lack of knowledge on the bioconversion of carotenoids in infants. The nutrition assessment concluded that limiting vitamin A content of infant formula only to that derived from preformed vitamin A was unlikely to pose a risk to infant health.

In light of uncertainty around its bioavailability, FSANZ's preliminary view in 2016 was to exclude β-carotene from the total amount of vitamin A in infant formula. FSANZ also supported expression of vitamin A requirements in units of µg alone (rather than RE), as this clarifies that β-carotene should not contribute to the vitamin A content. The Code would then align with Codex and other international regulations in relation to β-carotene contribution to vitamin A content but would differ in relation to the vitamin A units.

Stakeholder views

Seven submissions (five industry, two government) commented on β-carotene as a permitted form of vitamin A. Industry submitters supported retaining the current permissions in Standard 2.9.1 and commented that β-carotene is a colouring agent and anti-oxidant in foods and many products are formulated to include β-carotene for these purposes. Government submitters either opposed β-carotene addition or requested further consideration to justify β-carotene addition. All seven submitters agreed that β-carotene should be excluded from the total amount of vitamin A in infant formula.

Three industry submitters supported the use of µg RE to clarify the units for vitamin A requirements and to align with Codex STAN 72-1981 and other international regulations.

Nutrition risk assessment

No further nutrition risk assessment was considered on this issue.

Options and discussion

β-carotene is a natural component of milk. Human milk content of β-carotene is variable (Canfield et al, 2003) and in Australian mothers it was reported to be about 32 µg/L. β-carotene intakes based on this amount would be 26 µg/day. The Institute of Medicine (IoM 2000) reported the range of β-carotene intakes for infants 0–6 months to be 8–163 µg/day.

β-carotene occurs naturally in cow's milk at variable levels and it is enriched in the whey fraction of cow's milk which is an ingredient in infant formula products. The concentration of β-carotene in a commercial standard infant formula formulated for term infants was measured to be 25 µg/L (Hansen et al. 2016). Based on an intake volume of 0.8 L/day, this amount corresponds to a daily intake of about 20 µg/day which is comparable to intakes for a breastfed infant. Notably, β-carotene amounts are not consistent in commercial formulas across international jurisdictions or across different brands and some products contain no detectable amount of β-carotene (Sommerburg et al. 2000, Bohn 2019).

Food additive permissions under the Code (Schedule 15) and Codex do not include β-carotene.[10] Therefore, β-carotene is not permitted to be added to impart a technological

[10] Codex CAC/GL 10-1979 is the list of nutrient compounds (not food additives) that may be used in infant formula products. S16-3 of the Code permits carotene as colouring at GMP but this permission does not apply to infant formula (because it is not listed in S15 category 13.1 infant formula products)

function such as colour or anti-oxidant. However, its presence as a component of an ingredient (the whey fraction of cow's milk) does not pre-empt it from a technological function. This is not unusual for a vitamin. For example, both vitamin C and vitamin E are nutrients that have anti-oxidant functionality. Excluding β-carotene from the vitamin A calculation addresses the uncertainty surrounding its bioavailability from infant formula.

Proposed option

Based on the above discussion and alignment with Codex STAN 72-1981, the Codex Standard for Follow-Up Formula CXS 156-1987, the 2016 EU regulation and other international regulations, FSANZ proposes to:

- express vitamin A requirements as µg RE/100 kJ
- exclude β-carotene from the vitamin A calculation

Based on history of use, FSANZ proposes to retain the permission for β-carotene as a permitted form of vitamin A in section S29—7 however this will not be included within the vitamin A calculation.

7.2.2 Folic acid and folate equivalents

Folate refers to the methylated form of the vitamin that occurs naturally in food such as green leafy vegetables and is biologically functional. Folic acid is the synthetic form of folate that is added to food and supplements. Folate and folic acid differ in how efficiently they are absorbed in the gut. Dietary folate equivalents (DFE) are used to account for differences in the absorption efficiency.

Current regulations

Neither Standard 2.9.1 nor Codex STAN 72-1981 apply DFE to set requirements for infant formula. The minimum amount (2 µg) required in section S29—9 is expressed as µg/100 kJ folate, but folic acid is the only permitted form to be added under section S29—7. The Codex minimum amount (3.6 µg) is expressed as µg/100 kJ folic acid.

Recent EFSA (2014a) recommendations on the composition of infant formula have proposed the use of DFE using the 1998 IoM conversions (below; IOM 1998) This recommendation has been adopted into EU 2016/127. The EU range for folate is 3.6–11.4 µg/100 kJ.

1 DFE = 1 µg food folate = 0.6 µg folic acid from fortified food or as a supplement consumed with food = 0.5 µg of a folic acid supplement taken on an empty stomach.

Previous consideration

Milk and milk powder have naturally occurring levels of folate, thus infant formula generally contains a mixture of naturally occurring folate and added folic acid. Setting the minimum folate requirement as folic acid (as in the Codex standard) would exclude the contribution of naturally occurring folate. According to MacLean et al. (2010), up to 40% of the folate in the finished product is inherent in the ingredients used to produce infant formula.

DFE were first introduced as the units for the folate NRV in 2006 but this has not been incorporated into the Code. Currently the Code treats folic acid and folate as having equivalent bioavailability with values for folate and folic acid considered equal (FSANZ, 2005). A consultation paper on the use of the 2006 NRVs as the basis of a revision of the current regulatory NRVs (rNRV) in the Code was released in 2010 (FSANZ 2010). Submitters generally supported the approach to update the rNRV for folate to DFE. In 2018, Proposal P1047 *Review of regulatory nutrient reference values* was commenced and

introducing the term DFE into the Code is being considered as part of that review. However, the proposal is not currently being progressed.

Use of DFE for infant formula products would require the appropriate conversions to be specified in the Code such as that defined by the IoM and recently adopted into EU 2016/127.

FSANZ's preliminary view in 2016 was to retain the nutrient name as folate rather than folic acid, although this differs from Codex STAN 72-1981, and retain units of µg folate. We sought further information from stakeholders to determine whether DFE should be applied and whether the permitted range for folic acid should include or exclude the contribution of naturally occurring folate.

Stakeholder views

Eleven submissions (seven industry, four government) commented on the application of DFE to express folic acid amounts. All industry submitters and one government disagreed with the use of DFE for folate/folic acid expression as this would not be aligned with Codex STAN 72-1981. Several submitters also highlighted that despite EFSA's recommendation to use DFE, EFSA also considered that the evidence base for the IoM definition of DFE was uncertain. Three government submitters supported the application of DFE referring to EFSA's opinion (2014a) and updated EU 2016/127.

Ten submissions (seven industry, three government) commented on the contribution of folate to the total amount of the vitamin in infant formula. Two government submitters considered that folate should be included citing the evidence reported in 2010 by MacLean et al. (see "Previous consideration"). The remaining submissions supported excluding naturally occurring folate citing the lack of reliable methodology to quantify both forms and the minimal amount of folate that is likely to be present in infant formula products.

Nutrition risk assessment

No further nutrition risk assessment was considered on this issue.

Options and discussion

A recent study reported that concentrations of folate in ten cow's milk- and soy-based infant formulas were low or below the level of detection (Campos-Gimenez et al. 2018). The major component measured in all formulas was folic acid, added to meet the requirement for this vitamin. Existing official methodology for folate analysis was used, with modifications to ensure optimised extraction and detection of all folates from the food matrix. These results provide updated evidence from that reported in MacLean et al. (2010) and indicate that applying extra analysis to measure the contribution of folate from ingredients (e.g. cow's milk) in infant formula would not be justified.

The EU requires the use of DFE to express the folate amount in infant formula.[11] The regulation was based on the 2014 EFSA recommendation on the essential composition of infant formula (EFSA 2014b) which in turn references the 2014 EFSA Scientific Opinion on Dietary References Values (EFSA 2014a). However, as noted in submissions to FSANZ's 2016 Consultation paper, the evidence base for the definition for DFE and the figures used by the IoM is uncertain.

[11] The US FDA has issued guidance (i.e. voluntary) for using DFE in expressing folate amounts in conventional foods (FDA, 2019).

FSANZ notes that the folic acid requirement in the Codex Draft Standard for FUF (Codex REP20/NFSDU Appendix VI, 2019) is µg/100 kJ folic acid which aligns with the Codex infant formula standard Codex STAN 72-1981. In addition, excluding the contribution of folate from ingredients such as cow's milk (see above) eliminates the need for using DFE as units for expressing folic acid amounts.

Proposed option

Based on the above considerations, FSANZ proposes to express the requirements for folic acid/folate as µg folic acid/100 kJ. The contribution of folate from ingredients (naturally occurring folate) will not be included in the permitted range for this vitamin. As such there is no need to use DFE as units of expression in folic acid amounts.

7.2.3 Vitamin E and tocopherol equivalents

Vitamin E refers to a group of compounds that include naturally occurring tocopherols and tocotrienols and several synthetic homologues. Vitamin E activity is either identified as α-tocopherol only or α-Tocopherol Equivalents (α-TE). Vitamin E prevents oxidation of PUFA, including LC-PUFA, thus the amount required is influenced by the unsaturated fatty acid content of infant formula.

Current regulations

Section S29—9 lists the vitamin E range in units of mg /100 kJ with permitted forms of vitamin E are synthetic or natural forms of α-tocopherol (section S29—7). Codex STAN 72-1981 lists units of vitamin E as α-TE although a note specifies that 1 mg α-TE = 1 mg d-α-tocopherol.

Standard 2.9.1—12(3) and Codex STAN 72-1981 both specify a minimum amount of vitamin E per gram of PUFA. Standard 2.9.1—12(3) sets a minimum amount of 0.5 mg vitamin E per gram of any PUFA whereas Codex STAN 72-1981 also lists 'factors of equivalence' from 0.5 mg/g for LA and increasing in increments of 0.25 mg/g to 1.5 mg/g for DHA according to the number of fatty acid double bonds in individual PUFAs in an infant formula. These factors are applied to determine the minimum amount of vitamin E for a particular PUFA mixture in infant formula.

Previous consideration

In 2016 FSANZ considered that mg α-TE should be adopted as the units for vitamin E to indicate the relative activities of natural and synthetic forms of α-tocopherol.

FSANZ's preliminary view was also to retain the current approach to vitamin E requirements relating to the PUFA content of infant formula. It was not considered necessary to adopt the 'factors of equivalence' for α-TE to individual PUFA outlined in Codex STAN 72-1981.

Stakeholder views

Three submitters (two industry, one government) commented on the issues related to vitamin E equivalents and units of expression. All supported FSANZ's 2016 view to express vitamin E in units of mg α-TE/100 kJ and that the current requirements relating to the PUFA content are retained.

Nutrition risk assessment

No further nutrition risk assessment was considered on this issue.

Options and discussion

FSANZ notes that adopting mg α-TE as the units for vitamin E received no submitter comments in the 2012 consultation and all comments received in the 2016 consultation were in support of this change.

The 2016 nutrition risk assessment concluded that application of the Codex STAN 72-1981 conversions for PUFA content (i.e. 'factors of equivalence') makes only a marginal difference to the minimum vitamin E amount compared to the approach currently used in Standard 2.9.1. There was limited evidence to indicate that the use of different factors depending on the number of PUFA double bonds is warranted.

Proposed approach

Based on the conclusions of the 2016 nutrition risk assessment and support from stakeholders, FSANZ proposes that α-TE should be adopted as the units for vitamin E to indicate the relative activities of natural and synthetic forms of α-tocopherol. FSANZ also proposes that the current Standard 2.9.1 vitamin E requirements relating to the PUFA content of infant formula is retained.

7.2.4 Niacin equivalents

Preformed niacin is the term used to refer to the niacin present in foods. In humans, niacin can be synthesised from tryptophan. Niacin requirements are therefore commonly expressed as niacin equivalents (NE) which take account of the niacin in the diet as well as the conversion of tryptophan to niacin. Both Schedule 29 and Codex STAN 72-1981 list the niacin requirements as preformed niacin.

Current regulations

Both Schedule 29 and Codex STAN 72-1981 list the niacin requirements as preformed niacin.

Previous consideration

In 2016, FSANZ considered that it is appropriate to retain the requirement for niacin in infant formula to be limited to the contribution from preformed niacin.

Stakeholder views

No submitter comments were received on this issue.

Risk assessment

No further risk assessment was considered on this issue.

Options and discussion

As preformed niacin refers to the niacin present in foods and does not include the niacin that can be synthesised in the human body the permission of preformed niacin only in infant formula will be sufficient niacin to meet infant requirements.

Proposed approach

FSANZ proposes that the current requirement in Schedule 29 for niacin be retained. The niacin amount in infant formula will be restricted to preformed niacin.

7.3 Permitted ranges for micronutrients

A permitted range is established for each of the 25 vitamins, minerals and electrolytes required in infant formula. The table to section S29—9 lists the minimum amounts for every listed micronutrient, and maximum amounts only where necessary. GULs for the other micronutrients are located in section S29—10. In Codex STAN 72-1981, section 3.1 (d) and (e) set out minimum amounts and maximum amounts or GULs for vitamins and minerals. The approach adopted in the two standards is similar, with both setting minimum amounts and either a maximum amount or a GUL for the same range of micronutrients although the specified minimum and maximum amounts may vary.

This section discusses the suitability of aligning the permitted ranges with Codex STAN 72-1981, based on previous support for this approach from stakeholders (refer to 2016 Consultation paper). The conclusions of the 2016 nutrition risk assessment are taken into consideration along with submitter comments, potential implications on trade, and new information that has become available.

New information includes the revised EU regulations for infant formula products (EU 2016/127) which was published after the release of FSANZ's 2016 Consultation paper. The approach used to specify permitted range of vitamins and minerals in the EU 2016/127 was based on:

- EFSA Scientific Opinion on the essential composition of infant and follow-on formulae (2014)
- EFSA Opinion Nutrient requirements and dietary intakes of infants and young children in the EU (2014)

However, the EFSA Panel did not specifically evaluate UL/ML and thus they made limited comments on UL/ML. Where EFSA did comment, these have been noted in the section for that micronutrient. Additionally, FSANZ has noted EFSA's general comments on maximum limits (Box 7.1) which have also been taken into consideration.

Box 7.1: EFSA (2014) Codex STAN 72-1981 guidance on carbohydrates in infant formula

Abstract of the 2014 EFSA Scientific Opinion:
"From a nutritional point of view, the minimum contents of nutrients in infant and follow-on formula proposed by the Panel cover the nutritional needs of virtually all healthy infants born at term and there is no need to exceed these amounts in formulae, as nutrients which are not used or stored have to be excreted and this may put a burden on the infant's metabolism. Therefore the panel, emphasises that maximum amounts should be interpreted not as target values but rather as upper limits which should not be exceeded."

Summary of the 2014 EFSA Opinion (paragraph 5):
"Specifications for the currently permitted maximum amounts of micronutrients in formulae were mostly calculated as three to five times the minimum amounts established at the time and took into account established history of apparent safe use (Codex STAN 72-1981, Codex STAN 156-1987, the Directive 2006/141/EC and the SCF) and were not based on scientific evidence for adverse effects owing to the lack of such evidence for most nutrients."

Although infant formula for older infants aged 6 months and above (i.e. follow-on or follow-up formula) is not part of the scope for this proposal, FSANZ has also considered, where

relevant, the current draft of the revised Codex standard on the composition of follow-up formula. Generally there is considerable overlap in the requirements between the two Codex standards as this represents current international regulation on infant formula composition.

The nutrition risk assessment for the 2016 Consultation paper examined the basis for the minimum and maximum amounts for each micronutrient. As a result, micronutrients could be categorised into three groups:

- The permitted range already aligns with Codex STAN 72-1981 and potentially no change was needed.
- The permitted range is not aligned but the 2016 assessment suggested alignment was appropriate.
- There was uncertainty whether alignment was appropriate and further information was sought in the 2016 consultation.

The discussion below on the permitted ranges for micronutrients is organised according to these three categories.

7.3: Permitted range is aligned with Codex

This section covers vitamin A and vitamin D which are nutrients that are currently aligned with Codex STAN 72-1981 and the preliminary view from the 2016 Consultation paper was that the current permitted range should be retained.

7.3.1 Vitamin A (maximum)

Current regulations

Section S29—9 and Codex STAN 72-1981 vitamin A minimum and maximum are aligned at 14–43 µg/100 kJ. The maximum under EU Directive 2006 was 43 µg/100 kJ but this was decreased to 27.2 µg/100 kJ in EU 2016/127. FSANZ 2021 label survey showed the average vitamin A content in products on the ANZ market ranged between 17.99 and 38.88 µg/100 kJ (Figure 7.3.1).

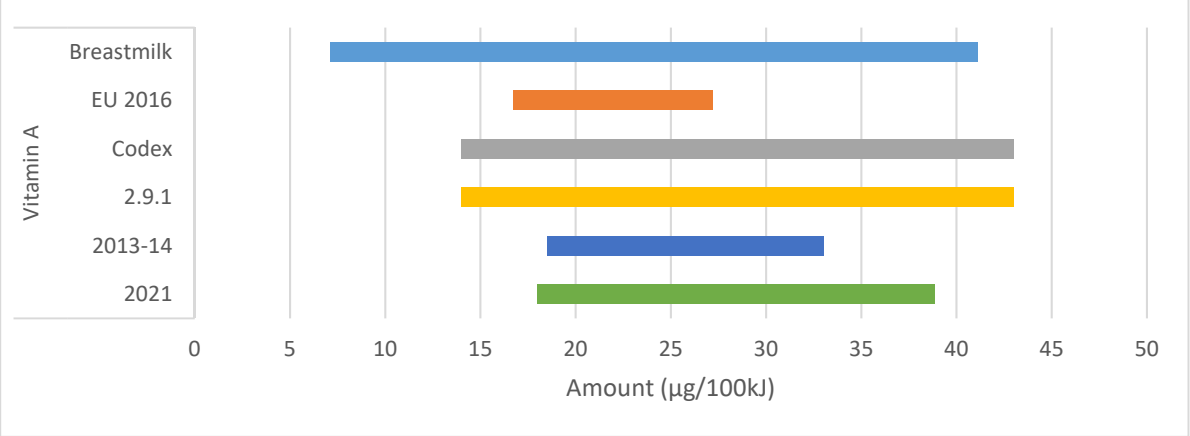


Figure 7.3.1 Comparison of the permitted ranges for vitamin A across standards (Standard 2.9.1, Codex STAN 72-1981 and EU 2016/127), human milk concentration, and the FSANZ survey of the average content in products on the ANZ market.

Previous consideration

In 2016 FSANZ proposed to retain the permitted range for vitamin A. The 2016 nutrition risk assessment determined that the existing maximum could lead to exceedance of the NHMRC UL for vitamin A (600 µg/day for infants 0–12 months) but this exceedance was unlikely to

occur continuously over the period of formula feeding. There was no additional evidence that the current maximum amount was associated with adverse health effects.

Stakeholder views

Two submitters (one government, one industry) commented on the permitted range for vitamin A. The government submitter supported a lower maximum (27.2 µg RE/100 kJ) to align with EU 2016/127. The industry submitter supported retaining the current maximum.

Nutrition risk assessment

Further nutrition risk assessment (SD1) considered the scientific basis for the maximum level set in EU 2016/127 and potential risks to infant health and safety if the maximum vitamin A amount was decreased to 27.2 µg RE/100 kJ. There was no explicit rationale explained in the 2014 EFSA opinion on infant formula composition. EFSA (2014b) also cited two recent studies which reported human milk concentrations of vitamin A to be 50–54 µg RE/100 kJ which is higher than the maximum amount set under Codex STAN 72-1981 and section S29—9.

Regarding potential risks to infant health and safety, the risk assessment concluded use of the EU 2016/127 minimum amount (16.7 µg RE/100 kJ) and maximum amount (27.2 µg RE/100 kJ) poses a low risk to infant health.

Options and discussion

Although not explicitly stated, EU 2016/127 appears to be based on the EFSA 2014 paper on DRVs which considered that the UL (800 µg RE/day; derived in 2002[12] and set for children aged one to three years, i.e. not infants) could be exceeded with regular consumption of formula containing vitamin A at the maximum level of 43 µg/100 kJ.

The maximum vitamin A amount is a regulated maximum upper level which means that the amount present in the formula at any time is 43 µg RE/100 kJ or less. Although evidence has been presented that the NHMRC UL can be exceeded at median intake if the maximum permitted amount is used, no evidence of adverse effects has been presented at this level. The 2021 FSANZ survey of the range of vitamin A content of products on the market confirmed that this maximum amount is unlikely to be exceeded (see Figure 7.3.1.1 for further details).

The recent review of the Codex standard of follow-up formula determined that the maximum vitamin A amount be retained at 43 µg/100 kJ. The lower maximum level set by the EU falls within the proposed permitted range of vitamin A, so would not present any concerns for trade from the EU (Figure 7.3.1.1). Figure 7.3.1.1 also shows that the Codex permitted range is consistent with human milk concentrations, whereas the EU range has a much lower maximum.

Proposed approach

Based on alignment with Codex STAN 72-1981, Codex Draft Standard for FUF and human milk concentrations, FSANZ proposes to retain the current maximum amount for vitamin A in section S29—9. This is also based on the absence of data indicating that the current maximum of 43 µg/100 kJ is associated with adverse health effects in infants, the

[12] https://ec.europa.eu/food/sites/food/files/safety/docs/sci-com_scf_out145_en.pdf

uncertainty around the basis for EU 2016/127, and the objective of this Proposal to align with Codex STAN 72-1981 where possible.

The minimum vitamin A amount is retained as no submissions indicated concerns about FSANZ's 2016 conclusions and no new information has been identified.

7.3.2 Vitamin D

Current regulations

The permitted range for vitamin D in section S29—9 (0.25 – 0.63 μg/100 kJ) is comparable to that in Codex STAN 72-1981 (0.25 – 0.6 μg/100 kJ). The permitted range for vitamin D under EU 2016/127 was recently revised to 0.48 – 0.6 μg/100 kJ (European Commission 2019).

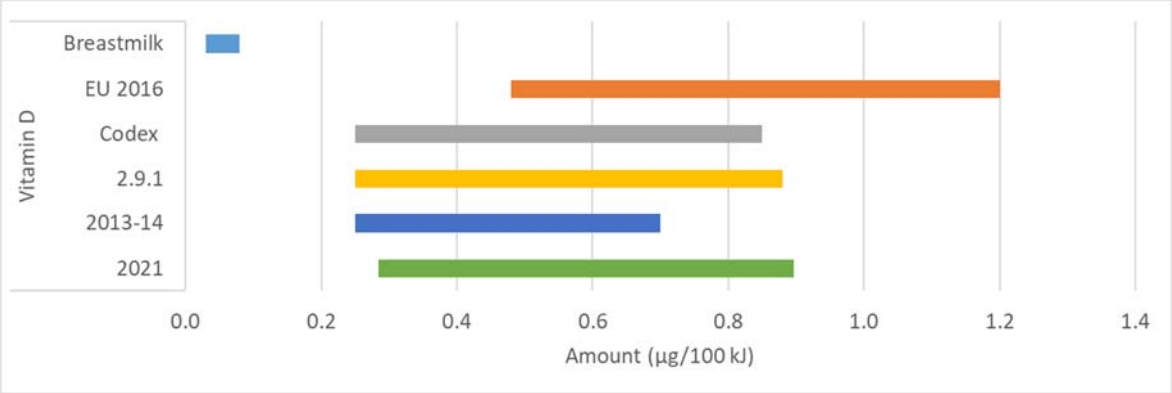


Figure 7.3.2 Comparison of the permitted ranges for vitamin D across standards (Standard 2.9.1, Codex STAN 72-1981 and EU 2016/127), human milk concentration, and the FSANZ survey of the average content in products on the ANZ market.

Previous consideration

In 2016 FSANZ considered it appropriate to retain the vitamin D range to 0.25 – 0.63 μg/100 kJ as this was unlikely to pose a risk to infant health and a change would result in inconsistency with Codex STAN 72-1981. FSANZ also concluded in 2016 that the current range was achievable for industry, thus not impacting on the manufacturing of infant formula.

Stakeholder views

Six submitters (one government, five industry) commented on the permitted range for vitamin D. One government submission supported retaining the current section S29—9 range. However, industry submitters supported alignment with the EU maximum (at that time set to 0.72 μg/100 kJ) to enable a broader common range between the Code, Codex STAN 72-1981 and EU 2016/127 regulations.

Nutrition risk assessment

No further nutrition risk assessment has been considered.

Options and discussion

Comments from industry submitters on the vitamin D maximum reflect the previous EU regulation. Since 2016, the EU has amended the vitamin D maximum level as it was concluded that some infants may consume amounts of vitamin D that exceed the upper

intake level (EFSA 2018). The EU permitted range was amended to 0.48 - 0.6 µg/100 kJ in 2019. FSANZ notes that the Codex Draft Standard for FUF (2020) has proposed a vitamin D range of 0.24 – 0.72 µg/100 kJ (i.e. the higher maximum but the same minimum as that set in the Code and Codex STAN 72-1981).

Proposed approach

FSANZ proposes to retain the current permitted range for vitamin D on the basis that no safety concerns have been identified using this range, the range aligns most closely with international regulations and is wide enough to be achievable for product formulation and manufacturing.

7.3: Permitted range is not aligned with Codex

This section covers the permitted range of eighteen micronutrients that are not currently aligned with Codex STAN 72-1981 and the preliminary view from the 2016 Consultation paper was that the range could be aligned.

No comments were raised in submissions for eleven of these nutrients (calcium, chloride, magnesium, manganese, folate, niacin, pantothenic acid, potassium, sodium, vitamin B12, and vitamin E). Therefore, no further consideration related to the permitted range was undertaken in this consultation paper. The proposed approach for these nutrients is to align with the Codex range (Table 7.4).

Table 7.4 Permitted range of micronutrients: propose to align with Codex

Micronutrient (units)	Standard 2.9.1 (Schedule 29)		Codex STAN 72-1981		Content in products on the market^
	Min	Max	Min	Max	
Vitamins					
Vitamin B12 µg/100 kJ	0.025	0.17 (GUL)	0.025	0.36 (GUL)	0.04–0.16
Folate (µg/100 kJ	2	8.0	2.5	12 (GUL)	NR
Pantothenic Acid (µg/100 kJ)	70	360 (GUL)	96	478 (GUL)	84.04–227.3
Niacin (preformed) (µg/100 kJ)	130	480 (GUL)	70	360 (GUL)	130.1–272.7
Vitamin E (mg/100 kJ)	0.11	1.1	0.12 (α-TE)	1.2 (GUL) (α-TE)	0.26–0.58
Minerals					
Calcium (mg/100 kJ)	12	33 (GUL)	12	35 (GUL)	15.38–23.57
Manganese (µg/100 kJ)	0.24	24	0.25	24 (GUL)	1.53–18.71
Magnesium (mg/100 kJ)	1.2	4.0	1.2	3.6 (GUL)	1.65–2.52
Electrolytes					
Potassium (mg/100 kJ)	20	50	14	43	20.79–31.65
Chloride (mg/100 kJ)	12	35	12	38	14.39–25
Sodium (mg/100 kJ)	5	15	5	14	5.71–11.47

^ *Product content range is reflective of the ANZ market during 2013–2014*
NR: Not recorded

Issues were raised by submitters for the remaining eight micronutrients (biotin, folate, riboflavin, thiamin, vitamin B6, and vitamin K, copper and phosphorus). These are examined further below.

7.3.3 Vitamin K, thiamin, riboflavin, vitamin B6, and biotin

Current regulations

Table 7.5 summarise the current regulations for vitamin K, thiamin, riboflavin, vitamin B6, and biotin.

Table 7.5 Permitted ranges for vitamin K, thiamin, riboflavin, vitamin B6 and biotin

Vitamin (µg/100 kJ)	Standard 2.9.1 (Schedule 29)		Codex STAN 72-1981		EU 2016/127		Content in products on the market
	Min	Max	Min	Max	Min	Max	
Vitamin K	1	5.0 (GUL)	1	6.5 (GUL)	0.24	6	1.25 – 3.69
Thiamin	10	48 (GUL)	14	72 (GUL)	9.6	72	17 – 48
Riboflavin	14	86 (GUL)	19	119 (GUL)	14.3	95.6	25.62 – 77.36
Vitamin B6	9	36	8.5	45 (GUL)	4.8	41.8	13.17 – 28.11
Biotin	0.36	2.7	0.4	2.4	0.24	1.8	0.50 – 1.73

Previous consideration

In 2016, FSANZ's nutrition risk assessment concluded that alignment with the Codex STAN 72-1981 for vitamin K, thiamin, riboflavin, vitamin B6, and biotin was appropriate. The Codex permitted range for these nutrients was reviewed against the nutrition risk assessment criteria, as reported in the 2016 nutrition risk assessment. No evidence was identified to indicate that the Codex permitted range was not appropriate and the permitted range (using maximum amounts or GULs) as specified in Codex STAN 72-1981 was determined to be unlikely to pose a risk to infant health.

Stakeholder views

Three submitters (one government, two industry) commented on the permitted range for vitamin K, thiamin, riboflavin, vitamin B6, and biotin. Industry submitters supported FSANZ's preliminary view to align the permitted range for these vitamins with the Codex amounts. The government submitter opposed alignment with Codex and recommended aligning with the EU 2016/127 values based on the recommendation by EFSA NDA and justification that these levels meets the nutritional needs of most infants, are consistent with human milk concentrations and corresponding intakes would be closer to the AI.

Nutrition risk assessment

Additional nutrition risk assessment (see SD1) for vitamin B6, vitamin K, riboflavin, and biotin re-examined FSANZ's preliminary view on the permitted range for these nutrients and considered whether the range set under EU 2016/127 poses a low risk to infant health.

Vitamin B6

The vitamin B6 minimum set in EU 2016/127 (4.8 µg/100 kJ) is the same amount that EFSA (2014) recommended. This recommendation aligns with the EFSA NDA Panel (EFSA 2013), which advised that an intake of 100 µg/day and 400 µg/day is considered adequate for the majority of infants in the first and second half-year of life, respectively. For the younger infants, this was based on an observed mean content in human milk (0.13 mg/L). EFSA (2014) used the vitamin B6 intake deemed adequate (100 µg/day) with an average energy intake of 500 kcal/day for infants aged 0–<6 months, to recommend that infant and FOF contain a minimum vitamin B6 content of 20 µg/100 kcal (4.8 µg/100 kJ).

The 2021 nutrition risk assessment (SD1) estimated vitamin B6 intake using the EU 2016/127 minimum amount against the ANZ AI. This estimation showed that infants aged 0–<6 months met the AI, however, was substantially lower than half the AI value for infants aged 6–<12 months. Therefore, the assessment concluded that use of the EU 2016/127 minimum amount of 4.8 µg/100 kJ may pose a risk to infant health. The minimum amount of 9 µg/100 kJ in Schedule 29, or 8.5 µg/100 kJ in Codex STAN 72-1981, would mitigate this risk.

FSANZ's considerations from the 2016 nutrition risk assessment determined that intakes based on the Codex permitted range are unlikely to pose a risk to infant health. It was also noted that there is no evidence indicating excessive vitamin B6 intakes in formula-fed infants. Use of a GUL would pose a low risk to infant health.

Vitamin K

The vitamin K minimum set in EU 2016/127 was based on the SCF findings from 1993 which concluded that intake of 1 µg per kg body weight per day appears adequate. The panel therefore proposed a minimum vitamin K content in infant formula and follow on formula of 0.24 µg/100 kJ. FSANZ's 2016 nutrition risk assessment indicated that intakes based on the Codex minimum exceed the AI twelve-fold, noting the AI is low as it assumes infants receive prophylactic vitamin K at birth. Estimated vitamin K intakes based on the lower minimum permitted amount set under EU 2016/127 more closely align with the NHMRC AI. Human milk vitamin K concentrations are low and vary widely and are therefore not informative. Based on these findings, the 2021 nutrition risk assessment (SD1) concluded that use of the EU 2016/127 minimum amount (0.24 µg/100 kJ) and maximum amount (6 µg/100 kJ) poses a low risk to infant health. This conclusion assumes that newborn infants receive prophylactic vitamin K at birth.

Riboflavin

The riboflavin minimum set in EU 2016/127 was based on EFSA (2014b). The EFSA recommendation was based on the human milk riboflavin concentration (350–600 µg/L, corresponding to 13–29 µg/100 kJ) and advice from the EFSA NDA Panel (2013) that a riboflavin intake of 300 µg/day and 400 µg/day is adequate for the majority of infants in the first and second half-year of life, respectively. FSANZ's considerations from the 2016 nutrition risk assessment determined that the Codex minimum was consistent with breast milk concentrations, would meet the AI for both age groups, and there was no evidence indicating that the Codex minimum would pose a risk to infant health. The estimated riboflavin intake based on the EU 2016/127 minimum amount also meets the AI value for infants aged 0–<12 months.

The riboflavin maximum set in EU 2016/127 was based on EFSA (2014b), which appears to be based on the Commission Directive 2006/141/EC (95 µg/100 kJ) maximum. This was not

based on scientific evidence for adverse effects, but was calculated as three to five times the minimum amounts, prescribed by European Commission Directive 2006/141/EC (European Commission 2006), at that time and considered the history of apparent safe use. No additional evidence has been identified to support the lower maximum specified by EU 2016/127, riboflavin toxicity has not been reported in ANZ formula-fed infants, and an ANZ UL has not been established due to no evidence of adverse effects.

The 2021 nutrition risk assessment (SD1) concluded that use of the EU 2016/127 range (14.3–95.6 µg/100 kJ) poses a low risk to infant health.

Biotin

The biotin minimum set in EU 2016/127 was based on EFSA (2014b) which recommended a minimum of 0.24 µg/100 kJ. The recommended minimum was derived from the reported average concentration in human milk (5 µg/L) and on biotin intakes of 4 µg/day and 6 µg/day that are considered adequate for the majority of infants in the first and second half-year of life, respectively. FSANZ's 2016 nutrition risk assessment determined that the Codex minimum was consistent with breast milk concentrations, would meet the AI for both age groups, and there was no evidence indicating that the Codex minimum would pose a risk to infant health. The estimated biotin intake based on the EU 2016/127 minimum amount also meets the AI value for infants aged 0–<12 months.

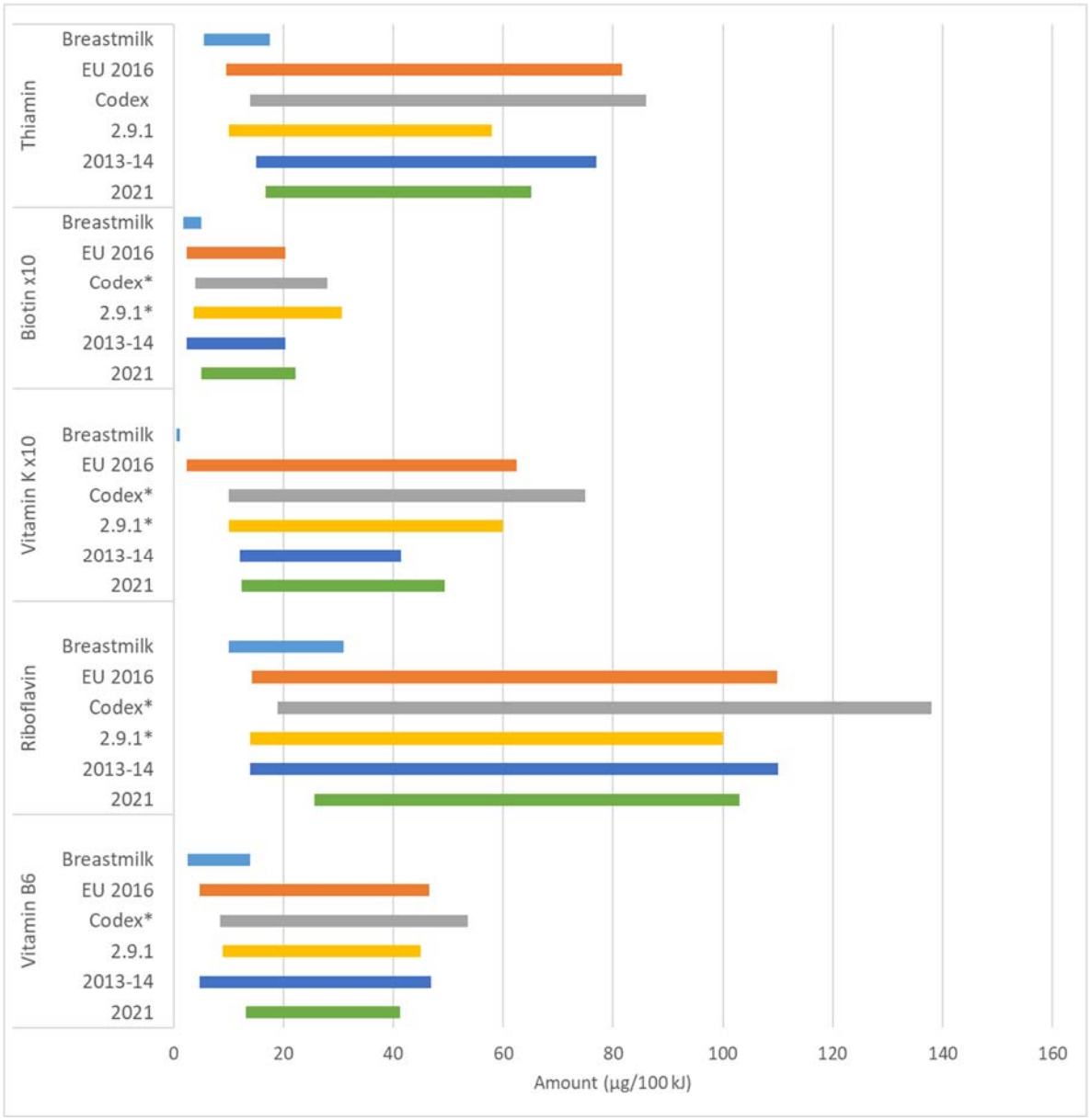
The biotin maximum set in EU 2016/127 was based on EFSA. However, the basis for this decision is not clear as EFSA (2014b) did not assess micronutrient maximum amounts. Maximum amounts were adopted from Commission Directive 2006/141/EC which calculated the maximums as three to five times the minimum amounts, prescribed by European Commission Directive 2006/141/EC (Directive 2006/141/EC; EC 2006), at that time and considered the history of apparent safe use. FSANZ's 2016 nutrition risk assessment proposed adopting the Codex STAN 72-1981 maximum amount as a GUL. No additional evidence has been identified to support the lower maximum specified by EU 2016/127, biotin toxicity has not been reported in ANZ formula-fed infants, and an ANZ UL has not been established due to no evidence of adverse effects.

The 2021 nutrition risk assessment (SD1) concluded that the EU 2016/127 range (0.24 - 1.8 µg/100 kJ) poses a low risk to infant health.

Options and discussion

Figure 7.3.3 directly compares the permitted ranges as specified in Schedule 29, Codex STAN 72-1981 and EU 2016/127, human milk concentration, and the 2021 surveys of the average content in products on the ANZ market. The graph highlights that the permitted ranges across standards are largely similar. It also shows that products on the ANZ market fall within permitted ranges outlined by the standards.

Issues and FSANZ responses for vitamin K, thiamin, riboflavin, vitamin B6, and biotin are summarised in Table 7.6. FSANZ notes that submitters supporting EU 2016/127 regarded these amounts to reflect the most up-to-date scientific evidence about infant nutritional requirements. However, human milk content and reference intakes on which recommendations of the EC SCF (2003), ESPGHAN (2005) (which underpin the Codex standard) and the 2014 EFSA opinion (which underpins the EU regulation) are based were derived from studies conducted in the 1980s and 90s and not new data.



*Guideline maximum

Figure 7.3.3 Comparison of the permitted ranges for vitamin K, thiamin, riboflavin, vitamin B6, and biotin in Standard 2.9.1, Codex STAN 72-1981 and EU 2016/127, human milk concentration, and the survey of the content in products on the ANZ market (2013-14 and 2021).

Table 7.6 Submitter comments and FSANZ responses for vitamin K, thiamin, riboflavin, vitamin B6, and biotin

Comment*	FSANZ response
Vitamin K: adopt lower minimum EU 2016/127 as this level meets the AI.	The minimums under Codex and EU 2016/127 were determined to pose a low risk to infant health. The EU minimum is unlikely to impact trade since products formulated at the lower minimum would still meet Codex STAN 72-1981. **Propose adopting EU minimum**.
Thiamin: adopt lower minimum level set under EU 2016/127 as this is consistent with the AI and with human milk concentration.	The current minimum (which is the same as EU 2016/127) is more consistent with human milk concentrations (Figure 7.3.2.1). No trade implications would result since products formulated at the lower minimum will still meet Codex STAN 72-1981. **Propose retaining current Standard 2.9.1 minimum.**

Riboflavin: adopt permitted range set under EU 2016/127 as the higher levels under the Codex standard provide unnecessary amounts of riboflavin.	FSANZ concluded that the permitted ranges under both Codex and EU 2016/127 would pose a low risk to infant health. The EU minimum is unlikely to impact trade since products formulated at the lower minimum would still meet Codex STAN 72-1981. The riboflavin content in infant formula currently sold in ANZ is consistent with EU 2016/127 (Figure 7.3.2.1). **Propose adopting EU permitted range.**
Vitamin B6: adopt lower minimum level set under EU 2016/127 as this is consistent with the AI and with human milk concentration.	Intakes based on the lower EU minimum would not meet the AI for infants 7-<12 months. **Propose adopting Codex STAN 72-1981 minimum.**
Biotin: adopt lower permitted range set under EU 2016/127 based on EFSA recommendations	FSANZ concluded that the permitted ranges under both Codex and EU 2016/127 would pose a low risk to infant health. The EU minimum is unlikely to impact trade since products formulated at the lower minimum would still meet Codex STAN 72-1981. **Propose adopting EU minimum**.

** As noted in submission/s opposing FSANZ's preliminary view to align with the Codex standard for these nutrients.*

FSANZ also notes that the Codex Draft Standard for FUF are aligned with the Codex STAN 72-1981 provisions for these nutrients (allowing for rounding).

Proposed approach

Proposed approaches for vitamin K, thiamin, riboflavin, vitamin B6, and biotin are indicated in Table 7.6.

7.3.4 Phosphorus

Phosphorus is assessed in detail within section 7.4.1 Phosphorus and the calcium: phosphorus ratio, in which FSANZ proposes to adjust the current phosphorus maximum (25 mg/100 kJ) in section S29—9 to a GUL of 24 mg/100 kJ. The minimum for phosphorus is already aligned with Codex STAN 72-1981 and EU 2016/127 and therefore is not considered in this paper. Please refer to section 7.4.1 for further details.

7.3.5 Copper

Current regulations

Both minimum and maximum amounts for copper in section S29—9 are higher than the Codex STAN 72-1981 minimum amount and GUL, respectively. EU 2016/12 set a range for copper of 14.3–24.0 µg/100 kJ. The permitted range under the Codex Draft Standard for FUF aligns with the current Codex STAN 72-1981 (8–29 (GUL) µg/100 kJ).

Table 7.7 Permitted range for copper

Micronutrient	Standard 2.9.1 (Schedule 29)		Codex STAN 72-1981		Content in products on the market^
	Min	Max	Min	Max	
Copper (µg/100 kJ)	14	43	8.5	29 (GUL)	14.01–20.64

^ Product content range is reflective of the ANZ market during 2013–2014

Previous consideration

The 2016 nutrition risk assessment indicated that estimated copper intakes of infants using the minimum amount specified in Codex STAN 72-1981 would not meet the AI for copper for older or younger infants. However, powdered infant formula is typically mixed with tap water. Codex STAN 72-1981 includes a footnote, “adjustments may be needed in these levels for infant formula made in regions with a high content of copper in the water supply”. Thus if the estimated intake is revised to account for the copper from tap water in Australia, the combined intake of copper from infant formula and tap water is likely to meet the AI for both younger and older infants. Therefore, alignment with the lower minimum in Codex STAN 72-1981 would be unlikely to pose a risk to infant health.

Section S29—9 sets a maximum for copper whereas Codex provides a lower GUL. FSANZ has not found a clear basis for these levels in any literature. There is no UL set for copper for infants. Copper toxicity is not known to occur in full-term breastfed or formula-fed infants and the nutrition risk assessment identified no recent studies suggesting adverse effects related to high copper intakes of formula-fed infants. The nutrition risk assessment concluded that adopting the GUL at the lower amount would be unlikely to adversely affect infant health.

FSANZ’s 2013–2014 label survey indicated that the copper content of infant formula lies within the minimum to maximum range specified in Codex STAN 72-1981.

FSANZ’s preliminary view from the 2016 Consultation paper was that alignment with the Codex STAN 72-1981 minimum amount and GUL amount is appropriate. However this may need to be considered in the context of the zinc to copper ratio. For further details please refer to section 7.3.3.4.

FSANZ also sought information from submitters in the 2016 Consultation paper on whether there were any technical issues if the lower Codex minimum and maximum levels for copper were to be incorporated into the Code.

Stakeholder views

Five submitters (two government, three industry) commented on the permitted range for copper with four of the five submissions supporting alignment with Codex. One government submitter supported alignment with Codex STAN 72-1981 for powder formula only, citing the use of liquid, ready-to-use infant formula in hospitals and the assumption that this product would be manufactured to meet the standard and would not have the added copper contribution from Australian drinking water. Thus there would be a risk that these infants’ copper requirements would not be met. The submitter suggested that the higher minimum be retained for liquid, ready-to-use infant formula.

Nutrition risk assessment

No further nutrition risk assessment was considered on this issue.

The 2021 nutrition risk assessment noted that if the vitamin C maximum amount listed in Section S29—10 is increased then consideration should be given to the relationship between iron and ascorbic acid and its negative effect on copper metabolism. This consideration is further assessed in section 7.4.3.

Options and discussion

The 2021 composition survey based on label data did not include liquid, ready-to-use formula because these products are not available for retail sale in ANZ. FSANZ does not

have information on the types of infant formula (i.e. infant formula or IFPSDU) products being used in hospitals.

The Codex minimum level has been adopted in the Codex Draft Standard for FUF (FAO/WHO 2018). As noted in the 2016 nutrition risk assessment, the Codex minimum amount of 232 µg/L is within the reported range in breast milk from studies conducted in Japan and the United States (150–400 µg/L) (Casey 1995; Yamawaki et al. 2005; Lönnerdal 2008). Based on European studies, EFSA 2014 reported a higher range of copper in breast milk (329–390 µg/L) which is the basis for the EU 2016/127 minimum (14.3 µg/100 kJ).

Excluding the amount of copper contributed by potable water, the estimated intake of copper for infants 0-6 months consuming formula prepared from powder is 186 µg/day, which is within 10% of the ANZ AI (200 µg/day). It is assumed that this estimated intake would not be consistent across the whole feeding period.

FSANZ notes that copper deficiency is rare in humans except in pre-term infants. Pre-term products are highly specialised, generally available through neo-natal paediatrics and supplied where medically necessary. Provisions for micronutrients for these products would not be set within this division of Standard 2.9.1. Further considerations of IFPSDU will be provided in Consultation paper 3 of this series.

Proposed approach

Based on the arguments above, the permitted range for copper is proposed to be aligned with Codex STAN 72-1981 at 8.5–29 (GUL) µg/100 kJ. See section 7.1 for discussion on setting maximum levels as a GUL.

7.3: Permitted range where further information was sought

This section covers the permitted range of micronutrients that are not currently aligned with Codex STAN 72-1981, and the preliminary view from the 2016 Consultation paper was that the permitted range under Codex STAN 72-1981 may not be appropriate. FSANZ specifically sought comments from stakeholders on these nutrients, which included vitamin C, chromium, molybdenum, iodine, zinc, iron, and selenium.

7.3.6 Vitamin C (maximum)

Current regulations

The maximum vitamin C level is a GUL in both standards, however the GUL in Codex STAN 72-1981 is 17 mg/100 kJ, whereas the GUL in section S29—10 is much lower at 5.4 mg/100 kJ. EU 2016/127 sets a mandatory maximum vitamin C level of 7.2 mg/100kJ.

The higher Codex GUL takes into account possible high losses and includes a footnote stating “this GUL has been set to account for possible high losses over shelf-life in liquid formulas; for powdered products lower upper limits should be aimed for”.

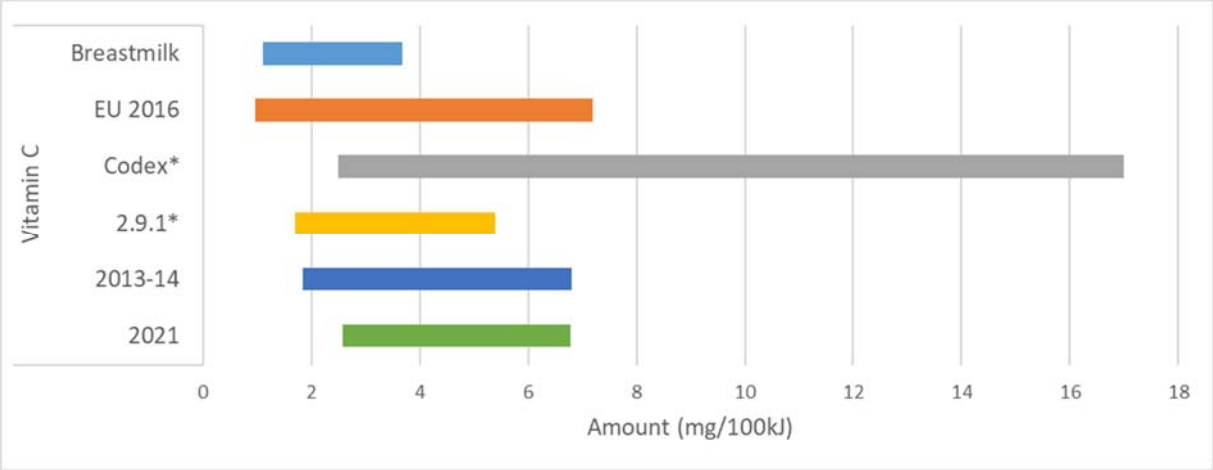


Figure 7.3.6 Comparison of the permitted ranges for vitamin C across standards (Standard 2.9.1, Codex STAN 72-1981 and EU 2016/127), human milk concentration, and the FSANZ survey of the content in products on the ANZ market (2013-14 and 2021).

Previous consideration

The 2016 nutrition risk assessment concluded that the increased maximum is unlikely to pose a risk to infant health.

FSANZ's 2013–2014 label survey indicated that the lowest reported vitamin C content in the sample was 1.8 mg/100 kJ, which is less than the Codex STAN 72-1981 minimum amount (2.5 mg/100 kJ). Therefore, if adopted, some manufacturers may need to adjust formulations to comply with the higher Codex minimum amount. The highest reported content was 6.8 mg/100 kJ. This survey mainly consisted of powdered products as few liquid products are available on the Australian and New Zealand market.

Vitamin C is chemically labile and is therefore prone to deterioration, which can create technological issues for manufacturing. Large losses may occur over shelf life since vitamin C degrades rapidly when exposed to air and water. Losses ranging from 30–75% have been reported in liquid products (MacLean et al. 2010). As few liquid products are available, further consideration is required on the need to align with the higher GUL amount (17 mg/100 kJ). Further information was sought to assist this consideration.

Stakeholder views

Eight submitters (three government, five industry) commented on the maximum amount for vitamin C. Most supported the higher Codex maximum with two government submitters opposing based on concerns about excess intakes. Industry noted that the higher level is set to account for high losses over the shelf life of liquid formula. Currently there are few retail liquid formulas as it is a product that is more commonly used in health care facilities. One submitter also commented that future innovation may increase the number of liquid ready-to-use products.

Nutrition risk assessment

Further nutrition risk assessment (SD1) considered the evidence base for maximum vitamin C amount determined in EU 2016/127. It was noted that the EFSA 2014 Opinion did not include an assessment of the maximum level of vitamin C. EU 2016/127 is likely to be based on the conclusions of the EC SCF (2003) and ESPGHAN (Koletzko et al. 2005) which estimated a maximum from the no observed adverse effect level for adult men and extrapolating to a body mass equivalent intake for infants. The nutrition risk assessment

concluded that the maximum amount of 7.2 mg/100 kJ as set in EU 2016/127 poses a low risk to infant health.

The 2021 nutrition risk assessment also noted that in setting a maximum amount for vitamin C, the maximum iron level and the normal physiologic concentrations of vitamin C should be considered in the context of copper metabolism. This consideration is further assessed in section 7.4.3.

Options and discussion

The Codex EWG review of the standard for FUF reviewed the evidence regarding vitamin C losses (see NZ MPI submission to the 2016 Consultation). They noted that during normal storage conditions significant losses in vitamin C can occur during the shelf life of products, ranging from 20 to 50% in powdered products and up to 75% in liquid products. The Codex EWG concluded that the GUL of 17 mg/100 kJ was appropriate to ensure minimum requirements are met regardless of deterioration.

Allowing for potential breakdown losses of 75%, 7.2 mg/100 kJ could be reduced over the shelf life of a liquid infant formula to 1.8 mg/100 kJ. Based on median energy intake (2725 kJ/L) and assuming consumption of 0.8 L/day, this amount translates to an intake of 39 mg/day. The NHMRC AI for vitamin C is 25 mg/day. Given that heat is also known to affect stability of vitamin C, it is possible that the level in infant formula could be further reduced during preparation.

Proposed approach

To ensure infants meet the minimum requirements for vitamin C, the proposed approach is to align with the maximum level set by Codex STAN 72-1981 (17 mg/100 kJ). This also allows for liquid formula products which are a small proportion of the ANZ market.

7.3.7 Chromium and molybdenum

Current regulations

Neither Codex or Schedule 29 set minimum amounts for chromium and molybdenum in infant formula. Schedule 29 sets GULs for both chromium and molybdenum at 2.0 µg/100 kJ and 3.0 µg/100 kJ, respectively. Codex STAN 72-1981 does not include a maximum or GUL for these minerals. EU 2016/127 specifies a maximum level for molybdenum at 3.3 µg/100 kJ and does not set levels for chromium (Table 7.8).

Under Division 4 (*Infant formula products for special dietary use*), Standard 2.9.1—15 (*Products for specific dietary use based on a protein substitute*) specifies that such infant formula products must contain chromium in an amount of no less than 0.35 µg/100 kJ and no more than 2.0 µg/100 kJ and molybdenum in an amount of no less than 0.36 µg/100 kJ and no more than 3.0 µg/100 kJ. Within Codex STAN 72-1981 *Section B Formula for Special Medical Purposes* chromium and molybdenum are prescribed at a range of 0.4 – 2.4 µg/100 kJ.

Table 7.8 Permitted ranges for chromium and molybdenum

Micronutrient	Product Type	The Code		Codex STAN 72-1981		EU 2016/127	
		Min	Max	Min	Max	Min	Max
Chromium (µg/100 kJ)	Infant formula	-	2.0*	-	-	-	-
	IFPSDU	≥ 0.35^	≤ 2.0^	0.4^^	2.4^^	-	-
Molybdenum (µg/100 kJ)	Infant formula	-	3.0*	-	-	-	3.3
	IFPSDU	≥ 0.36^	≤ 3.0^	0.4^^	2.4^^	-	-

**S29—10*
^2.9.1—15 Products for specific dietary use based on a protein substitute
^^ Codex STAN 72-1981, Section B Formula for Special Medical Purposes

Previous consideration

When Standard 2.9.1 was developed, the assessment concluded that there was no reliable biological or nutritional data to specify infant requirements or recommended intakes for chromium and molybdenum. Since then, AIs has been set for both younger (0–6 months) and older (7–12 months) infants (NHMRC and MoH 2006). Because no minimum amounts have been defined in either standard, the 2016 nutrition risk assessment did not assess the minimum intake to meet the AI amount.

The 2016 nutrition risk assessment also noted there is no Australian and New Zealand UL set for chromium or molybdenum, as there are no known adverse effects associated with high intakes of these minerals from food. Based on this the 2016 nutrition risk assessment concluded that removal of the guidance levels to align with Codex STAN 72-1982 was unlikely to impact on infant health.

Stakeholder views

The 2016 Consultation paper sought further information to consider whether there is a need to set a minimum requirement for chromium and molybdenum and to retain the current GULs. Four submitters (one government, three industry) commented on chromium and molybdenum. Industry submitters did not support a minimum, maximum, or GUL being set for chromium or molybdenum on the basis of insufficient evidence. The New Zealand government submission indicated that the 2016 New Zealand Total Diet Study (NZ TDS) included data on chromium and molybdenum levels in infant formula which could be used to estimate infant intakes.

The 2017 Consultation paper sought further information on the minimum and maximum amount of chromium and molybdenum prescribed in IFPSDU. Two submitters (one government, one health professional) provided comments. The government submission noted that a maximum value for chromium and molybdenum is difficult to manage due to natural variation in raw materials and recommended setting a maximum value that is large enough to avoid excessive technological constraints or if a maximum is unable to be established, it should be kept open in order to align with Europe or the United States. The health professional did not provide comments specific to chromium and molybdenum, however noted that there should be scientific rationale for any variations to the standard composition and that requirements should be guided by review of current literature and scientific opinion.

Nutrition risk assessment

No further nutrition risk assessment was considered on this issue.

Options and discussion

The 2016 Consultation paper estimated intakes of chromium and molybdenum from infant formula based on concentrations of these elements measured in the 22nd Australian Total Diet Study (ATDS). The theoretical infant diet estimated mean intakes for both chromium and molybdenum that were well above the AI. Results from the 2016 NZ TDS for chromium and molybdenum were below the limit of reporting and therefore not informative for comparison with the AI.

Currently no ULs are established for chromium and molybdenum in Australia and New Zealand, or in Europe or the United States as there are no known adverse effects associated with high intakes of chromium or molybdenum from food. Originally, the voluntary maximum was set as a precaution (ANZFA 1999a) however the EC SCF (2003) did not recommend setting maximum amounts. The 2016 nutrition risk assessment concluded that removing the voluntary maximum amounts for chromium and molybdenum from infant formula would be unlikely to pose a risk to infant health.

The range for chromium and molybdenum under section 2.9.1—15 for IFPSDU (products based on a protein substitute) were set to ensure minimum levels were achieved during the manufacture of IFPSDU. Infant formula does not require the addition of chromium and molybdenum as these levels are met through the base macronutrients levels prescribed in Standard 2.9.1. However, for purified or refined formulas, there is a need for the addition of chromium and molybdenum.

Proposed approach

Based on the above estimated intakes and the conclusions of the 2016 nutrition risk assessment, FSANZ proposes to align the permissions for chromium and molybdenum with Codex STAN 72-1981 by removing the current maximum level (GUL). FSANZ will retain the current permissions for chromium and molybdenum in IFPSDU under Standard 2.9.1—15. The regulation of IFPSDU will be further explored in the next Consultation paper.

7.3.8 Iodine (minimum, maximum)

Current regulations

The minimum iodine amount under Codex STAN 72-1981 is more than double the minimum specified in section S29—9. The use of the maximum iodine level as a GUL is discussed in Section 7.1. EU 2016/127 set a range for iodine of 3.6–6.9 µg/100 kJ (Table 7.9).

Table 7.9 Permitted range for iodine

Micronutrient	Standard 2.9.1		Codex STAN 72-1981		EU 2016/127		Content in products on the market
	Min	Max	Min	Max	Min	Max	
Iodine (µg/100 kJ)	1.2	10	2.5	14 (GUL)	3.6	6.9	2.19–8.42

Previous consideration

The 2016 nutrition risk assessment reported that estimated iodine intakes based on a minimum iodine level of 1.2 µg/100 kJ (Schedule 29) or 2.5 µg/100 kJ (Codex STAN 72-1981) do not meet the AI for younger or older infants. Raising the minimum iodine content may increase iodine intakes in formula-fed infants who would be then be more likely to meet the AI. However, it is also noted that studies in the period after mandatory iodine fortification suggest that Australian and New Zealand infants are not iodine deficient.

The 2016 nutrition risk assessment noted that there is no iodine UL for infants in ANZ, and concludes that a higher maximum of 14 µg/100 kJ would be unlikely to adversely pose a risk to infant health.

FSANZ's preliminary view was that alignment with the higher Codex minimum and GUL for iodine may be appropriate for Australian and New Zealand infants. We sought information on whether this is likely to require reformulation by manufacturers.

Stakeholder views

Eleven submitters (two government, eight industry, one health professional) commented on the permitted range for iodine. All submitters supported increasing the minimum level to at least the Codex STAN 72-1981 level and there was also support to increase the iodine minimum to align with EU 2016/127.

Additionally one submitter provided data of iodine content from a label survey of 40 infant formulas on the Australian market in 2010 (see below). The submitter requested further review of iodine levels in infant formula to ensure adequate iodine intakes.

Aligning the maximum level with Codex STAN 72-1981 was also supported by most submitters with one government submitter opposing alignment to the higher Codex amount, noting that the EU 2016/127 maximum (6.9 µg/100 kJ) is closer to the current maximum under the Code.

Nutrition risk assessment

The 2021 nutrition risk assessment concluded that the use of the EU 2016/127 minimum amount (3.6 µg/100 kJ) and maximum amount (6.9 µg/100 kJ) poses a low risk to infant health.

The nutrition risk assessment also considered a recent study by Huynh et al. (2017) which investigated the relationship between iodine status of lactating mothers and their infants following the mandatory iodine fortification of bread in Australia in 2009. The study concluded that the iodine status of lactating mothers and their infants in South Australia was sufficient after mandatory iodine fortification was introduced. The outcomes of this study address the concerns raised during consultation that formula-fed infants cannot obtain an adequate iodine intake under the current provisions in Standard 2.9.1/Schedule 29.

Options and discussion

Minimum

A submitter provided data of iodine content based on label information of 40 infant formulas on the market on 2010. These formulas had range of 4–12 µg/100 mL (1.5–4.4 µg/100 kJ) which was lower than that determined in FSANZ label surveys in 2013–2014 (2.1–5.9 µg/100 kJ) and 2021 (2.19–8.42 µg/100 kJ). The 2010 information suggested that formula-fed infants may not be meeting the AI for iodine. Indeed, estimated intakes (using the midpoint of the Codex energy range of 2725 kJ/L) based on the 2010 products would not meet the NHMRC AI for iodine. Comparing the 2010 information with surveys undertaken by FSANZ in 2013–2014 and 2021 suggests industry re-formulation has occurred (Figure 7.3.3.3).

The 2017 Huynh et al. study examined in the nutrition risk assessment supports increasing the iodine minimum to 3.7 µg/100 kJ. This is based on observed breast milk iodine

concentrations of 100 µg/L, which maintains iodine sufficiency in most infants, and the mean energy content of human milk is 2720 kJ/L (Nommsen et al. 1991). Estimated intakes based on this minimum would meet the ANZ AI and it is aligned with EU 2016/127 (derived from an observed mean content in human milk of 0.13 mg/L, with an intake of 0.8 L/day).

The 2016 NZTDS showed dietary iodine intake for infants was 76% of the AI, of which infant formula contributed 72%.

Maximum

The permitted range under EU 2016/127 is narrower than that specified in section S29—9 and Codex STAN 72-1981 and is the most consistent with human milk concentrations (Figure 7.3.8). The conclusion of the 2016 Consultation paper was that there were no safety concerns with the higher Codex maximum as there is no ANZ UL. However there was also no clear explanation for the much higher amount. The permitted range under the Codex Draft Standard for FUF aligns with the current Codex STAN 72-1981 (2.4–14.0 (GUL) µg/100 kJ).

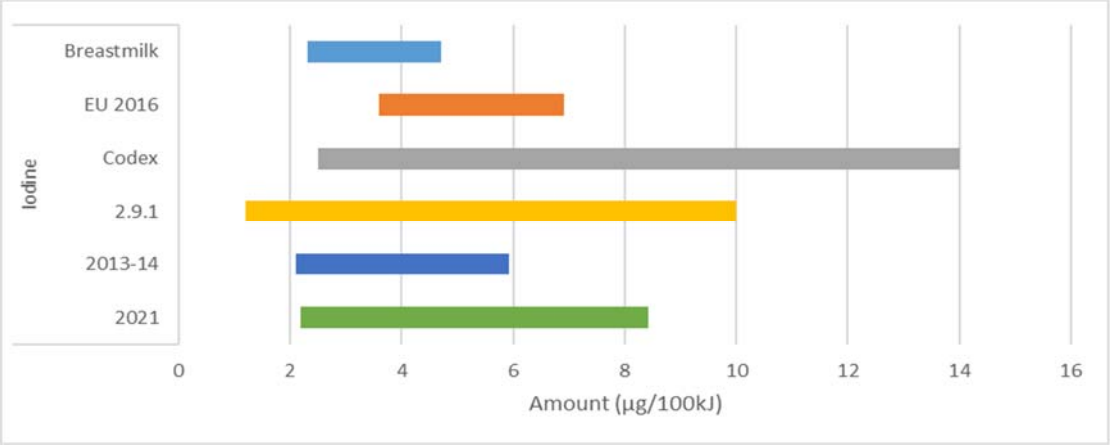


Figure 7.3.8 Comparison of the permitted ranges for iodine in Standard 2.9.1, Codex STAN 72-1981 and EU 2016/127, human milk concentration, and the survey of the content in products on the ANZ market.

Proposed approach

To ensure infants meet their requirements for iodine, the proposed approach is to align the minimum amount with EU 2016/127 (3.6 µg/100 kJ). FSANZ proposes to retain the existing section S29—9 maximum as this amount is comparable to expert recommendations and is an amount that manufacturers are able to meet already.

7.3.9 Zinc and Zn:Cu ratio

Current regulations

Standard 2.9.1, Codex STAN 72-1981 and EU 2016/127 are aligned for the minimum amount of zinc. Standard 2.9.1 has a higher maximum amount than the GUL in Codex STAN 72-1981 and the maximum in EU 2016/127. Standard 2.9.1 also prescribes a maximum ratio of zinc to copper (Zn:Cu) of 15:1, whereas Codex STAN 72-1981 and EU 2016/127 do not specify a ratio (Table 7.10).

Table 7.10 Permitted range for zinc

Micronutrient	Standard 2.9.1 (Section 29—9)		Codex STAN 72-1981		EU 2016/127		Content in products on the market
	Min	Max	Min	Max	Min	Max	
Zinc (mg/100 kJ)	0.12	0.43	0.12	0.36 (GUL)	0.12	0.24	0.15–0.29
					0.18*	0.30*	

** Infant formula manufactured from soya protein isolates, alone or in a mixture with cow's milk or goat's milk proteins*

Previous consideration

The 2016 nutrition risk assessment concluded that despite both the maximum in Schedule 29 and the lower GUL in Codex STAN 72-1981 potentially contributing to intakes exceeding the UL, there is no evidence of risk to infant health as the UL is overly conservative (FSANZ 2011). FSANZ considered alignment with the Codex GUL would be unlikely to pose a risk to infant health.

The 2016 nutrition risk assessment also noted limited evidence to support the need for a Zn:Cu ratio in formula and concluded that deleting the Zn:Cu ratio from Standard 2.9.1 would have minimal impact on micronutrient status of healthy term infants.

The assessment also considered that setting minimum amounts for certain minerals in soy-based formula should consider the phytic acid content of soy proteins and the potential for reduced availability of minerals. Literature reports suggest it is technologically possible to remove phytic acid from soy-based formula and noted that studies show reduction of phytic acid content by 50-100% in ready-to-feed formula improves zinc absorption (EFSA 2014b).

FSANZ sought further information from submitters to inform the appropriate amount of zinc, the Zn:Cu ratio and phytic acid content, particularly in light of the composition of soy-based formula.

The higher maximum amount in section S29—9 allowed for lower absorption of zinc from soy-based formula due to the presence of phytates, which can bind with zinc. The Zn:Cu ratio was included to manage the potential impact of zinc intakes on copper bioavailability (ANZFA 1999b). In 2005, the draft Codex GUL was reduced from the previous (2003) level on the basis that high intakes of zinc may interfere with the absorption and metabolism of other micronutrients, such as copper. At the time of gazettal of Standard 2.9.1, the Zn:Cu ratio was a new concept in infant nutrition and was considered a separate issue from the minimum and maximum limits of zinc and copper (ANZFA 2002). A cautious approach was taken and the ratio was included in the standard for several reasons:

- the Zn:Cu ratio of breast milk is 10:1 but there were no studies in infants to indicate the appropriate or optimal Zn:Cu ratio for formula
- infants have immature systems (absorption, metabolism, excretion) and are therefore considered a more vulnerable population
- when infant formula is the sole source of nutrition, infants are at a stage of development characterised by intense growth (which may make infants more vulnerable to factors such as copper deficiency)
- data on adverse effects are limited.

Stakeholder views

Five submitters (two government, three industry) commented on the permitted range for zinc and the need for a prescribed Zn:Cu ratio. Retaining the prescribed Zn:Cu ratio was not supported. Views on the maximum level were varied. Use of the Codex maximum was supported by three submitters who provided evidence indicating that the UL was inappropriately low, and that both Standard 2.9.1 and Codex maximum should accommodate higher levels of zinc in soy-based formula. One submitter supported retaining the current maximum (no rationale provided) and one supported aligning the zinc maximum with EU 2016/127 since this level would be closest to the ANZ UL. In the latter case, a separate, higher zinc maximum would be needed to allow higher levels of zinc in soy-based formula.

Four submitters (two government, two industry) commented on phytic acid content in soy-based formula. One government submitter noted support for setting separate limits for zinc in soy-based infant formula to align within EU 2016/127. An industry submitter noted that even though there may be less efficient zinc absorption from soy protein isolate formulas, higher levels of zinc intake could impact on the absorption of copper. The industry submitter recommended that a separate upper level of zinc for soy-based formula may not be ideal, however proposed an upper level for zinc for all formulas should account for any additional needs of soy-based formula. Two submitters provided a Systematic Review with Meta-Analysis (Vandenplas, 2014) that noted that soy protein isolate contains 1–2% of phytates and found feeding soy-based infant formula to young infants did not result in any negative impact on the levels of certain minerals including zinc and calcium nor on overall growth.

Nutrition risk assessment

The 2021 nutrition risk assessment considered range specified for zinc in EU 2016/127. Use of the EU 2016/127 minimum amount of 0.12 mg/100 kJ (for infant formula manufactured from cow's milk or goat's milk proteins or protein hydrolysates) is the same as the current value in the Code. The EU 2016/127 minimum amount of 0.18 mg/100 kJ (for infant formula manufactured from soya protein isolates, alone or in a mixture with cow's milk or goat's milk proteins) is higher than the Code value of 0.12 mg/100 kJ. Adoption of the EU 2016/127 minimum amounts will not result in any additional risk to infant health.

Use of the EU 2016/127 maximum amounts of 0.24 mg/100 kJ (for infant formula manufactured from cow's milk or goat's milk proteins or protein hydrolysates) and 0.3 mg/100 kJ (for infant formula manufactured from soya protein isolates, alone or in a mixture with cow's milk or goat's milk proteins) poses a low risk to infant health.

Options and discussion

FSANZ notes that EU 2016/127 was based on the 2014 EFSA Scientific Opinion which did not include a safety assessment of the maximum levels. The maximum level prescribed in EU 2016/127 is based on levels contained in formulas on the European market, not on safety considerations. FSANZ also reiterates the view of the 2016 Consultation paper which found that the potential exceedance of the UL based on the Codex maximum at the midpoint of energy content was unlikely to pose a risk to infant health.

FSANZ's 2021 label survey suggests that zinc content lies within the Codex permitted range, as all products were all below the Codex GUL (Figure 7.3.9). Other label information indicates that soy-based formula products contain higher amounts of zinc than standard formula.

EU 2016/127 provides separate zinc requirements for cow's milk- and soy-based formula, for which the minimum amount is 0.12 mg/100 kJ and 0.18 mg/100 kJ, respectively; These match the amounts recommended by EFSA (2014b). The EFSA (2014b) recommendation for soy-based formula (0.18 mg/100 kJ) maps to the level proposed by the EC SCF (2003). EFSA (2014b) cites evidence published between 1984 and 2004 that phytic acid reduces zinc absorption efficiency and states this as the reason for setting a higher minimum level for soy-based formula than cow's milk-based formula.

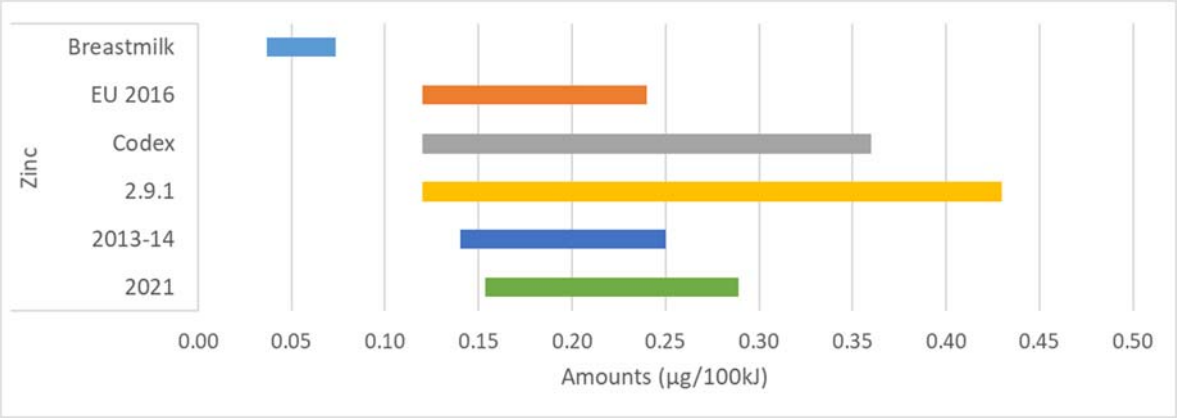


Figure 7.3.9 Comparison of the permitted ranges for zinc in Standard 2.9.1, Codex STAN 72-1981 and EU 2016/127, human milk concentration, and the survey of the content in products on the ANZ market.

Proposed approach

Based on the conclusions of the nutrition risk assessment, FSANZ proposes to align the permitted range with Codex STAN 1972-81 which includes a maximum that accommodates the higher concentration of zinc in soy-based formula. FSANZ also proposes that the prescribed Zn:Cu ratio be removed.

7.3.10 Iron (minimum, maximum)

Current regulations

The permitted range for iron varies across different standards and regulations (Table 7.11). Different ranges are set depending on infant age group and soy-based formulas. In more recently reviewed standards (EU 2016/127 and the Codex Draft Standard for FUF), minimum and maximum iron amounts are higher for formulas for older infants (6-12 months) and those based on soy protein.

Previous consideration

The 2016 nutrition risk assessment concluded that formula-fed infants have a lower risk of iron deficiency or iron deficiency anaemia (IDA) than breastfed infants but there is evidence of inadequate iron status in some population groups of older infants. The nutrition risk assessment concluded that lowering the minimum to the Codex STAN 72-1981 could pose a risk to infant health as the Codex STAN 72-1981 minimum is substantially lower than Standard 2.9.1.

No maximum level for iron is specified in Codex STAN 72-1981 but it is restricted through individual national authorities setting their own maximum. The current maximum specified by Standard 2.9.1 was considered to be unlikely to pose a risk to infant health since estimated intakes were below the NHMRC UL for iron.

FSANZ's 2013–14 and 2021 label survey of infant formula found the iron content of all formula was within both the Codex and Standard 2.9.1 provisions.

The preliminary view in 2016 was to retain current permitted range for iron. Because of uncertainty around iron requirements for isolated soy protein (ISP)-based formula, further information was requested from submitters on whether the current permitted range of iron should be retained.

Table 7.11 Permitted range for iron

Type of formula		Standard 2.9.1		Codex STAN 72-1981		EU 2016/127*		Range of average content in products on the market^
		Min	Max	Min	Max	Min	Max	
Cow's milk	Infant formula	0.2	0.5	0.1	N.S.**	0.07	0.31	0.20–0.44
	FOF***	0.2	0.5	0.24	0.48	0.14	0.48	
Soy-based	Infant formula	No values set		No values set		0.11	0.48	0.29–0.39
	FOF***	No values set		0.36	0.6	0.22	0.60	

N.S.: Not stated
** EU 2016/127 requirements for cow's milk are the same for goat's milk and protein hydrolysates*
*** Levels to be determined by national authorities.*
**** Formula for older infants 6-12 months. The specifications for FOF under Standard 2.9.1 are not in the scope of P1028. These values are shown with the Codex standard for this age group (Codex Draft Standard for FUF 2020) for comparison only.*
^ The survey only included infant formulas, no FUF was included.

Stakeholder views

Eight submitters (three government, five industry) provided comments on the permitted range for iron. There were mixed views on the permitted range which were not aligned by sector (Table 7.12). Four submitters (three industry, one government) supported FSANZ's 2016 view to retain the range currently specified in Standard 2.9.1. There was also support to adopt the Codex and EU 2016/127.

Table 7.12 Submitter comments on the permitted range for iron

Comment	Raised by	FSANZ response
Adopt Codex minimum; increase bioavailability by choosing appropriate forms of iron, reducing phytate content and/or adding absorption enhancers such as ascorbic acid.	Industry (1)	Permitted forms are considered in Section 7.5. FSANZ has not assessed methods to reduce phytate which would be out of scope for this consultation paper; any agents to reduce phytate content would require pre-market approval. FSANZ notes the proposed approach for ascorbic acid is to adopt the higher maximum set in Codex STAN 72-1981 (see Section 7.4.)
Adopt Codex range for international consistency citing ESPGHAN (2005) which reported a study where iron status was the same for infants fed formulas containing 0.06–0.24 mg/100 kJ.	Industry (1)	Noted. We commented on ESPGHAN 2005 in the 2016 Consultation paper: *ESPGHAN (Koletzko et al. 2005) … also reported on relatively new evidence that iron absorption from formula is comparable to breast milk and potential risks linked to excess iron. Although the evidence showed that adverse effects (lower length gain, higher prevalence of diarrhoea and upper*

		respiratory tract infection) were only associated with supplemental iron and not iron-fortified infant formula, ESPGHAN concluded that iron content should be kept as low as possible as long as iron deficiency is prevented.
Adopt Codex range with supporting evidence cited, including advice that breast milk is the primary reference. There was a question of whether iron deficiency is a widespread issue for ANZ infants and if so, whether a full review was required. Supports adopting EU 2016/127 maximum based on personal communication with EFSA that the value is based on the upper range of iron found in European formulas.	Government (2)	The 2016 nutrition risk assessment considered evidence across several criteria including breast milk concentration and evidence of nutrient deficiency. We reported on three studies indicating ANZ infants could be at risk of iron deficiency or IDA but these were based on breastfed and formula-fed infants collectively. In light of these studies, and the remaining questions on iron bioavailability from infant formulas, FSANZ notes its conclusion from the 2021 nutrition risk assessment that reducing the minimum iron level to the Codex level would increase the potential risk of iron deficiency or IDA for older infants.
Retain current minimum and maximum to allow wider range for IFPSDU.	Industry (2)	FSANZ assumes this refers to retaining current maximum which is higher than EU 2016/127, noting that the Codex minimum would allow a broader range.
Cautions about too much iron intake citing study showing poorer developmental outcomes in infants consuming high-iron infant formula.	Industry (1), Government (1)	The 2016 nutrition risk assessment determined that it was not appropriate to adopt a GUL for iron. Since that time, EU 2016/127 set a specified maximum of 0.3 mg/100 kJ which is consistent with that view. See Section 7.1 for further discussion.
Seeks clarification on statement from 2016 nutrition risk assessment that there is no international consensus on the minimum amount of iron in infant formula. Also cites minor error where the 2016 nutrition risk assessment implied that EFSA had suggested that ¾ of iron requirements should be met by complementary foods. Considers separate minimum and maximum limits for formulas based on isolated soy protein not required.	Government (2)	There is no regulatory alignment internationally on the permitted range for iron (see above – *"Current regulations"*). International recommendations are consistent with EC SCF (2003), ESPGHAN (2005) and EFSA (2014b) with all recommending a minimum content of 0.07 mg/100 kJ for cow's milk formulas and 0.11 mg/100 kJ for soy-based formulas. Regarding the amount of iron met by complementary foods in older infants, EFSA 2014 reported the following: *Based on the consideration that around 70 % of daily iron (equivalent to 5.7 mg iron per day) could be supplied by complementary foods, a minimum content of iron in FOF of 0.6 mg/100 kcal is proposed*, in line with the SCF (2003b).* * 0.14 mg/100 kJ.

Nutrition risk assessment

Further nutrition risk assessment (SD1) considered the iron concentrations in human milk, scientific basis for EU 2016/127, how these compare to EFSA 2014 recommendations (EFSA 2014b) and the FSANZ 2016 proposed range.

The 2021 nutrition risk assessment concluded that if infant formula for sale in ANZ is to meet the needs of both 0–<6 month and 6–<12 month infants, the minimum amount in Schedule 29–9 (0.2 mg/100 kJ) is preferred to the EU 2016/127 levels (0.07 mg/100 kJ for infant

formula manufactured from cow's milk or goat's milk proteins or protein hydrolysates; 0.11 mg/100 kJ for infant formula manufactured from soy protein isolates, alone or in a mixture with cow's milk or goat's milk proteins).

Use of EU 2016/127 maximum amounts of 0.31 mg/100 kJ (for infant formula manufactured from cow's milk or goat's milk proteins or protein hydrolysates) and 0.48 mg/100 kJ (for infant formula manufactured from soy protein isolates, alone or in a mixture with cow's milk or goat's milk proteins) poses a low risk to infant health.

Options and discussion

ANZ product market

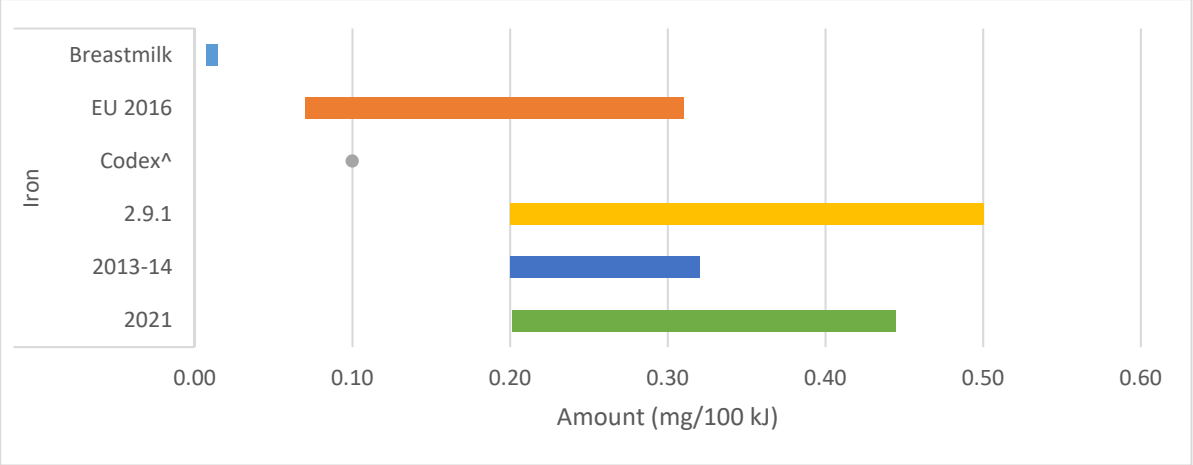
FSANZ's 2021 label survey of infant formula concluded similar findings to that of the 2013–2014 label survey. Iron content of all infant formula ranged between 0.20 and 0.44 mg/100 kJ, which was within both the Codex and Standard 2.9.1 provisions. The main difference was that products surveyed in 2021 had a higher maximum level of iron. This higher maximum is still lower than the prescribed maximums of Standard 2.9.1 and Codex STAN 72-1981, however does not align with the EU 2016/127 maximum. Figure 7.3.3.4 displays the misalignment of products in the 2021 label survey with EU 2016/127, which would have a potential impact on the ANZ market. Of the products surveyed that were manufactured in Australia, iron was noted to have the least overlap with EU 2016/127 compared with other micronutrients reviewed.

Moreover, further alignment could be achieved between EU 2016/127 and the ANZ market/Standard 2.9.1 by adopting the EU or Codex minimum. However, as addressed in the nutrition risk assessment, the lower minimum level has the potential to pose risk to the health of older infants. This was concluded in both 2016 and 2021 nutrition assessments.

FSANZ's 2021 label survey assessed 71 infant formula products, of which two were soy-based. Iron content of the soy-based formulas was 0.29 mg/100 kJ and 0.39 mg/100 kJ (Figure 7.3.10).

Breast milk

Most research shows that iron is better absorbed from human milk than from infant formulas (Lönnerdal et al. 2015). The iron in infant formula is reported to be less bioavailable than that in human milk, in the order of 10–20% (NHMRC and MoH 2006) or 7–14% (EFSA 2014b). The 2021 nutrition risk assessment compared the current minimum amount in Standard 2.9.1 to the levels in human milk. The Code's minimum amount (0.2 mg/100 kJ) would equate to an estimated absorbed iron of 0.02 mg/100 kJ from cow's milk-based formula and 0.014 mg/100 kJ from soy-based formula. The estimated iron absorbed from infant formula when using the Code's minimum level would be almost double that from human milk (0.012–0.013 mg/100 kJ).



^ *Codex specifies a minimum concentration of 0.1mg/100kJ for iron and does not specify a maximum permitted concentration.*

Figure 7.3.10 Comparison of the permitted ranges for iron in Standard 2.9.1, Codex STAN 72-1981 and EU 2016/127, human milk concentration, and the survey of the content in products on the ANZ market.

Soy-based infant formula

Iron in soy-based formula is considered to have lower bioavailability than human milk and cow's milk-based formula, due to soy protein isolate containing 1–2% phytate which inhibits intestinal iron absorption (Agostoni et al. 2006). Independent of phytate, soy protein itself may also be an inhibitor, with phytate-free soy protein isolates also reported to inhibit non-haem iron absorption (Hurrell et al. 1992). FSANZ understands that processing methods already reduce phytate content in soy-based formulas, which diminishes the need to prescribe phytate restrictions or set separate iron levels for soy-based formulas.

Infant formula for older infants

Standard 2.9.1 applies to formula for infants aged 0–12 months. Formula for older infants (6–12 months) is included in 2.9.1. However, the Codex Draft Standard for FUF specifically focuses on the older infants group, which is why the iron requirements are higher (0.24–0.48 mg/100 kJ for cow's milk and 0.36–0.6 mg/100 kJ for soy-based products). Due to the difference in target population group there is no need for alignment with the Codex Draft Standard for FUF, however FSANZ does acknowledge the increased iron needs of older infants. FSANZ also notes that there are additional recommendations to ensure adequate iron intakes in older infants in the Australian and New Zealand Infant feeding guidelines (NHMRC 2013; MoH 2008).

FSANZ is also proposing to increase the current vitamin C levels (ascorbic acid) within Standard 2.9.1 (see section 7.3.3.1). This aligns with industry recommendations to add absorption enhancers.

Proposed approach

The adequacy NRV for iron is an AI for younger infants (0–6 months) whereas an Estimated Average Requirement (EAR) is established for older infants (7–12 months). New Zealand infants with intakes below the EAR had an increased risk of iron deficiency compared to those with intakes meeting or exceeding the EAR, thus FSANZ considers that use of the lower Codex minimum could potentially pose a risk to infant health although the extent of risk is uncertain.

Based on the above considerations and conclusions from the 2016 and 2021 nutrition risk assessments, FSANZ proposes to retain the current minimum and maximum specified in section S29—9. Retaining the broader permitted range in standard S29—9 accounts for older infants and soy-based infant formula and aligns with the current ANZ market. Retaining the current standard also allows manufacturers to meet the Codex and EU ranges for iron, while still posing the least risk to infant health.

FSANZ is seeking further information from submitters on setting separate maximum iron levels for soy-based infant formula. Please see section 9 for further details.

7.3.11 Selenium

Current regulations

The minimum level for selenium in Standard 2.9.1 and Codex STAN 72-1981 are aligned, however the maximums differ (Table 7.13). EU 2016/127 set a permitted range for selenium of 0.72 to 2 µg/100 kJ.

Table 7.13 Permitted range for selenium

Micronutrient	Standard 2.9.1 (Section S29—9)	Codex STAN 72-1981	EU 2016/127	US FDA Final Rule (2015)	Draft Codex FUF (2020)
Selenium (µg/100 kJ)	0.25 – 1.19	0.24 – 2.2 (GUL)	0.72 – 2.0	0.48 – 1.70	0.48 – 2.2 (GUL)

Previous consideration

In 2016 FSANZ considered that increasing the minimum requirement for selenium in Standard 2.9.1 may be appropriate for the Australian and New Zealand context based on the following factors:

- The selenium content of soil varies between geographical locations including ANZ and this influences selenium content in food and crops (FSANZ, 2008).
- The 2016 nutrition risk assessment noted studies indicating lower breast milk selenium concentrations in Australian and New Zealand mothers, compared to other populations. Research has also reported a lower selenium status of Australian infants relative to other international studies, although this has not been associated with any clinical or adverse health outcomes.
- Estimated selenium intakes based on the current minimum infant formula requirements do not meet the Australian and New Zealand AI, thus could pose a risk to infant health. The assessment noted recent studies indicating the minimum should be increased.
- The nutrition risk assessment further noted that Codex STAN 72-1981 requires nearly double the maximum amount of Standard 2.9.1 and also sets it as a GUL (discussed in Section 7.1).
- FSANZ's 2013–2014 label survey indicated the product with the lowest selenium content contained 0.43 µg/100 kJ and 0.29 µg/100 kJ in the New Zealand and Australian samples respectively.

The FSANZ 2016 assessment concluded that adopting the Codex STAN 72-1981 minimum and maximum could pose a risk to infant health. Further information was sought from submitters to help inform the future proposal.

Stakeholder views

FSANZ asked whether submitters supported raising the minimum and maximum level of selenium and to provide a rationale for their response. Eight submitters (three government, five industry) commented on the permitted range for selenium (Table 7.14).

Table 7.14 Submitter comments on the permitted range for selenium

Comment	Raised by	FSANZ response
Support retaining Standard 2.9.1 minimum mainly based on argument that manufacturers already target a higher amount than the existing minimum (as confirmed by FSANZ 2013–2014 label survey).	Industry (5)	To be more consistent with human milk concentrations in the ANZ population, the minimum level should be increased. FSANZ also notes that the existing minimum is inconsistent with all recently revised regulations (see Table 7.3.3.6.1). FSANZ 2021 label survey supported the industry position with the range determined to be 0.43 – 1.14 µg/100 kJ.
Support increase in minimum and maximum based on breast milk concentrations from selenium-replete population and on arguments presented in the 2016 nutrition risk assessment.	Government (3)	Noted. FSANZ reiterates that the selenium status of ANZ is lower than other selenium sufficient countries. Selenium content of human milk is dependent on maternal diet and not necessarily reflective of infant requirements (see CCNFSDU 2nd Consultation Paper 2015 pg 60).
Support other public health initiatives to address selenium deficiency in Australian and New Zealand populations.	Government (2)	This is outside FSANZ's remit and out of scope for this proposal.
Supports maximum level that will not achieve intakes that are greater than the UL.	Government (2)	FSANZ noted in the 2016 nutrition risk assessment that estimated intakes based on the Codex STAN 72-1981 maximum (GUL) could exceed the ANZ UL but there was no evidence of excess intakes or associated adverse health effects. If the minimum is raised to meet infant requirements, adopting the Codex GUL means the new range would be comparable to the current range in Standard 2.9.1.

Nutrition risk assessment

The 2021 nutrition risk assessment (SD1) considered that use of the EU 2016/127 minimum amount (0.72 µg/100 kJ) and maximum amount (2.0 µg/100 kJ) poses a low risk infant health.

The 2021 assessment also reviewed recent evidence on human milk selenium concentrations in the ANZ population. The studies indicated that (1) infant formula should contain at least the same amount of selenium as human milk from that geographical area (Daniels 2008) and that (2) human milk selenium concentrations in ANZ ranged between 0.4 and 0.5 µg/100 kJ. The ANZ concentrations are lower than concentrations measured in North America and Europe which had a range of 0.55–0.66 µg/100 kJ. The assessment also found that selenium concentrations in human milk are influenced by maternal dietary intake and can differ based on the soil selenium levels of that region.

Options and discussion

The 2016 New Zealand Total Diet Study (NZTDS) was published in 2018 which is after FSANZ's 2016 consideration of the permitted range for selenium. The NZTDS reported that

selenium intakes were meeting the nutritional requirements for selenium in the NZ population. The NZTDS noted that for infants the key dietary source of selenium was infant formula products (Ministry for Primary Industries 2016). The NZTDS showed that infants did not have estimated mean dietary intakes close to the UL for selenium, indicating that the risk of selenium toxicity is highly unlikely.

The lower selenium content in ANZ human milk are consistent with that reported in the US FDA 2015 Final Rule, which prescribed a minimum selenium of 0.48 µg/100 kJ. This minimum is also more consistent with the minimum amounts seen in FSANZ's 2021 label survey (0.43–1.14 µg/100 kJ). Adopting the minimum amount specified in US FDA 2015 Final Rule is likely to require a small percentage of products to be reformulated.

In the Codex Draft Standard for FUF, the CCNFSDU has proposed the minimum amount for selenium to be 0.48 µg/100 kJ (FAO/WHO 2018).

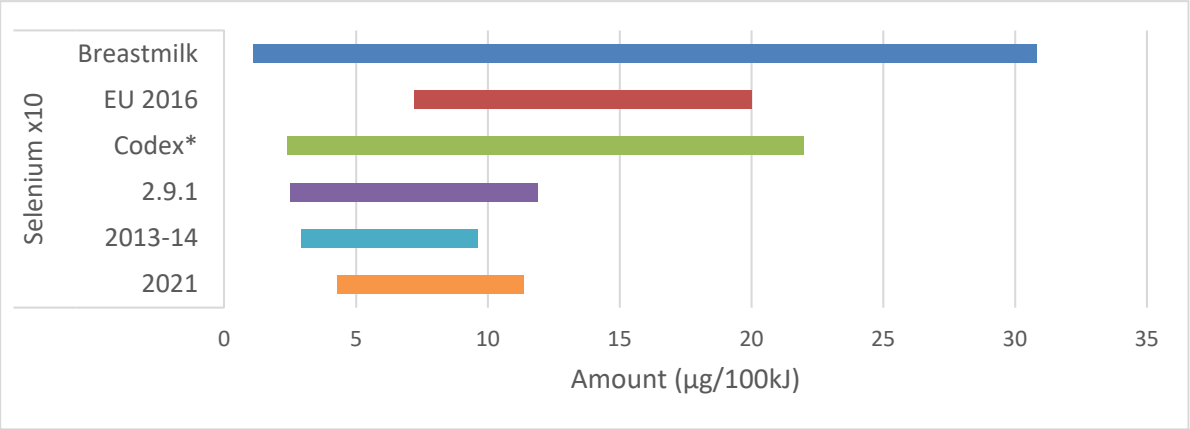


Figure 7.3.11 Comparison of the permitted ranges for selenium in Standard 2.9.1, Codex STAN 72-1981 and EU 2016/127, human milk concentration, and the survey of the content in products on the ANZ market.

Proposed approach

Based on the most recent information on selenium status of ANZ infants, FSANZ proposes to increase the minimum to 0.48 µg/100 kJ. This level is consistent with recent international regulations, would meet the ANZ AI, and is slightly higher than breast milk concentrations of ANZ mothers, a population that may not be selenium sufficient.

FSANZ proposes to also increase the maximum level to 2.0 µg/100 kJ which would align with EU 2016/127 and is comparable to the Codex STAN 72-1981 maximum. This amount would result in estimated intakes that do not exceed UL. The proposed permitted range (0.48 – 2.0 µg/100 kJ) is broader than the current range in the Code and is more aligned with international regulations which should minimise the amount of reformulation that would be required by manufacturers. Consideration on the proposed approach regarding the GUL status of the selenium maximum is discussed in section 7.1.

7.4 Other ratios, equivalents and nutrient interactions

7.4.1 Phosphorus and the calcium: phosphorus (Ca:P) ratio

Table 7.15 Regulatory requirements for calcium, phosphorus and the Ca:P ratio

Micronutrient (unit)	Standard 2.9.1 (Schedule 29)		Codex STAN 72-1981		EU 2016/127	
	Min	Max	Min	Max	Min	Max
Calcium (mg/100 kJ)	12	33 (GUL)	12	35 (GUL)	12	33.5
Phosphorus (mg/100 kJ)	6	25	6	24 (GUL)	6*	21.5*
					7.2^	24^
Ca:P ratio	1.2 : 1	2 : 1	1 : 1	2 : 1	>1	<2

** Infant formula manufactured from cow's milk or goat's milk proteins or protein hydrolysates*
^ Infant formula manufactured from soya protein isolates, alone or in a mixture with cow's milk or goat's milk proteins

Current regulations

Standard 2.9.1, Codex STAN 72-1981 and EU 2016/127 are generally aligned for the minimum and maximum amounts of calcium and phosphorus (Table 7.15). EU 2016/127 notes that the Ca:P ratio should not be less than 1 or greater than 2 and the amount of available phosphorus should be calculated as 70% of total phosphorus for infant formula manufactured from soya protein isolates and 80% of total phosphorous for infant formula manufactured from cow's milk protein, goat's milk protein or protein hydrolysates.

Previous consideration

In 2016 FSANZ considered it appropriate to change the current phosphorus maximum (25 mg/100 kJ) specified in section S29—9 to a GUL of 24 mg/100 kJ in alignment with Codex. FSANZ also proposed to adjust Standard 2.9.1 to align with the minimum Ca:P ratio of 1:1 as the nutrition risk assessment indicates that such a change would be unlikely to pose a risk to infant health, and the shift required to align is small.

Stakeholder views

Six submitters (three government, three industry) commented on the permitted range for phosphorus and the prescribed Ca:P ratio (Table 7.16). All submitters supported FSANZ's proposal to adjust Standard 2.9.1 to align with the minimum Ca:P ratio prescribed by Codex STAN 72-1981 of 1:1.

Table 7.16 Submitter comments on phosphorus maximum and phosphorus levels in soy-based infant formula

Comment	Submitter	FSANZ response
Phosphorus Maximum		
Adopt GUL of 24 mg/100 kJ. As it is not possible to establish an UL a GUL is most appropriate and allows alignment with Codex.	Industry (3)	Noted. FSANZ reiterates that proposed approach in 2016 was to change the current phosphorus maximum (25 mg/100 kJ) in Schedule 29 to a GUL of 24 mg/100 kJ in alignment with Codex.
Cautions about amending the maximum to a GUL, based on evidence of hypocalcaemia in neonates fed	Government (2)	The 2016 nutrition risk assessment considered research investigating hypocalcaemia in neonates fed infant

infant formula and ULs derived by the NHMRC/MoH for young children suggest that excessive intakes should be avoided as a precautionary approach for this age group. A government submitter suggested a review of the literature may further inform this issue.		formula which concluded that in several clinical reports of formula-fed early neonates (<14 days) the hypocalcaemia was considered to be associated with vitamin D deficiency resulting from low maternal vitamin D status. Two recent studies also support this conclusion.
Phosphorus levels in soy-based infant formula		
Support setting separate minimum and maximum phosphorus levels in soy-based infant formula in line with EU 2016/127.	Government (2)	FSANZ is seeking further information from industry submitters on this issue to inform future considerations.

Nutrition risk assessment

No further nutrition risk assessment was considered on this issue.

Options and discussion

The 2016 nutrition risk assessment considered research investigating hypocalcaemia in neonates fed infant formula. The assessment concluded that in several clinical reports of formula-fed early neonates (<14 days) the hypocalcaemia was considered to be associated with vitamin D deficiency resulting from low maternal vitamin D status (Thomas et al. 2012; Do et al. 2014; Cho et al. 2015). There was also no recent evidence indicating that older infants (>14 days) consuming infant formula develop hypercalcemia due to excess phosphorus intakes. Both government submitters that did not support FSANZ's pervious consideration to permit phosphorus at a GUL of 24 mg/100 kJ referenced the Cho et al study (2015) to support their concerns surrounding hypocalcaemia in formula-fed neonates.

No further nutrition risk assessment was done for this issue, however two studies have recently been published regarding hypocalcaemia in formula fed neonates. The studies published in 2015 and 2020 were consistent with the conclusions of the 2016 nutrition risk assessment noting the incidence of hypocalcaemia in formula-fed infants was associated with vitamin D deficiency (Qureshi et al. 2020; Jo et al. 2015). Therefore FSANZ reiterates the conclusions of the 2016 nutrition risk assessment, noting there is no recent literature to suggest otherwise, that the incidence of hypocalcaemia in neonates fed infant formula is associated with vitamin D deficiency not phosphorus levels in infant formula and therefore aligning with the Codex STAN 72-1981 voluntary maximum is unlikely to pose a risk to infant health.

Two government submitters noted support for setting a separate minimum and maximum level for phosphorus in soy-based infant formula in line with the approach of EU 2016/127. EU 2016/127 has set separate ranges for infant formula manufactured from soya protein isolates, alone or in a mixture with cow's or goat's milk proteins and infant formula manufactured from cow's or goat's milk protein or protein hydrolysates. Despite the separation both ranges are comparable and do not differ greatly, with phosphorus in soy-based infant formulas ranging between 7.2 and 24 mg/100 kJ and cow's or goat's milk-based infant formulas ranging between 6.0 and 21.5 mg/100 kJ. This approach was also not noted in any industry submissions. Codex STAN 72-1981 lists a GUL rather than a maximum amount to accommodate for higher phosphorus levels in isolated soy protein formula. The Codex Standard for Follow-Up Formula CXS 156-1987 prescribes a minimum phosphorus level of 14 mg/100 kJ, which applies to both cow's milk- and soy-based products. The Codex Standard for Follow-Up Formula does not set separate ranges for soy-based products for any nutrient. The FSANZ 2013–2014 label survey included three isolated

soy protein-based formulas, for which the labelled amount ranged from 8.57 to 16.22 mg/100 kJ, aligning with the current range in Standard 2.9.1 and Codex STAN 72-1981 and both ranges prescribed in EU 2016/127. Given this alignment, FSANZ proposes retaining a phosphorus range for all infant formula products (including soy-based infant formulas).

Proposed approach

Based on conclusions of the 2016 nutrition risk assessment and Codex STAN 72-1981 current regulations, FSANZ proposes to adjust Standard 2.9.1 to align with Codex's minimum Ca:P ratio of 1:1.

Based on the above discussion supported by recent research, alignment with Codex STAN 72-1981 and conclusions from the 2016 nutrition risk assessment, FSANZ proposes to adjust the current phosphorus maximum (25 mg/100 kJ) in section S29—9 to a GUL of 24 mg/100 kJ.

FSANZ also proposes retaining a phosphorus range that accounts for all infant formula products (including soy-based infant formulas), however is seeking further information from industry submitters to inform considerations regarding separate minimum and maximum phosphorus levels for soy-based infant formula. Please see section 9 for further details.

7.4.2 Vitamin E: fatty acids ratio

Current regulations

Both Standard 2.9.1 and Codex STAN 72-1981 specify a minimum amount of vitamin E per gram of PUFA. Standard 2.9.1 sets a minimum amount of 0.5 mg vitamin E per gram of any PUFA whereas Codex STAN 72-1981 also lists 'factors of equivalence' from 0.5 mg/g for LA and increasing in increments of 0.25 mg/g to 1.5 mg/g for DHA according to the number of fatty acid double bonds in individual PUFAs in an infant formula. These factors are applied to determine the minimum amount of vitamin E for a particular PUFA mixture in infant formula.

Previous consideration

In 2016 FSANZ considered it appropriate to retain the current approach to vitamin E requirements relating to the PUFA content of infant formula. It is not considered necessary to adopt the 'factors of equivalence' for α-TE to individual PUFA outlined in Codex STAN 72-1981.

Stakeholder views

Three submitters (one government, two industry) commented on the current approach to vitamin E requirements relating to the PUFA content of infant formula. All submitters supported retaining the current approach in Standard 2.9.1.

Nutrition risk assessment

No further nutrition risk assessment was considered on this issue.

Options and discussion

The 2016 nutrition risk assessment concluded that application of the Codex STAN 72-1981 conversions for vitamin E equivalents makes a marginal difference in the amount of vitamin E needed to be present compared to application of the approach currently used in Standard 2.9.1. There is limited evidence to indicate that the use of different factors depending on the

number of PUFA double bonds is warranted. Moreover, without evidence of harm of the current approach, not applying the specific Codex 'factors of equivalence' for α-TE to PUFA would be unlikely to pose a risk to infant health.

Proposed approach

Based on the 2016 nutrition risk assessment conclusions and stakeholder support, FSANZ's proposed approach is to retain the current permission for vitamin E requirements relating to the PUFA content of infant formula within Standard 2.9.1. It is not considered necessary to adopt the 'factors of equivalence' for α-TE to individual PUFA outlined in Codex STAN 72-1981.

7.4.3 Copper, vitamin C and iron: nutrient interaction

Current regulations

Copper, vitamin C and iron all have separate regulations specified in Standard 2.9.1 (see sections on these nutrients in section 7.3). Standard 2.9.1, Codex STAN 72-1981 and EU 2016/127 do not comment on the nutrient interactions between copper, vitamin C and iron.

Previous consideration

In 2016 FSANZ did not consider copper, vitamin C or iron in the context of this nutrient interaction.

Stakeholder views

No submitter comments on this issue.

Nutrition risk assessment

The 2021 nutrition risk assessment (see SD1) did not evaluate this nutrient interaction. However, it did note that nutrient interactions between copper, vitamin C and iron may be of relevance if the vitamin C maximum amount currently permitted in Standard 2.9.1 is increased. This is based on high intakes of iron and ascorbic acid potentially having a synergistic negative effect on copper metabolism.

Options and discussion

As discussed in section 7.3.3 for vitamin C, FSANZ is proposing to increase the vitamin C maximum level from the current permission of 5.5 mg/100 kJ, to a GUL of 17 mg/100 kJ to align with Codex STAN 72-1981. This increase was proposed to mitigate the significant vitamin C losses that occur during shelf life and preparation of infant formula. The proposed increase seems large, but an estimated vitamin C loss of 20–50% in powdered products and up to 75% in liquid products can occur before the product is consumed.

The 2021 nutrition risk assessment (SD1) considered limitations in the evidence on ascorbic acid, as there is difficulty in evaluating at which stage ascorbic acid interferes with copper metabolism (Lönnerdal 1998). The paper also noted that most of the data available is based on animal studies and there is uncertainty around whether copper metabolism differs in humans, with the possibility that ascorbic acid has a lesser effect on copper metabolism in humans.

Proposed approach

Based on the above discussion, FSANZ considers the proposed approaches for copper, vitamin C, and iron to be appropriate in regard to the potential interactions between these nutrients.

7.5 Permitted forms of vitamins, minerals and electrolytes

This section discusses FSANZ's comparison of the permitted forms of vitamins, minerals and electrolytes in Standard 2.9.1 with Codex GL 10-1979.

Current regulations

Schedule 29 lists the permitted forms for the vitamins, minerals and electrolytes intended for use as a nutrient when added to infant formula. Schedule 3 – Identity and Purity includes a list of acceptable sources of specifications e.g. FAO JECFA Monographs, Food Chemicals Codex (FCC), European Pharmacopoeia. The current list of permitted forms in the Code was developed during P93 to align with the 1991 European Commission Infant Formula Directive (91/321/EEC) and the previous regulations in Codex (GL 10-1979). The substances on these lists were assessed as part of the toxicology and risk assessment during assessment of P93.

The Codex GL 10-1979 list of the permitted forms of nutrients for use in infant formula was comprehensively reviewed by CCNFSDU around the time of the review of Codex STAN 72-1981. A set of criteria was devised to ensure that any permitted nutrient form would be safe and appropriate for use in products for infants. In addition, the CCNFSDU agreed that to ensure safety, permitted forms of nutrients must comply with certain specifications. The specifications indicate the identity, origin, production and acceptable level of purity for each substance.

Previous consideration

The 2016 Consultation paper compared the forms of vitamins, minerals and electrolytes that are permitted by Codex but which are not permitted for use in infant formula in the Code and whether each form has a specification source listed in S3. We also considered submissions to the 2012 Consultation paper. Overall conclusions in 2016 were:

- Submissions to the 2012 Consultation paper generally supported aligning the permitted forms of nutrients in Standard 2.9.1 with Codex GL 10-1979 on the basis that these forms have been evaluated by Codex for nutritional adequacy and safety in infant formula. Submitters did not support the removal of any currently permitted nutrient forms from Standard 2.9.1.
- Particular requests from 2012 were to clarify the permitted forms of niacin and vitamin A, and to consider additional permitted forms for niacin, pantothenic acid, copper, iron, magnesium, potassium and zinc in terms of technological justification. This information was sought in the 2016 Consultation paper.

Stakeholder views

A summary of submissions and FSANZ's responses on permitted forms of vitamin, minerals, and electrolytes is provided in Table 7.17.

Table 7.17 Submitter comments on permitted forms

Comment	Submitters*	FSANZ response (proposed approach)
General alignment: forms of nutrients permitted in Codex STAN 72-1981 should be permitted in Standard 2.9.1 for reasons of alignment, flexibility for manufacture and avoidance of trade barriers.	Industry (5)	See "Previous consideration". Except for niacin, vitamin A, pantothenic acid, copper, iron, magnesium, potassium and zinc there was general support to align permitted forms with Codex.
Vitamin A: β-carotene is a permitted as a provitamin A form in Standard 2.9.1 and Codex but it is not included in the total vitamin A amount (see section 7.2.1). FSANZ sought further information on the justification to retain β-carotene as a provitamin A form in Standard 2.9.1.	Industry (6), Government (2)	See discussion below. FSANZ proposes to retain permission for β-carotene as a permitted form but this will not be included in the vitamin A content.
Vitamin D: Both vitamin D_3 (cholecalciferol) and vitamin D_2 (ergocalciferol) are permitted forms in the Code. Codex GL 10-1979 permits only cholecalciferol (D_3) based on uncertainty of the bioavailability of vitamin D_2 in infants.	Industry (2), Government (1)	See discussion below. Based on current scientific evidence, FSANZ proposes to retain the current Standard 2.9.1 permitted forms for vitamin D.
Pantothenic acid: The Code lists dexpanthenol as the only permitted form of pantothenic acid. Codex GL 10-1979 lists D-panthenol, DL-panthenol, calcium D-pantothenate, and sodium D-pantothenate as permitted forms. FSANZ's preliminary view was that it is not appropriate to permit DL-panthenol and we sought further information and technological justification for calcium D-pantothenate and sodium D-pantothenate as suitable for use in infant formula.	0	FSANZ proposes to permit D-panthenol, calcium D-pantothenate, and sodium D-pantothenate as forms for pantothenic acid but not DL-panthenol.
Niacin: The Code and Codex list niacinamide (nicotinamide) as the permitted form for niacin but Codex also includes nicotinic acid.	0	FSANZ proposes not to permit nicotinic acid for use in infant formula.
Copper: Codex lists an additional form of copper (cupric carbonate) which is not included in S29 of the Code.	0	FSANZ proposes to include cupric carbonate as a permitted form for copper.
Magnesium: FSANZ sought further information on the technological justification for the use of magnesium hydroxide carbonate, magnesium hydroxide and magnesium salts of citric acid in infant formula.	0	FSANZ proposes to include magnesium hydroxide carbonate, magnesium hydroxide and magnesium salts of citric acid as permitted forms for magnesium.
Potassium: FSANZ sought further information on the technological justification for the use of potassium L-lactate in infant formula.	0	FSANZ proposes to include potassium L-lactate as a permitted form for potassium.
Zinc: FSANZ sought further information on the technological justification for the use of zinc lactate and zinc citrate (zinc citrate dehydrate or zinc citrate trihydrate) in infant formula	0	FSANZ proposes to include zinc lactate and zinc citrate (zinc citrate dehydrate or zinc citrate trihydrate) as permitted forms for zinc.
Iron: FSANZ sought further information on the technological justification for the use of ferric citrate, ferrous bisglycinate and ferrous sulphate in infant formula.	0	FSANZ proposes to include ferric citrate, ferrous bisglycinate and ferrous sulphate as permitted forms for iron.

** Submitters with a specific comment on this nutrient.*

Nutrition risk assessment

No further nutrition risk assessment was considered on the permitted forms of vitamins, minerals, and electrolytes.

Options and discussion

Table 7.5.1 lists FSANZ's proposed approach for permitted forms of vitamin, minerals, and electrolytes. Nothing further was considered regarding pantothenic acid, niacin, copper, magnesium, potassium, zinc and iron, and the proposed approach, which are aligned with Codex STAN 72-1981, as listed in Table 7.5.1. However, based on comments from submitters, issues for β-carotene and vitamin D_2 have been addressed below.

Proposed approach

FSANZ proposes that the proposed approach listed in Table 7.5.1 for permitted forms of vitamins, minerals, and electrolytes be implemented within Standard 2.9.1.

7.5.1 β-carotene

β-carotene is assessed in detail within section 7.2.1 (Vitamin A, β-carotene, and calculation of retinol equivalents), for which FSANZ proposes to retain permission for β-carotene as a permitted form but this will not be included in the vitamin A content. Refer to section 7.2.1 for further details.

7.5.2 Vitamin D_2

Current regulations

As a form of vitamin D (cholecalciferol-cholesterol), Standard 2.9.1 currently permits both vitamin D_3 (cholecalciferol) and vitamin D_2 (ergocalciferol) in infant formula (see section S29—7). Codex GL 10-1979 permits only cholecalciferol (D_3) based on uncertainty of the bioavailability of vitamin D_2 in infants.

Previous consideration

In 2016 FSANZ considered it appropriate to retain the two permitted forms vitamin D_3 (cholecalciferol) and vitamin D_2 (ergocalciferol).

Stakeholder views

Two submitters (one industry, one government) commented on the permitted forms of vitamin D. Industry supported retaining both forms whereas the government submitter considered that the vitamin D_2 permission should be retained only if there is clear evidence that the amounts present in infant formula are equally bioavailable as D_3.

Nutrition risk assessment

No further nutrition risk assessment was considered on this issue.

Options and discussion

FSANZ's 2016 nutrition risk assessment concluded that both forms are equally effective in raising serum 25-hydroxyvitamin D (25OHD) concentration (the marker for adequate vitamin D status) and use of vitamin D_2 would be unlikely to pose a risk to infant health. Recent evidence supported the suitability of both forms to be used in infant formula. A review of the

labelled ingredient lists on products sold in ANZ showed that both forms are currently used. Thus restricting the form of vitamin D to the D_3 form to align with Codex may impact on infant formula manufacturing.

Additional nutrition risk assessment examined whether any human clinical trials published from 2015 to 2018 had compared the efficacy of vitamin D_2 and vitamin D_3 in raising serum 25OHD concentrations. No clinical studies involving infants were identified from the literature search. However, a recently published randomised controlled trial of adult women supplemented with a low dose of vitamin D_2 or vitamin D_3 showed that the two forms were equally efficacious in raising serum 25OHD concentrations (FSANZ 2015).

FSANZ also notes that the current review of the Codex Draft Standard for FUF concluded that the requirement for vitamin D should encompass both vitamin D_2 and vitamin D_3.

Proposed approach

Based on the nutrition risk assessment evidence and the conclusions of the Codex Draft Standard for FUF permitted forms for this nutrient, FSANZ proposes to retain both vitamin D_2 and vitamin D_3 as permitted forms in Standard 2.9.1.

7.6 Fluoride

Fluoride is a mineral naturally present in food and drink and is considered a normal constituent of the human body (NHMRC and MoH 2006, revised 2017). Fluoride is necessary for mineralisation of teeth and bones and to stimulate formation of new bone. Sufficient intakes of fluoride prevent the formation of dental caries (tooth decay) (FSANZ 2011). Most public water supplies in Australia and New Zealand are fluoridated as a public health strategy to prevent dental caries. However, excess fluoride intakes can lead to dental fluorosis.

Current regulations

The Code, Codex STAN 72-1981, and EU 2016/127 do not permit the addition of fluoride to infant formula. Therefore consideration of the minimum amount of fluoride in infant formula is not addressed in this review.

Standard 2.9.1 manages the potential risk of dental fluorosis by requiring infant formula that contains:

- more than 17 µg of fluoride per 100 kJ prior to reconstitution, in the case of powdered or concentrated infant formula product; or
- more than 0.15 mg of fluoride per 100 mL, in the case of 'ready-to-drink' formula

to include a statement on the product label indicating the potential risk of dental fluorosis (subparagraph 2.9.1—23(1)(b)(i)) and a statement recommending that the risk of dental fluorosis should be discussed with a medical professional (subparagraph 2.9.1–23(1)(b)(ii)).

Codex STAN 72-1981 and EU 2016/127 manage fluoride content by specifying an upper limit for fluoride of 24 µg/100 kJ in infant formula prepared ready for consumption (i.e. when prepared following the manufacturer's instructions on the label).

Previous consideration

The issue of fluoride was not considered in the 2016 Consultation paper.

The 2012 Consultation paper noted that the approach in Standard 2.9.1 varied from both

Codex and the EU which specify maximum levels for fluoride and do not require a dental fluorosis statement.

Stakeholder views

Submitters to the 2012 Consultation paper expressed diverse views on issues relating to fluoride in infant formula. Some submitters supported alignment with Codex provisions (i.e. maximum level of 24 µg/100 kJ 'ready to drink'), while others considered the level should be lowered following a review of the evidence to consider the public health and safety issues relating to fluoride in infant formula. Some questioned the need for the dental fluorosis statements, and others considered these statements should be amended and made mandatory on products.

Nutrition risk assessment

No further nutrition risk assessment was considered on this issue.

Options and discussion

History of the requirement in the Code

During the time Standard 2.9.1 was being developed, there were concerns that formula-fed infants may be at risk for dental fluorosis when infant formula powder containing fluoride was made up with fluoridated water. Therefore, estimated fluoride intakes were assessed using the reported levels of fluoride in Australian and New Zealand infant formula at the time and assuming that the infant formula was prepared with water containing the maximum permitted fluoridation levels. The assessment noted the fluoride content of infant formula powder alone would not lead to daily intakes at a level of concern. As potentially high fluoride levels depended mainly on the fluoride concentration of the water used to reconstitute the products, it was considered difficult to regulate. Consequently it was concluded that the issue of fluoride in infant formula was adequately covered by the water quality guidelines at the time. FSANZ (then ANZFA) also noted that some manufacturers were moving to produce infant formula with low fluoride-containing water to reduce the fluoride levels in the final product and this was consistent with monitoring study (Riordan 1995). Due to concerns on the possibility of dental fluorosis from the use of some formulas, a labelling requirement was introduced as a measure to advise carers of this potential risk.

Other FSANZ assessments

The fluoride content of infant formula and infant foods (in addition to other foods) was analysed as part of the 23rd ATDS. Based on a model infant diet, infant formula was reported to be the major source of fluoride intake for infants, noting that the survey only considered dietary sources of fluoride. For 9 month old infants, estimated mean dietary intakes exceeded the AI, while the UL (0.9 mg/day) was exceeded in 9 month old infants at the 95th percentile (150% of the UL) (FSANZ 2011). This was consistent with the FSANZ assessment for Application A588 – Voluntary Addition of Fluoride to Packaged Water (FSANZ 2009). As part of the dietary exposure assessment for this Application, a proportion of infants and children up to 8 years of age were found to have fluoride intakes greater than the UL. However, these exceedances were not considered to represent a safety issue because:

- moderate dental fluorosis (the adverse effect on which the UL is based) is a rare condition in Australia and New Zealand
- the apparent exceedances were considered to be the result of comparing values based on actual consumption data for children up to 8 years of age to a UL that was

originally based on model data for these ages.

FSANZ concluded that the apparent exceedances of the UL in infants in the survey were not considered to represent a human health and safety risk (FSANZ 2011). Following this FSANZ started working with the NHMRC to review the UL for fluoride.

Upper Level of Intake for fluoride

The NHMRC review of the UL for fluoride was undertaken to address the apparent exceedance of recommended fluoride intakes without occurrence of adverse dental fluorosis. The review included a comprehensive review of studies published since the last review of the UL in 2006. The literature review found that studies conducted in 1930s and 1940s provided the best dose-response data for establishing the UL. Based on (1) the critical fluoride concentration in water that would minimise severe dental fluorosis, (2) nationally representative data on water and food consumption, and (3) updated bodyweight data for Australian and New Zealand populations, the UL for fluoride for infants and children up to 8 years old was estimated to be 0.2 mg fluoride/kg bodyweight/day (NHMRC and NZ MOH 2017). This converts to the values listed in Table 7.18 based on a mean bodyweight of 6 kg for infants 0–6 months and 9 kg for infants 7–12 months. The revised ULs, published in 2017, are considerably higher than the previous values.

Table 7.18 Fluoride Upper Level of Intake as established by the NHMRC

Infant age range	UL - NHMRC 2006 (mg/day)	UL - NHMRC 2017 (mg/day)
0–6 months	0.7	1.2
7–12 months	0.9	1.8

NHMRC Drinking Water Guidelines

The Australian Drinking Water Guidelines and New Zealand Drinking Water Standards both recommend water fluoridation levels in the range of 0.7–1.0 mg F/L with a maximum level in both countries of 1.5 mg F/L (NHMRC 2011; MOH 2005, revised 2018). Optimal levels of fluoridation are considered to be 1.0 mg F/L as this is the point at which maximal protection against dental caries is reached with minimum risk of dental fluorosis.

Calculated estimated exposure

FSANZ has calculated estimated fluoride exposures based on the fluoride content for several brands of infant formula powder and water fluoride concentrations of 0, 0.5, 1.0 and 1.5 mg F/L. It is important to note that the maximal level of 1.5 mg/L is not considered generally relevant to Australian and New Zealand conditions.

The calculations showed that at the optimal level of water fluoridation (1.0 mg/L) and current levels of fluoride concentration in infant formula powders (milk- and soy-based), it is unlikely that infants consuming infant formula as recommended would consume even half the UL recommendations for fluoride daily. An example of this calculation is provided in Appendix 3.

Proposed approach

Based on the above discussion, FSANZ is proposing to set a compositional limit of 24 µg/100 kJ when prepared ready for consumption and to remove the labelling statements

relating to dental fluorosis in paragraph 2.9.1—23(1)(b). This approach will still provide a mechanism to protect infant health and safety and will align with international regulations.

8 Other optional substances

Section S19—7 lists substances permitted for use as nutritive substances in infant formula and their permitted forms. In addition, Schedule 3 includes a list of acceptable sources of specifications e.g. FAO, JECFA Monographs, FCC, European Pharmacopoeia.

Codex STAN 72-1981 and EU 2016/127 prescribe the mandatory addition of three substances to infant formula which are considered optional in the Code: choline, L-carnitine, and inositol (Table 8.1). Many infant formulas contain these substances and no adverse effects in infants consuming these formulas have been reported. Thus, the prescribed optional amounts have an extended history of safe use both in Australia, New Zealand and overseas and the safety of infant formula supplemented with these nutrients has not been further examined.

Schedule 29 permits the optional addition of five specific nucleotides to infant formula as a nutritive substance. Comparison of the permitted forms of nucleotides across Schedule 29, Codex STAN 72-1981 and EU 2016/127 shows they are already aligned (Table 8).

Table 8.1 Regulatory requirements for choline, L-carnitine, inositol and nucleotides

Micronutrient (mg/100 kJ)	Standard 2.9.1 (Schedule 29)		Codex STAN 72-1981		EU 2016/127	
	Min	Max	Min	Max	Min	Max
Choline	1.7	7.1	1.7	12 (GUL)	6.0	12.0
L-carnitine	0.21	0.8	0.3	ns	0.3	ns
Inositol	1.0	9.5	1.0	9.5 (GUL)	0.96	9.6
Nucleotides						
Adenosine-5′-monophosphate	0.14	0.38	At discretion of national authorities		ns	0.36
Cytidine-5′-monophosphate	0.22	0.6			ns	0.60
Guanosine-5′-monophosphate	0.04	0.12			ns	0.12
Inosine-5′-monophosphate	0.08	0.24			ns	0.24
Uridine-5′-monophosphate	0.13	0.42			ns	0.42
Total nucleotide 5′-monophosphates	≤ 3.8	ns			≤ 1.2	ns

ns: Not specified.

8.1 Choline

Current regulations

The minimum level for choline in Schedule 29 and Codex STAN 72-1981 are aligned, however the maximums differ (Table 8). EU 2016/127 set a range for choline of 6.0–12.0 mg/100 kJ.

Within Schedule 29 choline is currently permitted as choline chloride and choline bitartrate, whereas Codex GL 10-1979 lists three forms of choline that are not permitted in Schedule 29 (choline, choline citrate, choline hydrogen tartrate).

Choline is permitted within Schedule 29 as a nutritive substance. EU 2016/127 permits it as a mandatory substance and Codex STAN 72-1981 permits it as an essential ingredient within infant formula.

Previous consideration

In 2016 FSANZ considered that choline should be permitted within Schedule 29 as a mandatory substance in infant formula with a mandatory range of 1.7–12.0 mg/100 kJ, to align with the Codex STAN 72-1981 maximum.

FSANZ also sought further information on the technological justification for the use of choline, choline citrate and choline hydrogen tartrate as permitted forms of choline in infant formula.

Stakeholder views

Thirteen submitters (two government, eleven industry) commented on the permitted range for choline. All industry and one government submission supported FSANZ's 2016 view to list choline as a mandatory substance in infant formula with a range of 1.7–12 mg/100 kJ. The majority also noted that the upper amount should be presented as a GUL as per Codex STAN 72-1981. One government submission supported alignment with the EU minimum (6 mg/100 kJ) because it would meet the Australian and New Zealand AI for choline and is consistent with the average amount found in breast milk.

Four industry submitters commented on the additional forms of choline and their technological justifications for use in infant formula. All submitters supported the inclusions of additional forms as they are safe, the bioavailability is comparable to other current permitted forms and choline hydrogen tartrate is an alternative name for choline bitartrate.

Nutrition risk assessment

No further nutrition risk assessment was considered on this issue.

Options and discussion

Since 2006, choline has been classed as an essential nutrient in the NRVs. Submissions to both 2012 and 2016 Consultation papers noted this and supported mandating choline in Schedule 29. Mandating choline would align Schedule 29 with Codex GL 10-1979 and EU 2016/127.

Twelve submitters supported FSANZ preliminary view. However, one submitter considered the EU minimum of 6 mg/100 kJ to be appropriate. This EU amount is based on the recommendation of EFSA 2014 which was based on the choline concentration in human milk of 160 mg/L (Holmes-McNary et al. 1996). This concentration includes all sources of choline; i.e. choline, phosphocholine, glycerophosphocholine, phosphatidylcholine and sphingomyelin. The lower Codex STAN 72-1981 and Schedule 29 amount is based on human milk concentration of about 20 mg/L (Zeisel and Blusztajn 1994, LSRO 1998) which does not include all available sources of choline. None of the additional choline sources found in breast milk are permitted forms for choline under either standard. Assessment of new permitted forms of nutritive substances (e.g. phosphatidylcholine and sphingomyelin) is out of scope for Proposal P1028.

Since the current minimum is a better reflection of breast milk concentration of choline itself, and not additional potentially bioactive forms, FSANZ proposes that using the range of 1.7–12.0 mg/100 kJ for this nutrient is appropriate. This approach is supported by the FSANZ 2016 nutrition risk assessment which noted that mandatory inclusion of choline in the range in Codex STAN 72-1981 is unlikely to pose a risk to infant health. FSANZ also notes that 11 out of 12 submitters suggested the upper limit should be set as a GUL rather than a mandatory maximum, to allow further alignment with Codex STAN 72-1981. The consideration proposed by FSANZ in 2016 to use a maximum rather than GUL was based on a review published in 2014 (Tang and Hazen 2014) although the relevance of this evidence for infants and children remains undetermined. Due to absence of an UL, the use of an GUL is more appropriate and maintains consistency between Schedule 29 and Codex STAN 72-1981.

Choline in milk is present in several forms: free choline, phosphocholine, glycerol-phosphocholine, phosphatidylcholine, and sphingomyelin. The amounts of these forms vary considerably (Holmes-McNary et al. 1996). FSANZ notes that numerous stakeholders across the 2012 and 2016 consultation supported the permission of additional forms of choline into Schedule 29 including choline, choline citrate and choline hydrogen tartrate. Addition of the above forms would allow alignment with both Codex GL 10-1979 and EU 2016/127. Choline hydrogen tartrate is also an alternative name for choline bitartrate which is already permitted within Schedule 29. Choline hydrogen tartrate and choline citrate have a history of use in EU infant formula and have not posed risk to infant health. Submitters have noted technological justification in permitting these forms such as similar bioavailability to currently permitted forms and alignment with international standards and uses. The safety of these forms is also supported by their permissions in Codex and the EU regulations. While some of these forms of choline may be used rarely, in the future they may contribute to the provision of an essential nutrient.

Proposed approach

Based on the above considerations, FSANZ proposes that choline be listed as a mandatory substance in infant formula with a range of 1.7–12.0 mg/100 kJ, to align with the Codex STAN 72-1981. The proposed approach also notes that the maximum should be presented as a GUL.

It is proposed that choline should be permitted as the following forms in Schedule 29: choline chloride, choline bitartrate, choline, choline citrate and choline hydrogen tartrate.

8.2 L-carnitine

Current regulations

Schedule 29 permits the addition of L-carnitine as an optional substance at 0.21–0.8 mg/100 kJ. However, Codex STAN 72-1981 has set a mandatory higher minimum amount of 0.3 mg/100 kJ, but has set no maximum amount. The EU 2016/127 also states that L-carnitine content shall be at least equal to 0.3 mg/100 kJ.

Schedule 29 does not permit other forms of L-carnitine, whereas Codex GL 10-1979 lists two other forms (L-carnitine hydrochloride and L-carnitine tartrate).

Previous consideration

In 2016 FSANZ considered that L-carnitine should be listed as a mandatory substance in infant formula with a mandatory range of 0.3–0.8 mg/100 kJ.

FSANZ also sought further information on a technological justification for additional forms of L-carnitine and evidence to demonstrate safety of these forms in infant formula is needed to inform future assessment.

Stakeholder views

Fourteen submitters (two government, eleven industry, one health professional) commented on L-carnitine's permitted range. All government and industry submissions supported FSANZ's 2016 view to list L-carnitine as a mandatory substance in infant formula. One health professional submission did not support the mandatory requirement for L-carnitine in infant formula without clinical data to support it.

The submissions also supported increasing the minimum level to align with the Codex STAN 72-1981 amount of 0.3 mg/100 kJ. The majority of these submissions did not support setting a mandatory maximum level and noted concerns of achieving the proposed maximum. Multiple industry submissions also noted that a GUL is more appropriate and the upper level set must account for the natural variation in L-carnitine content of milk. The proposed maximum is noted by submitters as problematic as it is too low to account for the variable contribution of naturally occurring L-carnitine from cow's or goat's milk. An industry submitter also commented that a barrier to trade would emerge with the proposed maximum being out of step with trading partners.

Seven submitters (one government, six industry) commented on the technological justification for use of L-carnitine hydrochloride and/or L-carnitine tartrate in infant formula. The majority of submitters supported the use due to no safety issues being raised, as shown by the inclusion in Codex STAN 72-1981. One industry submission did note that a functional benefit of L-carnitine tartrate is that it is less hygroscopic compared to L-carnitine, therefore produces less lumping in dry powder and premixes. Another industry submitter noted there is evidence to suggest that use of L-carnitine tartrate may result in sulphurous taste and odours, which may adversely affect finished product acceptance of the product by infants.

Nutrition risk assessment

Additional nutrition risk assessment (SD1) noted the mean total carnitine concentrations have been reported to be in the range of 0.2 to 0.4 mg/100 kJ in human milk, 0.8 to 1.6 mg/100 kJ in cow's milk and 0.8 to 1.1 mg/100 kJ in goat's milk. There is a lack of evidence published since 2015 to assess the risk of harm due to consumption of infant formula that contains L-carnitine at a level greater than the current maximum level in the Code (0.8 mg/100 kJ).

Options and discussion

FSANZ considers that L-carnitine is regarded as an essential nutrient in infant formula and formulas for special medical purposes intended for infants (Codex STAN 72-1981) and that L-carnitine and L-carnitine tartrate are listed in the advisory list of nutrient compounds for use in foods for special dietary uses intended for infants and young children (CAC/GL 10-1979). The Codex Standard for Follow-Up Formula CXS 156-1987 also notes that in addition to vitamins and minerals, other nutrients may be added when required to ensure that the product is suitable.

In 2016 FSANZ concluded that based on available evidence the mandatory inclusion of L-carnitine at the amount prescribed by Codex is unlikely to pose a risk to infant health.

A maximum amount has not been specified in Codex STAN 72-1981 and no discussion about this was provided in the EC SCF review (2003). EU 2016/127 does not specify a maximum level for L-carnitine, which is based on the ESPGHAN IEG recommendation that in the absence of any adverse effects associated with higher L-carnitine intakes for infants no maximum level is needed to be set (Koletzko et al. 2005). This recommendation aligns with the majority of submitter views received within the 2016 Consultation paper. FSANZ's current maximum in Schedule 29 (0.8 mg/100 kJ) reflects the upper levels present in breast milk and aligns with LSRO suggestion that a maximum level based on the upper end of the usual range found in human milk is also appropriate.

In 2016, the nutrition assessment considered that L-carnitine should retain its maximum level based on its alignment with breast milk and evidence showing that non-absorbed carnitine is metabolised by microbes in the large bowel to trimethylamine, a compound that may be associated with the development of cardiovascular disease (Koeth et al. 2013). The nutrition risk assessment also noted there is no evidence specific to infants or children indicating consumption of excess carnitine is linked with adverse health outcomes. The 2021 nutrition risk assessment searched for trials in infants receiving supplementary L-carnitine published between January 2015 and May 2021. Eleven publications were identified, however, none of the trials were designed to evaluate the occurrence or impact of excessive carnitine intake in infants without existing health conditions.

Industry submitters raised comments surrounding the applicability of the current maximum and its appropriateness given the use of cow's and goat's milk in infant formula. L-carnitine concentrations in milk differ between species, mean total carnitine concentrations have been reported to be in the range of 0.9–1.6 mg/100 kcal in human milk, whereas cow's milk and goat's milk range from 4.1–6.7 mg/100 kcal and 3.2–4.4 mg/100 kcal, respectively (Sandor et al. 1982; Penn et al. 1987; Ferreira 2003). Moreover, the submitters suggested in the absence of an UL no maximum should be set and instead a GUL should be applied to account for the natural L-carnitine levels present in cow's and goat's milk.

One submitter did not support making L-carnitine a mandatory substance in infant formula without clinical data to support it. FSANZ's assessment for application *A1102 – L-carnitine in Food* reviewed numerous human studies which showed that intake of L-carnitine up to 3 g/day is not associated with adverse effects and higher doses only presented minor adverse effects (FSANZ 2019b). Although, the above studies do not relate to infants specifically they do reinforce that L-carnitine is unlikely to pose public health risks or safety concerns. This application also assessed the use of two forms (L-carnitine and L-carnitine tartrate) of L-carnitine as a nutritive substance in 30 classes of foods. FSANZ conducted technical and nutrition risk assessments which concluded that no public health or safety concerns were associated with the estimated dietary intake of L-carnitine at maximum use levels in the requested foods.

Seven submitters supported the addition of L-carnitine hydrochloride and L-carnitine tartrate to infant formula. It is noted that L-carnitine tartrate has technological benefits such as being less hygroscopic. L-carnitine tartrate was also assessed within *Application A1102 – L-carnitine in Food* which noted no safety or public health concerns. Moreover, both forms of L-carnitine have no associated safety issues as shown by the inclusion in Codex STAN 72-1981.

The range previously proposed by FSANZ of 0.3–0.8 mg/100 kJ is consistent with the level found in breast milk, the amount considered adequate for infants and also aligns with the minimum level in Codex STAN 72-1981 and EU 2016/127.

Proposed approach

Based on the above considerations, FSANZ proposes that L-carnitine be listed as a mandatory substance in infant formula and should align with the permitted Codex and EU mandatory minimum of 0.3g/100 kJ.

FSANZ also proposes that the current maximum level within Schedule 29 (0.8 mg/100 kJ) should be retained, however presented as a GUL to account for the natural variability of L-carnitine content in differing milks, provide flexibility for manufacturers and avoid trade barriers. This is based on a lack of evidence specific to infants or children indicating consumption of excess carnitine being linked with adverse health outcomes and the absence of a UL.

Based on the safety conclusions of Codex STAN 72-1981 and *A1102 – L-carnitine in Food,* FSANZ proposes that L-carnitine should be permitted as L-carnitine hydrochloride and L-carnitine tartrate in Schedule 29.

8.3 Inositol

Current regulations

The Code (Schedule 29) permits the range of 1.0–9.5 mg/100 kJ for inositol which is basically aligned with Codex STAN 72-1981 and EU 2016/127. However, Codex and EU 2016/127 list inositol maximum amount as a GUL.

The above standards permit the same form of inositol, however Codex and EU 2016/127 list this form as myo-inositol which is the physiologically most relevant form.

Previous consideration

In 2016 FSANZ considered it appropriate to prescribe the mandatory inclusion of inositol in infant formula at the current minimum amount (which already aligns with Codex STAN 72-1981 and EU 2016/127) and list a GUL of 9.5 mg/100 kJ. FSANZ also considered listing the permitted form of inositol as myo-inositol to provide clarity and align with the Codex STAN 72-1981 and EU 2016/127.

Submissions

Nine submitters (two government, seven industry) commented on inositol's permitted range. All submissions supported FSANZ's 2016 view to list inositol as a mandatory substance in infant formula. Six industry submissions supported the change to a GUL rather than a maximum upper level, to align with Codex. A government submission requested further consideration on whether the upper level should be permitted as a maximum or GUL. Another government submitter noted that the proposed level is much lower than the level found naturally in breast milk.

Seven submitters (two government and five industry) commented on listing the permitted form of inositol as myo-inositol. All submitters were in support of this change and agreed that it provides clarity and consistency with Codex.

Nutrition risk assessment

No further nutrition risk assessment was considered on this issue.

Options and discussion

FSANZ notes recent reviews on infant formula composition have not set a mandatory maximum, and suggest that the upper level should be around that reported for breast milk (9.6 mg/100 kJ) (EFSA 2014b). The 2016 nutrition assessment also noted that no safety data or negative health effects related to inositol in infants or children had been reported. Thus alignment by setting a GUL instead of maximum amount is unlikely to pose a risk to infant health.

FSANZ notes stakeholder queries relating to the proposed levels being much lower than levels present in breast milk. Inositol has been found to reach a relatively stable concentration of around 130–325 mg/L (20–50mg/100 kcal) in mature human milk (EFSA 2014b). The GUL proposed by FSANZ fits within this this range. The proposed range for inositol is 4–40 mg/100kcal which is equivalent to 1–10 mg/100 kJ. This value is reflective of the rounded proposed range of 1–9.5 mg/100 kJ. It is also important to note that endogenous *de novo* synthesis of inositol appears to be efficient in newborn infants (EFSA 2014b).

Codex GL 10–1979 lists myo-inositol (previously referred to as meso-inositol) as the only permitted form of the inositols. The specification listed in Food Chemicals Codex (as referenced in Codex GL 10–1979 and Schedule 29) lists three alternative names for inositol: i-Inositol, meso-Inositol, myo-Inositol. In the literature inositol can also be used as the common name to refer to several compounds. Thus the permitted forms currently align, however the use of multiple names does create some potential for confusion and outlines the need for consistency.

Proposed approach

Based on the above discussion, FSANZ proposes that inositol be listed as a mandatory substance in infant formula with a minimum of 1.0 mg/100 kJ and a GUL of 9.5 mg/100 kJ to align with the Codex STAN 72-1981 range.

FSANZ also proposes listing the permitted form of inositol as myo-inositol to provide clarity and align with the Codex STAN 72-1981 and EU 2016/127.

8.4 Nucleotides

Current regulations

Schedule 29 permits the optional addition of five specific nucleotides to infant formula, which outlines a minimum and maximum for each of the permitted nucleotides. Standard 2.9.1—8 states that “infant formula product must contain no more than 3.8 mg/100 kJ of nucleotide-5’-monophosphates”. Codex STAN 72-1981 permits the addition of nucleotides at the discretion of national authorities. EU 2016/127 permits the optional addition of five specific nucleotides to infant formula. EU 2016/127 specifies varying minimum levels outlined in Table 8.

Comparison of the permitted forms of nucleotides in each standard shows they are already aligned.

Previous consideration

In 2016 FSANZ considered retaining the current permission and maximum combined total limit of nucleotides. FSANZ also sought feedback on the clarity of the drafting in the revised Code.[13]

Submissions

Four submitters (all industry) commented on nucleotides current permissions. All submitters supported retaining the current permission and maximum combined total limit of nucleotides.

Seven submitters (two government, five industry) commented on the clarity of the drafting for the maximum amount of nucleotides in the Code. Four industry submitters commented on considering that the combined total content should only apply when nucleotides are added to infant formula.

Nutrition risk assessment

No further nutrition risk assessment was considered on this issue.

Options and discussion

Comparison of the permitted forms of nucleotides in each standard shows there is already alignment. There have also been no submissions opposed to FSANZ's original proposal in 2016.

FSANZ is aware that there has been confusion amongst submitters between the prescribed maximum amount for individual nucleotides, and the combined total limit of nucleotides. The revised Code clarifies that the combined total nucleotide content is intended to include naturally occurring nucleotides which means that not all individual nucleotides can be present in infant formula at their individual maximum amounts from addition alone. The prescribed maximum for each nucleotide-5'-monophosphate sums to 0.76 mg/100 kJ.

Proposed approach

Based on above discussion, FSANZ proposes retaining both the current permission in Schedule 29 and the maximum total limit of nucleotides prescribed in Standard 2.9.1.

9. List of questions to submitters

FSANZ invites stakeholders to provide comment on the proposed approaches as outlined in this paper. To facilitate this feedback, FSANZ has proposed a series of questions for consideration. As noted in relevant sections, some of these questions pertain to a lack of information that will be needed to support proposed options in the 1st Call for Submissions paper.

In addition, the purpose of some of these questions will be to inform a CRIS should one be required. Additional information on costs and benefits would also be useful to help us consider cost/benefit in accordance with the FSANZ Act.

---

[13] Proposal P1025 Code Revision brought in a new section to Schedule 29 (S29—5) to list permitted nutritive substances for infant formula products, including nucleotides. This information was previously in the table to clause 7 of Standard 2.9.1. The revised Code came into effect 1 March 2016.

Questions for submitters
General question related to the Consultation paper
1. In addition to your submissions from previous Consultations for this Proposal, do you have any further comments on how any of our proposed options in this paper would affect market opportunities for infant formula? Please provide evidence of practical barriers and quantify impacts where possible. 2. With the proposed approaches for Standard 2.9.1 or Schedule 29 in this Consultation paper, will small or large businesses be disproportionately impacted if a new permission or restriction does not align with international regulations or standards? ? If so can you specify how by providing quantitative evidence where possible?
Questions about the minimum LA requirement. (Section 5.3)
3. Do you support retaining the current minimum requirement for LA (9% total fatty acids) in infant formula? Please provide your rationale and any supporting evidence. 4. Are there any technical issues related to increasing the LA minimum in Standard 2.9.1 to align with the higher EU 2016/127 level of 120 mg/100 kJ? 5. Can you provide data on the LA levels in commercially available infant formula internationally? This information can be provided as 'Commercial in confidence' if required.
Questions about setting separate maximum iron levels for soy-based infant formula. (Section 7.3.3.5)
6. Do you support setting a separate iron maximum for soy-based infant formula? Please provide your rationale and evidence to support your answer.
Questions about setting a separate phosphorus range for soy-based infant formula. (Section 7.4.1)
7. Do you support setting a separate phosphorus range for soy-based infant formula? Please provide your rationale and evidence to support your answer.

References

Agostoni C, Axelsson I, Goulet O, Koletzko B, Michaelsen KF, Puntis J, Rieu D, Rigo J, Shamir R, Szajewska H, Turck D (2006) ESPGHAN Committee on Nutrition: Soy Protein Infant Formulae and Follow-On Formulae. J. Pediatr. Gastroenterol. Nutr. 42(4): 352-361. doi: 10.1097/01.mpg.0000189358.38427.cd

Ahmed M, Khaleeq A, Munir R, Huma R, Muddassae M, and Naseem S (2017) Determination of macronutrients, micronutrients, non-essential elements in milk based-infant formulas by atomic absorption and inductively coupled plasma-optical emission spectroscopy after microwave and ultrasound assisted digestion. Spectroscopy Lett. 50(2):88-95.

ANZFA (1999a) Preliminary Inquiry Report. Proposal P93 – Infant Formula. Australia New Zealand Food Authority, Canberra. http://www.foodstandards.gov.au/code/proposals/Pages/proposalp93reviewofinfantformula/Default.aspx

ANZFA (1999b) Preliminary Inquiry Report - Explanatory notes. Proposal P93 – Infant Formula Products. Australia New Zealand Food Authority, Canberra http://www.foodstandards.gov.au/code/proposals/Pages/proposalp93reviewofinfantformula/Default.aspx

ANZFA (2002) Supplementary Final Assessment (Inquiry – S.24) Report. Proposal P93 – Review of Infant Formula. Australia New Zealand Food Authority, Canberra. http://www.foodstandards.gov.au/code/proposals/pages/proposalp93reviewofinfantformula/p93finalassessreport1397.aspx

Bohn T (2019). Determinants and Determination of Carotenoid Bioavailability from Infant Food Formulas and Adult Nutritionals Including Liquid Dairy Products. Journal of AOAC INTERNATIONAL 102(4) 1044–1058. https://doi.org/10.5740/jaoacint.19-0015

Campos-Giménez E, Bénet S, Oguey Y, Martin F, Redeuil K (2018) The contribution of minor folates to the total vitamin B9 content of Infant formula and clinical nutrition products. Food Chem. 249: 91-97. https://doi.org/10.1016/j.foodchem.2017.12.061.

Canfield LM, Clandinin MT, Davies DP, Fernandez MC, Jackson J, Hawkes J, Goldman WJ, Pramuk K, Reyes H, Sablan B, Sonobe T, Bo X (2003) Multinational study of major breast milk carotenoids of healthy mothers. Eur. J. Nutr. 42(3):133–141.

Casey CE, Smitt A, Zhang P (1995) Microminerals in human and animal milks. In: Jensen RG (ed) Handbook of Milk Composition. Academic Press, New York, NY, p. 622–674
CCNFSDU (2015) Report of the Thirty Seventh Session of the Codex Committee On Nutrition And Foods For Special Dietary Uses (REP16/NFSDU). Codex Alimentarius Commission, Rome. http://www.fao.org/fao-who-codexalimentarius/sh-proxy/en/?lnk=1&url=https%253A%252F%252Fworkspace.fao.org%252Fsites%252Fcodex%252FMeetings%252FCX-720-37%252FREP16_NFSDUe.pdf

Cho WI, Yu HW, Chung HR, Shin CH, Yang SW, Choi CW, Kim BI (2015) Clinical and laboratory characteristics of neonatal hypocalcemia. Ann. Pediatr. Endocrin. Metab. 20(2): 86–91.

Codex (1979) Advisory Lists of Nutrient Compounds for Use in Foods for Special Dietary Uses Intended for Infants and Young Children. Codex Alimentarius CAC/GL 10-1979. Codex Alimentarius Commission, Rome. www.codexalimentarius.org/input/download/standards/300/CXG_010e.pdf

Codex (1981) Standard for Infant Formula and Formulas for Special Medical Purposes Intended for Infants. Codex Alimentarius CODEX STAN 72-1981. Codex Alimentarius Commission, Rome. www.codexalimentarius.org/input/download/standards/288/CXS_072e_2015.pdf

Codex (1985) Guidelines on Nutrition Labelling. Codex Alimentarius CAC/GL 2-1985. Codex Alimentarius Commission, Rome.

Codex (2016) Nitrogen conversion factor for soy protein. 37th Session of the Codex Committee on Methods of Analysis Sampling. Budapest, Hungary. Item 107. CRD7-Agenda 2 (Information provided by AOCS). Available online at http://www.fao.org/fao-who-codexalimentarius/meetings/detail/en/?meeting=CCMAS&session=37

Daoud S, Bou-Maroun E, Waschatko G, Horemans B, Mestdagh R, Billecke N, Cayot P. (2020) Detection of Lipid Oxidation in Infant Formulas: Application of Infrared Spectroscopy to Complex Food Systems. Foods 9(10):1432. https://doi.org/10.3390/foods9101432

Da Silva SV, Mattanna P, Bizzi CA, dos Santos Richards NSP, and Barin JS (2013) Evaluation of the mineral content of infant formulas consumed in Brazil. J. Dairy Sci. 96(6): 3498-3505.

Delplanque, B, Gibson R, Koletzko B, Lapillonne A, Strandvik Birgitta (2015) Lipid Quality in Infant Nutrition, J. Pediatr. Gastroenterol. Nutr. 61(1):8-17. doi: 10.1097/MPG.0000000000000818

Do HJ, Park JS, Seo JH, Lee ES, Park CH, Woo HO, Youn HS (2014) Neonatal Late-onset Hypocalcemia: Is There Any Relationship with Maternal Hypovitaminosis D? Pediatr. Gastroenterol. Hepatol. Nutr: 17(1):47–51.

EC SCF (2003) Report of the Scientific Committee on Food on the Revision of Essential Requirements of Infant Formulae and Follow-on Formulae. European Commission, Brussels Available online at http://ec.europa.eu/food/fs/sc/scf/out199_en.pdf

EFSA (2012) Scientific opinion on dietary reference values for protein. EFSA Panel on Dietetic Products, Nutrition, and Allergies. The EFSA Journal 10(2):2557–2613. https://www.efsa.europa.eu/en/efsajournal/pub/2557

EFSA (2014a) NDA Panel (EFSA Panel on Dietetic Products, Nutrition and Allergies), Scientific Opinion on Dietary Reference Values for folate. The EFSA Journal 2014;12(11):3893. https://www.efsa.europa.eu/en/efsajournal/pub/3893

EFSA (2014b) Scientific Opinion of the Panel on Dietetic Products, Nutrition and Allergies (NDA) on the essential composition of infant and follow-on formula. The EFSA Journal 12(7):3760. http://www.efsa.europa.eu/en/efsajournal/pub/3760

EFSA (2018) Scientific opinion on the update of the tolerable upper intake level for vitamin D for infants. The EFSA Journal 2018;16(8):5365 https://efsa.onlinelibrary.wiley.com/doi/pdf/10.2903/j.efsa.2018.5365

EFSA (2020) Scientific Opinion on the re-evaluation of lecithins (E 322) as a food additive in foods for infants below 16 weeks of age and follow-up of its re-evaluation as food additive for uses in foods for all population groups. The EFSA Journal 2020;18(11):6266. https://doi.org/10.2903/j.efsa.2020.6266

European Commission (2006) Commission Directive 2006/141/EC on infant formulae and follow-on formulae. Official Journal of the European Union L 401:1–33. https://eur-lex.europa.eu/legal-content/EN/ALL/?uri=CELEX%3A32006L0141

European Commission (2016) Commission Delegated Regulation (EU) 2016/127 of 25 September 2015 supplementing Regulation (EU) No 609/2013 of the European Parliament and of the Council as regards the specific compositional and information requirements for infant formulae and follow-on formulae and as regards requirements on information relating to infant and young child feeding. Official Journal of the European Union. 59: 1-29. EUR-Lex - 32016R0127 - EN - EUR-Lex (europa.eu)

European Commission (2019) Commission Delegated Regulation (EU) 2019/828 of 14 March 2019 amending Delegated Regulation (EU) 2016/127 with regard to vitamin D requirements for infant formula and erucic acid requirements for infant formula and follow-on formula. Official Journal of the European Union. 62:12-14. EUR-Lex - 32019R0828 - EN - EUR-Lex (europa.eu)

FAO/WHO (2018) Report of the Fortieth Session of the Codex Committee on Nutrition and Foods for Special Dietary Uses. Berlin, Germany, November 2018. REP19/NFSDU Appendix II. Accessed June 2021.

FDA (U.S. Department of Health and Human Services, Food and Drug Administration, Center for Food Safety and Applied Nutrition) (2019) Converting Units of Measure for Folate, Niacin, and Vitamins A, D, and E on the Nutrition and Supplement Facts Labels: Guidance for Industry. FDA-2016-D-4484. United States, Maryland.

Ferreira I. (2003) Quantification of non-protein nitrogen components of infant formulae and follow-up milks: comparison with cows' and human milk. Br. J. Nutr. 90(01):127.

FSANZ (2005) Final Assessment Report. Application A500 – Fortification of Cereal-based Beverages. Food Standards Australia New Zealand, Canberra.
http://www.foodstandards.gov.au/code/applications/Pages/applicationa500addit2480.aspx

FSANZ (2006) Final Assessment Report. Application A563 - Medium chain Triglycerides in infant formula products. Food Standards Australia New Zealand, Canberra.
https://www.foodstandards.gov.au/code/applications/Pages/applicationa563mediu3018.aspx

FSANZ (2008) 22nd Australian Total Diet Survey. Food Standards Australia New Zealand Canberra.
http://www.foodstandards.gov.au/publications/Pages/22ndaustraliantotaldietstudy/Default.aspx

FSANZ (2009) Final Assessment Report. Application A588 – Voluntary Addition of Fluoride to Packaged Water. Food Standards Australia New Zealand, Canberra
https://www.foodstandards.gov.au/code/applications/pages/applicationa588volun3872.aspx

FSANZ (2010) Nutrient Reference Values in the Australia New Zealand Food Standards Code – Potential Revision Consultation Paper. Food Standards Australia New Zealand, Canberra.
Regulatory nutrient reference values (foodstandards.gov.au) Accessed June 2021.

FSANZ (2011) 23rd Australian Total Diet Survey. Food Standards Australia New Zealand, Canberra.
http://www.foodstandards.gov.au/publications/pages/23rdaustraliantotald5367.aspx

FSANZ (2012) Consultation Paper – Regulation of Infant Formula Products in the *Australia New Zealand Food Standards Code*. FSANZ, Canberra. Available online at
https://www.foodstandards.gov.au/code/infant/Pages/default.aspx

FSANZ (2016a): Consultation Paper – Proposal P1028 (amended 4 May 2016). Infant formula. FSANZ, Canberra. Available online at www.foodstandards.gov.au/code/proposals/Pages/P1028.aspx.

FSANZ (2016b) Consultation paper – Proposal P1028. Supporting Document 1, Attachment A1.1 - Nutrition Assessment. FSANZ, Canberra. Available online at
https://www.foodstandards.gov.au/code/proposals/Documents/P1028-Consult-SD1-Attach-A1.pdf

FSANZ (2016c) Consultation paper – Proposal P1028. Supporting Document 1: Definitions and Nutrient Composition – Proposal P1028 Infant Formula. FSANZ, Canberra.
Available online at https://www.foodstandards.gov.au/code/proposals/Pages/P1028.aspx

FSANZ (2017): Consultation Paper – Proposal P1028. Regulation of Infant formula – Infant formula products for special dietary use. FSANZ, Canberra. Available online at
https://www.foodstandards.gov.au/code/proposals/Pages/P1028.aspx

FSANZ (2019a) Approval Report – Application A1173 – Minimum protein in follow-on formula. Food Standards Australia New Zealand, Canberra.
https://www.foodstandards.gov.au/code/applications/Documents/A1173%20Approval%20Report.pdf

FSANZ (2019b) Supporting document 1: Risk and technical assessment. Application A1102 – L-carnitine in Food. Food Standards Australia New Zealand, Canberra.
https://www.foodstandards.gov.au/code/applications/Pages/A1102-L-carnitineInFood.aspx

FSANZ (2020) Application A1155 – 2'-FL and LNnT in infant formula and other products. Food Standards Australia New Zealand, Canberra. https://www.foodstandards.gov.au/code/applications/Pages/A1155.aspx

Greenfield H, Southgate DAT (2003) Food Composition Data. Food and Agriculture Organization of the United Nations, Rome http://www.fao.org/documents/card/en/c/7a6877a2-86b5-588c-a55c-c6a1e63f19c9/

Hanson C, Lyden E, Furtado J, Van Ormer M, Anderson-Berry A. (2016) A Comparison of Nutritional Antioxidant Content in Breast Milk, Donor Milk, and Infant Formulas. Nutrients. 8(11):681. https://doi.org/10.3390/nu8110681

Holmes-McNary MQ, Cheng WL, Mar MH, Fussell S, Zeisel SH (1996) Choline and choline esters in human and rat milk and in infant formulas. Am. J. Clin. Nutr. 64(4):572–576. http://ajcn.nutrition.org/content/64/4/572.full.pdf+html

Hurrell RF, Juillerat MA, Reddy MB, Lynch SR, Dassenko SA, Cook JD (1992) Soy protein, phytate, and iron absorption in humans. Am J Clin Nutr 56(3): 573-578.

Huynh, D, Condo, D, Gibson, R, Muhlhausler, B, Ryan, P, Skeaff, S, Zhou, S. (2017) Iodine status of postpartum women and their infants in Australia after the introduction of mandatory iodine fortification. British Journal of Nutrition, 117(12), 1656-1662. doi:10.1017/S0007114517001775

IOM (1998) Dietary Reference Intakes for Thiamin, Riboflavin, Niacin, Vitamin B_6, Folate, vitamin B12, pantothenic acid, biotin and choline: a report of Standing Committee on the Scientific Evaluation on Dietary Reference Intakes and its Panel on Folate, Other B Vitamins, and Choline and Subcommittee on Upper Reference Levels of Nutrients. National Academy Press, Washington D.C.

IOM (2000) Dietary Reference Intakes for vitamin C, Vitamin E, Selenium and Carotenoids: a report of the Panel on Dietary Antioxidants and Related Compounds, Subcommittees on Upper Reference Levels of Nutrients and Interpretation and Uses of Dietary Reference Intakes, and the Standing Committee on the Scientific Evaluation on Dietary Reference Intakes. National Academy Press, Washington D.C.

Jo, B. W., Shim, Y. J., Choi, J. H., Kim, J. S., Lee, H. J., & Kim, H. S. (2015). Formula fed twin infants with recurrent hypocalcemic seizures with vitamin D deficient rickets and hyperphosphatemia. Ann. Pediatric. Endocrin. Metab,. 20(2), 102–105. https://doi.org/10.6065/apem.2015.20.2.102

Koeth RA, Wang Z, Levison BS, Buffa JA, Org E, Sheehy BT, Britt EB, Fu X, Wu Y, Li L, Smith JD, DiDonato JA, Chen J, Li H, Wu GD, Lewis JD, Warrier M, Brown JM, Krauss RM, Tang WH, Bushman FD, Lusis AJ, Hazen SL (2013) Intestinal microbiota metabolism of L-carnitine, a nutrient in red meat, promotes atherosclerosis. Nat. Med. 19(5):576–585

Koletzko B, Baker S, Cleghorn G, Neto UF, Gopalan S, Hernell O, Hock QS, Jirapinyo P, Lonnerdal B, Pencharz P, Pzyrembel H, Ramirez-Mayans J, Shamir R, Turck D, Yamashiro Y, Zong-Yi D (2005) Global standard for the composition of infant formula: recommendations of an ESPGHAN coordinated international expert group. J. Pediatr. Gastroenterol. Nutr. 41(5):584–599.

Koletzko B (2016): Human Milk Lipids. Ann. Nutr. Metab. 69(S2): 28-40. DOI: 10.1159/000452819

Koletzko B, von KR, Closa R, Escribano J, Scaglioni S, Giovannini M, Beyer J, Demmelmair H, Anton B, Gruszfeld D, Dobrzanska A, Sengier A, Langhendries JP, Rolland Cachera MF, Grote V (2009) Can infant feeding choices modulate later obesity risk? Am. J. Clin. Nutr. 89(5):1502S–1508S.

Koletzko B, Bergmann K, Brenna JT, Calder PC, Campoy C, Clandinin MT, Colombo J, Daly M, Decsi T, Demmelmair H (2020) Should formula for infants provide arachidonic acid along with DHA? A position paper of the European Academy of Paediatrics and the Child Health Foundation. Am. J Clin. Nutr. 2020, 111, 10–16.

Kouwenhoven S, Finken N, Twisk J, Van der Beek E, Abrahamse-Berkeveld M, Van de Heijning B, Schierbeek H, Holdt L, B Van Goudoever J, Koletzko B (2020) A modified low-protein infant formula supports adequate growth in healthy, term infants: a randomized, double-blind, equivalence trial. Am. J. Clin. Nutr. 111(5): 962–974, https://doi.org/10.1093/ajcn/nqz308

LSRO (1998) Assessment of nutrient requirements for infant formulas. Life Sciences Research Office. J. Nutr. 128(11S):2059S–2294S.

Lönnerdal B (1998): Copper nutrition during infancy and childhood. Am. J. Clin. Nutr. 67(5): 1046S-1053S. DOI: 10.1093/ajcn/67.5.1046S

Lönnerdal B (2008) Intestinal regulation of copper homeostasis: a developmental perspective. Am. J. Clin. Nutr. 88(3):846S–850S.

Lönnerdal B, Georgieff MK, Hernell O (2015): Developmental Physiology of Iron Absorption, Homeostasis, and Metabolism in the Healthy Term Infant. J. Pediatr. 167(4): S8-S14. DOI: 1-.1016/j.peds.2015.07.014

MacLean J, Van Dael P, Clemens R, Davies J, Underwood E, Risky L, Rooney D, Schrijver J (2010) Upper levels of nutrients in infant formulas: Comparison of analytical data with the revised Codex infant formula standard. J. Food Comp. Anal. 23(1):44–53.

Maubois JL, Lorient D (2016) Dairy proteins and soy proteins in infant foods nitrogen-to-protein conversion factors. Dairy Sci. Technol. 1–11.

McSweeney S, O'Regan J, O'Callaghan D (2013) Nutritional formulae for infants and young children. Ch 21 In: Park YW, Haenlein GFW (eds) Milk and dairy products in human nutrition: production, composition and health. John Wiley & Sons Ltd, Chichester, 458-476.

Mendonça MA, Araújo WMC, Borgo LA, Alencar EdR (2017) Lipid profile of different infant formulas for infants. PLoS ONE 12(6): e0177812. https://doi.org/10.1371/journal.pone.0177812

Ministry of Health (2008) Food and Nutrition Guidelines for Healthy Infants and Toddlers (Aged 0–2): A background paper - Partially revised December 2012. Wellington: Ministry of Health.

Ministry of Health (2018) Drinking-water Standards for New Zealand 2005 (revised 2018). Wellington: Ministry of Health.

Ministry for Primary Industries (2016) 2016 New Zealand Total Diet Study. Ministry for Primary Industries, Wellington.
https://apo.org.au/sites/default/files/resource-files/2018-05/apo-nid173731.pdf

National Health and Medical Research Council (2011) Australian Drinking Water Guidelines, Paper 6 National Water Quality Management Strategy. National Resource Management Ministerial Council, Commonwealth of Australia, Canberra.

National Health and Medical Research Council (2013) Australian Dietary Guidelines. Canberra: National Health and Medical Research Council.

NHMRC and NZ MOH (2006) Nutrient Reference Values for Australia and New Zealand. Commonwealth of Australia, Canberra. http://www.nrv.gov.au/

NHMRC and NZ MOH (2017) Australia and New Zealand Nutrient Reference Values for Fluoride. Commonwealth of Australia, Canberra.
https://www.nrv.gov.au/sites/default/files/content/resources/2017%20NRV%20Fluoride%20Report.pdf

Nommsen LA, Lovelady CA, Heinig MJ, Lonnerdal B, Dewey KG (1991) Determinants of energy, protein, lipid, and lactose concentrations in human milk during the first 12 mo of lactation: the DARLING Study. Am. J. Clin. Nutr. 53(2):457–465.

Papachristodoulou C, Tsiamou MC, Sakkas H, and Papadopoulou (2018) Determination of minerals in infant milk formulae by energy dispersive X-ray fluorescence spectrometry. J. Food Comp. Anal. 72:39-47.

Pehrsson PR, Patterson KY, Khan MA (2014) Selected vitamins, minerals and fatty acids in infant formulas in the United States. J. Food Comp. Anal. 36 (1-2): 66-71.

Penn D, Dolderer M, Schmidt-Sommerfeld E (1987) Carnitine concentrations in the milk of different species and infant formulas. Neonatology. 52(2):70-79.

Qureshi UA, Bhat AS, Jan M, Qureshi U (2020) Late Onset Hypocalcemic Seizures in Formula-Fed, Vitamin D Deficient Babies: Revisited. J. Neonatol. 34(1-2):15-18.

Riordan, P.J (1995) Fluorosis: Diagnosis, Epidemiology, Risk Factors and Prevention. Health Department Of Western Australia, Dental Services. Como, Western Australia.

Sandor A, Pecsuvac K, Kerner J, Alkonyi I. (1982) On carnitine content of the human breast milk. Pediatr. Res. 16(2):89-91.

Sommerburg O, Meissner K, Nelle M, Lenhartz H, Leichsenring M. (2000) Carotenoid supply in breast-fed and formula-fed neonates. Eur. J. Pediatr. 159, 86–90. https://doi.org/10.1007/PL00013811

Stephen A, Champ M, Cloran S, Fleith M, Van Lieshout L, Mejborn H, Burley V (2017) Dietary fibre in Europe: Current state of knowledge on definitions, sources, recommendations, intakes and relationships to health. Nutr. Res. Rev. 30(2), 149-190. doi:10.1017/S095442241700004X.

Stokes A, Campbell K, Yu H, Szymlek-Gay E, Abbott G, He Q, Zheng M (2021) Protein Intake from Birth to 2 Years and Obesity Outcomes in Later Childhood and Adolescence: A Systematic Review of Prospective Cohort Studies. Adv. Nutr. 2021 nmab034. https://doi.org/10.1093/advances/nmab034

Tang WH, Hazen SL (2014) The contributory role of gut microbiota in cardiovascular disease. J. Clin. Investig. 124(10):4204–4211.

Thomas TC, Smith JM, White PC, Adhikari S (2012) Transient neonatal hypocalcemia: presentation and outcomes. Pediatrics 129(6):e1461–e1467.

US FDA (2015) Final Rule. Infant formula: the addition of minimum and maximum levels of selenium to infant formula and related labelling requirements. 21 CFR Part 107. Available online at: https://www.federalregister.gov/articles/2015/06/23/2015-15394/infant-formula-the-addition-of-minimum-and-maximum-levels-of-selenium-to-infant-formula-and-related.

WHO/FAO (2019) Nitrogen and protein content measurement and nitrogen to protein conversion factors for dairy and soy protein-based foods: a systematic review and modelling analysis. World Health Organization. https://apps.who.int/iris/handle/10665/331206. License: CC BY-NC-SA 3.0 IGO

Yamawaki N, Yamada M, Kan-no T, Kojima T, Kaneko T, Yonekubo A (2005) Macronutrient, mineral and trace element composition of breast milk from Japanese women. J. Trace Elem. Med. Biol. 19(2-3):171–181.

Zeisel SH and Blusztajn JK (1994) Choline and Human Nutrition. Ann. Rev. Nutr. 14:1, 269-296.

Zhang Z, Adelman AS, Rai D, Boettcher J, Lonnerdal B (2013) Amino acid profiles in term and preterm human milk through lactation: a systematic review. Nutrients 5(12):4800–4821.

Appendix 1: Summary of submitter comments and FSANZ proposed approach

Compilation of submitter comments to 2016 Consultation paper and FSANZ response. See relevant section in CP for explanation and reasoning for FSANZ's proposed option.

CP section	Issue	Submitters[1]	Submitter comments	FSANZ proposed option
GENERAL COMPOSITION				
2	General compositional issues, including addition of nutrients and substances, minimum and maximum levels of nutrients, technological calculation errors and use of factor 4.81 to convert kcal to kJ.	5 (3G, 2I)	- Nutrients and substances should only be added in amounts that serve a nutritional function or other benefit. - Minimum levels of nutrients should be used as target values. - Maximum levels should be regarded as upper limits. - Technical calculation errors within the nutrient composition specified in Codex STAN 72-1981 have led to some incorrect values being applied in Standard 2.9.1. - Use of 4.18 to convert kcal to kJ (main implication is for protein minimum).	- FSANZ agrees and reiterates the 2014 EFSA opinion that minimum amounts should be understood as target values and that that maximum amounts are driven by safety aspects while also taking into account technological considerations and should not be interpreted as target values but rather as upper limits of a range which should not be exceeded. - FSANZ to rectify these errors within Standard 2.9.1. - Calculations throughout this proposal are based on 4.18.
MACRONUTRIENTS				
3.1	Energy: energy content in Standard 2.9.1 is 2500–3150 kJ/L but in Codex is 2500–2950 kJ/L.	6 (2G, 4I)	All submitters supported lowering the maximum to align with Codex STAN 72-1981.	FSANZ proposes to decrease the maximum energy content 2950 kJ/L to align with Codex STAN 72-1981
3.2	Energy: difference between Standards 2.9.1 and 1.2.8 in factors used to calculate energy.	2 (2I)	Submitters supported use of energy factors as prescribed in Standard 1.2.8	The issue was resolved in recent Code revision (P1025).
4.1	Protein calculation: appropriate nitrogen conversion factors (NCF)	13 (1G, 12 I)	Submitters had numerous views on use of 5.71, 6.25, or 6.38 as NCF for dairy- or non-dairy-based formulas. See Table 4.1.4 in CP2 for summary of comments.	Based on FSANZ's consideration of the differences between Codex STAN 72-1981 and Standard 2.9.1 in defining NCF, recent reviews on NCF from Codex and JEMNU panels, and economic factors important for manufacturers, the proposed option is to adopt 6.25 as the NCF for all protein sources.

CP section	Issue	Submitters[1]	Submitter comments	FSANZ proposed option
4.2.1	Protein: permitted range for cow's milk based	8 (2G, 6I)	Only one submitter did not support FSANZ's preliminary view to retain the current permitted range of 0.45-0.7 g/100kJ (which is aligned with Codex STAN 72-1981). The submitter proposed adopting the EU 2016/127 maximum of 0.6 g/100 kJ.	The permitted protein range is proposed to be 0.43 – 0.72 g/100 kJ based on lack of evidence of harm to infant health for this range and alignment with the most recently reviewed the Codex Draft Standard for FUF.
4.2.2	Protein: minimum for soy-based formula	7 (4G, 3I)	All supported a higher minimum to be applied for soy-based formulas, noting that this needs to be considered in conjunction with the appropriate NCF for the protein source.	The minimum protein amount for soy-based formula is proposed to be 0.54 g/100 kJ, based on the 6.25 as the NCF. This is consistent with the regulations set under EU 2016/127 and the Codex Draft Standard for FUF.
4.3	Protein: source	6 (3G, 3I)	Industry supported FSANZ's preliminary the view that no change to protein source requirements (which regulate protein quantity and quality) was required. This view was opposed in government submissions.	Based on concerns about new proteins that may not be approved through pre-market approval, FSANZ proposes that the protein source be specified to be cow's milk protein, goat's milk protein, protein hydrolysates of one or more proteins normally used in infant formula, and soy protein isolate.
4.4	Protein: quality and use of protein scoring methods	4 (4I)	All supported FSANZ's preliminary view that human milk amino acid composition should remain as the reference. Implementation of the DIAAS method would be appropriate once the supporting science was complete.	FSANZ proposes to maintain the current requirements for protein quality by mandating minimum amino acid amounts.
4.5	Amino acid content: including expression of sulphur amino acids (cysteine and methionine) and aromatic amino acids (aromatic amino acids)	9 (1G, 8 I)	All agreed with FSANZ's preliminary view to align with Codex STAN 72-1981 for isoleucine, leucine, lysine, threonine, tryptophan and valine. All opposed FSANZ's preliminary view to retain current Standard 2.9.1 requirements for expression of sulphur amino acids and aromatic amino acids.	FSANZ proposes to align all amino acid minimum amounts with Codex STAN 72-1981. The ratios of Methionine:Cystine and Tyrosine:Phenyalanine consistent with the EU 2016/127 regulation will be listed as a condition in Schedule 29.
5.1	Fat content	6 (2G, 4I)	All supported FSANZ's preliminary view to align the permitted fat content with Codex STAN 72-1981 (1.05 -1.4 g/100 kJ.	FSANZ proposes to set the permitted range for fat to 1.05- 1.4 g/100 kJ which is aligned with Codex STAN 72-1981 and EU 2016/127 C and is consistent with levels found in human milk.
5.2	Fat: units of expression: mg/100 kJ or as a percentage of total fatty acids	3 (3I)	Submitters agreed with FSANZ's preliminary view that units of expression should be mg/100 kJ to align with Codex STAN 72-1981. They suggested that a calculation and appropriate assumptions be included in Standard 2.9.1 so that fatty acids acid can be expressed as a percentage of total fatty acids.	FSANZ's proposed option is to align with Codex STAN 72-1981. A calculation for converting fatty acids amounts from % fatty acids to mg/100 kJ will not be included.

CP section	Issue	Submitters[1]	Submitter comments	FSANZ proposed option
5.3	Essential fatty acid composition: LA and ALA minimum amounts	8 (4G, 3I, 1HP)	Industry submissions and one HP considered that the minimum LA amount should be lowered to the Codex STAN 72-1981 level (70 mg/100kJ), with appropriate consideration of the LA:ALA ratio. Government submitters supported increasing the minimum LA amount to align with EU 2016/127 and EFSA's 2014 Scientific Opinion (120 mg/100 kJ).	Based on the stability and palatability concerns associated with higher LA levels, history of safe use at current levels and no emerging safety or adequacy concerns for infants, FSANZ proposes to retain the current minimum requirement for LA within Standard 2.9.1. FSANZ is also seeking further information on nutritional adequacy and technological concerns in meeting a higher level of LA in infant formula.
5.4	Long chain PUFA: mandatory or optional addition of DHA And other LC PUFA, ratios and sources	8 (3G, 5I) 3 (3I)	There was no clear agreement on the preferred approach. Two industry submitters supported FSANZ's preliminary view to retain the voluntary addition of DHA. All other submitters supported adopting the EU 2016/127 requirements with or without concomitant addition of arachidonic acid. All submissions agreed with FSANZ's preliminary view that to maintain the current requirement for EPA content to be no more than DHA content, maintain the current requirement that a maximum proportion of no more than 1% total fatty acids when AA is present and replace the minimum ratio of total n-6 to total n-3 with the Codex STAN 72-1981 minimum ratio of AA:DHA.	FSANZ proposes to retain the current voluntary permission for DHA based on the conclusions of Koletzko et al. (2019). When DHA is present, the amount should be controlled with a guidance limit, by adopting the Codex STAN 72-1981 GUL amount for DHA of 0.5% total fatty acids. Based on submitter support FSANZ proposed options for source of LC-PUFA, EPA, AA, and ratios of DHA, AA, and LC-PUFA are unchanged from the previous consideration of these topics in the 2016 Consultation paper.
5.5	Fat source: define by permitting or prohibiting certain fat sources	9 (2G, 6I, 1 HP)	Six submitters supported the current approach where Standard 2.9.1 does not specify or prohibit any particular sources of fat but instead sets specific requirements which restrict fat composition Two submissions considered more specification was needed on certain fat sources.	FSANZ considers that the current approach which restricts fat composition should be retained. Clarification around fat sources permitted to be used is related to the question around pre-market assessment of new macronutrient types or form which is discussed in CP3.
5.6.1	Restrictions on certain fats: MCTs	6 (3G, 3I)	Government submitters supporting the existing restriction. Industry submitters supported removal of existing restrictions on MCT to align with Codex STAN 72-1981 and allow greater choice of fat sources to be used.	In conjunction with the proposed option to not specify permitted sources of fat, and in line with the nutrition risk assessment conclusions, the proposed option is to retain the current restrictions on MCTs.
5.6.2	Restrictions on certain fats: TFA	6 (1G, 5I)	Industry submitters support maintaining the current restriction on total TFA at a maximum of 4% of total fatty acids, whereas the government submitter supported the option to lower the maximum to 3% of total fatty acids to align with Code STAN 72-1981.	FSANZ proposes to retain the current restriction on TFA. Aligning with Codex STAN 72-1981 for TFA wo require a change in the definition of TFA in the Code. FSANZ considers this to be out of scope for this proposal.

CP section	Issue	Submitters[1]	Submitter comments	FSANZ proposed option
5.6.3	Restrictions on certain fats: Phospholipids (PL)	9 (3G, 6I)	Government submitters supported restriction of total PL to 2g/L (72 mg/100 kJ) to align with Codex STAN 72-1981. Industry submitters supported the current approach (no maximum limit on PL) or supported alignment with Codex STAN 72-1981.	The issue is complicated by the existence of two maximums for PL: one for PL as a nutritive substance source of LC PUFA in infant formula, and one for PL as a component of lecithin which is a food additive or processing aid permitted to be used in infant formula. In order to clarify the permissions, FSANZ proposes to align with the Codex STAN 72-1981 maximum permitted amount. This will included PL present as source of LC PUFA and as a component of added lecithin.
5.6.4	Other fatty acids: myristic, lauric, and erucic acids	3 (3I)	Submitters supported FSANZ's preliminary view to retain current restrictions in Standard 2.9.1 for erucic acid, lauric and myristic acids.	FSANZ proposes to retain the current restrictions in Standard 2.9.1 for these fatty acids.
6.1	Carbohydrate: definitions and calculations	3 (1G, 2I)	All submitters supported FSANZ's preliminary view that that definitions in the current Code are appropriate for infant formula. We considered that the classification of carbohydrates as available or unavailable was best left to manufacturers. Energy factors were considered to be appropriate as specified in Schedule 11.	FSANZ proposes to retain current requirements in Standard 2.9.1.
6.2	Dietary fibre: need for a definition and/or prescribed methods of analysis	4 (2G, 2I)	There was no agreement in submitter views on dietary fibre. Currently the Code is aligned with Codex STAN 72-1981 and the EU 2016/127in not prescribing methods of analysis for dietary fibre.	Given that there is no identified safety issues with the current approach, and since it is already aligned with international regulations, FSANZ proposes no change to the existing requirements.
6.3	Carbohydrate source: need for provisions to define or restrict unsuitable carbohydrate sources	10 (4G, 6I)	Government submitters supported consideration of the EFSA 2014 opinion and alignment with Codex STAN 72-1981, which restricts certain types of carbohydrates. Industry supported the current approach (no restrictions) citing the lack of evidence suggesting safety concerns or adverse effects. Industry also noted that sucrose was not used in infant formulas manufactured in ANZ.	FSANZ proposes to adopt limits on sucrose and fructose that are aligned with Codex STAN 72-1981. This option is supported by safety concerns cited by government submitters, by FSANZ's safety (risk) assessment conducted in 2002, and by international requirements that will come into place in 2020 that in line with the Codex STAN 72-1981.
6.4	Carbohydrate: permitted range for total carbohydrate content	2 (2I)	Submitters agreed with the current approach under Standard 2.9.1, in which carbohydrate content is calculated by difference from protein, fat and energy content.	The proposed option is to retain the current approach in Standard 2.9.1, which does not specify a permitted range for carbohydrate content.
MICRONUTRIENTS				

CP section	Issue	Submitters[1]	Submitter comments	FSANZ proposed option
7.1	GULs and regulatory maximums	11 (3G, 8I)	Generally, use of GULs for micronutrients was supported industry submitters and opposed by government submitters. Specific comments were provided and considered on vitamin C, iodine, phosphorus, selenium and folate.	**Regulatory maximums** applied to: vitamin A, vitamin D, chloride, sodium, potassium, iron, iodine and selenium. **GULs applied to**: vitamin E, vitamin K, vitamin C, niacin, thiamin, riboflavin, vitamin B6, folate, pantothenic acid, vitamin B12, biotin, calcium, phosphorus, magnesium, iron, copper, zinc, manganese, chromium, and molybdenum.
VITAMIN DIETARY EQUIVALENTS AND CONVERSION FACTORS				
7.2.1	Including β-carotene in total vitamin A content	7 (5I, 2G)	All supported excluding β-carotene from vitamin A content based on uncertainty around its bioavailability and to align with international regulations.	FSANZ proposes to exclude β-carotene from the vitamin A calculation.
	Units of expression: vitamin A	3 (3I)	All supported the using µg of RE to clarify the units of expression for vitamin A content and to align with Codex STAN 72-1981 .	FSANZ proposes to express vitamin A requirements as µg RE/100 kJ.
7.2.2	Use of Dietary Folate Equivalents (DFE) to express folic acid amounts	11 (7I, 4G)	Industry submitters and one government submitter did not support use of DFE as this would not align with Codex STAN 72-1981. Three government submitters supported the application of DFE referring to EFSA's opinion (2014) and updated EU regulations.	FSANZ proposes to express the requirements for folic acid/folate as µg folic acid/100 kJ. The contribution of folate from ingredients (naturally occurring folate) will not be included in the permitted range for this vitamin, in turn there is no need for using DFE as units of expression in folic acid amounts.
	Including folate from ingredients (such as cow's milk) to the total folic/folate amount	10 (7I, 3G)	Two government submitters considered that folate should be included citing the evidence reported in 2010 by MacLean. The remaining submitters supported exclusion of naturally occurring folate from the total folic/folate amounts as there are no straightforward and reliable methods to quantify both forms. The amount of naturally occurring folate in infant formula (from ingredients such as cows' milk) is likely to be minimal.	FSANZ proposes to exclude folate from the permitted range for folic acid. Recent studies have shown that folate amounts in infant formula is minimal compared to folic acid that is added.
7.2.3	Adopt mg α-TE/100 kJ as units for vitamin E and whether the Codex STAN 72-1981 equivalence factors for PUFA content should be applied.	3 (2I, 1G)	All supported FSANZ's preliminary view to express vitamin E in units of mg α-TE/100 kJ and that the current Standard 2.9.1 requirements relating to the PUFA content is retained.	FSANZ proposes to adopt units of mg α-TE/100 kJ for vitamin E and no change to the current requirements to account for PUFA content.
PERMITTED RANGE FOR MICRONUTRIENTS				

CP section	Issue	Submitters[1]	Submitter comments	FSANZ proposed option
7.3.1	Vitamin A: Codex STAN 72-1981 and Standard 2.9.1 are aligned but conflict with EU 2016/127	2 (1I, IG)	The government submitter proposed lowering the maximum to 27.2 µg RE/100 kJ to align with the EU 2016/127. The industry submitter supported retaining the current maximum level.	FSANZ proposes retain the current maximum vitamin A amount based on the absence of data indicating that the current maximum of 43 µg/100 kJ is associated with adverse health effects, the uncertainty around the basis for the EU 2016/127, and that the objective of this Proposal to align with Codex STAN 72-1981 where possible.
7.3.1	Vitamin D: Codex STAN 72-1981 and Standard 2.9.1 are aligned but conflict with EU 2016/127	6 (5I, 1G)	Industry submitters supported alignment with the EU 2016/127 as the current range is too narrow to allow compliance with both Codex STAN 72-1981 and EU 2016/127. The government submitter supported retaining current Standard 2.9.1.	The EU 2016/127 maximum was recently lowered and is now aligned with Codex STAN 72-1981 at 0.6 µg/100 kJ. FSANZ proposes to retain the current permitted range as this meets ANZ recommended daily intakes, no safety concerns have been identified, and the range is achievable for industry.
7.3.2	11 micronutrients (calcium, chloride, magnesium, manganese, folate, niacin, pantothenic, potassium, sodium, vitamin B12, and vitamin E) not currently aligned with Codex STAN 72-198.	0	Preliminary view from the 2016 CP was to align with Codex STAN 72-1981 (i.e. no were issues identified). No submitters commented on the permitted range for these micronutrients.	FSANZ proposes to align with the Codex STAN 72-1981 permitted range for calcium, chloride, magnesium, manganese, folate, niacin, pantothenic, potassium, sodium, vitamin B12, and vitamin E.
7.3.2	Vitamin K, thiamin, riboflavin, vitamin B6, biotin: propose alignment with Codex STAN 72-1981	3 (2I, 1G)	Industry submitters supported FSANZ's preliminary view to align the permitted range with the Codex STAN 72-1981 amounts. The government submitter opposed alignment on the basis that the EU 2016/127 minimum was more consistent with human milk concentration and intakes would be closer to the AI.	Based on additional nutrition risk assessment and consideration of submitter comments, FSANZ proposes the following: Vitamin K: adopt EU 2016/127 minimum Thiamin: retain Standard 2.9.1 Riboflavin: adopt EU 2016/127 permitted range Vitamin B6: retain Standard 2.9.1 Biotin: adopt EU 2016/127 minimum Maximums for these micronutrients are noted in section 7.1.
7.3.2	Copper	5 (3I, 2G)	Four submitters supported alignment with Codex STAN 72-1981. One submitter commented that the use of liquid, ready-made infant formula in hospitals would not have copper form contribution and therefore copper requirements not met for these infants.	FSANZ proposes that the permitted range for copper is proposed to be aligned with Codex STAN 72-1981 at 8.5- 29 (GUL) ug/100 kJ.

CP section	Issue	Submitters[1]	Submitter comments	FSANZ proposed option
7.3.3	Vitamin C: maximum is much higher under Codex STAN 72-1981	8 (5I, 3G)	Most submitters supported adopting the Codex STAN 72-1981 maximum for vitamin C however, two government submitters expressed concerns about excessive intakes and supported adoption of the EU 2016/127 maximum.	FSANZ identified no safety concerns with the maximum set under Codex STAN 72-1981 or EU 2016/127. To allow for vitamin C degradation over the product shelf life and ensure infants have adequate intakes, and for harmonisation reasons, the proposed option to is to align with the maximum level set by Codex STAN 72-1981 (17 mg/100 kJ).
7.3.3	Chromium and Molybdenum: need for a minimum level and whether to retain the current GUL	4 (3I, 1G)	Industry submitters do not support a minimum, maximum or GUL being set for chromium and molybdenum on the basis of insufficient evidence for these restrictions. NZ MPI commented that the 2016 NZ TDS included data on on chromium and molybdenum levels in infant formula to be considered.	Results for chromium and molybdenum from the 2016 NZ Total Diet Study were below the limit of reporting and therefore not useful to estimate intakes. Therefore, based on the conclusions in the 2016 Consultation paper, FSANZ proposes to align the permissions for chromium and molybdenum with Codex STAN 72-1981.
7.3.3	Iodine: minimum under Codex STAN 72-1981 is two-fold higher than minimum in Standard 2.9.1	11 (8I, 2G, 1 HP)	All submitters supported increasing the minimum level to at least that specified in Codex STAN 72-1981.	To ensure infants meet their requirements for iodine, the proposed approach is to align the minimum amount with EU 2016/127 (3.6 µg/100 kJ). FSANZ proposes to retain the existing Standard 2.9.1 maximum as this amount is comparable to expert recommendations and is an amount that manufacturers are able to meet already.
7.3.3	Zinc , the Zn:Cu ratio and appropriate maximum for soy-based formula	5 (2G, 3I)	Retaining the prescribed Zn:Cu ratio was not supported. Views on the maximum level were varied. Use of the Codex STAN 72-1981 maximum was supported by three submitters, one submitter supported retaining the current maximum and one supported aligning the zinc maximum with EU 2016/127 since this level would be closest to the ANZ UL. One government submitter noted support for setting separate limits for zinc in soy-based infant formula to align within EU 2016/127. An industry submitter did not support setting separate levels for zinc as higher levels of zinc intake could impact on the absorption of copper, however proposed an upper level for zinc for all formulas should account for any additional needs of soy-based formula.	FSANZ proposes to remove the prescribed Zn:Cu ratio. FSANZ proposes to align the permitted range with Codex STAN 1972-81 which includes a maximum that accommodates the higher concentration of zinc in soy-based formula.

CP section	Issue	Submitters[1]	Submitter comments	FSANZ proposed option
7.3.	Iron: permitted range (minimum and maximum)	8 (3G, 3I)	Four submitters supported FSANZ's 2016 view to retain the range currently specified in Standard 2.9.1. There was also support to adopt the Codex STAN 72-1981 and EU 2016/127. An industry submitter supported increasing bioavailability by choosing appropriate forms of iron, reducing phytate content and/or adding absorption enhancers such as ascorbic acid. A submission also noted caution regarding high-iron infant formula being associated with poorer developmental outcomes in infants.	FSANZ proposes to retain the current minimum and maximum in Standard 2.9.1. Retaining the broader permitted range in Standard 2.9.1 accounts for older infants and soy-based infant formula and aligns with the current ANZ market. Retaining the current standard also allows manufacturers to meet the Codex STAN 72-1981 and EU 2016/127 ranges for iron, while still posing the least risk to infant health.
7.3.3	Selenium	8 (5I, 3G)	Government submitters supported FSANZ's preliminary view to increase the selenium minimum. Industry submitters supported retaining Std. 2.9.1 level on basis that manufacturers already target a higher amount.	FSANZ proposes to set the selenium permitted range to 0.48 - 2.2 ug/100 kJ. The increased minimum would align with recent international regulations, would meet the ANZ AI, and is slightly higher than breast milk concentrations of ANZ mothers, a population that may not be selenium sufficient. The increased maximum would align with Codex STAN 72-1981 and allows a range that is comparable to other international regulations.
RATIOS AND EQUIVALENTS				
7.4.1	Phosphorus and the Ca:P ratio	6 (3G, 3I)	All submitters supported FSANZ proposal to adjust Standard 2.9.1 to align with the minimum Ca:P ratio prescribed by Codex STAN 72-1981 of 1:1. Industry submitters supported adopting the Codex STAN 72-1981 GUL of 24mg/100 kJ. Government submitters raised cautions about adopting the GUL based on evidence of hypocalcaemia in neonates fed infant formal and ULs derived by the NHMRC/MoH for young children suggest that excessive intakes should be avoided. Government submitters were in support of setting a separate minimum and maximum for phosphorus levels in soy-based infant formula.	FSANZ proposes to adjust Standard 2.9.1 to align with the Codex STAN 72-1981 minimum Ca:P ratio of 1:1. FSANZ notes that the evidence suggesting hypocalcaemia in neonates fed infant formal and UL, concluded hypocalcaemia was considered to be associated with vitamin D deficiency. Based on Codex STAN 72-1981 and conclusions from the 2016 nutrition assessment FSANZ proposes to adjust the current phosphorus maximum (25 mg/100 kJ) in Standard 2.9.1 to a GUL of 24 mg/100 kJ. FSANZ also proposes retaining a phosphorus range that accounts for all infant formula products (including soy-based infant formulas), however is seeking further information on this issue to inform future considerations.

CP section	Issue	Submitters[1]	Submitter comments	FSANZ proposed option
7.4.2	Vitamin E: fatty acids ratio	3 (1G, 2I)	All submitters supported retaining the current approach in Standard 2.9.1.	Based on the 2016 nutrition assessment conclusions and stakeholder support FSANZ's proposes to retain the current permission for vitamin E requirements relating to the PUFA content of infant formula within Standard 2.9.1. It is not considered necessary to adopt the 'factors of equivalence' for α-TE to individual PUFA outlined in Codex STAN 72-1981.
7.4.3	Copper, vitamin C and iron: nutrient interaction			
PERMITTED FORMS				
7.5	Permitted forms	5 (5I)	Industry submitters considered that all the forms of nutrients permitted in Codex STAN 72-1981 should be permitted in Standard 2.9.1 for reasons of alignment, flexibility for manufacture and avoidance of trade barriers.	FSANZ proposes to permit the Codex STAN 72-1981 permitted forms for pantothenic acid, niacin, copper, magnesium, potassium, zinc, and iron.
7.5.1	β-carotene: purpose of its use as a permitted form of vitamin A and whether it is included in the total vitamin A content	8 (6I, 2G)	Industry submitters supported retaining the current Standard 2.9.1 permission and commented that β-carotene is a colouring agent and anti-oxidant in foods and many products are formulated to include this nutrient for these purposes. Government submitters either opposed β-carotene addition or requested further consideration to justify its addition.	For international harmonisation, FSANZ proposes to retain permission for β-carotene as a permitted form but this will not be included in the vitamin A content.
7.5.2	Vitamin D_2 and bioavailability compared to vitamin D_3	2 (1I, 1G)	Industry supported retaining both forms of vitamin D as permitted forms. The government submitter considered that vitamin D_2 should only be permitted with evidence that it is equally bioavailable to vitamin D_3.	Based on further nutrition risk assessment and the conclusions of the Codex Draft Standard for FUF, FSANZ proposes to retain both vitamin D_2 and vitamin D_3 as permitted forms in Standard 2.9.1.
OTHER OPTIONAL SUBSTANCES				
8.1	Choline: permitted range and forms	13 (11I, 2G)	All submitters supported listing choline as a mandatory substance in infant formula with a range of 1.7 – 12 mg/100 kJ. The majority also noted that the upper amount should be presented as a GUL as per Codex STAN 72-1981. Industry submitters supported the inclusions of the additional forms.	FSANZ proposes that choline should be permitted within Schedule 29 as a mandatory substance in infant formula with a range of 1.7 – 12 mg/100 kJ, to align with the Codex STAN 72-1981. The proposed approach also notes that the maximum should be presented as a GUL. It is proposed that choline should be permitted as the following forms in Schedule 29: choline chloride, choline bitartrate, choline, choline citrate and choline hydrogren tartrate.

CP section	Issue	Submitters[1]	Submitter comments	FSANZ proposed option
8.2	L-carnitine: permitted range and forms	14 (11I, 2G, 1HP)	Majority of submitters supported listing L-carnitine as a mandatory substance in infant formula. Submitters also supported the use of a higher minimum level to align with the Codex STAN 72-1981. The majority noted concerns of achieving the proposed maximum and noted that a GUL is more appropriate. The majority of submitters supported the use of L-carnitine hydrochloride and/or L-carnitine tartrate in infant formula and provided technological justification.	For international harmonisation, FSANZ proposes to permit L-carnitine as a mandatory minimum of 0.3g/100 kJ and a GUL of 0.8mg/100kJ. Based on the safety conclusions of Codex STAN 72-1981 and *A1102 – L-carnitine in Food,* FSANZ proposes that L-carnitine should be permitted as L-carnitine hydrochloride and L-carnitine tartrate in Schedule 29.
8.3	Inositol: permitted range and forms	9 (7I, 2G)	All submitters supported listing inositol as a mandatory substance in infant formula and listing the permitted form of inositol as myo-inositol. Industry submitters supported the change to a GUL rather than a maximum upper level, to align with Codex STAN 72-1981.	Based on alignment with Codex STAN 72-1981, FSANZ proposes that inositol should be permitted within Schedule 29 as a mandatory substance in infant formula with a minimum of 1.0 mg/100 kJ, GUL of 9.5 mg/100 kJ and listing the permitted form of inositol as myo-inositol.
8.4	Nucleotides: permitted range and forms	7 (5I, 2G)	Industry supported retaining the current permission and maximum combined total limit of nucleotides. All submitters commented on the clarity of the drafting for the maximum amount of nucleotides in the Code, of which four industry submitters commented on considering that the combined total content should only apply when nucleotides are added to infant formula.	FSANZ proposes retaining the current permission and maximum total limit of nucleotides within Schedule 29.
OTHER COMPOSITION ISSUES RAISED IN SUBMISSIONS				
Nil raised.				

[1] *Indicates number of submissions that commented on this issue; I = Industry, G = Government, HP = Health Professional*

Appendix 2: Nitrogen conversion factors - examples for illustrative purposes

Protein source	NCF	Basis
Soy	1 g N = 5.71 g protein	Experimentally determined, science-based NCF for soy protein sources (Maubois and Laurient 2015).
General	1 g N = 6.25 g protein	An approximated conversion factor for all protein sources based on average nitrogen content of mixed food proteins which is approximately 16%
Cow's milk	1 g N = 6.38 g protein	Experimentally determined, science-based NCF for dairy protein sources (Maubois and Laurient 2015).

How much SPI is needed for 100 g IF at minimum protein level of 0.45 g/100 kJ using NCF of 5.71 or 6.25?

Required minimum: 0.45 g P /100 kJ = 1.23 g P /100 g IF
(assuming 2725 kJ/L and 1ml IF = 1 g IF)

For illustrative purposes, the measured nitrogen in SPI is 10 g N/100 g SPI.

Using NCF = 5.71:

$$\frac{10\ g\ N}{100\ g\ SPI} \times \frac{5.71\ g\ protein}{g\ N} = \frac{0.517\ g\ protein}{g\ SPI}$$

$$\frac{0.571\ g\ protein}{g\ SPI} \times X\ g\ SPI = \frac{1.23\ g\ protein}{100\ g\ IF}$$

Concentration of protein in source (measured as N)

Calculate how much SPI to give 1.23 g Protein per 100 g IF

Minimum level of protein under FSC

$$X\ g\ SPI = \frac{1.23\ g\ protein}{100\ g\ IF} \times \frac{g\ SPI}{g\ 0.571\ g\ protein} = \frac{2.51\ g\ SPI}{100\ g\ IF}$$

Using NCF = 6.25

$$X\ g\ SPI = \frac{1.23\ g\ protein}{100\ g\ IF} \times \frac{g\ SPI}{g\ 0.6.25\ g\ protein} = \frac{1.97\ g\ SPI}{100\ g\ IF}$$

Therefore, using 6.25 (instead of 5.71) as the NCF means that 8.4% less SPI needs to be added to meet the minimum protein amount. In other words, using 6.25, the protein content is over-estimated from the true protein content. One way to address this would be to use NCF of 6.25 but increase minimum protein content for soy-based formulas by 10%.

For cow's milk protein

How much cow's milk protein is needed for 100 g IF at minimum protein level of 0.45 g/100 kJ using NCF of 6.25 or 6.38?

For illustrative purposes, the measured nitrogen in cow's milk protein is 10 g N/100 g protein.

Similar calculation:

Required minimum: 0.45 g P /100 kJ = 1.23 g P /100 g IF
(assuming 2725 kJ/L and 1ml IF = 1 g IF)

Using NCF = 6.25:

$$\frac{10\ g\ N}{100\ g\ protein} \times \frac{6.25\ g\ protein}{g\ N} = \frac{0.625\ g\ protein}{g\ protein}$$

Concentration of protein in source (measured and N)

Calculate how much cow's milk protein to give 1.23 g protein per 100 g IF

Minimum level of protein under FSC

$$\frac{0.625\ g\ protein}{g\ protein} \times X\ g\ cow's\ milk\ protein = \frac{1.23\ g\ protein}{100\ g\ IF}$$

$$Amount\ cows'\ milk\ protein = \frac{1.23\ g\ protein}{100\ g\ IF} \times \frac{g\ cow's\ milk\ protein}{g\ 0.625\ g\ protein} = \frac{1.97\ g}{100\ g\ IF}$$

Using NCF = 6.38

$$Amount\ cow's\ milk\ protein = \frac{1.23\ g\ protein}{100\ g\ IF} \times \frac{g\ cow's\ milk\ protein}{0.638\ g\ protein} = \frac{1.93\ g}{100\ g\ IF}$$

Therefore, using 6.25 (instead of 6.38) as the NCF means that 2.0% more cows' milk protein needs to be added to meet the minimum protein amount.

Appendix 3: Fluoride and infant formula calculation

The recently revised AU and NZ NRVs for fluoride have:

- Reaffirmed the AI for children aged 7 months to 8 years to be 0.05 mg/kg bw/day
- Withdrawn the AI for infants aged 0 - 6 months
- Revised the UL for fluoride for infants and children up to 8 years from 0.10 to 0.20 mg/kg bw/day. Updated bodyweight information was used to present the UL as 1.2 mg/day for infants aged 0 – 6 months and 1.8 mg/day for infants aged 7 – 12 months

NHMRC Nutrient Reference Values

Age	Upper level of intake
0 – 6 months	1.2 mg/day
7 - 12 months	1.8 mg/day

Under Australian Drinking water guidelines (NHMRC 2011)

- Maximum permitted fluoride concentration in drinking water = 1.5 mg/L
- Minimum level for a protective effect against dental caries is about 0.5 mg/L
- The critical figure is 1.0 mg/L as this is the point at which maximal protection against dental caries is reached with minimum risk of dental fluorosis.

Under Standard 2.9.1 Infant formula, fluorosis statement if:

- Fluoride level in IF powder > 17µg/100kJ

Under Codex STAN72- 1981 when prepared '*as recommended*':

- Maximum fluoride should not exceed 24µg/ 100kJ

Question 1: Does powdered infant formula prepared with tap water contain levels of fluoride that may pose a risk to health and safety if consumed?

Several calculations were performed using a popular brands of infant formula powder and water fluoride contents of 0, 0.5, 1.0 and 1.5 mg F/L. It is important to note that the critical level for water fluoridation is 1.0 mg/L and the maximal level of 1.5 mg/L is not considered generally relevant to Australian conditions.

Example brand 1 formula powder for one-month-old male infant (4.4 kg):

1. Formula energy content = 280 kJ/100 mL as prepared
2. Recommended energy intake (EER) = 2000 kJ/day
3. Prepared with 12.5 g powder + 90mL water (to provide 280 kJ)
4. Estimated formula volume = 715 mL Estimated water volume = 626 mL water (and 87 g infant formula powder) per 2000 kJ

Table A1: Male infant one-month-old using brand 1 formula powder

(1) F level in water mg/L[14]	(2) F level in IF powder µg/100kJ[15] (µg/2000 kJ or µg/day[16])	(3) F intake water mg/day (per 626 mL)	(4) F intake IF powder mg/day	(3) + (4) Total est. F intake mg/day
Median level found in Au IF powder	0 (0)	0	0.00	0.00
	2 (40)	0	0.04	0.04
	4 (80)	0	0.08	0.08
0	8 (160)	0	0.16	0.16
2.9.1 Fluorosis statement required >17 µg/100kJ	16 (320)	0	0.32	0.32
	20 (400)	0	0.40	0.40
STAN 72-1981 max	24 (480)	0	0.48	0.48
	25 (500)	0	0.50	0.50
Median level found in Au IF powder	0 (0)	0.31	0.00	0.31
	2 (40)	0.31	0.04	0.35
	4 (80)	0.31	0.08	0.39
0.5	8 (160)	0.31	0.16	0.47
2.9.1 Fluorosis statement required >17 µg/100kJ	16 (320)	0.31	0.32	0.63
	20 (400)	0.31	0.40	0.71
	25 (500)	0.31	0.50	0.81
Median level found in Au IF powder	0 (0)	0.63	0.00	0.63
	2 (40)	0.63	0.04	0.67
	4 (80)	0.63	0.08	0.71
1.0[17]	8 (160)	0.63	0.16	0.79
2.9.1 Fluorosis statement required >17 µg/100kJ	16 (320)	0.63	0.32	0.95
	20 (400)	0.63	0.40	1.03
	25 (500)	0.63	0.50	1.13
Median level found in Au IF powder	0 (0)	0.94	0.00	0.94
	2 (40)	0.94	0.04	0.98
	4 (80)	0.94	0.08	1.02
1.5[18]	8 (160)	0.94	0.16	1.10
2.9.1 Fluorosis statement required >17 µg/100kJ	16 (320)	0.94	0.32	1.26
	20 (400)	0.94	0.40	1.34
	25 (500)	0.94	0.50	1.44

F = Fluoride
IF = Infant Formula

[14] Water fluoridation levels from 0 to 1.5 mg/L were used in these calculations to account for water fluoride concentration variation. While 1.5 is the maximum allowed fluoride content in Australian tap water, in practice 1.0 mg/L is recognised as the optimum level for both reduction of dental caries and minimisation of risk of severe dental fluorosis.
[15] A wide range of fluoride content of milk based infant formula powder was used (0 – 25 µg/100 kJ) in these calculations in order to encompass the STAN 72- 1981 maximum allowed and the Standard 2.9.1 labelling requirement at 17 µg/100 kJ). The Codex standard is marked with a green background in the table and the Standard 2.9.1 trigger for labelling in gold. The median concentration of fluoride was 2.37 µg/100 kJ in milk based formula powder (Clifford et al. [2009]) and this is indicated with the blue shading. It is important to note that the STAN 72- 1981 refers to formula reconstituted as recommended, and Standard 2.9.1 refers to infant formula powder prior to reconstitution so the only STAN 72-1981 figure to consider for each Table is that which uses water with zero fluoride content.
[16] To convert µg F/100KJ to µg F/day (2000 kJ) multiply by 20
[17] Optimally fluoridated water (1.0 mg/L) results in a daily fluoride intake from reconstituted milk based formula of approximately half the UL.
[18] It is extremely unlikely that water with a fluoride concentration of 1.5 mg/L would be used to reconstitute infant formula powder. As the median fluoride level found in milk based infant formula in Australia was less than 2.5 µg/100 kJ it would require concentrations of fluoride six times higher than normal to reach a level that would (a) trigger labelling requirements and (b) reach the UL for infants.

Example brand 2 formula powder for three-month-old male infant (6 kg):

1. Formula energy content = 280 kJ/100 mL as prepared
2. Recommended energy intake (EER) = 2400 kJ/day
3. Prepared with 12.5 g powder + 90mL water provides 280 kJ
4. Estimated formula volume = 857 mL
5. Estimated water volume = 749 mL water (and 104 g infant formula powder) per 2400 kJ

Table A2: Male infant three-month-old using brand 2 formula powder

(1)	(2)	(3)	(4)	(3) + (4)
F level in water mg/L	**F level in IF powder µg/100kJ (µg/2400 kJ or µg/day)**	**F intake water mg/day (per 749 mL)**	**F intake IF powder mg/day (per 104 g)**	**Total est. F intake mg/day**
Median level found in Au IF powder	0 (0)	0	0.00	0.00
	2 (48)	0	0.05	0.05
	4 (96)	0	0.10	0.10
0	8 (192)	0	0.19	0.19
2.9.1 Fluorosis statement required >17 µg/100kJ	16 (384)	0	0.38	0.38
	20 (480)	0	0.48	0.48
STAN 72-1981 max	24 (576)	0	0.58	0.58
	25 (600)	0	0.60	0.60
Median level found in Au IF powder	0 (0)	0	0	0.00
	2 (48)	0.37	0.05	0.47
	4 (96)	0.37	0.10	0.47
0.5	8 (192)	0.37	0.19	0.56
2.9.1 Fluorosis statement required >17 µg/100kJ	16 (384)	0.37	0.38	0.75
	20 (480)	0.37	0.48	0.85
	25 (600)	0.37	0.60	0.97
	0 (0)	0.75	0	0.75
Median level found in Au IF powder	2 (48)	0.75	0.05	0.80
	4 (96)	0.75	0.10	0.85
	8 (192)	0.75	0.19	0.94
1.0[19]	16 (384)	0.75	0.38	1.13
2.9.1 Fluorosis statement required >17 µg/100kJ	20 (480)	0.75	0.48	1.23
	25 (600)	0.75	0.60	1.35
Median level found in Au IF powder	0 (0)	1.12	0	1.12
	2 (48)	1.12	0.05	1.17
	4 (96)	1.12	0.10	1.22
	8 (192)	1.12	0.19	1.31
1.5	16 (384)	1.12	0.38	1.50
2.9.1 Fluorosis statement required >17 µg/100kJ	20 (480)	1.12	0.48	1.60
	25 (600)	1.12	0.60	1.72

F = Fluoride
IF = Infant Formula

[19] A 3-month-old male infant consuming reconstituted milk based infant formula at recommended levels would reach the UL when optimally fluoridated water was used only if the milk powder contained levels of fluoride seven times that currently found (Clifford et al. 2009).

Example brand 3 formula powder form male seven-month-old infant (8.4 kg):

1. Formula energy content = 275 kJ/100 mL as prepared
2. Recommended energy intake (EER) = 2800 kJ/day
3. Prepared with 13 g powder + 90 mL water provides 275 kJ
4. Estimated formula volume = 1018 mL
5. Estimated water volume = 920 mL water (and 133 g infant formula powder) per 2800 kJ

Table A3: Male infant seven-month-old (8.4 kg) consuming 2800 kJ/day of brand 3 formula powder

(1)	(2)	(3)	(4)	(3) + (4)
F level in water mg/L	**F level in IF powder µg/100kJ (µg/2800kJ or day[20])**	**F intake water mg/day (at 920 mL)**	**F intake IF powder mg/day**	**Total est. F intake mg/day**
Median level found in Au IF powder	0 (0)	0	0.00	0.00
	2 (56)	0	0.06	0.06
	4 (112)	0	0.11	0.11
0	8 (224)	0	0.22	0.22
2.9.1 Fluorosis statement required >17 µg/100kJ	16 (448)	0	0.45	0.45
	20 (560)	0	0.56	0.56
STAN 72-1981 max	24 (672)	0	0.62	0.62
	25 (700)	0	0.70	0.70
	0 (0)	0.46	0.00	0.00
Median level found in Au IF powder	2 (56)	0.46	0.06	0.52
	4 (112)	0.46	0.11	0.57
	8 (224)	0.46	0.22	0.68
0.5	16 (448)	0.46	0.45	0.91
2.9.1 Fluorosis statement required >17 µg/100kJ	20 (560)	0.46	0.56	1.02
	25 (700)	0.46	0.70	1.16
	0 (0)	0.92	0.00	0.92
Median level found in Au IF powder	2 (56)	0.92	0.06	0.98
	4 (112)	0.92	0.11	1.03
	8 (224)	0.92	0.22	1.14
1.0	16 (448)	0.92	0.45	1.37
2.9.1 Fluorosis statement required >17 µg/100kJ	20 (560)	0.92	0.56	1.48
	25 (700)	0.92	0.70	1.62
	0 (0)	1.38	0.00	1.38
Median level found in Au IF powder	2 (56)	1.38	0.06	1.44
	4 (112)	1.38	0.11	1.49
	8 (224)	1.38	0.22	1.60
1.5[21]	16 (448)	1.38	0.45	1.83
2.9.1 Fluorosis statement required >17 µg/100kJ	20 (560)	1.38	0.56	1.94
	25 (700)	1.38	0.70	2.08

F = Fluoride
IF = Infant Formula

[20] To convert F level in infant formula powder from µg/100 kJ to µg/day (2400 kJ) multiply by 24
[21] Fluoride levels in reconstituted infant formula would not reach the UL unless water fluoridated at the maximum allowable level was used, and infant formula powder contained approximately 8 times the amount of fluoride currently seen.

Example brand 4 formula powder for 3-month-old male infant (6 kg):

1. Formula energy content = 281 kJ/100 mL as prepared
2. Recommended energy intake (EER) = 2400 kJ/day
3. Prepared with 13 g powder + 90mL water provides 281 kJ
4. Estimated formula volume = 854 mL
5. Estimated water volume = 752 mL water (and 109 g infant formula powder) per 2400 kJ

Table A4: Male infant 3-month-old (6kg) consuming brand 4 formula powder

(1)	(2)	(3)	(4)	(3) + (4)
F level in water mg/L	**F level in IF powder µg/100kJ[22] (µg/2400 kJ or day)**	**F intake water mg/day (at 752 mL)**	**F intake IF powder mg/day**	**Total est. F intake mg/day**
	0 (0)	0	0.00	0.00
Median level found in Au IF powder	4 (96)	0	0.10	0.10
	5 (120)	0	0.12	0.12
	8 (192)	0	0.19	0.19
0	16 (384)	0	0.38	0.38
2.9.1 Fluorosis statement required >17 µg/100kJ	20 (480)	0	0.48	0.48
STAN 72-1981 max	24 (576)	0	0.58	0.58
	25 (600)	0	0.60	0.60
	0 (0)	0.38	0.00	0.00
Median level found in Au IF powder	4 (96)	0.38	0.10	0.48
	5 (120)	0.38	0.12	0.50
	8 (192)	0.38	0.19	0.57
0.5	16 (384)	0.38	0.38	0.76
2.9.1 Fluorosis statement required >17 µg/100kJ	20 (480)	0.38	0.48	0.86
	25 (600)	0.38	0.60	0.98100kJ
	0 (0)	0.75	0	0.75
Median level found in Au IF powder	4 (96)	0.75	0.10	0.85
	5 (120)	0.75	0.12	0.87
	8 (192)	0.75	0.19	0.94
1.0[23]	16 (384)	0.75	0.38	1.13
2.9.1 Fluorosis statement required >17 µg/100kJ	20 (480)	0.75	0.48	1.23
	25 (600)	0.75	0.60	1.35
	0 (0)	1.13	0.00	1.13
Median level found in Au IF powder	4 (96)	1.13	0.10	1.23
	5 (120)	1.13	0.12	1.25
	8 (192)	1.13	0.19	1.32
1.5	16 (384)	1.13	0.38	1.51
2.9.1 Fluorosis statement required >17 µg/100kJ	20 (480)	1.13	0.48	1.61
	25 (600)	1.13	0.60	1.73

F = Fluoride
IF = Infant Formula

[22] A wide range of fluoride concentrations in soy based infant formula was used in these calculations to include the Standard 2.9.1 label trigger of 17 µg F/100kJ formula powder and the STAN 72-1981 maximum level of 24 µg F/ 100 kJ when made as recommended. The median concentration of fluoride in soy based formula powder was 5.15 µg/100 kJ (Clifford et al [2006]).

[23] A male 3-month-old infant would only have a fluoride intake over the UL if powder were reconstituted at the optimal level with powder containing approximately four times the levels currently found (Clifford et al. 2009) or water at the maximum fluoride level allowed was to be used for reconstitution.