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

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Supporting Document 1: Nutrition assessment

Proposal P1028 **–** Infant Formula

Executive summary

Infant formula contains macronutrients, vitamins, and minerals that are required for infant growth and development. Other substances such as docosahexaenoic acid, L-carnitine, choline and inositol can be voluntarily added. Compositional requirements and other permissions are established in order to reduce the risk of harm to infant health due to an inadequate or excessive intake. These are prescribed in the *Australia New Zealand Food Standards Code* (the Code) Standard 2.9.1 – Infant formula products, and Schedule 29 – Special purpose foods.

In 2016, FSANZ published a comparative assessment of requirements in the Code and *Codex Alimentarius* Standard 72-1981 Standard for Infant Formula and Formulas for Special Medical Purposes Intended for Infants (Codex STAN 72-1981; Codex 1981). The purpose of the 2016 assessment was to determine whether harmonising with the compositional requirements in Codex STAN 72-1981 would pose any nutritional risks to Australian and New Zealand (ANZ) infants. The risk of nutrient inadequacy or harm for ANZ infants was found to be low for most of the Codex STAN 72-1981 nutrient compositional requirements. For linoleic acid, iron and selenium, FSANZ determined that use of Codex STAN 72-1981 could pose a risk to infant health.

The nutrition assessment questions considered in this Supporting Document were developed to address submissions to the FSANZ 2016 Consultation Paper (FSANZ 2016a) and to further consider the potential risks related to compositional requirements for linoleic acid, iron and selenium. The questions relate to outlining the rationale and/or risk of harm to infant health related to the compositional requirements set by the European Commission Delegated Regulation (EU) 2016/127 (EU 2016/127) for six vitamins, four minerals, protein, and L-carnitine. Other questions include evaluating the appropriateness of the scoring method for protein quality, the minimum level for linoleic acid, and the impact of using the Code's energy conversion factor. Conclusions from the current assessment are:

Vitamin A (minimum and maximum)

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.

Vitamin B6 (minimum and maximum)

Use of the EU 2016/127 minimum amount of 4.8 µg/100 kJ may pose a risk to infant health. Use of 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.

Use of the EU 2016/127 maximum amount of 41.8 µg/100 kJ poses a low risk to infant health.

Vitamin C (maximum)

Use of the EU 2016/127 maximum amount of 7.2 mg/100 kJ poses a low risk to infant health.

Vitamin K (minimum and maximum)

Assuming that newborn infants receive prophylactic vitamin K at birth, 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.

Riboflavin (minimum and maximum)

Use of the EU 2016/127 minimum amount (14.3 µg/100 kJ) and maximum amount (95.6 µg/100 kJ) poses a low risk to infant health.

Biotin (minimum and maximum)

Use of the EU 2016/127 minimum amount (0.24 µg/100 kJ) and maximum amount (1.8 µg/100 kJ) poses a low risk to infant health.

Iron (minimum and maximum)

The minimum amount in Schedule 29–9 (0.2 mg/100 kJ) presents a lower risk to infant health than 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, and 0.11 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).

Use of the 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 soya protein isolates, alone or in a mixture with cow's milk or goat's milk proteins) poses a low risk to infant health.

Selenium (minimum and maximum)

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 to infant health.

Iodine (minimum and maximum)

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.

Zinc (minimum and maximum)

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.

Protein quality

Use of the amino acid composition of human milk as the reference for determining minimum amino acid requirements in infant formula is currently recommended in preference to .the digestible indispensable amino acid score (DIAAS) or protein digestibility corrected amino acid score (PDCAAS).

Protein maximum level

The lowered maximum permitted protein levels in EU 2016/127 are based on estimated upper bounds of the adequate range of protein intake. The EFSA (2014a) 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 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 or goat's milk-based formulas, was not provided.

Linoleic acid

Use of a minimum amount of linoleic acid between 110 mg/100 kJ and 140 mg/100 kJ poses a low risk to infant health.

L-carnitine

Mean levels of total carnitine have been reported to be 0.2–0.4 mg/100 kJ in human milk, 0.8–1.6 mg/100 kJ in cow's milk and 0.8–1.1 mg/100 kJ in goat's milk. There insufficient 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). Therefore, the lack of a specification for a maximum amount of L-carnitine in infant formula, as is the case for Codex STAN 72-1981 and EU 2016/127, may pose a risk to infant health.

Conversion between kcal and kJ

The Codex standard specifies vitamin and mineral amounts as per 100 kcal and per 100 kJ. Multiplying the 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.

Table 1: Summary of the risk posed to infant health associated with aligning to EU 2016/127 minimum and maximum amounts[1]

Nutrient[1]	Units	EU 2016/127 minimum		EU 2016/127 maximum	
		Amount	Low risk posed to infant health	Amount	Low risk posed to infant health
Vitamin A	µg RE/100 kJ	16.7	✓	27.2	✓
Vitamin B6	µg/100 kJ	4.8	×[2]	41.8	✓
Vitamin C	mg/100 kJ	n/a	n/a	7.2	✓
Vitamin K[3]	µg/100 kJ	0.24	✓	6	✓
Riboflavin	µg/100 kJ	14.3	✓	95.6	✓
Biotin	µg/100 kJ	0.24	✓	1.8	✓
Selenium	µg/100 kJ	0.72	✓	2.0	✓
Iodine	µg/100 kJ	3.6	✓	6.9	✓

RE: retinol equivalents; ✓: poses a low risk to infant health; ×: may pose a risk to infant health; n/a: not applicable (not assessed).

[1] See Executive Summary text for the assessment's conclusions for iron and zinc.

[2] See Executive Summary text for alternate values that could mitigate the risk related to the EU 2016/127 minimum amount for vitamin B6.

[3] Conclusion assumes that newborn infants receive prophylactic vitamin K at birth.

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Glossary

95% CI	95% confidence interval
2012 Consultation paper	Regulation of Infant Formula Products in the Australia New Zealand Food Standards Code: Consultation paper, 26 September 2012
2016 Consultation paper	Proposal P1028 - Infant Formula: Consultation paper, 23 February 2016
α-TE	Alpha-tocopherol equivalent
AAP	American Academy of Pediatrics
AI	Adequate intake
ALA	Alpha-linolenic acid or α-linolenic acid
Amino acids	In this paper, refers to L-amino acids only
ANZ	Australia and New Zealand
BMIC	Breast milk iodine concentration
CCNFSDU	Codex Committee on Nutrition and Foods for Special Dietary Uses
Codex	Refers to Codex Alimentarius
Complementary feeding	Complementary feeding is the gradual introduction of solid food and fluids along with the usual milk feed (human milk or infant formula) to an infant's diet (Ministry of Health, 2008).
DFE	Dietary folate equivalents
DIAAS	Digestible indispensable amino acid score
DPA	Docosapentaenoic acid C22:5, n-3
EAR	Estimated average requirement
EC	European Commission
EC SCF	European Commission Scientific Committee on Food
EFSA	European Food Safety Authority
EFSA NDA Panel	European Food Safety Authority Panel on Nutrition, Novel Foods and Food Allergens
ESPGHAN	European Society for Paediatric Gastroenterology, Hepatology and Nutrition
EU	European Union
EU 2016/127	Commission Delegated Regulation (EU) 2016/127
FA	Fatty acid
FAO	Food and Agriculture Organization of the United Nations
FNB:IOM	Food and Nutrition Board, US Institute of Medicine

Follow-on formula	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.
GUL	Guidance upper level
HBGV	Health-based guidance value
Human milk	A general term for human milk provided from a mother's breast and is described as mature milk (to distinguish it from colostrum).
IFPSDU	An infant formula product for special dietary use, as defined in Standard 2.9.1
Infant	A person under the age of 12 months; as defined in Standard 2.9.1
Infant formula	An infant formula product represented as a human milk substitute for infants and which satisfies the nutritional requirements of infants aged up to four to six months; as defined in Standard 2.9.1
Infant formula product	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 2.9.1
IOM	US Institute of Medicine
kcal	Kilocalorie
kJ	Kilojoule
LA	Linoleic acid
LC-PUFA	Long chain polyunsaturated fatty acid
LOAEL	Lowest observed adverse effect level
LSRO	Life Sciences Research Office
Mature human milk	Human milk from four weeks post-partum
MoH	Ministry of Health (New Zealand)
MUFA	Monounsaturated fatty acid
NHMRC	National Health and Medical Research Council (Australia)
NOAEL	No observed adverse effect level
NPN	Non-protein nitrogen which consists mainly of free amino acids, peptides, and urea. Human milk contains 20–25% total nitrogen as NPN
NRV	Nutrient Reference Value established by NHMRC (2006)
OR	Odds ratio
PDCAAS	Protein digestibility-corrected amino acid score
PER	Protein efficiency ratio
Policy Guideline	The Policy Guideline on the *Regulation of Infant Formula Products* notified to FSANZ by the Australia and New Zealand Food Regulation Ministerial Council

PUFA	Polyunsaturated fatty acid
RDI	Recommended dietary intake
RE	Retinol equivalents
Requirement	Refers to nutritional requirements that are established by NHMRC/MoH, EFSA, IOM or other expert body for the nutrient amount that denotes a concentration or intake level that supports normal growth and development
RR	Relative risk
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
The Code	*Australia New Zealand Food Standards Code*; which ceases to have effect on 1 March 2016
The revised Code	*Australia New Zealand Food Standards Code;* which came into effect on 1 March 2016. A list of standards and relevant schedules is available at: http://www.foodstandards.gov.au/code/Pages/Revised-code-list-of-standards-and-schedules.aspx
UIC	Urinary iodine concentration
UL	Upper level of intake
US	United States of America
WHO	World Health Organization

1 Introduction

Because infant formula is used as a sole source of nutrients for some infants, or as a supplement to human milk and/or complementary feeding (i.e. solid foods introduced around 6 months), its compositional requirements are explicitly defined by regulatory authorities.

The nutrient composition of infant formula comprises all the essential nutrients in addition to some nutritive substances which may be added as optional ingredients. Essential nutrients are macronutrients (protein, essential amino acids, carbohydrate, and lipids including essential fatty acids) and micronutrients (vitamins and minerals). In food standards, essential nutrients are generally defined in terms of minimum amounts per 100 kcal or 100 kJ to ensure that they are present in amounts that support normal growth and development. For some nutrients, maximum amounts are specified to reduce the risk of excessive intake. In addition, other factors such as permitted forms, sources, conversion factors, ratios to other nutrients, and other restrictions (e.g. limits on certain fatty acids) may also be defined in regulations.

1.1 History of infant formula regulations (ANZ, Codex and EU)

In Australia and New Zealand, the nutrient composition of infant formula is regulated by the *Australia New Zealand Food Standards Code* (the Code) Standard 2.9.1 - Infant formula products and Schedule 29 – Special purpose foods. The Standard was developed in the late 1990s and early 2000s. In general, nutrient composition requirements for Standard 2.9.1 were based on: (1) recommendations of the Life Sciences Research Office (LSRO) which published the comprehensive review *Assessment of Nutrient Requirements for Infant Formulas* (LSRO 1998); or, (2) provisions specified by Codex Standard 72-1981 *Standard for Infant Formula and Formulas for Special Medical Purposes Intended for Infants* (Codex STAN 72-1981), as well as European regulations in place at the time.

At the time of developing Standard 2.9.1, Codex STAN 72-1981 had been in place since 1981 and nutrient composition provisions were, by and large, based on scientific research conducted in the 1970s. The present Codex STAN 72-1981 was developed from a full review of nutrient composition conducted in 2003 by the European Commission Scientific Committee on Food (EC SCF; SCF 2003).

Some of the EC SCF (2003) recommendations were the same as those in the LSRO (1998) assessment or were amended based on additional scientific evidence available at the time. A subsequent report summarising the recommendations in the EC SCF (2003) was published in 2005 by the European Society for Paediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN; Koletzko et al. 2005a & 2005b). With a few exceptions, the ESPGHAN recommendations were adopted into Codex STAN 72-1981 and European Commission (EC) regulations.

Despite the staggered timing of the scientific assessments that underpin Standard 2.9.1 and Codex STAN 72-1981, the two standards are largely comparable for most nutrients.

The current European Commission Delegated Regulation (EU) 2016/127 (EU 2016/127; EC 2015) came into force in September 2015 following the publication of an EFSA opinion on the essential composition of infant and follow-on formulae (EFSA 2014a). EU 2016/127 was amended in January 2018 following the publication of an EFSA opinion on protein content of follow-on formulae (EFSA 2017), and in March 2019 following the publication of EFSA opinions on vitamin D requirements for infant formula (EFSA 2018), and erucic acid requirements for infant formula and follow-on formula (EFSA 2016).

2 FSANZ 2016 nutrition assessment

2.1 Objectives and scope

The FSANZ 2016 nutrition assessment (FSANZ 2016b) reviewed infant formula nutrient composition with the aim of determining whether harmonising with the compositional requirements in Codex STAN 72-1981 would pose a risk of nutritional harm to Australian and New Zealand (ANZ) infants.

Depending on the nutrient, Standard 2.9.1 and Codex STAN 72-1981 prescribe minimum amounts per 100 kJ, maximum amounts per 100 kJ (mandatory or voluntary), sources, permitted forms, restrictions, ratios, and conversion factors (for example, where permitted forms require a calculation of equivalent amounts).

For some nutrients, provisions are identical in Codex STAN 72-1981 and the Code. In these cases, the nutrient was reviewed to assess whether new science has emerged since 2003 when Codex STAN 72-1981 was last fully reviewed. For nutrient provisions that were not identical, the reason for the difference was investigated.

The scope of the FSANZ 2016 nutrition assessment covered energy, protein, amino acids, carbohydrates, fat, fatty acids, vitamins, minerals, and certain nutritive substances (L-carnitine, choline, and inositol; FSANZ 2016b).

The scope of the nutrition assessment did not include consideration of:

- non-essential nutritive substances that are not currently permitted in Standard 2.9.1 (but are permitted in Codex STAN 72-1981).
- nucleotides (inosine monophosphate, adenosine monophosphate, and guanosine monophosphate) and taurine, which are nutritive substances currently permitted as optional additions to infant formula but are considered non-essential in both Standard 2.9.1 and Codex STAN 72-1981, and more recently by EFSA (EFSA 2014a).
- fluoride, which will be covered in subsequent assessment reports in Proposal P1028.

2.2 Approach

The FSANZ 2016 nutrition assessment (FSANZ 2016b) followed an approach in which the Codex STAN 72-1981 provisions for each nutrient were assessed against a set of criteria. These assessment criteria were (where applicable):

- origin of the current standards
- recommendations of key expert bodies
- comparison with human milk concentrations
- estimation of intakes and comparison with ANZ Nutrient Reference Values (NRVs) for adequate and excess intakes
- physiological, biochemical or functional outcomes
- identification of new or emerging scientific evidence.

Compositional requirements for 33 constituents of infant formula—protein, carbohydrate, fat, vitamins (13), minerals and electrolytes (14), and nutritive substances (three)—as well as the energy content were reviewed.

2.3 Conclusions of the FSANZ 2016 nutrition assessment

For all but three of the 33 constituents it was concluded that the use of the constituents' compositional requirements in Codex STAN 72-1981 posed a low risk to infant health. For linoleic acid, iron, and selenium, it was concluded that the use of Codex STAN 72-1981 may pose a risk to infant health.

For linoleic acid, the Codex STAN 72-1981 minimum amount does not meet recommendations made by EFSA, and is substantially lower than the minimum amount in Standard 2.9.1. There is current debate within the scientific community about infant requirements for essential fatty acids.

For iron, the Codex STAN 72-1981 minimum amount is substantially less than the minimum amount in Standard 2.9.1. At the time, FSANZ (2016b) determined that estimated intakes based on the Codex STAN 72-1981 minimum would not meet the ANZ adequate intake (AI) for infants aged 0–<6 months, and would meet approximately one quarter of the estimated average requirement (EAR) derived for infants aged 6–<12 months. There is debate about the absorption of iron from infant formula compared with human milk, and there is evidence that NZ infants are at risk of iron deficiency anaemia.

For selenium, an estimated intake based on the Codex STAN 72-1981 minimum amount would not meet the ANZ AI for selenium for infants aged 0–<12 months. An estimated intake based on the Codex STAN 72-1981 maximum amount would exceed the ANZ upper level of intake (UL). However, there was no evidence of excess intakes or associated adverse health effects.

3 2021 nutrition assessment

3.1 Objectives and scope

The current nutrition assessment builds on the FSANZ 2016 assessment by addressing questions and concerns raised by submitters, while for some nutrients further assessment has been undertaken to consider whether aligning with the EU 2016/127 would pose a risk to infant health. The nutrition assessment questions are provided in Section 4.

3.2 Approach

The approach used for the current assessment generally follows that of the FSANZ 2016 nutrition assessment. However, as some nutrition assessment questions are discrete or framed with a different purpose in mind, not all of the current assessment follows a uniform approach. The numbering of the nutrition assessment questions referred to below follows that outlined in Section 4.

Question 1: For five vitamins (vitamin A, B6, K, riboflavin, and biotin) and four minerals (iron, selenium, iodine, and zinc), the EU 2016/127 provisions for each nutrient's minimum and maximum levels were assessed against a set of criteria. These assessment criteria included (where applicable):

- outline of the scientific basis of the current standards
- comparison with human milk concentrations, focusing on ANZ populations
- comparison with EFSA (2014a) recommendations and FSANZ (2016b) proposed levels

- estimation of intakes and comparison with ANZ NRVs for adequate and excess intakes (non-ANZ NRVs were used in circumstances when an ANZ value was not available)
- other relevant factors unique to the nutrient of interest such as the impact of manufacturing or other nutrients on the nutrient's bioavailability, history of apparent safe use, or the ANZ infant or maternal population
- when a potential risk was identified based on comparisons to human milk concentrations and NRVs, a review of scientific evidence which focused on primary research published after the FSANZ 2016 assessment and on ANZ populations
- if a potential risk was identified, a comparative assessment of the risk associated with the compositional requirements of the Code and Codex STAN 72-1981 was conducted.

Question 2: For one vitamin (vitamin C), the assessment addressed the maximum level only and the criteria included:

- outline of the scientific basis of the standards or recommendations given by EU 2016/127, EFSA (2014a), and EC SCF (2003)
- estimation of intakes using the EU 2016/127 regulatory limits
- consideration of the risk of excess intake based on non-ANZ NRVs and published scientific evidence.

Questions 3 to 7: These are discrete questions, not requiring further explanation of criteria since they are embedded within the questions (see Section 4).

3.3 Assumptions

Unless otherwise specified, the current assessment assumes the following:

Infant age groups

Standard 2.9.1 defines infant formula product as *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* where an infant is defined as a person under the age of 12 months. Therefore, nutrient composition of infant formula must be suitable to meet the nutrient requirements of infants aged 0–<12 months.

Estimated nutrient intake

Intakes were estimated for two age groups: 0–<6 months (also referred to as "younger infants" or "first half-year of life"); and, 6–<12 months (also referred to as "older infants" or "second half-year of life"). The estimated intake was calculated using the midpoint of the energy content (2725 kJ/L, according to Codex STAN 72-1981) and assumed a mean volume of intake of 0.8 L/day for infants aged 0–<6 months (FSANZ 2007, p.44; EFSA 2013, p.12) and 0.6 L/day for infants aged 6–<12 months. The rationale for this midpoint and volumes are further described in the 2016 nutrition assessment (FSANZ 2016b). We note that EFSA (2014a) assume a volume of intake of 0.8 L/day to determine micronutrient intakes deemed adequate for younger infants. The NHMRC (2006) often use 0.78 L/day and 0.6 L/day for the 0–6 and 7–12 month age groups, respectively, in establishing the ANZ NRVs.

Comparison with nutrient reference values

The ANZ NRVs (NHMRC 2006) are used to assess nutrient adequacy of a group, not to derive a minimum and maximum level based on the NRV. To assess the likelihood of a group of infants consuming an adequate intake we compared the estimated intake from formula calculated using the regulatory or recommended minimum level of interest, with the EAR or, if an EAR has not been determined, the AI value. To assess the likelihood of a group of infants consuming an excessive intake, calculated using the regulatory or recommended maximum level, we compared the estimated intake with the UL value. We note, however, that an UL has not been defined for all essential nutrients generally due to insufficient evidence to support an UL for infants in the 0–<12 month age group.

The AI represents the nutrient intake of a group of apparently healthy people that are assumed to be adequate. The EAR represents the requirements of half the healthy individuals in a group (i.e. the median or the 50th centile, but not necessarily the average or mean intake of healthy individuals, despite the use of the word "average"). Definitions for AI, EAR, and UL are provided in Table 3.1.

Table 3.1: Nutrient reference values and their definitions

Nutrient reference value	Definition
Adequate intake (AI)	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 (used when an EAR cannot be determined).
Estimated average requirement (EAR)	Nutrient level required to meet the needs of approximately half the healthy individuals in a sex and particular life stage group.
Upper level of intake (UL)	The highest average daily nutrient intake level likely to pose no adverse health effects to almost all individuals in the general population. As intake increases above the UL, the potential risk of adverse effects increases.

Source: NHMRC (2017).

For infants aged 6–<12 months, unless otherwise stated, we assume that 50% of the nutrient intake is derived from human milk or breast milk substitutes and 50% from complementary feeding (including non-milk beverages). This is based on model diets for 9 month infants (FSANZ 2009). We note that for 12 month infants the contribution from complementary foods increases to 65% of energy (Hitchcock et al. 1986).

Unless stated otherwise, when we compare older infants' estimated nutrient intakes to the NRVs, we consider an estimated nutrient intake from infant formula of: half the AI value or more to represent a low risk of harm to infant health due to inadequacy; half the UL value or less to represent a low risk of harm to infant health due to excess; and, half the EAR value (or more) to represent that 50% (or more) will and 50% (or less) will not meet their nutrient needs.

In recognition of the uncertainty in infant NRVs, comparisons where the estimated intakes for younger infants were ≤15% lower than the AI or ≤15% greater than the UL supported a conclusion that the regulatory or recommended minimum or maximum level posed a low risk to infant health. For older infants, we applied the same approach, but using the thresholds: ≤15% lower than half the AI; and, ≤15% greater than half the UL (as outlined by FSANZ 2016b, Section 2.2.3). Where an EAR value was used, if the estimated intakes for older

infants were ≤15% lower than half the EAR, we assumed that 50% of this group will and 50% will not meet their nutrient needs.

Human milk nutrient concentrations

Comparisons with human milk are based on mean or median nutrient concentrations measured in mature breast milk from healthy mothers, where mature human milk refers to that sampled from mothers at ≥4 weeks post-partum.

Limitations of using human milk as a benchmark include:

- changes in nutrient concentrations in human milk based on maternal health, diet and nutritional status, post-partum sampling period, circadian cycle, and time of collection (fore-milk versus hind-milk)
- difficulty in measuring human milk intakes in human milk-fed infants
- differences in bioavailability and metabolism of certain nutrients in human milk compared with the corresponding nutrients in infant formula.

4 Nutrition assessment questions

1. For the following vitamins and minerals—vitamin A, vitamin B6, vitamin K, riboflavin, biotin, iron, selenium, iodine, zinc:

a) What is the scientific basis for the minimum and maximum amounts in the European Commission Delegated Regulation (EU) 2016/127 (EU 2016/127)?
b) How do these amounts compare to: the EFSA (2014a) recommendation, FSANZ 2016 proposed levels, and levels found in human milk (including the EFSA 2013 Opinion)?
c) What is the risk of harm, due to inadequate or excessive intakes, if FSANZ adopted the EU 2016/127 minimum and maximum values, respectively? If there is a potential risk, would this be mitigated by retaining the current Code value or the Codex value?

2. Vitamin C:

a) What is the scientific basis for the maximum amount specified for vitamin C in:
   (i) EU 2016/127
   (ii) EFSA (2014a)
   (iii) EC SCF (2003)?
b) What is the estimated daily intake of vitamin C using the EU 2016/127 maximum of 7.2 mg/100 kJ for infants aged 0–<6 months and 6–<12 months?
c) Does the EU 2016/127 maximum amount pose a risk to infant health?

3. Protein quality:

Does the evidence base for the digestible indispensable amino acid score (DIAAS) and protein digestibility-corrected amino acid score (PDCAAS) methods of protein scoring support these as alternative methods to the current approach for ensuring protein quality, i.e. using the amino acid composition of human milk as the reference for determining minimum amino acid requirements in infant formula?

4. Protein level:

What is the scientific basis for the lowered protein maximum amounts in the EU 2016/127 for:

a) infant formula manufactured from cow’s or goat’s milk proteins

b) infant formula manufactured from soya protein isolates, alone or in a mixture with cow's or goat's milk proteins
c) infant formula manufactured from protein hydrolysates?

5. Linoleic acid:

What does the evidence suggest is an appropriate minimum amount of linoleic acid considering:

a) the variation of linoleic acid concentrations in human milk
b) the factors that influence linoleic acid levels in human milk
c) the minimum level to prevent deficiency
d) infant adequate intake recommendations in different populations and appropriateness for the ANZ population
e) the other proposed polyunsaturated fatty acid (PUFA) requirements?

6. L-carnitine:

a) What is the range of carnitine that occurs in cow's and goat's milk?
b) Is there any evidence published since 2015 to suggest that the lack of a maximum amount or GUL value for carnitine in Codex STAN 72-1981 and EU 2016/127 may pose a risk of harm to infants?

7. For all the vitamins and minerals: if the Codex values per 100 kilocalorie (kcal) are converted using the kcal to kilojoule (kJ) conversion factor of 4.18 specified in the Code, what are the differences in the respective Codex and Code values?

5 Vitamins and minerals

5.1 Vitamins

Provisions for vitamins in infant formula include minimum amounts, maximum amounts (either as a mandatory or voluntary limit) and in some cases permitted forms and conversion factors. Following public consultation in 2016, provisions for some vitamins required further consideration by FSANZ; mainly to consider information provided in submissions and to further consider the evidence base for the levels proposed by EFSA (2014a). These vitamins are vitamin A, B6, C, K, riboflavin, and biotin. For these vitamins, the EFSA (2014a) recommended levels, and the minimum and maximum amounts in three regulations are shown in Table 5.1.

Table 5.1: Regulatory requirements for infant formula and the EFSA (2014a) recommended levels

		The Code Schedules 29–9 and 29–10		Codex STAN 72-1981		EFSA (2014a)		EU 2016/127	
	Units	min	max	min	max	min	max	min	max
Vitamin A	µg RE/ 100 kJ	14	43	14	43	16.7	NS	16.7	27.2
Vitamin B6	µg/100 kJ	9	36	8.5	45 (GUL)	4.8	NS	4.8	41.8
Vitamin C	mg/100 kJ	1.7	5.4[1]	2.5	17 (GUL)	0.96	NS	0.96	7.2
Vitamin K	µg/100 kJ	1	5.0[1]	1	6.5 (GUL)	0.24	NS	0.24	6
Riboflavin	µg/100 kJ	14	86[1]	19	119 (GUL)	14.3	NS	14.3	95.6
Biotin	µg/100 kJ	0.36	2.7[1]	0.4	2.4 (GUL)	0.24	NS	0.24	1.8

RE: retinol equivalents; GUL: guidance upper level; NS: not specified.
[1] Guideline for maximum amounts in infant formula products, specified in Schedule 29–10.

5.1.1 Vitamin A (minimum and maximum)

Current requirements for the minimum and maximum amounts of vitamin A in the Code, Codex STAN 72-1981, EFSA (2014a) and EU 2016/127 are shown in Table 5.2, together with the range in human milk.

Table 5.2: Vitamin A regulatory requirements for infant formula, EFSA (2014a) recommended levels, and levels in human milk

		The Code Schedules 29–9 and 29–10		Codex STAN 72-1981[1]		EFSA (2014a)		EU 2016/127		Human milk concentration[2]
	Units	min	max	min	max	min	max	min	max	range
Vitamin A	µg RE/ 100 kJ	14	43	14	43	16.7	NS	16.7	27.2	3–38.3

RE: retinol equivalents; NS: not specified.
[1] The FSANZ 2016 proposed levels.
[2] Sources: EFSA (2014a), NHMRC (2006), EFSA (2013), and EC SCF (2003).

Minimum amount

The minimum amount of vitamin A in EU 2016/127 is 16.7 µg RE/100 kJ which is the same as the EFSA (2014a) recommendation. The EFSA (2014a) recommendation is based on the vitamin A intake deemed adequate (350 µg RE/day assuming a mean content in human milk of 450 µg RE/L) and an average energy intake of 500 kcal/day.

The minimum amount of vitamin A in EU 2016/127 is within the range of levels in human milk which are broad (see Table 5.2).

The estimated vitamin A intake from formula containing the EU 2016/127 minimum amount exceeds the AI value for infants aged 0–<6 months (364 µg RE/day versus 250 µg/day of retinol as retinyl esters; see Table 5.3). It also exceeds half the AI value for infants aged 6–<12 months (273 µg RE/day versus 215 µg RE/day). Therefore, the risk of harm to infant health due to an inadequate intake would be low if FSANZ adopted the EU 2016/127 minimum amount (16.7 µg RE/100 kJ).

Maximum amount

The maximum amount in EU 2016/127 is 27.2 µg RE/100 kJ. The basis of the maximum amount and lowering the value between Directive 2006/141/EC (43 µg RE/100 kJ) and EU 2016/127 (27.2 µg RE/100 kJ) is not known by FSANZ. It is about one-third lower than the amount FSANZ proposed in 2016, and is within the range of levels in human milk (see Table 5.2).

The estimated vitamin A intake from formula containing the EU 2016/127 maximum amount is lower than the ANZ UL for infants aged 0–<6 months (593 µg/day versus 600 µg/day; see Table 5.3). For infants aged 6-<12 months it is about 1.5 times higher than half the UL (445 µg/day versus 300 µg/day). Assuming a contribution of 244 µg/day vitamin A from complementary foods (NHMRC, 2006), the estimated total intake from both food and formula is 689 µg/day, and within the range considered to pose low risk to infant health (≤15% greater than the UL i.e. 690 µg/day; see Section 3.3).

On that basis FSANZ considers the risk of harm to infant health due to an excessive intake of vitamin A would be low if FSANZ adopted the EU 2016/127 maximum amount (27.2 µg RE/100 kJ).

Table 5.3: Alignment of the estimated intake of vitamin A using the EU 2016/127 minimum or maximum amount with nutrient reference values

Source	Vitamin A (µg/100 kJ)	Intake for 0–<6 months (µg/day)		Intake for 6–<12 months (µg/day)	
		Estimated from minimum or maximum[1]	Reference value	Estimated from minimum or maximum[1]	Reference value
EU 2016/127 minimum amount	16.7	364	250[2]	273	430[2]
EU 2016/127 maximum amount	27.2	593	600[3]	445	600[3]

[1] Calculated using midpoint of the energy content (2725 kJ/L) and mean volume of intake of 0.8 L/day for infants 0–<6 months and 0.6 L/day for infants 6–<12 months. Calculations are outlined in Appendix 1.
[2] ANZ adequate intake.
[3] ANZ upper level of intake.

5.1.2 Vitamin B6 (minimum and maximum)

Current requirements for the minimum and maximum amounts of vitamin B6 in the Code, Codex STAN 72-1981, EFSA (2014a) and EU 2016/127 are shown in Table 5.4, together with the range in human milk.

Table 5.4: Vitamin B6 regulatory requirements for infant formula, EFSA (2014a) recommended levels, and levels in human milk

		The Code Schedules 29–9 and 29–10		Codex STAN 72-1981[1]		EFSA (2014a)		EU 2016/127		Human milk concentration[2]
	Units	min	max	min	max	min	max	min	max	range
Vitamin B6	µg/100 kJ	9	36	8.5	45 (GUL)	4.8	NS	4.8	41.8	2.6–11.4

GUL: guidance upper level; NS: not specified.
[1] The FSANZ 2016 proposed levels.
[2] Sources: EFSA (2014a), IOM (1998), EC SCF (2003), and NHMRC (2006). EC SCF (2003) values were converted from µg/L to µg/100 kJ, assuming the midpoint of the Codex STAN 72-1981 energy amount (2725 kJ/L) and an intake of 0.8 L/day for younger infants.

Minimum amount

The minimum amount of vitamin B6 in EU 2016/127 is 4.8 µg/100 kJ which is the same as the EFSA (2014a) recommendation. The EFSA (2014a) recommendation is based on the vitamin B6 intake deemed adequate (100 µg/day for infants in the first half-year of life assuming a mean content in human milk of 0.13 mg/L) and an average energy intake of 500 kcal/day.

The minimum amount of vitamin B6 in EU 2016/127 is within the range of levels in human milk (see Table 5.4).

The estimated vitamin B6 intake from formula containing the EU 2016/127 minimum amount is close to the ANZ AI value for infants aged 0–<6 months (104 µg/day versus 100 µg/day; see Table 5.5). Therefore, the risk of harm to younger infants' health due to an inadequate intake would be low if FSANZ adopted the EU 2016/127 minimum amount (4.8 µg/100 kJ).

However, the estimated vitamin B6 intake for infants aged 6–<12 months (78.5 µg/day) is substantially lower than half the ANZ AI value (150 µg/day) and may pose a risk to older infants' health. This risk could be mitigated by retaining the current minimum amount in Schedule 29–9 of the Code (9 µg/100 kJ) or adopting Codex STAN 72-1981 (8.5 µg/100 kJ).

Maximum amount

The maximum amount of vitamin B6 in EU 2016/127 is 41.8 µg/100 kJ. The basis of the maximum amount was not described in the EFSA (2014a) report and is not known by FSANZ. It is higher than the range of levels reported in human milk and about nine times higher than the value reported by the IOM (1998) of 130 µg/L (4.8 µg/100 kJ).

The estimated vitamin B6 intake from formula containing the EU 2016/127 maximum amount is 911 µg/day and 683 µg/day for younger and older infants, respectively (see Table 5.5). There is no ANZ UL for vitamin B6 for infants 0-12 months (source of intake should be breast milk, formula or food only) and FSANZ (2016b) stated there are no reports of vitamin B6 toxicity in ANZ formula fed infants. The risk of harm to infant health due to an excessive intake if FSANZ adopted the EU 2016/127 maximum amount (41.8 µg/100 kJ) is therefore considered low.

Table 5.5: Alignment of the estimated intakes of vitamin B6 using regulatory minimum or maximum amounts with nutrient reference values

Source	Vitamin B6 (µg/100 kJ)	Intake for 0–<6 months (µg/day)		Intake for 6–<12 months (µg/day)	
		Estimated from minimum or maximum[1]	Reference value	Estimated from minimum or maximum[1]	Reference value
Minimum vitamin B6 levels and corresponding estimated intakes					
The Code Schedule 29–9	9	196	100[2]	147	300[2]
Codex STAN 72-1981	8.5	185		139	
EU 2016/127	4.8	104		78.5	
Maximum vitamin B6 levels and corresponding estimated intakes					
EU 2016/127	41.8	911	Not established[3]	683	Not established[3]

[1] Calculated using midpoint of the energy content (2725 kJ/L) and mean volume of intake of 0.8 L/day for infants 0–<6 months and 0.6 L/day for infants 6–<12 months. Calculations are outlined in Appendix 1.
[2] ANZ adequate intake which was converted from original AI values of 0.1 mg/day (0–<6 month infants) and 0.3 mg/day (6–<12 month infants).
[3] Not established by NHMRC (source of intake should be breast milk, formula or food only).

5.1.3 Vitamin C (maximum)

Current requirements for the maximum amount of vitamin C in the Code, Codex STAN 72-1981, EFSA (2014a) and EU 2016/127 are shown in Table 5.6, together with the range in human milk.

Table 5.6: Vitamin C regulatory requirements for infant formula and the EFSA (2014a) recommended levels, and levels in human milk

		The Code Schedules 29–9 and 29–10		Codex STAN 72-1981[2]		EFSA (2014a)		EU 2016/127		Human milk concentration[3]
	Units	min	max	min	max	range	max	min	max	range
Vitamin C	mg/100 kJ	1.7	5.4[1]	2.5	17 (GUL)	0.96	NS	0.96	7.2	1.3–3.3

GUL: guidance upper level; NS: not specified.
[1] Guideline for maximum amount in infant formula products, specified under Schedule 29–10.
[2] The FSANZ 2016 proposed levels.
[3] Source: EFSA (2014a).

Maximum amount

The maximum amount of vitamin C in EU 2016/127 is 7.2 mg/100 kJ. The basis of this maximum amount is not known by FSANZ and was not described in EFSA (2014a) or EC SCF (2003). The estimated vitamin C intake from formula containing the EU 2016/127 maximum amount is 157 mg/day and 118 mg/day for infants aged 0–<6 months and 6–<12 months, respectively (see Table 5.7). An ANZ UL has not been established for any age group, though the NHMRC observed that 1000 mg/day is a prudent limit for adults. The

NHMRC note that the common effects of acute, high doses of vitamin C are gastrointestinal effects.

Table 5.7: The estimated intake of vitamin C using the EU 2016/127 maximum amount

Source	Vitamin C (mg/100 kJ)	Intake for 0–<6 months (mg/day)	Intake for 6–<12 months (mg/day)
		Estimated from maximum[1]	Estimated from maximum[1]
EU 2016/127	7.2	157	118

[1] Calculated using midpoint of the energy content (2725 kJ/L) and mean volume of intake of 0.8 L/day for infants 0–<6 months and 0.6 L/day for infants 6–<12 months.

Comparison against NRVs for vitamin C in other jurisdictions

The guidance level of 1000 mg/day for adults was suggested by the UK Expert Group on Vitamins and Minerals (2003). A 'no observed adverse effect level' (NOAEL) of 1000 mg/day was derived from a 'lowest observed adverse effect level' (LOAEL) of 3000-4000 mg/day and an uncertainty factor of 3. The US Food and Nutrition Board used the same data but applied an uncertainty factor of 1.5, resulting in a NOAEL of 2000 mg/day for adults. From this, a Tolerable Upper Intake for children aged 1-3 years of 400 mg/day was adopted (IOM 2000b).

No ANZ UL has been established, however the estimated vitamin C intake from infant formula containing the EU 2016/127 maximum amount is well below the UL established by the IOM for children aged 1-3 years. On that basis, FSANZ considers the risk associated with the maximum vitamin C level in EU 2016/127 to be low.

5.1.4 Vitamin K (minimum and maximum)

Vitamin K is a collective term for a group of dietary essential fat-soluble vitamins that are involved in the blood clotting process. Vitamin K inadequacy is associated with serious and life threatening adverse effects. Current requirements for the minimum and maximum amounts of vitamin K in the Code, Codex STAN 72-1981, EFSA (2014a) and EU 2016/127 are shown in (see Table 5.8), together with the range in human milk.

Table 5.8: Vitamin K regulatory requirements for infant formula, the EFSA (2014a) recommended levels, and levels in human milk

		The Code Schedules 29–9 and 29–10		Codex STAN 72-1981[2]		EFSA (2014a)		EU 2016/127		Human milk concentration[3]
	Units	min	max	min	max	min	max	min	max	range
Vitamin K	µg/100 kJ	1	5.0[1]	1	6.5 (GUL)	0.24	NS	0.24	6	0.022–0.37

GUL: guidance upper level; NS: not specified.
[1] Guideline for maximum amount in infant formula products, specified under Schedule 29–10.
[2] The FSANZ 2016 proposed levels.
[3] Sources: EFSA (2014a), IOM (2001), and EC SCF (2003). EC SCF (2003) values were converted from µg/L to µg/100 kJ, assuming the midpoint of the Codex STAN 72-1981 energy amount (2725 kJ/L) and an intake of 0.8 L/day for younger infants.

Minimum amount

The minimum amount of vitamin K in EU 2016/127 is 0.24 µg/100 kJ which is the same as the EFSA (2014a) recommendation. The EFSA (2014a) recommendation is based on the vitamin K intake deemed adequate (5 µg/day for infants in the first half-year of life, assuming

a guidance value of 1 µg/kg body weight per day) and an average energy intake of 500 kcal/day.

The minimum amount of vitamin K in EU 2016/127 is within the range of levels in human milk (see Table 5.8).

The estimated vitamin K intake from formula containing the EU 2016/127 minimum amount exceeds the AI value for infants aged 0–<6 months (5.2 µg/day versus 2 µg/day; see Table 5.9). It also exceeds half the AI value for infants aged 6–<12 months (3.9 µg/day versus 1.3 µg/day). Assuming that newborn infants receive prophylactic vitamin K at birth, the risk of harm to infant health due to an inadequate intake if FSANZ adopted the EU 2016/127 minimum amount (0.24 µg/100 kJ) is low.

Maximum amount

The maximum amount in EU 2016/127 is 6 µg/100 kJ. The basis of the maximum amount is not known by FSANZ and is not specified in EFSA (2014a). It is much higher than the range of levels in human milk; about 18 times higher than the upper end of the range (0.34 µg/100 kJ; see Table 5.8).

The estimated vitamin K intake from formula containing the EU 2016/127 maximum amount is 131 µg/day and 98.1 µg/day for younger and older infants, respectively (see Table 5.9). An ANZ UL has not been established because no adverse effects have been associated with vitamin K consumption as food or supplements in humans or animals. Therefore, the risk of harm to infant health due to an excessive intake if FSANZ adopted the EU 2016/127 maximum amount (6 µg/100 kJ) is low.

Table 5.9: Alignment of the estimated intake of vitamin K using the EU 2016/127 minimum or maximum amount with nutrient reference values

Source	Vitamin K (µg/100 kJ)	Intake for 0–<6 months (µg/day)		Intake for 6–<12 months (µg/day)	
		Estimated from minimum or maximum[1]	Reference value	Estimated from minimum or maximum[1]	Reference value
EU 2016/127 minimum amount	0.24	5.2	2[2]	3.9	2.5[2]
EU 2016/127 maximum amount	6	130	Not established	98	Not established

[1] *Calculated using midpoint of the energy content (2725 kJ/L) and mean volume of intake of 0.8 L/day for infants 0–<6 months and 0.6 L/day for infants 6–<12 months. Calculations are outlined in Appendix 1.*
[2] *ANZ adequate intake.*

5.1.5 Riboflavin (minimum and maximum)

Current requirements for the minimum and maximum amounts of riboflavin in the Code, Codex STAN 72-1981, EFSA (2014a) and EU 2016/127 are shown in (see Table 5.10), together with the range in human milk.

Table 5.10: Riboflavin regulatory requirements for infant formula, the EFSA (2014a) recommended levels, and levels in human milk

		The Code Schedules 29–9 and 29–10		Codex STAN 72-1981[2]		EFSA (2014a)		EU 2016/127		Human milk concentration[3]
	Units	min	max	min	max	min	max	min	max	range
Riboflavin	µg/100 kJ	14	86[1]	19	119 (GUL)	14.3	NS	14.3	95.6	9.8–22.0

GUL: guidance upper level; NS: not specified.
[1] *Guideline for maximum amount in infant formula products, specified under Schedule 29–10.*
[2] *The FSANZ 2016 proposed levels.*
[3] *Sources:* EFSA (2013), IOM (1998), EFSA (2014a), EC SCF (2003), and NHMRC (2006).

Minimum amount

The minimum amount or riboflavin in EU 2016/127 is 14.3 µg/100 kJ which is the same as the EFSA (2014a) recommendation. The EFSA (2014a) recommendation is based on the riboflavin intake deemed adequate (300 µg/day for infants in the first half-year of life, assuming a mean content in human milk of 0.35 mg/L) and an average energy intake of 500 kcal/day.

The minimum amount of riboflavin in EU 2016/127 is within the range of levels in human milk (see Table 5.10).

The estimated riboflavin intake from formula containing the EU 2016/127 minimum amount exceeds the ANZ AI value for infants aged 0–<6 months (312 µg/day versus 300 µg/day; see Table 5.11). It also exceeds half the ANZ AI value for infants aged 6–<12 months (234 µg/day versus 200 µg/day). Therefore, the risk of harm to infants' health due to an inadequate intake of riboflavin would be low if FSANZ adopted the EU 2016/127 minimum amount (14.3 µg/100 kJ).

Maximum amount

The maximum amount in EU 2016/127 is 95.6 µg/100 kJ. The basis of the maximum amount is not known by FSANZ and was not specified in EFSA (2014a).

The maximum level in EU 2016/127 is 20% lower than the level FSANZ proposed in 2016 and is much higher than the range of levels in human milk; about four times higher than the upper level of the range reported by EFSA (2014a) of 600 µg/L (22 µg/100 kJ; see Table 5.10).

The estimated riboflavin intake from formula containing the EU 2016/127 maximum amount is 2084 µg/day and 1563 µg/day for younger and older infants, respectively (see Table 5.11). An ANZ UL for riboflavin has not been established by the NHMRC and riboflavin toxicity has not been reported in ANZ formula-fed infants. Therefore, the risk of harm to infants' health due to an excessive intake of riboflavin would be low if FSANZ adopted the EU 2016/127 maximum amount (95.6 µg/100 kJ).

Table 5.11: Alignment of the estimated intakes of riboflavin using the EU 2016/127 minimum or maximum amount with nutrient reference values

Source	Riboflavin (µg/100 kJ)	Intake for 0–<6 months (µg/day)		Intake for 6–<12 months (µg/day)	
		Estimated from minimum or maximum[1]	Reference value	Estimated from minimum or maximum[1]	Reference value
EU 2016/127 minimum amount	14.3	312	300[2]	234	400[2]
EU 2016/127 maximum amount	95.6	2080	Not established	1560	Not established

[1] Calculated using midpoint of the energy content (2725 kJ/L) and mean volume of intake of 0.8 L/day for infants 0–<6 months and 0.6 L/day for infants 6–<12 months. Calculations are outlined in Appendix 1.
[2] ANZ adequate intake which was converted from original AI values of 0.3 mg/day (0–<6 month infants) and 0.4 mg/day (6–<12 month infants).

5.1.6 Biotin (minimum and maximum)

Current requirements for the minimum and maximum amounts of biotin in the Code, Codex STAN 72-1981, EFSA (2014a) and EU 2016/127 are shown in (see Table 5.12), together with the range in human milk.

Table 5.12: Biotin regulatory requirements for infant formula, the EFSA (2014a) recommended levels, and levels in human milk

		The Code Schedules 29–9 and 29–10		Codex STAN 72-1981[2]		EFSA (2014a)		EU 2016/127		Human milk concentration[3]
	Units	min	max	min	max	min	max	min	max	range
Biotin	µg/100 kJ	0.36	2.7[1]	0.4	2.4 (GUL)	0.24	NS	0.24	1.8	0.2–0.3

GUL: guidance upper level; NS: not specified.
[1] Guideline for maximum amount in infant formula products, specified under Schedule 29–10.
[2] The FSANZ 2016 proposed levels.
[3] Sources: EFSA (2014b), EC SCF (2003), and NHMRC (2006).

Minimum amount

The minimum amount of biotin in EU 2016/127 is 0.24 µg/100 kJ which is the same amount as the EFSA (2014a) recommendation. The EFSA (2014a) recommendation is based on the biotin intake considered adequate for younger infants (4 µg/day, assuming an average biotin concentration in human milk of 5 µg/L) and an intake of 500 kcal/day.

The minimum amount of biotin in EU 2016/127 within the range of levels in human milk (see Table 5.12).

The estimated biotin intake from formula containing the EU 2016/127 minimum amount slightly exceeds the ANZ AI value for infants aged 0–<6 months (5.2 µg/day versus 5 µg/day; see Table 5.13). It also exceeds half the ANZ AI value for infants aged 6–<12 months (3.92 µg/day versus 3 µg/day). Therefore, the risk of harm to infants' health due to an inadequate intake of biotin would be low if FSANZ adopted the EU 2016/127 minimum amount (0.24 µg/100 kJ).

Maximum amount

The maximum amount in EU 2016/127 is 1.8 µg/100 kJ. The basis of the maximum amount is not known by FSANZ and was not specified in EFSA (2014a). It is higher than the range of levels in human milk; six times higher than the upper level of the range reported by EC SCF (2003) of 9 µg/L (0.3 µg/100 kJ; see Table 5.12).

The estimated biotin intake from formula containing the EU 2016/127 maximum amount is 39.2 µg/day and 29.4 µg/day for younger and older infants, respectively (see Table 5.13). An ANZ UL has not been established because there is insufficient evidence of adverse effects associated with high biotin intake in humans or animals and biotin toxicity has not been reported in ANZ formula-fed infants. Therefore, the risk of harm to infant health from excessive intake would be low if FSANZ adopted the EU 2016/127 maximum amount (1.8 µg/100 kJ).

Table 5.13: Comparison of biotin intakes (calculated using regulatory minimum and maximum amounts) with nutrient reference values

Source	Biotin (µg/100 kJ)	Intake for 0–<6 months (µg/day)		Intake for 6–<12 months (µg/day)	
		Estimated from minimum or maximum[1]	Reference value	Estimated from minimum or maximum[1]	Reference value
Minimum biotin levels and corresponding estimated intakes					
EU 2016/127	0.24	5.2	5[2]	3.9	6[2]
Maximum biotin levels and corresponding estimated intakes					
EU 2016/127	1.8	39	Not established	29	Not established
Codex STAN 72-1981	2.4 (GUL)	52		39	

GUL: guidance upper level.
[1] Calculated using midpoint of the energy content (2725 kJ/L) and mean volume of intake of 0.8 L/day for infants 0–<6 months and 0.6 L/day for infants 6–<12 months. Calculations are outlined in Appendix 1.
[2] ANZ adequate intake.

5.2 Minerals

Provisions for minerals in infant formula include minimum amounts, maximum amounts (either as a mandatory or voluntary limit), and in some cases ratios with other nutrients. Following public consultation in 2016, some provisions for minerals required further consideration by FSANZ; mainly to consider information provided in submissions and to further consider the evidence base for the levels proposed by EFSA (2014a). These minerals are iron, selenium, iodine, and zinc. For these minerals, the EFSA (2014a) recommended levels, and the minimum and maximum amounts in the three regulations are shown in Table 5.14.

Table 5.14: Regulatory requirements for minerals in infant formula and the EFSA (2014a) recommended levels

		The Code Schedule 29–9		Codex STAN 72-1981		EFSA (2014a)		EU 2016/127	
	Units	min	max	min	max	min	max	min	max
Iron (cow's milk-based formula)[1]	mg/100 kJ	0.2	0.5	0.1	NS	0.07	NS	0.07	0.31
Iron (soy-based formula)[1]	mg/100 kJ	0.2	0.5	0.1	NS	0.11	NS	0.11	0.48
Selenium	µg/100 kJ	0.25	1.19	0.24	2.2 (GUL)	0.72	NS	0.72	2
Iodine	µg/100 kJ	1.2	10	2.5	14 (GUL)	3.6	NS	3.6	6.9
Zinc (cow's milk-based formula)	mg/100 kJ	0.12	0.43	0.12	0.36 (GUL)	0.12	NS	0.12	0.24
Zinc (soy-based formula)	mg/100 kJ	0.12	0.43	0.12	0.36 (GUL)	0.18	NS	0.18	0.3

GUL: guidance upper level; NS: not specified.
[1] These values represent requirements for infant formula. The minimum amount set by EFSA (2014a), and minimum and maximum amount set by EU 2016/127, for follow-on formula, is different to the corresponding tabulated values for infant formula (refer to Tables 5.16 and 5.17)

5.2.1 Iron (minimum and maximum)

Current requirements for the minimum and maximum amounts of iron in the Code, Codex STAN 72-1981, EFSA (2014a) and EU 2016/127 are shown in Table 5.15, together with the range in human milk.

Table 5.15: Iron regulatory requirements for infant formula, the EFSA (2014a) recommended levels, and levels in human milk

		The Code Schedule 29–9		Codex STAN 72-1981		EFSA (2014a)		EU 2016/127		Human milk concentration[2]
	Units	min	max	min	max	min	max	min	max	range
Iron (cow's milk-based formula)[1]	mg/100 kJ	0.2	0.5	0.1	NS	0.07	NS	0.07	0.31	0.007–0.014
Iron (soy-based formula)[1]	mg/100 kJ	0.2	0.5	0.1	NS	0.11	NS	0.11	0.48	

NS: not specified.
[1] The minimum amount set by EFSA (2014a) and minimum and maximum amount set by EU 2016/127 for follow-on formula, is different to the corresponding values for infant formula (refer to Tables 5.16 and 5.17).
[2] Sources: EFSA (2014a), the IOM (2001), and Concha et al. (2013). The bioavailability of iron from human milk, cow's milk-based infant formula, and soy-based infant formula differs. Therefore, a direct comparison between regulatory requirements and levels in human milk is inappropriate.

Minimum amount in cow's milk- and soy-based formula and requirements for infant and follow-on formula.

EU 2016/127 provides separate iron requirements for cow's milk- and soy-based formula, and separate requirements for infant and follow-on formula. For infant formula, the minimum amount in EU 2016/127 is 0.07 mg/100 kJ for cow's milk-based and 0.11 mg/100 kJ for soy-based. For follow-on formula, the minimum amount in EU 2016/127 is 0.14 mg/100 kJ for cow's milk-based and 0.22 mg/100 kJ for soy-based. If the same formula is intended to be used by infants for the whole first year of life, EFSA (2014a) recommends the minimum amount should be 0.14 mg/100 kJ for cow's milk-based formula and 0.22 mg/100 kJ for soy-based formula.

The EFSA (2014a) recommendation for cow's milk-based infant formula (0.07 mg/100 kJ) is based on the absorbed iron intake deemed adequate (0.15 mg/day; based on a mean content in human milk of 0.35 mg/L, 0.8 L/day, and 50% absorption of iron from human milk), a lower bioavailability of iron from formula than human milk (10%), and an average intake of 2725 kJ/L and 0.8 L/day. The EC SCF (2003) proposed iron minimum and maximum levels 1.5 times higher in soy- compared to cow's milk-based formula (SCF 2003 pp. 135–6). The value takes into account the possibility of lower iron absorption efficiency due the presence of phytic acid in soy-based formula (Hurrell et al. 1992; EC SCF 2003).

If the same formula is intended to be used by infants for the whole first year of life, EFSA (2014a) recommends the minimum amount should be 0.14 mg/100 kJ for cow's milk-based formula and 0.22 mg/100 kJ for soy-based formula. EFSA (2013) considered an iron intake of 8 mg/day to be adequate for the majority of infants in the second half-year of life. The EFSA (2014a) recommendation for follow-on formula assumes that iron needs are higher in the second than first half-year of life and that 5.7 mg/day could be supplied by complementary food.

The minimum amounts in EU 2016/127 for infant formula are lower than the average amount in human milk when accommodating for differences in absorption. Reported average iron concentrations in human milk include 0.012 mg/100 kJ and 0.013 mg/100 kJ (IOM 2001 and Concha et al. 2013) while EFSA (2014a) reported a range of 0.007–0.014 mg/100 kJ but cited no evidence. The minimum levels in the EU 2016/127 for infant formula are comparable to the lower end of the range and are about half that of the average concentration in human milk, taking into account 10% absorption from cow's milk-based formula and a factor of 1.5 applied for inhibition of iron absorption by phytic acid in soy-based formula. The minimum levels in the EU 2016/127 for follow-on formula are comparable to the average and upper end of the range of iron concentrations in human milk, using the same conditions.

To receive the same amount of absorbed iron as human milk-fed infants who meet the ANZ AI (0.2 mg/day), cow's milk-based formula-fed infants aged 0-<6 months should have an iron intake of 1–2 mg/day (Table 5.16). The estimated iron intakes using the EU 2016/127 minimum amounts for cow's milk-based infant and follow-on formula (1.53 mg/day and 3.05 mg/day) is at or above the target intake of 1–2 mg/day for infants aged 0–<6 months. The estimated iron intakes using the EU 2016/127 minimum amounts for soy-based formula, also exceed the corrected AI value when considering the lower iron absorption efficiency. Therefore, the risk of harm to younger infants' health due to an inadequate iron intake would be low if FSANZ adopted the EU 2016/127 minimum amounts for cow's milk- and soy-based infant formula.

The estimated iron intakes using the EU 2016/127 minimum amounts for cow's milk-based infant and follow-on formula (1.14 mg/day and 2.29 mg/day, respectively) is substantially lower than half the EAR value for infants aged 6–<12 months (3.5 mg/day). Estimated iron intakes using the EU 2016/127 minimum amounts for soy-based formula, is also substantially lower than half the EAR value for this age group when considering the lower iron absorption efficiency. For 6–<12 month olds, we consider meeting half the EAR value via formula, together with half the EAR value via complementary foods, sufficient to meet the iron needs of 50% of older, formula-fed infants when assuming the EAR is based on normally distributed intakes. This risk to older infants could be mitigated by retaining the current minimum amount in Schedule 29–9 of the Code (0.2 mg/100 kJ).

Since infant formula for sale in ANZ must 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) presents a lower risk to infant health than 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 soya protein isolates, alone or in a mixture with cow's milk or goat's milk proteins).

Table 5.16: Comparison of iron intakes (calculated using regulatory minimum amounts) with nutrient reference values

Source	Iron minimum (mg/ 100 kJ)	Intake for 0–<6 months (mg/day)		Intake for 6–<12 months (mg/day)	
		Estimated from minimum[1]	Reference value (AI)	Estimated from minimum[1]	Reference value (EAR)
Cow's milk- and soy-based formula					
The Code Schedule 29–9	0.2	4.36	0.2[2]	3.27	7
Cow's milk-based formula only					
Infant formula: EU 2016/127	0.07	1.53	0.2[2]	1.14	7
Follow-on formula EU 2016/127	0.14	3.05		2.29	
Soy-based formula only					
Infant formula EU 2016/127	0.11	2.40	0.2[2]	1.80	7
Follow-on formula EU 2016/127	0.22	4.80		3.60	

[1] *Calculated using midpoint of the energy content (2725 kJ/L) and mean volume of intake of 0.8 L/day for infants 0–<6 months and 0.6 L/day for infants 6–<12 months. Calculations are outlined in Appendix 1.*
[2] *The ANZ NRV guidelines state that this adequate intake is for breastfed babies only and that the bioavailability of iron in infant formula is 10–20% that of breast milk (NHMRC 2006). This would suggest that the iron intake of formula-fed infants aged 0-<6 months should be 1–2 mg/day, in order to receive the same absorbed iron as human milk-fed infants.*

Maximum amount

EU 2016/127 provides separate iron requirements for cow's milk- and soy-based formula, and separate requirements for infant and follow-on formula. The maximum amount in EU 2016/127 is 0.31 mg/100 kJ for cow's milk-based infant formula and 0.48 mg/100 kJ for soy-based infant formula. The maximum amount in EU 2016/127 is 0.48 mg/100 kJ for cow's milk-based follow-on formula and 0.6 mg/100 kJ for soy-based follow-on formula. The basis of the maximum amounts are not known by FSANZ.

The estimated iron intake from cow's milk- and soy-based infant formula containing the EU 2016/127 maximum amount is 6.76 mg/day and 10.5 mg/day for younger infants, respectively, and 5.07 mg/day and 7.85 mg/day for older infants, respectively (see Table 5.17). The estimated iron intake from cow's milk- and soy-based follow-on formula containing the EU 2016/127 maximum amount is 10.5 mg/day and 13.1 mg/day for younger infants, respectively, and 7.85 mg/day and 9.81 mg/day for older infants, respectively (see Table 5.17).

The estimated iron intakes from formula for infants aged 0–<6 months using the four EU 2016/127 maximum amounts are lower than the UL. Estimated iron intakes for infants aged 6–<12 months using the four EU 2016/127 maximum amounts are lower than half the UL (10 mg/day). Therefore, the risk of harm to infant health due to an excessive iron intake if FSANZ adopted any of the EU 2016/127 maximum amounts is low.

Table 5.17: Comparison of iron intakes (calculated using regulatory maximum amounts) with nutrient reference values

Source	Iron (mg/100 kJ)	Intake for 0–<6 months (mg/day)		Intake for 6–<12 months (mg/day)	
		Estimated from maximum[1]	Reference value[6]	Estimated from maximum[1]	Reference value[6]
Infant formula (cow's milk-based)					
EC SCF (2003)[2] EU 2016/127	0.31	6.76	20	5.07	20
Follow-on formula (cow's milk-based)					
EC SCF (2003)[3]	0.41	8.94	20	6.70	20
EU 2016/127	0.48	10.5		7.85	
Infant formula (soy-based)					
EC SCF (2003)[4]	0.45	9.81	20	7.36	20
EU 2016/127	0.48	10.5		7.85	
Follow-on formula (soy-based)					
EC SCF (2003)[5] EU 2016/127	0.6	13.1	20	9.81	20

[1] Calculated using midpoint of the energy content (2725 kJ/L) and mean volume of intake of 0.8 L/day for infants 0–<6 months and 0.6 L/day for infants 6–<12 months. Calculations are outlined in Appendix 1.
[2] EC SCF (2003) and ESPGHAN (Koletzko et al. 2005a) value for cow's milk-based formula calculated from an original value of 1.30 mg/100 kcal.
[3] EC SCF (2003) value for cow's milk-based formula calculated from an original value of 1.70 mg/100 kcal.
[4] EC SCF (2003) value for soy-based formula calculated from an original value of 1.9 mg/100 kcal.
[5] EC SCF (2003) value for soy-based formula calculated from an original value of 2.50 mg/100 kcal.
[6] ANZ upper level of intake.

5.2.2 Selenium (minimum and maximum)

Current requirements for the minimum and maximum amounts of selenium in the Code, Codex STAN 72-1981, EFSA (2014a) and EU 2016/127 are shown in Table 5.18, together with levels in human milk.

FSANZ (2016b) concluded that the Codex STAN 72-1981 minimum amount could pose a risk to infant health due to the: lack of international consensus on the appropriate minimum level to set in infant formula; estimated intake based on this amount not meeting the ANZ AI for infants (NMHRC 2006); and, recent studies indicating that the minimum level in infant formula should be increased.

FSANZ (2016b) concluded that the Codex STAN 72-1981 maximum amount (specified as a GUL) could pose a risk to infant health due to the lack of international consensus on the appropriate maximum, and estimated intake calculated using the Codex maximum exceeding the ANZ UL.

Table 5.18: Selenium regulatory requirements for infant formula, the EFSA (2014a) recommended levels, and levels in human milk

		The Code Schedule 29–9		Codex STAN 72-1981		EFSA (2014a)		EU 2016/127		Human milk concentration
	Units	min	max	min	max	min	max	min	max	range
Selenium	µg/100 kJ	0.25	1.19	0.24	2.2 (GUL)	0.72	NS	0.72	2	0.4–0.5 (ANZ; median or mean)[1] 0.1–3.1 (European; range of means)[2]

GUL: Guidance upper level; NS: not specified.
[1] Median or mean selenium content in the human milk of ANZ women. Sources: Cumming et al. (1992), Daniels et al. (2000), Daniels et al. (2008), Dolamore et al. (1992), Jin et al. (2019).
[2] Range of selenium content in the human milk of European women. Sources: EFSA (2014a), and EFSA (2013).

Minimum amount

The EU selenium minimum amount of 0.72 µg/100 kJ is the same value that EFSA (2014a) recommended. In deriving the value, EFSA cited a mean human milk concentration in Europe of 16 µg/L, with a wide range of mean values in individual studies: 3 to 84 µg/L (0.5–13 µg/100 kcal, equivalent to 0.1–3.1 µg/100 kJ).

Selenium concentrations in human milk are influenced by maternal dietary intake. Selenium intakes are low in New Zealand (University of Otago and Ministry of Health 2011) and in some Australian populations (Lyons et al. 2005; Lymbury et al. 2008). The EU minimum amount is about 60% higher than levels reported in ANZ human milk (range of mean values: 0.4–0.5 µg/100 kJ).

For infants 0–<6 months, estimated selenium intake calculated from the EU 2016/127 minimum amount is 16 µg/day, which exceeds the ANZ AI value of 12 µg/day.

For infants 6–<12 months, estimated selenium intake calculated from the EU 2016/127 minimum amount is 12 µg/day, which exceeds half the ANZ AI value for infants aged 6–<12 months (7.5 µg/day) (Table 5.19). For infants 6–<12 months, we consider meeting half the AI value via formula to be sufficient, on the assumption that complementary foods will provide 50% of older infants' selenium needs.

Therefore, if FSANZ adopted the EU 2016/127 minimum amount for selenium (0.72 µg/100 kJ), the risk of harm to infant health due to inadequate intake is low.

Table 5.19: Comparison of selenium intakes (calculated using EU minimum amount) with nutrient reference values

Source	Selenium minimum amount (µg/100 kJ)	Intake for 0–<6 months (µg/day)		Intake for 6–<12 months (µg/day)	
		Estimated from minimum[1]	Reference value	Estimated from minimum[1]	Reference value
EU 2016/127	0.72	16	12[2]	12	15[2]

[1] Calculated using midpoint of the energy content (2725 kJ/L) and mean volume of intake of 0.8 L/day for infants 0–<6 months and 0.6 L/day for infants 6–<12 months.
[2] ANZ adequate intake.

Maximum amount

The maximum amount in EU 2016/127 is 2 µg/100 kJ, which is higher than mean levels reported in ANZ human milk, but within the range of mean levels in European human milk (0.1–3.1 µg/100 kJ; Table 5.18).

Estimated selenium intakes calculated using the EU 2016/127 maximum amount are 44 µg/day and 33 µg/day for younger and older infants, respectively (see Table 5.20).

The estimated selenium intake using the EU 2016/127 maximum amount is below the UL for infants aged 0–<6 months (44 µg/day versus 45 µg/day, respectively).

For infants 6–<12 months, we consider an intake of half the UL value or less via formula to represent a low risk of harm to infant health due to excess, on the assumption that complementary foods will provide 50% of older infants' selenium needs. Estimated selenium intake is slightly higher than half the UL value for infants aged 6–<12 months (33 µg/day versus 30 µg/day, respectively).

FSANZ notes that the ANZ UL for young infants was based on studies showing that a human milk concentration of 60 µg/L (equivalent to 2.2 µg/100 kJ; i.e. 10% greater than the EU maximum of 2 µg/100 kJ) was not associated with adverse effects.

Therefore, if FSANZ adopted the EU 2016/127 maximum amount of 2 µg/100 kJ, the risk of harm to infant health due to excessive intake is low.

Table 5.20: Comparison of selenium intakes (calculated using EU maximum amount) with nutrient reference values

Source	Selenium (µg/100 kJ)	Intake for 0–<6 months (µg/day)		Intake for 6–<12 months (µg/day)	
		Estimated from maximum[1]	Reference value	Estimated from maximum[1]	Reference value
EU 2016/127	2	44	45[2]	33	60[2]

[1] *Calculated using midpoint of the energy content (2725 kJ/L) and mean volume of intake of 0.8 L/day for infants 0–<6 months and 0.6 L/day for infants 6–<12 months.*
[2] *ANZ upper level of intake.*

5.2.3 Iodine (minimum and maximum)

Current requirements for iodine minimum and maximum amounts in the Code, Codex STAN 72-1981, EFSA (2014a) and EU 2016/127 are shown in Table 5.21, together with levels in human milk.

FSANZ (2016b) concluded that adopting the Codex minimum and maximum (specified as a GUL) amounts was unlikely to pose a risk to infant health.

Table 5.21: Iodine regulatory requirements for infant formula, the EFSA (2014a) recommended levels, and levels in human milk

		The Code Schedule 29–9		Codex STAN 72-1981		EFSA (2014a)		EU 2016/127		Human milk concentration
	Units	min	max	min	max	min	max	min	max	range
Iodine	µg/100 kJ	1.2	10	2.5	14 (GUL)	3.6	NS	3.6	6.9	1.9–3.8 (range of means, European studies[1]) 4.7 (median, ANZ data[2])

GUL: Guidance upper level; NS: not specified.
[1] EFSA (2014a).
[2] Huynh (2015) and Huynh et al. (2017).

Minimum amount

The EU minimum of 3.6 µg/100 kJ is the same value that EFSA (2014a) recommended and based on EFSA (2014d) and the levels in human milk (mean concentrations from European studies of 50–100 µg/L, equivalent to 1.9–3.8 µg/100 kJ).

Estimated iodine intakes calculated using the EU minimum are 79 µg/day and 59 µg/day for younger and older infants, respectively (Table 5.22). The value of 79 µg/day is 13% lower than the ANZ AI for infants 0–<6 months (90 µg/day), while the value of 59 µg/day exceeds half the AI value for infants 6–<12 months (55 µg/day). For infants 6–<12 months, we consider meeting half the AI via formula to be sufficient, on the assumption that complementary foods will provide 50% of older infants' iodine needs.

Based on this comparison, there is a low risk to infant health due to inadequate iodine intake if FSANZ adopted the EU minimum. The risk would be greater if the minimum amount of 1.2 µg/100 kJ in Schedule 29 was retained or if the Codex minimum of 2.5 µg/100 kJ was adopted.

Table 5.22: Comparison of iodine intakes (calculated using EU minimum amount) with nutrient reference values

Source	Iodine minimum amount (µg/100 kJ)	Intake for 0–<6 months (µg/day)		Intake for 6–<12 months (µg/day)	
		Estimated from minimum[1]	Reference value	Estimated from minimum[1]	Reference value
EU 2016/127	3.6	79	90[2]	59	110[2]

[1] Calculated using midpoint of the energy content (2725 kJ/L) and mean volume of intake of 0.8 L/day for infants 0–<6 months and 0.6 L/day for infants 6–<12 months.
[2] ANZ Adequate Intake (AI).

Maximum amount

Estimated iodine intakes from infant formula calculated using the EU maximum are 150 µg/day and 110 µg/day for younger and older infants, respectively (Table 5.23). An ANZ UL for infants 0–12 months has not been established, however these estimated intakes are below the iodine UL for children 1–3 years (200 µg/day). Also, FAO/WHO (2001) states that approximate intakes which appear to not impair thyroid function are 150 and 140 µg/kg bw/day for 0–6 month and 7–12 month old infants, respectively. These values are substantially higher and equivalent to iodine intakes of about 900 and 1100 µg/day,

calculated using bodyweights of 6 and 8 kg for infants 3 months and 9 months old, respectively.

Therefore, if FSANZ adopted the EU 2016/127 maximum amount of 6.9 µg/100 kJ, the risk of harm to infant health due to excessive iodine intake is low.

Table 5.23: Comparison of iodine intakes (calculated using EU maximum amount) with nutrient reference values

Source	Iodine maximum amount (µg/100 kJ)	Intake for 0–<6 months		Intake for 6–<12 months	
		Estimated from maximum (µg/day)[1]	Reference value (µg/day)	Estimated from maximum (µg/day)[1]	Reference value (µg/day)
EU 2016/127	6.9	150	200[2] 900[3]	110	200[2] 1100[3]

[1] Calculated using midpoint of the energy content (2725 kJ/L) and mean volume of intake of 0.8 L/day for infants 0–<6 months and 0.6 L/day for infants 6–<12 months.
[2] 200 µg/day is the ANZ Upper Level of Intake (UL) for children 1–3 years. A UL for infants 0–12 months has not been established.
[3] Approximate intakes which appear to not impair thyroid function in infants (FAO/WHO 2001).

5.2.4 Zinc (minimum and maximum)

Current requirements for the minimum and maximum amounts of zinc in the Code, Codex STAN 72-1981, EFSA (2014a) and EU 2016/127 are shown in Table 5.24, together with mean levels in human milk. FSANZ (2016b) concluded that adopting the Codex STAN 72-1981 maximum amount (specified as a GUL), which is only slightly lower than the Code maximum amount, was unlikely to pose a risk to infant health.

Table 5.24: Zinc regulatory requirements for infant formula, the EFSA (2014a) recommended levels, and levels in human milk

		The Code Schedule 29–9		Codex STAN 72-1981		EFSA (2014a)		EU 2016/127		Human milk concentration[1]
	Units	min	max	min	max	min	max	min	max	mean
Zinc (cow's milk-based formula)	mg/100 kJ	0.12	0.43	0.12	0.36 (GUL)	0.12	NS	0.12	0.24	0.071 (1–2 months) 0.037 (3–5 months)
Zinc (soy-based formula)	mg/100 kJ	0.12	0.43	0.12	0.36 (GUL)	0.18	NS	0.18	0.3	0.029 (6–11 months)

GUL: guidance upper level; NS: not specified.
[1]Source: EFSA (2014a).

Minimum amount

The minimum amount in EU 2016/127 is 0.12 mg/100 kJ for cow's milk-based infant formula and 0.18 mg/100 kJ for soy-based infant formula—the same values that EFSA (2014a) recommended. The EFSA (2014a) recommended minimum amounts are higher than the

mean levels in human milk due to the lower bioavailability of zinc from both cow's milk-based and soy-based infant formula.

Caution is needed when comparing estimated intakes to the ANZ AI and EAR, because zinc absorption is higher from human milk than from formula, but neither EFSA (2014a) or NHMRC (2006) quantify this difference. For infants aged 0–<6 months, the estimated zinc intake from cow's milk-based formula (2.6 mg/day) calculated using the EU 2016/127 respective minimum amount, is higher than the ANZ AI value of 2.0 mg/day. For infants aged 6–<12 months, the respective estimated intake (2.0 mg/day) is higher than half the EAR value of 1.3 mg/day (Table 5.25). Estimated zinc intakes using the EU 2016/127 minimum amounts for soy-based formula (3.9 and 2.9 mg/day for younger and older infants) should compare similarly to the NRVs, assuming the reduced zinc absorption efficiency due to the phytic acid present in formula containing isolated soy protein is offset by the higher minimum amounts.

The EU 2016/127 minimum amount of 0.12 mg/100 kJ (for cow's milk-based infant formula) is the same as the current value in the Code. The EU 2016/127 minimum amount of 0.18 mg/100 kJ (for soy-based infant formula) 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.

Table 5.25: Comparison of zinc intakes (calculated using EU minimum amounts) with nutrient reference values

Source	Zinc minimum amount (mg/ 100 kJ)	Intake for 0–<6 months (mg/day)		Intake for 6–<12 months (mg/day)	
		Estimated from minimum[1]	Reference value	Estimated from minimum[1]	Reference value
EU 2016/127 (cow's milk-based formula)	0.12	2.6	2.0[2]	2.0	2.5[3]
EU 2016/127 (soy-based formula)	0.18	3.9		2.9	

[1] *Calculated using midpoint of the energy content (2725 kJ/L) and mean volume of intake of 0.8 L/day for infants 0–<6 months and 0.6 L/day for infants 6–<12 months.*
[2] *ANZ Adequate Intake (AI).*
[3] *ANZ Estimated Average Requirement (EAR).*

Maximum amount

The maximum amount for zinc in EU 2016/127 is 0.24 mg/100 kJ for cow's milk-based infant formula and 0.3 mg/100 kJ for soy-based infant formula. EFSA (2014a) did not specify maximum amounts for zinc, stating that maximum amounts for most micronutrients were calculated as three to five times the minimum amounts, and were not based on scientific evidence for adverse effects owing to the lack of such evidence for most nutrients.

The EU maximum amounts are lower than the level FSANZ proposed in 2016 irrespective of the protein source, and are higher than the mean levels in human milk. FSANZ (2016b) proposed using the Codex STAN 72-1981 maximum amount (expressed as a GUL) of 0.36 mg/100 kJ irrespective of the protein source. The maximum level in EU 2016/127 for cow's milk-based formula is lower than this by one-third.

The estimated zinc intake from cow's milk- and soy-based infant formula containing the EU 2016/127 maximum amount is 5.2 mg/day and 6.5 mg/day for younger infants, respectively, and 3.9 mg/day and 4.9 mg/day for older infants, respectively (see Table 5.26).

The estimated zinc intake for infants aged 0–<6 months using the EU 2016/127 maximum amount for cow's milk-based formula (5.2 mg/day) is higher than the ANZ UL (4 mg/day; NHMRC 2006). The estimated zinc intake for infants aged 6–<12 months using the EU 2016/127 maximum amount for cow's milk-based formula (3.9 mg/day) is higher than half the ANZ UL (2.5 mg/day).

However, FSANZ has previously reviewed the ANZ UL for zinc and considers that it is based on a study with a number limitations which indicate an overly conservative basis for the UL (FSANZ 2011, pp. 102–104). Therefore, the risk of harm to infant health due to an excessive intake would be low if FSANZ adopted the EU 2016/127 maximum amounts of (0.24 mg/100 kJ and 0.3 mg/100 kJ for cow's milk- and soy-based formula, respectively).

Table 5.26: Comparison of zinc intakes (calculated using EU maximum amounts) with nutrient reference values

Source	Zinc maximum amount (mg/ 100 kJ)	Intake for 0–<6 months (mg/day)		Intake for 6–<12 months (mg/day)	
		Estimated from maximum[1]	Reference value	Estimated from maximum[1]	Reference value
EU 2016/127 (cow's milk-based formula)	0.24	5.2	4[2]	3.9	5[2]
EU 2016/127 (soy-based formula)	0.3	6.5		4.9	

[1] *Calculated using midpoint of the energy content (2725 kJ/L) and mean volume of intake of 0.8 L/day for infants 0–<6 months and 0.6 L/day for infants 6–<12 months.*
[2] *ANZ Upper Level of Intake (UL).*

6 Protein

6.1 Protein quality

Protein quality represents the ability of a protein source to meet amino acid requirements. FSANZ's previous assessment of infant formula protein quality considered scoring methods and minimum amino acid amounts (FSANZ 2016b). Neither Standard 2.9.1 or Codex STAN 72-1981 incorporate protein quality scoring systems such as PDCAAS[1] or DIAAS[2].

Standard 2.9.1 (and Schedule 29) and Codex STAN 72-1981 regulate protein quality by mandating minimum amounts of L-amino acids. The amounts listed in Schedule 29 are mainly based on human milk amino acid content reported by WHO (1985).

The minimum amino acid requirements in Codex STAN 72-1981 were derived from the ESPGHAN analysis (Koletzko et al. 2005a). FSANZ (2016b) concluded that the minimum amounts of essential amino acids in Codex STAN 72-1981 were unlikely to pose a risk to infant health.

This assessment considers whether the evidence base for DIAAS and PDCAAS are suitable alternatives to the current approach for ensuring protein quality in infant formula (i.e. using the amino acid composition of human milk as the reference for determining minimum amino acid requirements in infant formula).

[1] Protein Digestibility-Corrected Amino Acid Score.
[2] Digestible Indispensable Amino Acid Score.

Scoring methods

FAO/WHO (1991) recommended the use of PDCAAS for evaluating protein quality. PDCAAS uses an animal-based assay to measure faecal protein digestibility (defined in terms of the balance of amino acids or nitrogen measured from the mouth to anus), and chemical analysis to quantify individual amino acids in a protein source. The PDCAAS score is calculated as the ratio of the amount of the limiting amino acid in the tested protein (expressed as mg of amino acid per gram of test protein) divided by the amount of the corresponding amino acid in a reference protein, and multiplied by a digestibility factor.

FAO (2013) recommended using DIAAS which is a modified version of PDCAAS that allows for a more accurate estimation of protein quality. DIAAS uses ileal digestibility instead of faecal digestibility, and does not truncate protein quality scores that are greater than 100%. DIAAS also uses age-relevant reference amino acid pattern (that of human milk for infants 0–12 months).

FAO (2018) considered the use of DIAAS and PDCAAS methods for Follow-Up Formula for Young Children (FUF-YC), but did not comment on methods with respect to formula for infants aged 0 to <6 months. FAO (2018) advised that the DIAAS method is the ideal metric, but that true ileal digestibility values of individual amino acids are incomplete, and therefore the DIAAS method is not ready to be implemented for regulatory purposes but could be considered in the future.

In the absence of a revised FAO/WHO opinion on protein quality scoring for infant formula, FSANZ considers that amino acid minimum amounts should continue to be based on the amino acid content of human milk.

6.2 Maximum permitted protein level

FSANZ (2016) assessed protein in relation to quantification of protein content, meeting adequate intake requirements for total protein and essential amino acids, protein quality, and current research on health effects related to protein including the risk of childhood obesity. Comparisons to human milk composition and the origin of current infant formula standards were also considered. FSANZ (2016b) concluded that the maximum protein level should be retained at the current amounts now listed in Standard 2.9.1–9 and Codex STAN 72-1981.

Maximum amount

Regulatory requirements for the maximum permitted level of protein are presented in Table 6.1.

The maximum protein level in cow's or goat's milk-based infant formula specified in EU 2016/127 (0.6 g/100 kJ) is lower than the previous EC 2006 Directive (0.72 g/100 kJ). The permitted maximum amounts for soy protein isolate and protein hydrolysate formulas were also lowered between the EC 2006 Directive and EU 2016/127, from 0.72 g/100 kJ to 0.67 g/100 kJ, respectively. The lower maximum permitted protein levels in the current EU 2016/127 are the same as that advised by EFSA (2014a).

EFSA (2014a) states that there was no scientific data available to establish precise cut-off values for the maximum protein content in infant formula. The recommendations are based on the observation that there is no evidence of a physiological need for protein intakes at amounts of 3.0 g/100 kcal (calculated to be 0.72 mg/100 kJ) in infancy, and that protein intakes by infants in the EU are well above requirements.

The higher permitted maximum amounts in EU 2016/127 for formula based on isolated soy proteins, compared with cow's 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 (EFSA 2014a).

A rationale for the higher maximum level set for formula containing protein hydrolysates, compared with cow's or goat's milk-based formulas, was not provided.

Table 6.1: Maximum protein recommendations and regulatory requirements by formula protein source

	Cow's or goat's milk protein		Soy protein isolates		Protein hydrolysates	
	g/100 kJ	g/100 kcal	g/100 kJ	g/100 kcal	g/100 kJ	g/100 kcal
SCF (2003)	NS	3.0	NS	3.0	NS	3.0
EC 2006 Directive	0.7	3	0.7	3	0.7	3
EFSA (2014a), EU 2016/127	0.6	2.5	0.67	2.8	0.67	2.8
Standard 2.9.1	0.7	2.93	0.7	2.93	0.7	2.93
Codex STAN 72-1981	0.7	2.93	0.7	2.93	0.7	2.93

NS: not specified.

7 Linoleic acid

The minimum amount of linoleic acid (LA) differs between international regulations: 120 mg/100 kJ (EU 2016/127); 90 mg/100 kJ (calculated from 9% of total fatty acids (FAs), Schedule 29–8); and, 70 mg/100 kJ (Codex STAN 72-1981). EFSA (2014a), ESPGHAN (1991) and the EC SCF (2003) recommended a minimum amount of 120 mg/100kJ (Table 7.1).

Submissions to the FSANZ 2016 Consultation paper (FSANZ 2016a) did not all agree with FSANZ's preliminary view to retain the current minimum amount of ~~linoleic acid (~~LA~~)~~ specified in Standard 2.9.1 (Schedule 29–8 in the revised Code): no less than 9% of the total fatty acids (equivalent to ~90 mg/100 kJ; Table 7.1). Therefore, the current assessment reconsiders the basis for the minimum amount of LA.

Consideration of the α-linolenic acid (ALA) minimum amount is also required because Standard 2.9.1 prescribes an LA:ALA ratio range of 5:1–15:1 to ensure acceptable levels of metabolic conversion of LA to arachidonic acid, and ALA to docosahexaenoic acid and eicosapentaenoic acid.

Table 7.1: Linoleic acid and α-linolenic acid regulatory requirements and the EFSA (2014a) recommendation for minimum levels in infant formula

	Units	The Code Standard 2.9.1 or Schedule 29	Codex STAN 72-1981	EFSA (2014a) & EU 2016/127
Total fat (minimum amount)	g/100 kJ	1.05	1.05	n/a
Total FA	g/100 kJ[1]	1.00	1.00	n/a
LA (minimum amount)	% of total FA mg/100 kJ	9[2] 90[3]	NS 70	NS 120
ALA (minimum amount)	% of total FA mg/100 kJ	1.1[2] 11[3]	NS 12	NS 12

FA: fatty acid; LA: linoleic acid; ALA: α-linolenic acid; NS: not specified; n/a: not applicable (LA and ALA values do not require calculation).
[1] Calculated from minimum fat amounts, assuming FA content is 95% of total fat (Greenfield and Southgate 2003).
[2] Limits reported in Schedule 29–8.
[3] Calculated from the % of total FA and total FA (g/100 kJ) shown in Table 7.1 using calculations detailed in Appendix 1.

The assessment of an appropriate minimum LA level considers the following:

- ensuring other proposed PUFA requirements can be met, specifically ALA
- the variation of LA concentrations in human milk
- the factors that influence LA levels in human milk
- the AI recommendations for LA and their applicability to ANZ infants
- the minimum LA to prevent deficiency.

Existing regulatory or recommended minimum levels include:

- 60 mg/100 kJ (calculated to ensure the minimum ALA level in formula can be met; see below)
- 70 mg/100 kJ (Directive 2006/141/EC and Codex STAN 72-1981)
- 90 mg/100 kJ (Schedule 29–8 of the Code)
- 106 mg/100 kJ (calculated from the lower boundary of the range of LA in human milk of 8% of total fatty acids reported by LSRO 1998)
- 120 mg/100 kJ (EU 2016/127, EFSA 2014a, ESPGHAN 1991, and EC SCF 2003).

Ensuring other proposed PUFA requirements can be met

Any proposed changes to the minimum level of LA must accommodate the existing PUFA requirements in the Code or those proposed in FSANZ (2016b).

FSANZ (2016b) recommended adopting the maximum ALA used by Codex STAN 72-1981 which, rather than specifying an exact concentration, limits ALA by applying the maximum LA:ALA ratio (15:1) to the Codex GUL of 330 mg/100 kJ. The resulting ALA maximum is 22 mg/100 kJ (Table 7.2).

Table 7.2: Proposed linoleic acid and α-linolenic acid regulatory requirements for infant formula in the Code

		Regulatory requirements proposed by FSANZ (2016a)	
	Units	**min**	**max**
LA	mg/100 kJ	NS	330 (voluntary)
ALA	mg/100 kJ	12	22[1]

LA: linoleic acid; ALA: α-linolenic acid; NS: not specified (currently under review).
[1] The maximum ALA amount is calculated from the voluntary LA maximum (330 mg/100 kJ) and the maximum LA:ALA ratio of 15:1.

To determine the lowest possible minimum LA amount for consideration, we multiplied the proposed minimum ALA (12 mg/100 kJ) by five (applying the minimum LA:ALA of 5:1), which gives an LA amount of 60 mg/100 kJ.

Factors that influence linoleic acid levels in human milk

Contributors to the variability of human milk LA concentrations include differences in dietary intake, maternal body fat stores (Sosa-Castillo et al. 2017), differing research methodologies, the sex of the infant (Thakkar et al. 2013), and the role of nutrigenomics and nutrigenetics (Sosa-Castillo et al. 2017). The mean and variation of LA concentrations in ANZ human milk have been shown to differ to that of other geographic areas, as described below. We have prioritised human milk LA concentration data from ANZ, in recommending a minimum level of LA.

Linoleic acid concentrations in human milk

The studies of Yuhas et al. (2006) and Butts et al. (2018) are considered the best available data on human milk LA levels in ANZ populations.

Yuhas et al. (2006) evaluated the fatty acid profile of mature milk (post-partum day ≥ 30) from mothers of full-term infants living in nine countries. The overall mean LA concentration was 12.9% (wt% of total fatty acids), and mean levels ranged from 7.9% (Philippines) to 17.8% (Chile). This closely aligns with the range of 8–17% reported by LSRO (1998) but is lower than the upper bound of the range (24%, equivalent to 300 mg/100 kJ) cited by EFSA (2014a). The LA concentration in Australian women was 10.7 ± 0.3 (% of total FA; mean ± standard error; n = 48; equivalent to 142 ± 4.5 mg/100 kJ) which was not significantly different to that of Canada and the United Kingdom, but significantly lower than that of the United States (14.8 ± 0.4; n = 49; $P < 0.05$) and significantly higher than that of the Philippines ($P < 0.05$).

Butts et al. (2018) measured LA concentrations in New Zealander human milk within 6–8 weeks post-partum, in three small sub-samples: Asian (n = 8); Māori and Pacific Islander (n = 17); and, European (n = 53). Respective mean LA concentrations were 0.52, 0.35 and 0.36 g/100 g, equivalent to 164, 139 and 138 mg/100 kJ (Appendix 1).

Meeting recommendations for adequate intake of linoleic acid

Table 7.3 presents estimated LA intakes for the 0–<6 month and 6–<12 month age groups calculated using potential minimum LA values.

Table 7.3: Comparison of estimated linoleic acid intakes with nutrient reference values

Source	Linoleic acid minimum (mg/ 100 kJ)	Intake for 0–<6 months (g/day)		Intake for 6–<12 months (g/day)	
		Estimated from minimum[1]	Reference value[2]	Estimated from minimum[1]	Reference value[2]
Proposed ANZ level (upper end; current assessment)	140	3.1	2.4	2.3	3.1
EU 2016/127, ESFA (2014a), ESPGHAN (1991) & EC SCF (2003)	120	2.6		2.0	
LSRO (1998) and Yuhas et al. (2006)[3], & Proposed ANZ level (lower end; current assessment)	106	2.3		1.7	
The Code Schedule 29–8[4]	90	2.0		1.5	
Directive 2006/141/EC & Codex STAN 72-1981	70	1.5		1.1	
Minimum LA to achieve minimum ALA of 12 mg/100 kJ[5]	60	1.3		1.0	

LA: linoleic acid; ALA: α-linolenic acid.
[1] Calculated using midpoint of the energy content (2725 kJ/L) and mean volume of intake of 0.8 L/day for infants 0–<6 months and 0.6 L/day for infants 6–<12 months.
[2] EFSA (2013) reported adequate intakes (AI) for infants aged 0–12 months as % energy: LA = 4%. Conversion to g/day is shown in Appendix 1.
[3] Calculated from the lower boundary (8%) of the range (8–17% of total FAs) of LA in human milk reported by LSRO (1998) and Yuhas et al. (2006). Calculations are outlined in Appendix 1.
[4] Schedule 29–8 specifies the minimum LA as 9% of total fatty acids. Percentage was converted to mg/100 kJ using the total fat minimum (1.05 g/100 kJ), assuming 95% of fat is fatty acid (Greenfield and Southgate 2003).
[5] Minimum level calculated based on LA:ALA of 5:1 and ALA at 12 mg/100 kJ.

ANZ NRVs for LA have not been established. The EFSA AI for LA (4% of energy for infants) was derived from the lowest estimated mean intake in various European countries that was not accompanied by LA deficiency symptoms (EFSA 2013).

A minimum LA amount of ~110 mg/100 kJ is required to reach the EFSA AI for infants 0–<6 months (2.4 g/day); this will also meet half the EFSA AI for 6–<12 months (1.6 g/day). The estimated LA intake based on the Code's minimum amount (equivalent to ~90 mg/100 kJ) is within the range considered to pose low risk to infant health (≤15% lower than the EFSA AI for younger infants and ≤15% lower than half the EFSA AI for older infants; see Section 3.3). The lowest reported mean level of LA in human milk is 8% of total fatty acids (LSRO 1998 and the Philippines sample from Yuhas et al. 2006) which is also equivalent to ~110 mg/100 kJ.

An LA level of 140 mg/100 kJ closely matches the mean human milk LA concentration in Australians (142 mg/100 kJ; Yuhas et al. 2006) and New Zealanders (139 and 138 mg/100 kJ in two of three sub-samples; Butts et al. 2018). It is 15% lower than the mean for the Asian New Zealander sub-sample (164 mg/100 kJ; Butts et al. 2018). At an LA level of 140 mg/100 kJ, the estimated daily LA intake from formula for infants aged 0–< 6 months (3.1 g/day) and infants aged 6–<12 months (2.3 g/day) would also meet the EFSA AI (2.4 g/day and half of 3.1 g/day i.e. 1.6 g/day, respectively; Table 7.3).

The levels of LA in ANZ human milk (~140 mg/100 kJ) are higher than the lowest reported mean levels in other countries (~110 mg/100 kJ). However, the mean intake in populations

with no apparent deficiency, such as ANZ, may be higher than the minimum requirement to prevent deficiency. Based on the lowest overall mean level, and ANZ levels, of LA in human milk, the risk of harm to infants' health due to inadequate LA or ALA intake would be low if FSANZ adopted a minimum LA amount between 110 and 140 mg/100 kJ.

8 L-carnitine

Mean levels of total carnitine have been reported to be 0.2–0.4 mg/100 kJ in human milk, 0.8–1.6 mg/100 kJ in cow's milk and 0.8–1.1 mg/100 kJ in goat's milk (EFSA 2014; Olagaray et al. 2018).

EU 2016/127 and Codex STAN 72-1981 do not set a maximum level for L-carnitine, specified as either a mandatory or GUL value. Standard 2.9.1 permits L-carnitine to be added as a nutritive substance in the range of 0.21–0.8 mg/100 kJ.

FSANZ (2016b) reported there is no evidence in infants or in children indicating that they consume excess carnitine or that carnitine consumption is linked with adverse health outcomes. However, FSANZ (2016b) also stated that recent studies suggest that non-absorbed carnitine is metabolised by microbes in the large bowel to trimethylamine (TMA), a compound that may be associated with the development of cardiovascular disease. TMA is absorbed and then metabolised in the liver to trimethylamine-N-oxide (TMAO), and since 2013 several observational studies have reported positive associations between plasma TMAO concentrations and adverse cardiovascular outcomes.

As part of its assessment of application A1102 (L-carnitine in food), FSANZ concluded that the evidence available at the time (from studies in adults) did not support TMAO playing a causal role in initiating or promoting adverse cardiovascular effects (FSANZ 2019). At L-carnitine doses ≥ 3 g/day, nausea, gastrointestinal disturbances, and fishy body odour and/or urine odour have been observed in adults. However, these effects are mild in severity and have rarely warranted cessation of dosing in clinical studies. No adverse effects attributable to L-carnitine intake have been identified at doses of up to 3 g/day.

We 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.

On the basis of a lack of suitable information to assess the safety of high L-carnitine concentrations, it cannot be ruled out that the lack of a specification for a maximum amount of L-carnitine in infant formula, as is the case for Codex STAN 72-1981 and EU 2016/127, may pose a risk to infant health. This is consistent with FSANZ's previous conclusion (FSANZ 2016b).

9 Conversion between kilocalories and kilojoules

Levels for vitamins and minerals in Codex STAN 72-1981 are specified as both 'per 100 kcal' and 'per 100 kJ'. Here, we assess if the Codex values 'per 100 kcal' are all converted using the kcal to kJ conversion factor specified in the Code (4.18), and what, if any, the differences are to the Codex values specified in kJ.

In submissions to FSANZ's Consultation paper (2016a), stakeholders noted that the values for minimum and maximum nutrient levels in Codex STAN 72-1981 have not consistently been converted between units per kcal and kJ. As the Code specifies the kcal to kJ

conversion factor of 4.18 for nutrient levels, FSANZ wishes to determine the differences, if any, between the nutrient levels (per 100 kJ) as specified in Codex STAN 72-1981 and converted from nutrient levels (per 100 kcal) using the conversion factor specified in the Code.

When all the minimum and maximum amounts for all vitamins and minerals are converted using the kcal to kJ conversion factor specified in the Code (4.18), minimal differences were found between the Codex stated values and the converted values (see Tables 9.1 to 9.4). The largest difference was a 10% lower amount in the biotin minimum amount when converted using the specified conversion.

Table 9.1. Comparison of minimum values stated in Codex and values converted from kcal to kJ using factor of 4.18 for all vitamins

Vitamins (units)	Stated Codex minimum (unit/100 kcal)	Stated Codex minimum (unit/100 kJ)	Codex minimum (unit per 100 kcal) converted to unit/100 kJ[1]	Difference of minimum (unit/100 kJ)[2]	% difference of Codex minimum (per 100 kJ)
Vitamin A (µg RE)	60	14	14.4	0.354	2.5
Vitamin D3 (µg)	1	0.25	0.239	-0.011	-4.3
Vitamin E (mg α-TE)	0.5	0.12	0.120	0.000	-0.3
Vitamin K (µg)	4	1	0.957	-0.043	-4.3
Thiamin (µg)	60	14	14.4	0.354	2.5
Riboflavin (µg)	80	19	19.1	0.139	0.7
Niacin (µg)	300	70	71.8	0.177	2.5
Vitamin B6 (µg)	35	8.5	8.37	-0.127	-1.5
Vitamin B12 (µg)	0.1	0.025	0.024	-0.001	-4.3
Pantothenic acid (µg)	400	96	95.7	-0.306	-0.3
Folic acid (µg)	10	2.5	2.39	-0.108	-4.3
Vitamin C (mg)	10	2.5	2.39	-0.108	-4.3
Biotin (µg)	1.5	0.4	0.359	-0.041	-10.3

[1] *Converted using the kcal to kJ conversion factor of 4.18.*
[2] *Difference calculated by converted values minus Codex stated values.*

Table 9.2. Comparison of maximum or GUL values stated in Codex and values converted from kcal to kJ using factor of 4.18 for all vitamins

Vitamins (units)	Maximum or GUL value	Stated Codex value (unit/100 kcal)	Stated Codex value (unit/100 kJ)	Codex value (unit per 100 kcal) converted to unit/100 kJ[1]	Difference of value (unit/100 kJ)[2]	% difference of Codex value (per 100 kJ)
Vitamin A (µg RE)	Maximum	180	43	43.1	0.062	0.1
Vitamin D3 (µg)	Maximum	2.5	0.6	0.598	-0.002	-0.3
Vitamin E (mg α-TE)	GUL	5	1.2	1.20	0.004	-0.3
Vitamin K (µg)	GUL	27	6.5	6.46	-0.041	-0.6
Thiamin (µg)	GUL	300	72	71.8	-0.230	-0.3
Riboflavin (µg)	GUL	500	119	120	0.617	0.5
Niacin (µg)	GUL	1500	360	359	-1.15	-0.3
Vitamin B6 (µg)	GUL	175	45	41.9	-3.13	-7.0
Vitamin B12 (µg)	GUL	1.5	0.36	0.359	0.001	-0.3
Pantothenic acid (µg)	GUL	2000	478	478	0.469	0.1
Folic acid (µg)	GUL	50	12	12	0.038	-0.3
Vitamin C (mg)	GUL	70	17	16.7	-0.254	-1.5
Biotin (µg)	GUL	10	2.4	2.39	-0.008	-0.3

GUL, guidance upper level.
[1] Converted using the kcal to kJ conversion factor of 4.18.
[2] Difference calculated by converted values minus Codex stated values.

Table 9.3. Comparison of minimum values stated in Codex and values converted from kcal to kJ using factor of 4.18 for all minerals

Minerals (units)	Stated Codex minimum (unit /100 kcal)	Stated Codex minimum (unit/100 kJ)	Codex minimum (unit 100 kcal) converted to unit/100 kJ[1]	Difference of minimum (unit/100 kJ)[2]	% difference of Codex minimum (per 100 kJ)
Iron (mg)	0.45	0.1	0.108	0.008	7.7
Calcium (mg)	50	12	12	0.038	-0.3
Phosphorus (mg)	25	6	5.98	-0.019	-0.3
Magnesium (mg)	5	1.2	1.20	0.004	-0.3
Sodium (mg)	20	5	4.78	-0.215	-4.3
Chloride (mg)	50	12	12	0.038	-0.3
Potassium (mg)	60	14	14.4	0.354	2.5
Manganese (µg)	1	0.25	0.239	-0.011	-4.3
Iodine (µg)	10	2.5	2.39	-0.108	-4.3
Selenium (µg)	1	0.24	0.239	-0.001	-0.3
Copper (µg)	35	8.5	8.37	-0.127	-1.5
Zinc (mg)	0.5	0.12	0.120	0.000	-0.3

[1] *Converted using the kcal to kJ conversion factor of 4.18.*
[2] *Difference calculated by converted values minus Codex stated values.*

Table 9.4. Comparison of maximum or GUL values stated in Codex and values converted from kcal to kJ using factor of 4.18 for all minerals

Minerals (units)	Maximum or GUL value	Stated Codex value (unit/ 100 kcal)	Stated Codex value (unit/ 100 kJ)	Codex value (unit/100 kcal) converted to unit/100 kJ[1]	Difference of value (unit/100 kJ)[2]	% difference of Codex value (per 100 kJ)
Iron (mg)	NS	n/a	n/a	n/a	n/a	n/a
Calcium (mg)	GUL	140	35	33.5	-1.51	-4.3
Phosphorus (mg)	GUL	100	24	23.9	-0.077	-0.3
Magnesium (mg)	GUL	15	3.6	3.59	-0.011	-0.3
Sodium (mg)	Maximum	60	14	14.4	0.354	2.5
Chloride (mg)	Maximum	160	38	38.3	0.278	0.7
Potassium (mg)	Maximum	180	43	43.1	0.062	0.1
Manganese (µg)	GUL	100	24	23.9	-0.077	-0.3
Iodine (µg)	GUL	60	14	14.4	0.354	2.5
Selenium (µg)	GUL	9	2.2	2.15	-0.047	-2.1
Copper (µg)	GUL	120	29	28.7	-0.292	-0.01
Zinc (mg)	GUL	1.5	0.36	0.359	-0.001	-0.3

NS: not specified; n/a: not applicable; GUL: guidance upper level.
[1] Converted using the kcal to kJ conversion factor of 4.18.
[2] Difference calculated by converted values minus Codex stated values.

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Appendix 1: Calculations

Estimation of daily nutrient intake from infant formula: Minimum and maximum nutrient amounts (in mass per 100 kJ) were multiplied by the midpoint of the energy content (2725 kJ/L) and the mean daily intake volume (0.8 L/day or 0.6 L/day for younger or older infants, respectively) to obtain estimated daily nutrient intakes. This enabled comparison of the estimated daily nutrient intakes using the minimum nutrient levels to AIs or EARs, and the estimated daily nutrient intakes using the maximum nutrient levels to the ULs.

The application of these calculations has been shown in the example provided below.

Example (1) – estimated daily intake of vitamin A from infant formula containing the minimum and maximum amount in EU 2016/127 for infants aged 0–<6 months:

$$\boldsymbol{Minimum\ intake\ of\ vitamin\ A} = \frac{16.7\ \mu g}{100\ kJ} \times \frac{2725\ kJ}{L} \times \frac{0.8\ L}{day} = \frac{364\ \mu g}{day}$$

$$\boldsymbol{Maximum\ intake\ of\ vitamin\ A} = \frac{27.2\ \mu g}{100\ kJ} \times \frac{2725\ kJ}{L} \times \frac{0.8\ L}{day} = \frac{593\ \mu g}{day}$$

Linoleic acid and α-linolenic acid calculations:

Example (2) – standardising linoleic acid and α-linolenic acid regulatory requirements for infant formula:

	Specified LA Amount		Specified ALA Amount	
	The Code (% total FA)	Codex STAN 72-1981 (mg/100 kJ)	The Code (% total FA)	Codex STAN 72-1981 (mg/100 kJ)
Minimum	**9**	**70**	**1.1**	**70**
Maximum	**26**	**330**	**4**	**330 (GUL)**

The following calculations assume 95% of fat is fatty acid (Greenfield and Southgate 2003).

Conversion of the Code's LA and ALA amounts from '% of total FA' to 'mg/100 kJ':

$$\boldsymbol{Amount\ FA} = \%\ total\ FA \times \frac{g\ total\ fat}{100\ kJ} \times \frac{0.95\ g\ FA}{g\ fat} \times \frac{1000\ mg}{g} = \frac{mg\ FA}{100\ kJ}$$

$$\boldsymbol{Minimum\ LA} = 9\%\ LA \times \frac{1.05\ g\ total\ fat}{100\ kJ} \times \frac{0.95\ g\ FA}{g\ fat} \times \frac{1000\ mg}{g} = \frac{90\ mg\ LA}{100\ kJ}$$

$$\boldsymbol{Maximum\ LA} = 26\%\ LA \times \frac{1.5\ g\ total\ fat}{100\ kJ} \times \frac{0.95\ g\ FA}{g\ fat} \times \frac{1000\ mg}{g} = \frac{371\ mg\ LA}{100\ kJ}$$

$$\boldsymbol{Minimum\ ALA} = 1.1\%\ ALA \times \frac{1.05\ g\ total\ fat}{100\ kJ} \times \frac{0.95\ g\ FA}{g\ fat} \times \frac{1000\ mg}{g} = \frac{11\ mg\ ALA}{100\ kJ}$$

$$\textbf{Maximum ALA} = 4\%\ ALA \times \frac{1.5\ g\ total\ fat}{100\ kJ} \times \frac{0.95\ g\ FA}{g\ fat} \times \frac{1000\ mg}{g} = \frac{57\ mg\ ALA}{100\ kJ}$$

Example (3) – conversion of EFSA Adequate Intake value from '% energy' to 'g/day':

There are no ANZ AI amounts set for LA and ALA set by the NHMRC (2006) The EFSA NDA Panel (2013) reported values for adequate intake for LA and ALA as 4% and 0.5% of daily energy intake, respectively, for infants aged 0–12 months. In order assess whether intakes based on various regulatory requirements or recommendations for minimum amounts would meet these EFSA values (as an indicative comparison), the latter were converted from '% daily energy intake' to 'g/day' based on the assumptions:

- Mean EER for infants aged 0–<6 months is 2333 kJ/day. Mean EER for infants aged 6–<12 months is 3033 kJ/day from food and formula, or 1517 kJ/day from formula (see Table 5 in Section 3.2.2 of the FSANZ 2016 nutrition assessment; FSANZ 2016b).
- 1 g fat is equivalent to 37 kJ (Standard 1.2.8) where a correction to allow for the fatty acid content of fat (95%) was applied (Greenfield and Southgate 2003).

Conversion of EFSA adequate intakes amounts to g/day for infants aged 0-<6 months:

$$\textbf{Adequate intake LA} = \frac{4\ kJ\ LA}{100\ kJ} \times \frac{2333\ kJ}{day} \times \frac{1\ g\ fat}{37\ kJ} \times \frac{0.95\ g\ FA}{g\ fat} = \frac{2.4\ g}{day}$$

$$\textbf{Adequate intakes ALA} = \frac{0.5\ kJ\ LA}{100\ kJ} \times \frac{2333\ kJ}{day} \times \frac{1\ g\ fat}{37\ kJ} \times \frac{0.95\ g\ FA}{g\ fat} = \frac{0.30\ g}{day}$$

Example (4) – Conversion of human milk linoleic acid amounts from '% total FA' to 'mg/100 kJ':

Human milk from North American mothers was reported to contain LA at 8–17% of total fatty acids (LSRO 1998). Linoleic acid amounts were converted to mg/100 kJ using the average total fat content (38 g/L) (Hester et al. 2012) and the mean energy content of human milk (2720 kJ/L; EC SCF 2003, Hester et al. 2012, EFSA 2014a).

$$\textbf{Average total FA} = \frac{38\ g\ fat}{L} \times \frac{L}{2720\ kJ} \times \frac{0.95\ g\ FA}{g\ fat} = \frac{1.33\ g\ FA}{100\ kJ}$$

$$\textbf{Minimum LA} = 8\%\ LA \times \frac{1.33\ g\ total\ FA}{100\ kJ} \times \frac{1000\ mg}{g} = \frac{106\ mg\ LA}{100\ kJ}$$

$$\textbf{Maximum LA} = 17\%\ LA \times \frac{1.33\ g\ total\ FA}{100\ kJ} \times \frac{1000\ mg}{g} = \frac{226\ mg\ LA}{100\ kJ}$$