Comments from the Victorian Department of Health and the Victorian Department of Jobs, Precincts and Regions.

Due date of submission – 19 August 2021 (extended to 2 September 2021)

Contents

Introduction

The Victorian Departments of Health and Jobs, Precincts and Regions (the departments) welcome the opportunity to respond to this consultation paper *P1028– Infant formula: Nutrient composition*.

The departments recognise that breastfeeding is the normal and recommended way of feeding infants and that the regulation of infant formula has implications for breastfeeding rates as well as the health outcomes of formula-fed infants. Infant formula products are essential products for a vulnerable population and careful consideration is vital to ensure that infants' health and interests are the primary focus of regulatory decisions.

FSANZ, as the country's independent food standards scientific body and risk assessor, has an important responsibility to protect infant health and safety by ensuring that infant formula regulations are updated to keep pace with scientific knowledge about the nutritional requirements of infants to assist in reducing the negative health outcomes experienced by formula-fed infants relative to their breastfed counterparts.

Principles guiding the departments' positions:

1. The primary aim of Proposal P1028 is to update regulations that are twenty years old to ensure they are consistent with scientific knowledge about the nutritional requirements of infants, rather than primarily to align with Codex.
2. Protection of infant health and safety is the primary objective in reviewing Standard 2.9.1. Harmonisation with international regulations is an important consideration but only once infant health and safety has been satisfied. This is consistent with FSANZ's primary objective and Food Ministers expectations set in the *Policy Guidelines for the Regulation of Infant Formula Products* (Policy Guidelines), which recognises the vulnerability of the population for whom these products are intended, the importance of these products in the diets of formula fed infants and that the regulatory framework should recognise this greater level of risk.

   To meet this objective, the departments consider that risk assessments and established history of safe use for new food additives (from Paper 1) as well as nutrition assessments to determine compositional requirements are essential preconditions for setting provisions in infant formula regulations. Specifically in relation to nutrient composition, consideration of health and safety must include:

   a. Meeting infant nutritional requirements, in line with updated scientific evidence and comparability with breast milk composition, unless there is clear scientific justification for not doing so, consistent with the Policy Guidelines. This includes consideration of when a voluntary ingredient should be mandated to ensure equitable access for all infants.

   b. Avoiding the addition of unnecessary substances or amounts of substances that might burden infants' immature systems, in line with accepted expert opinion[1]. This includes consideration of both maximum levels and evidence of benefit for voluntary ingredients.

[1] Koletzko, B., et al., Global standard for the composition of infant formula: recommendations of an ESPGHAN coordinated international expert group. Journal of Pediatric Gastroenterology and Nutrition, 2005. 41(5): p. 584-599

The departments also note that decisions must be evidence-based and primarily in infants' interests and a majority approach to submission views to support proposed approaches may not be helpful in achieving this outcome. Adequate consultation with infant feeding experts (such as paediatric dietitians, paediatricians, maternal child health nurses and academics with expertise in infant feeding) is critical, as raised in previous consultations.

3. The regulatory nutrient composition of infant formula products must not give the impression that these products are superior to breastmilk in any way (for example by adding amount of nutrients above those found in breastmilk, unless there is a scientific justification for doing so, for example, differences in bioavailability).

Alignment with international regulations

At the 2016 consultation, the departments noted that the compositional levels in new EU regulations for infant formula had moved away from Codex levels in many cases, based on updated scientific assessment, and that these should be considered over Codex STAN 72-1981, noting the significant trade in infant formula between Australia and the EU. In this consultation paper, FSANZ has indicated it still prioritises aligning with Codex, however proposes to align some nutrient levels with Codex STAN 72-1981, some with EU 2016/127 and some it proposes keeping as they are, which align with neither Codex nor the EU. We note this is similar to other international standards, such as the proposed Chinese infant formula standards. Given this variable approach, the argument to align with Codex to facilitate trade, as FSANZ has stated in some instances, does not appear justified particularly where Codex levels are not consistent with the latest evidence on infant requirements. From a trade perspective, the principal priority should be maintaining Australia and New Zealand's reputation for high quality infant formula; a formula that is based on infant health and safety will better meet this priority.

In the first Call for Submissions, the departments would like to see a rationale, supported by scientific assessment, that is focused first on infant health and safety, including meeting infant nutritional requirements and avoiding excess levels, with harmonisation with international regulations wherever possible as a secondary consideration.

Scope

The departments note that FSANZ has stated that the scope of Proposal P1028 includes all requirements for infant formula products in Standard 2.9.1, excluding follow-on formula (FOF). As indicated in our response to Consultation Paper 1 – Safety and Food Technology, the departments consider this problematic in that the resulting changes to regulatory provisions would only apply to one class of product. This will result in two sets of nutritional composition permissions being created for infant formula and follow-on formula, without scientific justification and with potential trade implications. Changing the regulatory approach for products targeted to infants 6 months or over represents a new regulatory approach that would need proper justification and assessment of risks and benefits. **While P1028 may not consider the question of whether a breastmilk substitute for infants aged 6-12 months should contain different levels of nutrients than infants aged 0-6 months, the departments consider that Standard 2.9.1 must retain consistent nutritional compositional requirements across both products where these exist already, with the levels based on P1028.**

In addition, the departments request that FSANZ indicates when follow-on formula will be addressed.

Section 3 - Energy

3.1 Energy content

The departments note no further nutrition risk assessment was considered on this issue and **support the proposed approach to retain the minimum energy content at 2500 kJ/L and to lower the maximum energy content from 3150 kJ/L to 2950 kJ/L** on the basis that it better meets the energy requirements for infants. The departments note this range is consistent with Codex STAN 72-1981 and EU regulations (EU 2016/127).

3.2 Calculation of energy content

The departments note the previous conflict regarding the calculation of energy content between Standard 1.2.8 and Standard 2.9.1 was resolved in Proposal P1025 and no further changes are proposed.

Section 4 - Protein

4.1 Calculation of protein content

Summary position: The departments support Option 1 to adopt the NCF of 6.25 for all protein sources, with a higher minimum for soy.

The departments note that the Australia New Zealand Food Standards Code (the Code) currently assigns a nitrogen conversion factor (NCF) of 6.38 for cow's milk protein and 6.25 for soy protein to allow for the different bioavailability of soy protein. Codex STAN 72-1981 and EU 2016/127 both assign a NCF of 6.25 for all protein sources but alter the permitted range for soy protein to allow for bioavailability differences. FSANZ proposes two possible options for the calculation of protein, with Option 1 being FSANZ's proposed approach:

1) Adopt 6.25 as the nitrogen conversion factor (NCF) for all protein sources, including soy, with a higher minimum protein for soy (which aligns with the EU 2016/127 regulations and Codex).

2) Adopt all three NCF (5.71, 6.25, 6.38). This approach enables the highest degree of flexibility for manufacturers to apply the most appropriate NCF for a particular protein source (e.g., 5.71 for soy, 6.25 for whey-based protein, and 6.38 for other dairy), with manufacturers able to use 6.25 which is aligned with international regulations.

The departments note that no further nutrition risk assessment was considered on this issue. There is not yet consensus in the scientific literature as to what is the most appropriate NCF to use when determining protein content in infant formula, with recent conflicting opinions from the Codex Committee on Methods of Analysis Sampling in 2016 and the Joint FAO/WHO Expert Meetings on Nutrition in 2020. The departments note that the NCF influences the amount of protein that will be added and a lower NCF will require manufacturers to add more 'protein source' to achieve the same amount of protein. FSANZ has considered the cost to manufacturers of the additional protein source, if the NCF was lower, but not the impact on infant growth and risk of obesity.

Given the lack of consensus on the most appropriate NCF, and the impact on the amount of protein provided, the departments support a consistent NCF across international jurisdictions to ensure ideal growth (aligned with breastfed infants) can be determined and achieved. **Therefore, the departments support Option 1 to adopt a NCF of 6.25**, with a higher minimum for soy to account for the lower protein quality and availability.

4.2 Protein range

Cow's milk-based

Summary position: The departments support the proposed minimum protein of 0.43 g/100kJ but support a maximum that aligns with EU 2016/127 (0.6g/100kJ).

The departments note that FSANZ's proposed approach is to align its permitted protein range with the EU minimum of 0.43 g/100kJ and retain the current maximum, 0.7g/100kJ for cow's milk based formula, which is aligned with Codex. **The departments support the proposed minimum protein but remain concerned that the upper level of the range is too high**. **The departments propose aligning with the EU maximum of 0.6g/100kJ.** These levels assume a nitrogen conversion factor of 6.25.

The departments note that the EU reduced its maximum from the Codex level to 0.6g/100kJ based on the EFSA 2014 opinion that there is no evidence of a physiological need for protein intakes at 0.7g/100kJ[2]. The departments note that FSANZ states there is an absence of evidence of harm at 0.7g/100kJ. The departments disagree.

High protein intake in infants has been long recognised as a risk factor for obesity. In the large, multi-centre, randomised control trial (The European Childhood Obesity Trial) it was found that infants fed a formula with 0.7g protein/100kJ had a significantly higher weight at 3, 6 and 12 months of age than infants fed a formula at the lower permitted level (0.43g/100kJ) and breastfed infants[3]. A follow-up of these children at 6 years of age found a significantly higher risk of obesity in those children fed the formula with 0.7g/100kJ of protein[4]. While the departments note that, in its scientific assessment of infant formula composition in 2014, EFSA stated 'there are no scientific data available which allow the establishment of precise cut-off values for the maximum protein content in infant formula[5] , it would be prudent, and consistent with FSANZ's objectives, to select a lower maximum than one that associated with adverse health outcomes. This would also be consistent with the 2013 Infant Feeding Guidelines which recommend that it is preferable to use a formula with a lower protein level[6]. While it unclear at this stage whether protein levels of 0.6g/100kJ may also increase the risk of obesity, the risk is likely to be lower than that of the current level and has the benefit of harmonising with EU regulations.

In terms of industry's ability to achieve a maximum level of 0.6g/100kJ, the departments note that in its infant formula label survey from the 2016 consultation, FSANZ indicated protein levels ranged from 0.46-0.63g/100kJ. No updated information has been provided by FSANZ but a desktop review of the brands currently available in supermarkets indicates that all products reviewed range from

[2] EFSA (EFSA Panel on Dietetic Products Nutrition and Allergies), Scientific opinion on the essential composition of infant and follow-on formulae. EFSA Journal, 2014.12(7): p. 3760-3866

[3] European Childhood Obesity Trial Study Group, Lower protein in infant formula is associated with lower weight up to age 2 y: a randomized clinical trial, The American Journal of Clinical Nutrition, Volume 89, Issue 6, June 2009, Pages 1836–1845, https://doi.org/10.3945/ajcn.2008.27091

[4] Martina Weber, Veit Grote, Ricardo Closa-Monasterolo, Joaquín Escribano, Jean-Paul Langhendries, Elena Dain, Marcello Giovannini, Elvira Verduci, Dariusz Gruszfeld, Piotr Socha, Berthold Koletzko, for The European Childhood Obesity Trial Study Group, Lower protein content in infant formula reduces BMI and obesity risk at school age: follow-up of a randomized trial, The American Journal of Clinical Nutrition, Volume 99, Issue 5, May 2014, Pages 1041–1051

[5] EFSA (EFSA Panel on Dietetic Products Nutrition and Allergies), Scientific opinion on the essential composition of infant and follow-on formulae. EFSA Journal, 2014.12(7): p. 3760-3866

[6] National Health and Medical Research Council, Infant Feeding Guidelines. 2013, NHRMC: Canberra

0.44-0.52g/100kJ protein and therefore are already beneath the EU lower maximum level of 0.6g/100kJ and would not require reformulation[7].

Soy-based

The departments note no further nutrition risk assessment was considered on this issue but **support FSANZ's proposed approach to require a higher minimum protein level for soy-based formulas** (0.54g/100kJ) to account for lower levels of some essential amino acids, lower digestibility of plant proteins and the nitrogen conversion factor of 6.25, which overestimates the true protein content of soy protein. This creates a new minimum level for soy-based products in the Code and is consistent with the EU regulations and the Codex Draft Standard for Follow-up Formula.

General approach to provisions for soy-based formula

In relation to FSANZ's questions about separate ranges for certain nutrients (whose bioavailability is impacted) for soy-based formula, the departments consider it important to have separate ranges, rather than a single broader range that covers both cow and soy-based products. **This ensures sufficient amounts of nutrients are provided through soy formula (rather than a manufacturer adding the lower end of the range suitable for cow's milk only), minimises excess nutrients being added to cow-based formula, and also serves to indicate to manufacturers and formula developers the difference in bioavailability that needs to be considered. This will also be important with the growing interest in other plant-based protein sources.**

4.3 Protein source

Summary position: The departments support listing permitted protein sources but request the wording be reviewed and clarified for enforcement purposes.

The departments support the proposal for the Standard to clearly state the protein sources that have undergone pre-market assessment and are permitted in infant formula products. This aligns with the Ministerial Policy Guideline on Infant Formula Products, which specifies that all new substances used in infant formula in Australia and New Zealand should undergo pre-market assessment. This will ensure that permitted protein sources are suitable and issues such as bioavailability of the protein and the presence of anti-nutritive factors (such as trypsin inhibitors, lectins and phytic acid found in soy), and relevant contaminants (such as mycotoxins), are accounted for and kept as low as possible. The departments note that this is consistent with the EU and with the draft Codex approach for 'follow-up formula'.

In terms of enforceability, the departments request further consideration be given to the following proposed wording, which could be ambiguous in terms of what might be considered 'normally used in formula': '*cow's milk protein, goat's milk protein, protein hydrolysates of one or more proteins normally used in infant formula, and soy protein isolate'*.

4.4 Protein quality

Summary position: The departments support FSANZ'S proposed approach.

The departments note the assessment and recent international consideration of alternative protein quality methods and the conclusions that, while the protein digestibility corrected amino acid score (PDCAAS) and the digestible indispensable amino acid score (DIAAS) protein scoring systems have been considered ideal methods, the evidence base relevant for human infants is incomplete and they are not considered ready to use for regulatory purposes. **The departments support FSANZ's**

[7] Brands reviewed: Nan Optipro, A2 Platinum, Bellamy's Organic, Bub's Goat, Aptamil Gold, Karicare, S26 Premium

proposed approach to continue to use the amino acid composition of human milk as the reference for determining minimum amino acid requirements in infant formula products.

Until a superior method is confirmed, this is consistent with the Ministerial Policy Guideline on Infant Formula Products which recognise the composition of breastmilk should be used as a primary reference for determining the composition of infant formula. The departments note this also aligns with Codex.

4.5 Amino acid content

Summary position: The departments support FSANZ'S proposed approach.

The departments note that both Standard 2.9.1 and Codex STAN 72-1981 specify minimum amounts of 11 essential and semi-essential amino acids and that isolated amino acids should be added to infant formula only to improve its nutritional quality. **The departments support the proposed approach to align the minimum amounts of all essential and semi-essential amino acids with Codex STAN 72-1981 (which are closely aligned with EU regulations) and specify ratio requirements for methionine to cysteine and tyrosine to phenylalanine (using the example of the EU regulations) to ensure the amino acid composition remains closely aligned to breast milk composition.** This approach ensures amino acid requirements are met while offering the greatest harmonisation with international regulations.

Section 5 - Fat

5.1 Fat content

The departments support the proposed approach to retain the minimum fat content of 1.05g/ 100kJ and lower the maximum fat requirement in infant formula to 1.4g/100kJ on the basis that it is consistent with the fat content of human milk, the scientific recommendations of EFSA in 2014[8] and EU and Codex regulations.

5.2 Units of expression

The departments support the proposed approach to express permitted amounts of linoleic acid (LA), alpha-linoleic acid (ALA) and docosahexaenoic acid (DHA) in mg/100kJ on the basis that international regulations have moved away from expressing fatty acids as a percentage of total fatty acids and consistent units will simplify regulations. We note this approach is consistent with the most recent scientific opinion by EFSA and international regulations (Codex 72-1981 and EU 2016/127).

The departments note that individual fatty acids have a minimum and maximum range and are currently expressed as a percentage of total fat, which also has a range. This means that the figure obtained when converting between percentage fatty acid contents and mg per 100kJ will depend on whether a minimum/maximum or midpoint of the fatty acid in question is used. Instead of providing guidance on what method should be used to ensure a consistent approach, FSANZ indicates that '*Defining a calculation for converting fatty acid amounts from percentage of total fatty acids to mg/100 kJ is not needed as no safety issue has been identified and this approach would be inconsistent with the general view of manufacturers on minimum effective regulation*.' **The departments support providing guidance on a method of calculation based on what best meets**

[8] EFSA (EFSA Panel on Dietetic Products Nutrition and Allergies), Scientific opinion on the essential composition of infant and follow-on formulae. EFSA Journal, 2014.12(7): p. 3760-3866

the nutritional requirements of infants to ensure a consistent approach is taken and that this aspect of the standard is enforceable.

5.3 Essential fatty acid composition: Linoleic acid and Alpha-linolenic acid

Summary position: Linoleic acid: The departments do not support FSANZ's proposed approach. Support Option 1: Adopt EU 2016/127 minimum LA level of 120 mg/100 kJ, and a maximum Guideline Upper Level of 300mg/100kJ (in line with EU).
Alpha-linolenic acid: The departments support the proposed minimum ALA level of 12mg/100kJ and retaining the current ratio of LA:ALA of 5:1 To 15:1.

Linoleic acid (LA)
Proposed minimum of 90mg/100kJ

The departments note the minimum compositional levels for linoleic acid vary across international regulations with Codex requiring 70mg/100kJ, the Code 90mg/100kJ and the EU 120mg/100kJ (which was increased from the Codex level in 2016 to meet infant requirements).

FSANZ has considered two options for the linoleic acid minimum and it proposes aligning with Option 2:

Option 1: Adopt EU 2016/127 minimum LA level of 120 mg/100 kJ. This option supports alignment with the most recently updated regulation standards and alignment with the minimum LA levels noted within breast milk of the ANZ population.

Option 2: Retain the current minimum LA level of 90 mg/100 kJ within Standard 2.9.1 (S29—8). This option mitigates risks surrounding infant formula stability and palatability when LA levels are increased. It also represents the best available option for alignment with Codex and would mitigate risk of reformulation or trade implications.

The departments do not support FSANZ's proposed approach and instead support aligning with Option 1, which is a minimum of 120mg/100kJ for linoleic acid. This aligns with the EU regulations and longstanding scientific positions on infant requirements[9],[10] .

The primary consideration for determining nutritional compositional requirements for infant formula must be ensuring infant nutritional requirements are met. This is set out in principle f of the Policy Guideline for the Regulation of Infant Formula Products, which states: *f) The essential composition of infant formula and follow on formula should be prescribed in regulation and must satisfy the nutritional requirements of infants.*

While the National Health and Medical Research Council (NHMRC) Nutrient Reference Values do not set a specific Adequate Intake for LA, EFSA established an Adequate Intake of 4% of energy for infants (equivalent to ~110mg/100kJ), which was based on the lowest estimated mean intake in various European countries that was not associated with LA deficiency symptoms and was consistent with levels in breastmilk; FSANZ's nutritional assessment indicates the lowest reported average content in breastmilk is also equivalent to~110mg/100kJ, with 140mg/100kJ considered to be the average amount found in Australian and New Zealand women's breastmilk (142 mg/100 kJ in Australian women and 139 and 138mg/100 kJ in New Zealanders). **FSANZ notes adequate LA intake**

[9] EFSA (EFSA Panel on Dietetic Products Nutrition and Allergies), Scientific opinion on the essential composition of infant and follow-on formulae. EFSA Journal, 2014.12(7): p. 3760-3866
[10] SCF (Scientific Committee on Food), 2003. Report of the Scientific Committee on Food on the revision of essential requirements of infant formulae and follow-on formulae.

will not be achieved with the proposed minimum level of 90mg LA/100kJ and that 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. A proposal to provide less than the minimum requirement for infants of an essential nutrient is not consistent with FSANZ's primary objective to protect health and safety.

FSANZ indicates further information is needed to address the issues surrounding the stability and palatability of infant formula when LA levels are increased. We note FSANZ's recent label survey found the LA content of current market products ranged between 146 – 267mg/100kJ, **indicating there appear to be no technological issues, including around stability and palatability** at these higher levels.

FSANZ also suggests that adopting a higher minimum LA level may create some trade barriers as Codex STAN 72-1981 sets a lower minimum LA requirement (noting FSANZ has stated the much lower Codex minimum of 70mg/100kJ is not suitable and its proposed level will still not align with Codex). Given Australian (and presumably European) products currently have levels above 120mg/100kJ, it is unclear specifically what trade barriers FSANZ is concerned about. Australian exports to countries with lower minimums would still meet compositional requirements. However, **the departments would like to emphasise that the protection of health and safety, particularly for the very vulnerable population of infants, must always be the primary consideration.**

Proposed LA maximum (GUL) of 330 mg/100 kJ

There does not appear to be any physiological or technical justification to set a higher upper level of 330mg/100kJ when the highest levels found in human milk are 300mg/100kJ[11] (and there is the suggestion of issues with stability and palatability at higher levels). Based on ensuring the composition of infant formula meets the requirements of infants and does not overburden their systems[12], **the departments support setting the Guideline Upper Level maximum LA level in line with EU 2016/127 of 300mg/100kJ**. FSANZ's market survey indicates no reformulation would be required to meet this level with the current range of 146 – 267mg/100kJ, noting the maximum is a Guideline Upper Level (GUL).

Alpha-linolenic acid (ALA)

The departments support the proposed minimum ALA level of 12mg/100kJ, which is aligned with Codex and EU regulations and considered to be adequate for the majority of infants[13]. **The departments support retaining the current ratio of LA:ALA of 5:1 to 15:1**. We note although a

[11] EFSA (EFSA Panel on Dietetic Products Nutrition and Allergies), Scientific opinion on the essential composition of infant and follow-on formulae. EFSA Journal, 2014.12(7): p. 3760-3866

[12] The International Expert Group position statement on the composition of infant formula states: 'infant formulae should only contain components in such amounts that serve a nutritional purpose or provide another benefit. The inclusion of unnecessary components, or unnecessary amounts of components, may put a burden on metabolic and other physiologic functions of the infant. Those components taken in the diet, which are not utilized or stored by the body, have to be excreted, often as solutes in the urine. Since water available to form urine is limited and the infant's ability to concentrate urine is not fully developed during the first months of life, the need to excrete any additional solutes will reduce the margin of safety, especially under conditions of stress, such as fever, diarrhea or during weight loss'. Koletzko, B., et al., Global standard for the composition of infant formula: recommendations of an ESPGHAN coordinated international expert group. Journal of Pediatric Gastroenterology and Nutrition, 2005. 41(5): p. 584-599.

[13] EFSA (EFSA Panel on Dietetic Products Nutrition and Allergies), Scientific opinion on the essential composition of infant and follow-on formulae. EFSA Journal, 2014.12(7): p. 3760-3866

maximum ALA is not proposed, the restrictions on the ratio of LA:ALA will in effect pose a limit on ALA.

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

Summary position: The departments do not support FSANZ's proposed approach to retain the current voluntary permission for DHA.

Assessment is required to determine whether DHA is a partially essential nutrient and therefore should be mandated in all infant formula. If DHA is not required, the permission for DHA should be removed.

If mandated, the departments support FSANZ's proposed provision that the content of DHA should not exceed the AA amount but consider the optimal minimum amount in line with recent literature.

Docosahexaenoic acid (DHA) is currently permitted under the Code as an optional ingredient up to a maximum of 1% of long chain omega 3 series fatty acids (no minimum requirement). EU 2016/127 specifies the mandatory addition of DHA in the range of 4.8 – 12mg/100kJ (approx. 0.36 – 1.23%FA) The departments note that FSANZ proposes to retain the current voluntary permission for DHA but adopt the Guideline Upper Level for DHA of 0.5% total fatty acids. FSANZ indicates it has not conducted further scientific assessment on whether DHA, which has been an optional ingredient for 20 years, is important for infant growth and development and therefore should be mandated across all infant formula. **The departments do not support FSANZ's proposed approach to retain the current voluntary permission for DHA**.

In our 2016 comments, the departments supported specifying a mandatory minimum level for DHA in all infant formula, in line with the EU 2016/127 regulations and rationale that DHA should be present in infant formula based on its structural role in the nervous tissue and the retina and its involvement in normal brain and visual development, the need of the developing brain to accumulate large amounts of DHA in the first two years of life and the consideration that the intake of pre-formed DHA generally results in an erythrocyte DHA status more closely resembling that of a breast-fed infant than is achieved with ALA alone[14]. In its assessment in 2016, we note FSANZ acknowledged that DHA is an essential component of nerve and retinal cells, is involved in normal brain and visual function; and it accumulates in brain cells in the first two years of life. The departments consider that Principle J of the Policy Guideline on infant formula, which requires there to be a substantiated beneficial role in the normal growth and development of infants, has been met.

FSANZ's decision to maintain a voluntary permission is based on its conclusion in 2016 that 'the efficacy of DHA supplementation on infant growth and development has not been fully established'. The departments are aware there is a range of conflicting literature on determining specific functional outcomes from supplementing infants with DHA, which it has been noted are complicated by the wide range of DHA levels evaluated as well as the range of functional outcomes considered,

[14] EFSA (EFSA Panel on Dietetic Products Nutrition and Allergies), Scientific opinion on the essential composition of infant and follow-on formulae. EFSA Journal, 2014.12(7): p. 3760-3866

including visual and mental development as well as other outcomes[15],[16]. However, given DHA is already considered to be an essential component for infant development, **the question is whether it is a partially essential nutrient**; that is, whether infants can synthesise enough to meet requirements or whether infants partially rely on the amounts provided in breastmilk or formula to meet their requirements (similar to niacin and inositol). The departments note a number of papers suggest that although infants are able to synthesize DHA from essential fatty acids the conversion rate may not be sufficient to meet requirements, and that brain DHA content mainly relies on dietary supply, so it is important for infants to obtain an adequate amount of DHA from dietary sources (breastmilk or formula)[17,18,19,20]. **The departments consider that, if there is evidence that infants are not always able to synthesize enough DHA, then it should be made available in all formula in the levels present in breastmilk. An essential nutrient that is permitted to remain optional and available only in more expensive premium products results in inequality of access. In the First Call for Submissions, further detailed assessment by FSANZ is required to determine whether DHA is a partially essential nutrient and therefore should be mandated in all infant formula.** Given P1028 has continued for a protracted period and will likely require some manufacturers to reformulate formula products, the departments consider it is not appropriate to defer further consideration of DHA to a later date (separate to P1028), as this would incur further reformulation and labelling costs for industry.

The departments note the concerns raised in a recent position paper published by the European Academy of Pediatrics and the Child Health Foundation about the EU regulatory decision to require DHA without a concomitant requirement for arachidonic acid (AA), but also note that this position paper recommended infant formula should provide *both* DHA and AA and that the DHA minimum should be at least 0.3% of FA (equal to the mean content in breastmilk), but preferably 0.5% of FA (equal to mean + 1 SD content in breastmilk) to cover higher needs of some groups[21]. **The departments note FSANZ has proposed that the content of DHA does not exceed the AA amount and support this proposal but that the GUL should be 0.5% total fatty acids,** which is not consistent with the expert position. If mandated, the departments recommend aligning levels with the recent, published, expert positions rather than with EU 2016/127.

If the evidence does not support the need for an external source of DHA in infants, then the voluntary permission for DHA should be revoked. The primary aim of permitting optional ingredients is to encourage industry innovation to improve infant formula to reduce the adverse health outcomes experienced by formula fed infants, while allowing industry to recover research

[15] Uauy R, Dangour AD. Fat and fatty acid requirements and recommendations for infants of 0-2 years and children of 2-18 years. Ann Nutr Metab. 2009;55(1-3):76-96. doi: 10.1159/000228997. Epub 2009 Sep 15. PMID: 19752537.

[16] Lauritzen L, Brambilla P, Mazzocchi A, Harsløf LB, Ciappolino V, Agostoni C. DHA Effects in Brain Development and Function. Nutrients. 2016 Jan 4;8(1):6. doi: 10.3390/nu8010006. PMID: 26742060; PMCID: PMC4728620.

[17] nnis SM. Impact of maternal diet on human milk composition and neurological development of infants. Am J Clin Nutr. 2014 Mar;99(3):734S-41S. doi:

[18] Gao C, Liu G, Whitfield KC, et al. Comparison of Human Milk Fatty Acid Composition of Women From Cambodia and Australia. Journal of Human Lactation. 2018;34(3):585-591.

[19] Koletzko B et al (2020) Should formula for infants provide arachidonic acid along with DHA? A position paper of the European Academy of Paediatrics and the Child Health Foundation. Am. J Clin. Nutr. 2020, 111, 10–16.

[20] Tounian P, Bellaïche M, Legrand P. ARA or no ARA in infant formulae, that is the question. Arch Pediatr. 2021 Jan;28(1):69-74. doi: 10.1016/j.arcped.2020.10.001. Epub 2020 Oct 22. PMID: 33268182.

[21] Koletzko B et al (2020) Should formula for infants provide arachidonic acid along with DHA? A position paper of the European Academy of Paediatrics and the Child Health Foundation. Am. J Clin. Nutr. 2020, 111, 10–16.

and development costs. If, after 20 years, an external source (from breastmilk substitutes) of the optional ingredient is found not to be required for infants, it should not remain in infant formula. Manufacturers describe formula with optional ingredients as 'premium' or 'gold' formulas, and charge a significantly higher price than standard formula, implying that there is a benefit in using this formula over standard formula. **A regulatory system that permits ingredients to remain optional for decades regardless of need or benefit to infants promotes industry innovation for product differentiation and market advantage rather than infant benefit.** If FSANZ determines that DHA is not required in infant formula, retaining the permission and its use in premium formulas could mislead carers into believing there is a benefit.

5.5 Fat source

Summary position: The departments support Option 1, with the addition of restrictions around industrial trans fatty acids.

The departments note that international regulations around sources of fat differ: the EU prohibits the use of sesame seed oil and cotton seed oil, Codex prohibits the use of commercially hydrogenated fats and oils, while the Code does not prohibit any sources of fat (but does place some restrictions around types of fat e.g. medium chain triglycerides). FSANZ notes when certain fats or fatty acids were considered harmful, restrictions were put in place in the Code to protect infants from adverse health consequences. A similar approach is taken in Codex STAN 72-1981. FSANZ proposes two options:

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

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

T**he departments support Option 1 at this stage (unless further evidence becomes available to warrant restricting specific sources of fat), with the exception of prohibiting commercially hydrogenated oils that may contain industrial TFA, in line with Codex** (see below).

5.6 Restriction on certain fats

5.6.1 Medium chain triglycerides (MCTs)

Summary position: The departments support FSANZ's proposed approach on MCTs

The departments support retaining the current restrictions on MCTs, where these can be present only as a natural constituent of a milk-based formula ingredient; or as a component of a processing aid in the preparation of a permitted fat-soluble vitamin. The departments support the rationale that inclusion of MCTs in infant formula does not provide any benefit to infant health, that MCTs are not normally present in significant amounts in breast milk and that they may present safety concerns such as potential risk of deficiency of necessary unsaturated fatty acids and some fat-soluble vitamins. The departments note they are permitted in certain infant formula products for special dietary use where they are used to manage severe fat malabsorption. The departments note that neither Codex STAN 72-1981 or EU 2016/127 specify MCT.

5.6.2 Trans fatty acids (TFA)

Summary position: The departments do not have a position on whether trans fat permissions should be 3 or 4% at this stage and request FSANZ provides further information on the percentage of naturally occurring dairy trans fats present in formula if commercially hydrogenated oils are not permitted.

The departments also support aligning with Codex and prohibiting commercially hydrogenated oils that may contain industrial TFA.

The departments do not support FSANZ's proposed approach at this stage. The departments note no further nutrition risk assessment was considered on this issue and that Codex, the EU and China set a maximum of 3% for trans fatty acids (TFA), with Codex further specifying that commercially hydrogenated oils that may contain industrial TFA are not permitted in infant formula.

We understand that FSANZ proposes to retain the current limit for trans fatty acids (TFA) at 4% of total fatty acids because the definition for TFAs in Codex excludes conjugated linoleic acid (naturally found in dairy fat) while the Code includes it. FSANZ indicates a lower percentage limit may therefore impact on the amount of dairy fat that can be present in infant formula and changing the Code definition for TFA is out of scope of this Proposal. Given the increased understanding of the deleterious effects of industrial trans fats over the past 20 years, **the departments support a prohibition on commercially hydrogenated oils that may contain industrial TFA, in line with Codex and request FSANZ provides more information on the remaining percentage of naturally occurring dairy trans fats likely in formula to determine whether a 3% of total fatty acids limit is still feasible.**

5.6.3 Phospholipids

Summary position: Lecithin as a food additive: The departments support FSANZ's proposed approach to set a limit 1g/L, in line with the EU.

The departments consider than in order to support retaining a permission for phospholipids as a nutritive substance at a limit of 2g/L, FSANZ should provide further assessment to determine a scientific rationale for their addition as a nutritive substance and for the amounts permitted.

The departments note that phospholipids are added as a source of long chain-PUFA (i.e. as a nutritive substance) and also as a component of lecithin which is a processing aid or food additive emulsifier. In 2016 FSANZ considered that the amount of phospholipids in infant formula should not exceed that which normally occurs in breast or cow's milk (approximately 0.25g/L), due to their potential bioactivity, a lack of safety data, and insufficient evidence of their benefit. This would mean setting a level below that set by Codex STAN 72-1981 (2g/L). FSANZ now proposes to set the maximum permitted amount of phospholipids as 2 g/L (72 mg/100 kJ) and the maximum lecithin amount to 1 g/L, in line with Codex and the EU.

In terms of permissions for the use of lecithin as a food additive, the departments support FSANZ's proposed approach to set a limit 1g/L, in line with EFSA's 2020 re-evaluation of its safety[22].

FSANZ has not provided a rationale for the permission for phospholipids to be added as a nutritive substance, or at a level which is eight times that found in breastmilk. The departments note that EFSA's scientific assessment concluded that there is no need to add LCPUFAs as Phospholipids: 'Taking into account the lack of convincing evidence for a beneficial effect of LCPUFAs supplied as PLs instead of TAG in IF or FOF, the Panel considers that there is no necessity to use phospholipids as a source of LCPUFAs instead of TAG in IF and FOF'. '

At this stage, the departments cannot support the proposed approach to retain a permission for phospholipids as a nutritive substance and set a limit of 2g/L. In order to be consistent with the

[22] EFSA (2020) Scientific Opinion on the re-evaluation of lecithins (E 322) as a food additive in foods for infants below 16 weeks of age and follow-up of its re-evaluation as food additive for uses in foods for all population groups. The EFSA Journal 2020;18(11):6266.

policy guidelines, **FSANZ should provide further scientific assessment to justify adding phospholipids** as a nutritive substance together with justification for the levels permitted (relative to the amounts found in breastmilk).

5.6.4 Other fatty acids: myristic, lauric and erucic acids

The departments support FSANZ's rationale and proposed approach to retaining current restrictions in relation to erucic and not applying a restriction to myristic and lauric acids. We note that the Code, Codex Stan 72-1981 and EU 2016/127 permit erucic acid at a maximum of 1% of total FA. Myristic and lauric acid do not have restrictions in Standard 2.9.1 or EU 2016/127. However, Codex STAN 72-1981 permits both fatty acids at a maximum of 20% of total fatty acid content.

We note the EFSA's 2014 Scientific Opinion paper (which remains the most recent comprehensive review of infant formula composition) considered that there was insufficient evidence to establish a permitted range for specific types of saturated fatty acids, including myristic and lauric acid. On this basis and to support harmonisation with international regulations where possible, the departments support not imposing restrictions on the levels of myristic and lauric acid at this stage.

Section 6 Carbohydrate

6.1 Definitions and calculations relevant to carbohydrate identity

The departments support FSANZ's proposed view that no changes to definitions and calculations are needed. These are now set out in Standard 1.1.2 to apply across the Code.

6.2 Dietary fibre

The departments question the relevance of the dietary fibre definition to infants and infant formula but recognise the existing definitions in the Code are linked to calculation of energy content. We note that the definition for fibre does not include some oligosaccharides permitted in infant formula and that the Code prescribes methods for analysis for dietary fibre. **At this stage we support FSANZ's proposed approach to not specify prescribed methods of analysis for oligosaccharides (noting that these can be analysed for individually)** but note with the growing industry interest in prebiotics, there may need to be further consideration of this issue in the future.

6.3 Carbohydrate source

Summary position: The departments support Option 3 for sugars

The departments support the proposed approach to place restrictions on the sugars permitted in infant formula, in line with the scientific opinions by EFSA (2014) and stated by FSANZ in its original consideration of infant formula, P93.
FSANZ proposes three options regarding provisions for the source of carbohydrate:
Option 1: Retain current Standard 2.9.1 (no restrictions on carbohydrate source)

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

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

The departments support Option 3 - Adopt guidelines from EU 2016/127 and set a list of permitted carbohydrates, for the reason that this includes glucose, in addition to sucrose and fructose, while Codex does not. Both EFSA and the European Society for Paediatric Gastroenterology Hepatology and Nutrition's Medical Position Statement on infant formula composition indicated that sucrose, glucose and fructose should not be added to infant formula as sucrose and fructose do not have any advantage over lactose and pose a serious risk to infants with hereditary fructose intolerance and saccharase deficiency. Glucose is considered unsuitable as it may form Maillard products and

increases the osmolality of infant formula[23,24]. These should only be added where necessary, such as to specialised formula based on protein hydrolysates.

6.4 Permitted range for total carbohydrate content

Summary position: The departments support FSANZ's proposed approach to not specify a carbohydrate range.

The departments note that while both Codex STAN 72-1981 and EU 2016/127 set a carbohydrate range of 2.2–3.3 g/100 kJ, the Code does not specify a minimum and maximum as it is indirectly controlled by the regulations on protein, fat and energy content. FSANZ indicates it has calculated carbohydrate amounts based on Standard 2.9.1 provisions for energy, fat, and protein content and this demonstrated carbohydrate minimum and maximum levels are effectively aligned with Codex and the EU. For this reason, FSANZ proposes retaining the current approach to not set carbohydrate limits. **The departments support this approach.**

Section 7 Micronutrients

7.1 Guideline and maximum amounts

The departments note no further nutrition risk assessment was considered on this issue. **We support the nature of the maximum levels for the individual nutrients proposed by FSANZ (a guideline upper level versus a set maximum) with the exception of zinc,** which should be retained as a set maximum (discussed below under zinc). Individual nutrient permission ranges are also discussed separately below.

7.2 Vitamin equivalents and conversion factors

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

Summary position: The departments support expressing vitamin A requirements as µg RE/100 kJ and excluding β-carotene from the vitamin A calculation but do not support the permission to add β-carotene as a form of vitamin A.

The departments note no further nutrition risk assessment was considered on this issue. **The departments support FSANZ's approach to**:

- **express vitamin A requirements as µg RE/100 kJ** as this is consistent with international use and reduces confusion, and
- **exclude β-carotene from the vitamin A calculation** due to the lack of evidence on the on the bioconversion of carotenoids in infants. This is consistent with both Codex and the EU.

The departments do not support FSANZ's proposal to retain the permission for β-carotene as a permitted form of vitamin A in section S29—7. It is contradictory to permit β-carotene addition as a nutritive substance, as a permitted form of vitamin A, while simultaneously excluding it from total vitamin A calculation due to a lack of evidence about its bioconversion to vitamin A in infants. FSANZ's rationale is that the permission should remain as there are no safety issues, however there is no clear purpose for its addition to infant formula. This is contrary to the Policy Guidelines in that substances added to infant formula should have a specific role, either technological or health based.

[23] Koletzko, B., et al., Global standard for the composition of infant formula: recommendations of an ESPGHAN coordinated international expert group. Journal of Pediatric Gastroenterology and Nutrition, 2005. 41(5): p. 584-599.

[24] EFSA (EFSA Panel on Dietetic Products Nutrition and Allergies), Scientific opinion on the essential composition of infant and follow-on formulae. EFSA Journal, 2014. 12(7): p. 3760-3866.

It also represents an unnecessary substance and at odds with the principle of avoiding placing a burden on infants' metabolism[25].

Folic acid and folate equivalents

Summary position: The departments do not support FSANZ's proposed approach. We support use of Dietary Folate Equivalents, including all sources of folate and a permitted range of 3.6 – 11.4 µg/100 kJ, in line with the EU.

The departments do not support FSANZ's proposed approach to regulate folate only as µg folic acid/100 kJ on the basis that it is not consistent with consideration of infant's nutritional requirements nor current accepted understanding and use of Dietary Folate Equivalents in Australia. The departments note no further nutrition risk assessment was considered on this issue. Infants have no requirement for folic acid *per se*. Moreover, excluding any naturally occurring folate from calculations of total folate and the representation of folic acid as being equivalent to folate is misleading. **The departments instead support the use of Dietary Folate Equivalents (DFEs) and including all forms of folate present**. The 2006 Nutrient Reference Values for Australia and New Zealand recognise the difference in bioavailability between folic acid and folate adopts the use of DFEs. The use of DFEs has also been adopted by health professionals. The EU has changed its regulations, using DFEs, and there have been recent discussions about the US Food and Nutrition Board's 2016 decision to adopt DFEs into food and supplements[26]. FSANZ indicates excluding folate from ingredients is justified on the basis that a 2018 study, looking at testing methods, found that in 10 infant formula samples, folic acid was the major contributor of folates with only small amounts contributed by folate from the ingredients[27]. This is in contrast to the 2010 study that looked at 21,388 batches of formula and found up to 40% of folate is provided from folate containing ingredients[28]. Given the lack of consistency in results, lack of evidence that infant formula manufacturers use consistent processing methods that remove folate, together with the reasons listed above, all sources of folate should be included and represented as Dietary Folate Equivalents. Changing the units to take into account the relative activities of the natural and synthetic forms of folate is also consistent with the approach FSANZ has taken for vitamin E.

Permitted levels

FSANZ does not appear to indicate what the proposed compositional requirements will be. The Code currently requires 2 – 8 µg folate /100 kJ (not specifying whether DFEs) which is equivalent to 44-174 µg folate/day (based on FSANZ's standard calculation of 2725kJ/L and 0.8L intake per day), the minimum being below the NHMRC Adequate Intake of 65 µg folate/day. In comparison Codex permissions are 2.5-12 µg/100 kJ folic acid and EU: 3.6 – 11.4 µg DFE/100 kJ. **The departments**

[25] Koletzko, B., et al., Global standard for the composition of infant formula: recommendations of an ESPGHAN coordinated international expert group. Journal of Pediatric Gastroenterology and Nutrition, 2005. 41(5): p. 584-599.

[26] Leila G Saldanha, Johanna T Dwyer, Carol J Haggans, James L Mills, Nancy Potischman, Perspective: Time to Resolve Confusion on Folate Amounts, Units, and Forms in Prenatal Supplements, Advances in Nutrition, Volume 11, Issue 4, July 2020, Pages 753–759, https://doi.org/10.1093/advances/nmaa017

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

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

support a range of 3.6 – 11.4 µg DFE/100 kJ which aligns with the EU. This better reflects infant requirements (equivalent to 3 µg DFE/100 kJ) without providing excessive amounts.

Vitamin E and tocopherol equivalents

Summary position: The departments support FSANZ's proposed approach.

The departments support FSANZ's proposed approach to change the units used for vitamin E from mg alpha tocopherol to mg alpha-Tocopherol Equivalents to take into account the relative activities of natural and synthetic forms of alpha-tocopherol. **The departments also support FSANZ's approach to retaining the requirements in Standard 2.9.1 for vitamin E relative to polyunsaturated fatty acid content** rather than adopting the Codex STAN-72 factors of equivalence, given that this has minimal effect on the levels prescribed.

Permitted range of vitamin E

Summary position: The departments support raising the minimum level to meet infant requirements

The departments note that the permitted range is very similar across regulations, being 0.11-1.1 mg/100kJ (as a-TE) in the Code, 0.12-1.2 mg/100kJ in Codex and 0.14-1.2 mg/100kJ in EU 2016/127. The EU minimum level was based on a requirement of 3mg/day from breastmilk content of 3.5/L (noting levels have been recorded down to 2.3mg/L). The NHMRC AI of 4mg/day was based on a reported average intake of a much higher 4.9mg/L. This level would be closer to 0.18mg/100kJ, indicating the current minimum level of 0.11mg/100kJ would be insufficient. FSANZ has not indicated what it proposes the range should be but current minimum levels do not appear to be sufficient for infant requirements. The departments note the market product range reported by FSANZ in 2016 was 0.26-0.57 mg/100kJ indicating formula was meeting infant levels. **The departments support raising the minimum level to meet infant requirements,** whether that be based on the more recent EFSA assessment of 3mg/day or the NHMRC of 4mg/day, **depending on what is considered more current by a FSANZ assessment**. **This would mean the minimum should be at least 0.13 mg/100kJ (to meet 3 mg/day).**

Niacin equivalents

The departments support FSANZ's proposed approach to retain the current provisions in Schedule 29 where niacin requirements are listed as preformed niacin, noting this includes sufficient niacin to meet infant requirements. This does not include the niacin formed by the body from tryptophan. This is consistent with the approach in Codex STAN 72-1981 and the EU 2016/127.

7.3 Permitted ranges for micronutrients

General comments

The departments support the principle highlighted by FSANZ from the EFSA scientific assessment of infant formula composition that: "From a nutritional point of view, the minimum contents of nutrients in infant and follow-on formula proposed by the Panel cover the nutritional needs of virtually all healthy infants born at term and there is no need to exceed these amounts in formulae, as nutrients which are not used or stored have to be excreted and this may put a burden on the infant's metabolism. Therefore the panel, emphasises that maximum amounts should be interpreted not as target values but rather as upper limits which should not be exceeded"[29]. This is consistent

[29] EFSA (EFSA Panel on Dietetic Products Nutrition and Allergies), Scientific opinion on the essential composition of infant and follow-on formulae. EFSA Journal, 2014. 12(7): p. 3760-3866

with the ESPHGAN International Expert Group position paper highlighting it is important to not provide unnecessary amounts of substances[30].

Permitted range of micronutrients aligned with Codex

Vitamin A

Summary position: The departments support the minimum level for Vitamin A but not the maximum level, which should be lowered to 27.2 µg RE/ 100kJ, in line with the EU.

The departments do not support FSANZ's proposal to retain the current permitted range for Vitamin A of 14–43 µg/100 kJ in order to align with Codex STAN 72-1981 . The departments instead support a maximum limit of 27.2 µg RE/ 100kJ, which aligns with EU 2016/127, on the basis that this best meets the nutritional requirements of infants and protects infant health and safety, based on the science available.

Minimum levels

The minimum level proposed was based on the vitamin A intake deemed adequate from a mean content of breastmilk of 450 µg RE/L. EFSA reported breastmilk ranges of vitamin A as usually being 450-600 µg RE/L (16.5-22 µg RE/ 100kJ), with two recent studies showing much lower levels of 80 and 85 µg RE/ L (2.9 and 3.1 µg RE/ 100kJ). These levels were similarly reported in EFSA's scientific assessment of requirements[31]. The Australia New Zealand NHMRC Nutrient Reference Values quote a lower AI of 250 µg/day based on an average concentration of 310 µg/L from a study which indicates a Vitamin A range of 291-454 µg RE/ L [32].

A recent study of replete Indonesian infants (based on EU Adequate Intake) found breastmilk median vitamin A content was 320-614 µg RE/L (median 598 µg RE/L or 22 µg /100kJ), which equates to intakes of 279-664 µg RE/ day[33]. Another recent study assessing vitamin A requirements cited breastmilk levels of 165-773 µg RE/ L and concluded that a minimum of 147-221 µg RE/ L was needed to reach an adequate liver concentration by age 2 mo and maintain this concentration through age 6 mo (and this was near the lower range of Vitamin A concentrations in breast milk considered sufficient)[34]. Given the current minimum level of 14 µg/100 kJ would provide infants with 381 µg RE/ L (305 µg RE/ day), the departments consider that this would meet infants' requirements, as would the minimum level of 16.7 µg/100 kJ. **The departments would be supportive of either level.**

Maximum levels

[30] Koletzko, B., et al., Global standard for the composition of infant formula: recommendations of an ESPGHAN coordinated international expert group. Journal of Pediatric Gastroenterology and Nutrition, 2005. 41(5): p. 584-599.

[31] EFSA NDA Panel (EFSA Panel on Dietetic Products, Nutrition and Allergies), 2013. Scientific Opinion on nutrient requirements and dietary intakes of infants and young children in the European Union. EFSA Journal 2013;11(10):3408, 103 pp. doi:10.2903/j.efsa.2013.3408

[32] Canfield, L., Clandinin, M., Davies, D. et al. Multinational study of major breast milk carotenoids of healthy mothers. Eur J Nutr 42, 133–141 (2003). https://doi.org/10.1007/s00394-003-0403-9

[33] Daniels L, Gibson RS, Diana A, et al. Micronutrient intakes of lactating mothers and their association with breast milk concentrations and micronutrient adequacy of exclusively breastfed Indonesian infants. Am J Clin Nutr. 2019;110(2):391-400. doi:10.1093/ajcn/nqz047

[34] Ford JL, Lopez-Teros V. Prediction of Vitamin A Stores in Young Children Provides Insights into the Adequacy of Current Dietary Reference Intakes. Curr Dev Nutr. 2020;4(8):nzaa119. Published 2020 Jul 13. doi:10.1093/cdn/nzaa119

In terms of maximum levels, reviews of vitamin A note that the safety margin between the Tolerable Upper Intake Level (UL) and the 95th percentile of intake as well as the dietary reference intake is very small.[35,36]. The NHMRC UL for infants of 600 µg RE/day is based on reports of hypervitaminosis A in infants (rather than being extrapolated from the UL for older children or adults, as for some nutrients). The maximum level provided by the EU 2016/127 provides an amount just under this UL of 593 µg/day.

FSANZ in its assessments indicates that higher maximum levels are justified as breastmilk can contain up to 38.3 µg RE/100 kJ (1044 µg RE/ L), and states two studies cited by EFSA record levels as high as 50–54 µg RE/100 kJ (1363-1472 µg RE/ L) which are higher than the maximum amount set under Codex STAN 72-1981 and section S29—9. The departments have reviewed the references provided by FSANZ and cannot find references to breastmilk levels above 773 µg RE/ L (or 28 µg/100kJ). **The EU 2016/126 maximum of 27.2 µg/100kJ appears more in line with maximum breastmilk concentrations**.

FSANZ also suggests there is an absence of data indicating that the current maximum of 43 µg/100 kJ is associated with adverse health effects, however EFSA's scientific assessment stated, in relation to maximum nutrient levels that exceed ULs, that '*while there may be no reports of adverse effects associated with the use of formula at these levels, there are no studies available which were designed to investigate the short- or long-term health consequences of consumption of formulae containing the currently permitted maximum amounts of micronutrients*'. This is supported by FSANZ's 2016 market survey which indicated the higher range of vitamin A present in products was below this at 33 µg RE/100kJ.

The departments also note from its nutrition assessment that FSANZ concluded the lower EU maximum of 27.2 µg/100kJ resulted in an estimated slight exceedance of the UL for infants aged 6-12 months, including food intake, but was within the range considered to pose low risk to infant health (≤15% greater than the UL). This would not be the case if the current maximum was retained. **For the reasons above, the departments support a maximum limit of 27.2 µg RE/ 100kJ.**

Vitamin D

Summary position: The departments support FSANZ's proposed approach for the permitted range for vitamin D.

The departments note that the EU has reduced the maximum level for vitamin D since 2016 over concerns about exceeding the Upper Level. We note the advice in Australia through the Victorian Royal Children's Hospital clinical guidelines and the public facing Raising Children Network is that infant formula currently provides sufficient vitamin D and that supplementation is only required if infants have a risk factor for vitamin D deficiency and are breastfed. In line with our position in 2016, **the departments support FSANZ's proposed approach to retain the current vitamin D permissions in the Code 0.25 – 0.63 µg/100 kJ, which are appropriate for Australian conditions.**

[35] German Federal Institute for Risk Assessment 2021. Updated recommended maximum levels for the addition of vitamins and minerals to food supplements and conventional foods

[36] SCF (Scientific Committee on Food), 2002. Opinion on the Tolerable Upper Intake Level of preformed vitamin A (retinol and retinyl esters).

7.3 Permitted range is not aligned with Codex: vitamin B12, Folate, Pantothenic acid, Niacin, Vitamin E, Calcium, Manganese, Magnesium, Potassium, Chloride, Sodium

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

Micronutrient (units)	Standard 2.9.1 (Schedule 29)		Codex STAN 72-1981		EU	Content in products on the market^
	Min	Max	Min	Max		
Vitamins						
Vitamin B12 µg/100 kJ	0.025	0.17 (GUL)	0.025	0.36 (GUL)	0.02-0.12	0.04–0.16
Folate (µg/100 kJ	2	8.0	2.5	12 (GUL)	3.6-11.4 (DFE)	NR
Pantothenic Acid (µg/100 kJ)	70	360 (GUL)	96	478 (GUL)	100-480	84.04–227.3
Niacin (preformed) (µg/100 kJ)	130	480 (GUL)	70	360 (GUL)	100-360 (GUL)	130.1–272.7
Vitamin E (mg/100 kJ)	0.11	1.1	0.12 (α-TE)	1.2 (GUL) (α-TE)	0.14-1.2 (as a-TE)	0.26–0.58
Minerals						
Calcium (mg/100 kJ)	12	33 (GUL)	12	35 (GUL)	12 – 33.5	15.38–23.57
Manganese (µg/100 kJ)	0.24	24	0.25	24 (GUL)	0.24 - 24	1.53–18.71
Magnesium (mg/100 kJ)	1.2	4.0	1.2	3.6 (GUL)	1.2 – 3.6	1.65–2.52
Electrolytes						
Potassium (mg/100 kJ)	20	50	14	43	19.1 – 38.2	20.79–31.65
Chloride (mg/100 kJ)	12	35	12	38	14.3 – 38.2	14.39–25
Sodium (mg/100 kJ)	5	15	5	14	6 – 14.3	5.71–11.47

For the above listed vitamins and minerals, **the departments support permitted ranges that align with EU2016/127** (added to the table above) rather than Codex STAN 72-1081, noting that some of these permissions are very similar for some nutrients. This is because EU 2016/127 is based on science that has been reviewed more recently than Codex (2014 versus 2005) and **better reflects infant nutritional requirements and levels in breastmilk.** From FSANZ's market survey, all products in the market currently meet EU ranges, with exception of pantothenic acid – some products contain levels below both Codex and EU so would need to reformulate if adopted the proposed Codex level. The departments also consider from a trade perspective that EU products have a reputation of being high quality and that aligning with these permissions where appropriate will better protect trade interests than aligning with an older, out of date Codex standard.

Vitamin B6

Summary position: The departments do not support FSANZ's proposed approach for Vitamin B6. We support a minimum level of 4.8 µg/100 kJ in line with EU 2016/127 and a maximum level that is based on the maximum levels in breastmilk.

The departments note that the current compositional requirements for Vitamin B6 vary across jurisdictions: with 9-36 µg/100 kJ in the Code, 8.5 – 45 µg/100 kJ in Codex STAN 72-1981 and 4.8 – 41.8 µg/100 kJ in EU 2016/127 and recommended by EFSA (2014). Only the EFSA levels have been recently reviewed and were directly linked to infant requirements based on breastmilk. Reported breastmilk concentrations are 2.6-11.4 µg/100 kJ (equal to 57 - 248 µg/day, based on 800mL of breastmilk) with an average concentration cited as 4.8 µg/100kJ by EFSA (equal to 104 µg /day)[37,38].

FSANZ's nutrition assessment found that the minimum EU level met the requirements of infants aged 0-6 months, however it may not meet the vitamin B6 requirements for infants aged 7-12 months on the basis that it does not meet 50% of the NHMRC Adequate Intake of 300 µg/day (assuming 600mL of formula is consumed and 50% is met via food). In contrast the Codex minimum level provides 62% of requirements of 7-12 months old.

The departments question whether formula is required to meet 50% of vitamin B6 requirements for 7-12 month olds, noting that vitamin B6 is widely available in first foods (meat, vegetables and fruit). We note that in the NHMRC Australian and New Zealand Nutrient Reference Values, many requirements set for infants of 7-12 months **are based on a calculation where breastmilk provides less than 50%.** A rough example meal plan typical of an infant's diet from fresh (not fortified infant foods) indicated more than two thirds of vitamin B6 requirements could easily be met by foods, with the AI met by a combination of food and formula with 4.8 µg/100kJ.

In terms of the maximum limits, the departments note these are very similar in both Codex and the EU (45 versus 41.8 µg/ 100kJ) and are four times the upper levels found in breastmilk. These would result in a daily intake of 911 -981 µg/day. The departments question why such high maximum levels are required, considering the principle identified by FSANZ from EFSA's scientific assessment of infant formula composition: that nutrients which are not used or stored have to be excreted and this may put a burden on the infant's metabolism. FSANZ has indicated current products on the market contain vitamin B6 up to 28.11 µg/ 100kJ, which is well below the proposed maximum level (GUL). The departments note that while an UL has not been set in Australia, the maximum is well below the UL set in the EU of 5000 µg/day.

The departments preferred view is to align with the minimum levels assessed by EFSA and implemented in EU 2016/127 on the basis this best reflects the levels in breastmilk. **The departments request that FSANZ determine a maximum guideline upper level that better reflects the upper levels in breastmilk, or consider retaining the current maximum of 36 µg/100 kJ, with scientific justification.**

Vitamin K

Summary position: The departments support FSANZ's proposed approach for vitamin K.

[37] EFSA NDA Panel (EFSA Panel on Dietetic Products, Nutrition and Allergies), 2013. Scientific Opinion on nutrient requirements and dietary intakes of infants and young children in the European Union. EFSA Journal 2013;11(10):3408, 103 pp. doi:10.2903/j.efsa.2013.3408

[38] EFSA (EFSA Panel on Dietetic Products Nutrition and Allergies), Scientific opinion on the essential composition of infant and follow-on formulae. EFSA Journal, 2014. 12(7): p. 3760-3866.

The departments note the provisions for vitamin K vary across regulations with 1-5 µg/100 kJ in the Code, 1-6.5 µg/100 kJ in Codex and 0.24 – 6 µg/100 kJ in EU 2016/127. **The departments support FSANZ's proposed approach to align the permissions for Vitamin K in the Code with EU 2016/127 levels of 0.24 – 6 µg/100 kJ** listed in Table 7.5 given the reduced minimum better aligns with the NHMRC AI. The departments note that the current market use of Vitamin K in formula ranges from 1.25 – 3.69 µg/100 kJ and therefore will not be affected by a reduction in the minimum level.

Riboflavin

Summary position: The departments support FSANZ's proposed approach for riboflavin

The current permitted range for riboflavin in the Code is 14 – 86mg/100kJ, while Codex sets 19-119mg/100kJ. **The departments support FSANZ's proposed approach to align the Code with the EU 2016/127 permitted range for riboflavin, being 14.3 – 95.6 µg/100 kJ** based on nutritional adequacy for infants, noting that formula currently in the Australian and New Zealand market currently meets this range.

Biotin

Summary position: The departments support FSANZ's proposed approach to align the minimum requirement for biotin with EU 2016/127.

The departments also support aligning the maximum with the EU with a range of 0.24-1.8 µg/100 kJ.

The departments note the current provisions for biotin are 0.36-2.7 µg/100 kJ in the Code, 0.4-2.4 µg/100 kJ in Codex and 0.24 - 1.8 µg/100 kJ in the EU. FSANZ has proposed aligning with the EU minimum but appears to be silent on the maximum. **The departments support aligning the compositional requirements for biotin with EU 2016/127 of 0.24-1.8 µg/100 kJ** to best meet infant requirements and based on the average content of breastmilk. While the EU maximum level was not based on toxicity, the EU approach prioritises ensuring unnecessary burden is not placed on infants' systems. Given formula on the ANZ market is currently within the EU range (0.50 – 1.73 µg/100 kJ), **the departments consider the lower EU maximum would better protect the health and safety of infants** and reformulation would not be required.

Thiamin

Summary position: The departments support FSANZ's proposed approach for the minimum level for thiamin. FSANZ is silent on the maximum; we support retaining the current maximum (GUL).

The compositional requirements for thiamin vary from 10-48 µg /100kJ in the Code, 14-72 µg /100kJ in Codex and 9.6-72 µg /100kJ in the EU. The departments note that FSANZ's proposed approach is to retain the current minimum level for thiamin in Standard 2.9.1 of 10 µg /100kJ (equivalent to EU level) but is silent on the maximum level (GUL). The departments note the maximum levels vary considerably between the Code, Codex and the EU. These upper limits do not seem to have been linked to infant requirements.

The departments note that the levels of thiamin in breastmilk have been reported by EFSA as ranging from 150-330 µg/L (equivalent to 5.5-12 µg /100kJ). A 2012 review of B vitamin contents of breastmilk reports levels in US and Canadian women of 170 – 250 µg/L, up to 350 µg/L in Russian women, with other populations as high as 290 µg/L with maternal supplementation[39]. The current

[39] Allen LH. B vitamins in breast milk: relative importance of maternal status and intake, and effects on infant status and function. *Adv Nutr*. 2012;3(3):362-369. Published 2012 May 1. doi:10.3945/an.111.001172

Codex and EU maximums provide 1962 µg/L (approximately 6 times higher than upper levels in breastmilk). No rationale has been provided for the high levels.

The departments support retaining the current range of 10- 48 µg /100kJ for thiamin on the basis that this best supports infant requirements and limits the provision of unnecessary amounts of thiamin. We note products on the ANZ market are currently within this range and therefore reformulation would not be required.

Copper

Summary position: The departments do not support aligning the minimum and maximum levels for copper with Codex and instead suggest the minimum needs to be at least 9.2 µg/100 kJ and the maximum should be 24 µg/100 kJ, in line with EU 2016/127

The departments note no further nutrition risk assessment was considered on this issue. The copper provisions range from 14-43 µg/100 kJ in the Code to 8.5-29 µg/100 kJ in Codex and 14.3 – 24 µg/100 kJ in EU 2016/127. FSANZ is proposing reducing copper levels to align with Codex.

Copper minimum

The FSANZ nutritional assessment has indicated that while the minimum level set by Codex STAN 72-1981 (8.5 µg/100 kJ) provides only 186 µg/day for infants and does not meet the daily requirement of 200µg/day, infants' copper needs are met by the additional copper present in Australian potable water (providing a total of 465µg/ day of copper once the formula has been made up). At the last consultation, we raised the issue of ready-to-feed formulas, often used in hospitals, potentially being manufactured to meet the standard's compositional limits and not factoring in the amount to be derived from Australian potable water. In its response FSANZ indicated it does not have information on the types of infant formula (i.e. infant formula or IFPSDU) products being used in hospitals and currently ready-to-feed formula is not available for retail sale in ANZ. FSANZ also noted setting a level that did not meet infant requirements was acceptable because it was within 10% of the AI.

The departments do not support reducing the minimum copper levels to align with Codex and instead consider that the compositional requirements should meet infants' requirements. Ready-to-feed formula are for retail sale overseas and it is important to ensure the standards are 'future proof' in case this market develops in Australia. **The departments suggest the minimum should be at least at 9.2 µg/100 kJ,** based on the minimum required to meet the NHMRC AI. This is particularly the case given FSANZ is also proposing higher zinc levels and removing the Zinc: Copper ratio, which may impact on the amount of copper available to infants (see more below under zinc and Zinc: Copper ratio). Products on the market are already within this range and would not be affected.

Copper maximum

The departments do not support aligning the maximum (GUL) with Codex and instead support aligning it with the EU max of 24 µg /100kJ (GUL) as this best reflects breastmilk levels. Compared to the upper levels found in breastmilk (400 µg /L), 24 µg /100kJ provides 654 µg /L, while the Codex maximum provides 790 µg /L. The EU levels are less likely to create a burden on infants' systems from unnecessary amounts.

7.3 Permitted range where further information was sought

Vitamin C

Summary position: The departments support FSANZ's approach to align the minimum level of vitamin C with Codex, but do not support aligning the maximum with Codex. Instead, we support a range of 2.5mg – 7.2 mg/100kJ (aligning with the EU maximum GUL).

FSANZ is proposing to increase both the minimum and maximum (GUL) for vitamin C to align with Codex. This would change the current permission from 1.7-5.4 mg/100kJ to 2.5 to 17mg/100kJ, noting EU 2016/127 requires 0.96 to 7.2 mg/100kJ.

In 2016, the departments supported aligning with the Codex minimum but retaining the current maximum of 5.4mg/100kJ in the Code. This was on the basis that, even with maximum losses of vitamin C over shelf life (up to 75% in liquid formula, noting losses are less in powder formula), the amount left still meets minimum requirements as assessed by EFSA, being 20mg/day for 0 to 12 months of age[40]. The departments note that the higher maximum in Codex is accompanied by the footnote: "this GUL has been set to account for possible high losses over shelf-life in liquid formulas; for powdered products lower upper limits should be aimed for". While it is important to ensure sufficient amounts of vitamin C in liquid formula, as FSANZ indicated for copper, only powdered formula are currently available for retail sale in Australia therefore providing unnecessarily high amounts (when the lower level would be sufficient) is not ideal. FSANZ has also not considered that the current maximum of 5.4mg/100kJ has not been reportedly associated with vitamin C inadequacy resulting from shelf life losses.

The departments note that the EFSA Adequate Intake is lower than the NHMRC AI (25-30 mg/day for 0-12 months), but also that the figures are derived differently: the EFSA AI was derived as three times the amount known to prevent scurvy while the NHMRC AI was based directly on the amount found in breastmilk. Both the NHMRC and EFSA indicate that levels in breastmilk reflect maternal intake rather than infant requirements and are likely higher than required. We note that no UL was able to be established for infants, but that if the UL from the U.S. Institute of Medicine for 1 to 3 year olds (400mg/day) was extrapolated by reference weight to infants (215 and 276mg/day for 2-6 and 7-12 month olds), the Codex maximum would exceed this (providing 370mg/day)[41].

On the basis of allowing for shelf life losses but not providing unnecessary excess and aligning with international regulations where possible**, the departments support a range of 2.5mg – 7.2 mg/100kJ (aligning with the Codex minimum but the EU maximum GUL)**. This lower maximum will also minimise the risk of any nutrient interactions, for example with iron and copper (see below). We note that the highest reported amount in the product market survey was 6.8 mg/100 kJ, which is within this range, but also note that the GUL maximum is a voluntary guidance level and the exceedances would not cause compliance or trade issues.

[40] If a formula contained the GUL of 5.4mg/100kJ vitamin C and the upper end of typical losses of 50% occurred, this would leave a vitamin C content of 2.7mg/100kJ, which is still above the minimum of 0.96mg/100KJ which EFSA NDA considered to meet the nutritional needs of most infants (by providing a level three times the amount needed to prevent scurvy). If a loss of 75% of vitamin C occurred, the resulting vitamin C content would be 1.35mg/100kJ which remains well above the level that EFSA NDA considered as sufficient for the majority of infants. Given most infant formula available is in powdered form, losses would be expected to be less than this.

[41] Institute of Medicine (IOM) Dietary reference intakes for vitamin C, vitamin E, selenium and carotenoids., Food and Nutrition Board: Institute of Medicine, Editor. 2000, National Academy Press: Washington D.C.,. p. 284-324.

Chromium and Molybdenum

Summary position: The departments support FSANZ's approach for molybdenum and chromium.

The departments note neither Codex nor the Code set minimum amounts for chromium and molybdenum in infant formula. Schedule 29 sets GULs for both chromium and molybdenum at 2.0 µg/100 kJ and 3.0 µg/100 kJ, respectively. Codex STAN 72-1981 does not include a maximum or GUL for these minerals. EU 2016/127 specifies a maximum level for molybdenum at 3.3 µg/100 kJ and does not set levels for chromium. **The departments support FSANZ's proposed approach to remove regulatory provisions for chromium and molybdenum for standard infant formula products**, noting that infant formula does not require the addition of these trace elements because the Adequate Intakes are met through the macronutrient provisions. We note provisions are required for IFPSDU as these are more refined, and this will be addressed in the next consultation paper.

Iodine

Summary position: The departments support FSANZ's approach to align the minimum with the EU level of 3.6µg/ 100kJ but do not support retaining the current maximum; instead we support adopting the EU maximum of 6.9 µg/100kJ.

Iodine Minimum

The departments support the proposed approach to increase the minimum and align with the EU level of 3.6µg/ 100kJ. This amount of iodine provides 86-118µg/day, taking into account the quoted range of iodine in Australian water reported by FSANZ in the 2016 consultation paper (10–50 µg/L or 8-40 µg/day). This amount of iodine better meets the estimated requirements of infants, set as 90µg/day in the Australia and New Zealand NRVs or 70µg/day based on the most recent scientific opinion of EFSA[42]. In comparison, the minimum level set in Codex STAN 72-1981 provides 63-95µg/day (including a water contribution of 8-40µg/day in Australia) whereas the current level in Standard 2.9.1 of 1.2µg/100kJ only provides 34-66µg/day (allowing for water contribution). We note that FSANZ has indicated that South Australian research on the iodine status of lactating mothers and infants addresses the concerns raised during consultation that formula-fed infants cannot obtain an adequate iodine intake under the current provisions in Standard 2.9.1/Schedule 29, despite the minimum amount in formula not meeting the AI for iodine. In confirming the final position on the minimum compositional requirement it is important to note that, while this iodine status might be reasonably attributed to infants across South Australia, we do not believe that it can be assumed that all formula-fed infants in Australia would have a sufficient iodine status, given iodine status (and water content of iodine) varies based on location. Before iodine fortification, South Australia was one of the states in Australia that was considered iodine replete[43]. This would indicate that soil and water levels of iodine are likely to be higher in South Australia than other states with lower iodine status. As 61% of the Australian population resides in states known to be iodine deficient prior to fortification[44] the results by Huynh cannot be assumed to apply to the majority of the Australian formula fed infants.

Iodine Maximum

[42] EFSA (EFSA Panel on Dietetic Products Nutrition and Allergies), Scientific opinion on the essential composition of infant and follow-on formulae. EFSA Journal, 2014. 12(7): p. 3760-3866.
[43] Li M, et al., Are Australian children iodine deficient? Results of the Australian National Iodine Nutrition Study. The Medical Journal Of Australia, 2006. 184: p. 165-169.
[44] ABS, *Australian Demographic Data September 2015*. 2015.

FSANZ proposes retaining the current set maximum of 10µg/100kJ. This level equates to infant intakes of 218µg/day (226-258µg/day including water contribution). This is above the UL of 200µg/day for one to three year olds set by NHMRC (and consistent with the EU UL)[45]. The departments note that EU reduced the maximum limit for iodine on the basis that it resulted in intakes that exceed the UL. The EU maximum of 6.9 µg/100kJ was considered by FSANZ not to pose a risk and results in intakes of 150 µg/day (158-190 µg/day with water). **The departments do not support the proposal to retain the current maximum and instead support adopting the EU maximum of 6.9 µg/100kJ.** The departments note that FSANZ's market survey indicated an iodine range of 2.19 – 8.42 µg/100kJ indicating that reformulation will be required for some manufacturers to meet both the minimum levels proposed by FSANZ and the EU maximum.

Zinc and Zn:Cu ratio

Summary position: The departments do not support FSANZ's proposal to align the zinc maximum with Codex, but instead support aligning with the EU maximum of 0.24mg/100kJ and that this should be a compositional limit rather than a GUL.

The departments also support providing guidance in the standard that zinc and copper should be provided in a ratio as close to 10:1 ratio as possible.

The departments note the minimum levels for zinc are aligned across Standard 2.9.1, Codex STAN 72-1981 and EU 2016/127 (0.12 mg/100kJ), but the maximum levels vary considerably at 0.43, 0.36 and 0.24mg/100 kJ respectively. Standard 2.9.1 also prescribes a maximum ratio of zinc to copper (Zn:Cu) of 15:1, whereas Codex STAN 72-1981 and EU 2016/127 do not specify a ratio. FSANZ proposes to align the maximum level for zinc with Codex STAN 1972-81 which accommodates a higher concentration of zinc for soy-based formula and to remove the maximum ratio of zinc to copper. **The departments do not support aligning the maximum with Codex and instead support aligning with the EU maximum of 0.24mg/100kJ**. **The departments also support setting different levels for cow's milk and soy formula**, consistent with the approach for other nutrients where lower bioavailability in soy products exists. **This ensures sufficient amounts of nutrients are provided through soy formula and also serves to indicate to manufacturers and formula developers the difference in bioavailability that needs to be considered.**

The UL is currently 4mg/day for infants aged 0 to 6 months. The Standard 2.9.1 level results in daily intakes of 9.4mg/day, Codex results in an intake of 7.8mg/day and the EU regulations result in an intake of 5.2 mg/day. The EU value was previously aligned with Codex and reduced recently (EFSA did not discuss the rationale but noted current levels exceed the UL). While we note that the bioavailability of zinc from formula is lower and that FSANZ's review of the study underpinning the 4 mg/day UL had a number of limitations which indicate an overly conservative basis for this level, FSANZ has equally not provided evidence suggesting it is safe to provide double the UL on a regular basis. AS previously mentioned, EFSA noted there are no studies available which were designed to investigate the short- or long-term health consequences of consumption of formulae containing the currently permitted maximum amounts of micronutrients in infant or follow-on formula[46]. For this reason, the **departments also support retaining a set maximum limit for zinc rather than a voluntary GUL maximum**. We also note from the FSANZ's 2016 market label survey that the highest

[45] NHMRC, Nutrient Reference Values for Australia and New Zealand, Commonwealth of Australia, Editor. 2006: Canberra.

[46] EFSA (EFSA Panel on Dietetic Products Nutrition and Allergies), Scientific opinion on the essential composition of infant and follow-on formulae. EFSA Journal, 2014. 12(7): p. 3760-3866.

level being added to formula was 0.25mg/100kJ, which indicates a set maximum should have no impact on current products.

Zinc: copper ratio (Zn:Cu ratio)

In our 2016 response, the departments did not have a position on whether the Zn:CU ratio should be retained but noted that breastmilk has a Zn:Cu ratio of 10:1 and supported the principle that infant formula should be primarily based on the composition of breastmilk, noting the ratio was initially created to manage the potential impact of zinc intakes on copper bioavailability. We requested more information on how the proposed changes for zinc and copper levels impacted on the ratio of Zn:Cu to help determine whether a set ratio was required. FSANZ provided no further assessment on this.

In considering FSANZ's current proposed levels for zinc and copper we note that, at the minimum copper level (which does not meet infant requirements for ready-to-feed formula), the minimum Zn:Cu ratio would be 14:1. This would be higher if levels of zinc above the minimum were added. Presumably this presents a risk for meeting infant copper requirements, particularly in liquid products which may not meet requirements for copper. This supports 'future-proofing' the standard and ensuring copper compositional requirements are sufficient to meet requirements. If the Zn: Cu ratio requirement is removed, **the departments suggest guidance is included in Standard 2.9.1 for industry to provide zinc and copper in a ratio as close to 10:1 ratio as possible.**

Iron

Summary position: The departments do not support FSANZ's proposed approach to retain current iron permissions at 0.2-0.5mg/100kJ. Instead, the departments support a range of 0.14-0.31 mg/100kJ in cow's milk-based formula. The departments support a separate range for soy-based formula.

The departments note that the compositional requirements for iron in the Code are higher than those in both Codex STAN 72-1981 and EU 2016/127 at 0.2 – 0.5 mg/100kJ, 0.1 – N.S mg/100kJ and 0.07 to 0.31 mg/100kJ respectively. FSANZ proposes retaining the current levels in the Code as this is consistent with the current levels in the market and due to the concern that the lower levels set by Codex and EU provide less than 50% of the EAR for 7-12 month old infants and may place them at risk of deficiency.

The departments note relatively recent assessments of infant iron requirements indicate that in the EU, infant formulas have contained 4-8mg/L iron (0.15 to 0.29mg/100kJ) with very low prevalence of iron deficiency at 6 months[47]. In EFSA's scientific assessment, it recommended a minimum of 0.14mg/100kJ for follow-on formula and formula designed to cover 0-12 months, recognising food provides more than 50% of iron requirements for older infants[48].

The departments support a lower minimum iron level of 0.14mg/100kJ for cow's milk-based infant formula for 0-12 months, in line with EFSA's recommendations and a maximum of 0.31mg/100kJ, to avoid excess iron.

Support for these lower levels is based on:

[47] Domellof M, Braegger C, Campoy C, Colomb V, Decsi T, Fewtrell M, Hojsak I, Mihatsch W, Molgaard C, Shamir R, Turck D, van GJ (2014) Iron requirements of infants and toddlers. J Pediatr Gastroenterol Nutr 58(1):119–129

[48] EFSA (EFSA Panel on Dietetic Products Nutrition and Allergies), Scientific opinion on the essential composition of infant and follow-on formulae. EFSA Journal, 2014. 12(7): p. 3760-3866

- There is good evidence that excess iron intake in iron replete infants is associated with poorer long term developmental outcomes, infection risk and status of trace minerals[49,50,51,52]. The proposed maximum level of 0.5mg/100kJ is greater than levels associated with poorer outcomes.
- From FSANZ's market survey, products on the market currently contain up to 0.44mg/100kJ, approaching the levels associated with poorer developmental outcomes in iron replete infants.
- Studies that show while low iron status occurs in some Australian infants and young children, the vast majority of infants are iron replete (76% of 9-24 months olds replete, with 5.4% with iron deficiency in a Sydney population and similar levels in an Adelaide population) and therefore may be disadvantaged by the levels proposed at the upper end of the proposed range[53,54].
- The minimum level set by EU 2016/127 (0.07 mg/100kJ) is consistent with the level of iron found in breastmilk and meets infant requirements[55] once differences in absorption in iron from formula and breastmilk are accounted for. Studies also show that providing formula at the minimum EU level vs the maximum EU level (0.07mg/100kJ versus 0.31mg/100kJ) is not associated with increased risk of iron deficiency at 6 months of age[56]. The estimated iron *absorbed* from infant formula when using the Code's minimum level would be almost double that absorbed from human milk (0.012–0.013 mg/100 kJ) and therefore not in line with the Policy Guideline. Recognising that infant formula is recommended to be continued from 0-12 months by health professionals (rather than requiring a switch to a follow-on formula), the departments support the level that is closest to breastmilk levels (ie. 0.14mg/100kJ rather than 0.2 mg/100kJ).
- Follow-on formula is a breastmilk substitute, not a treatment modality, and should use breastmilk from healthy mothers and breastfed infants as the primary reference (taking into account differences in absorption efficiency), consistent with the Policy Guideline. FSANZ's rationale is that iron levels in follow-on formula should meet 50% of the NHMRC EAR of 7mg/day

[49] Koletzko, B., et al., Global standard for the composition of infant formula: recommendations of an ESPGHAN coordinated international expert group. Journal of Pediatric Gastroenterology and Nutrition, 2005. 41(5): p. 584-599.

[50] Lozoff B, Castillo M, Clark KM, Smith JB. Iron-Fortified vs Low-Iron Infant Formula: Developmental Outcome at 10 Years. Arch Pediatr Adolesc Med. 2012;166(3):208–215. doi:10.1001/archpediatrics.2011.197

[51] Hare DJ, Cardoso BR, Szymlek-Gay EA, Biggs BA. Neurological effects of iron supplementation in infancy: finding the balance between health and harm in iron-replete infants. Lancet Child Adolesc Health. 2018 Feb;2(2):144-156. doi: 10.1016/S2352-4642(17)30159-1. Epub 2017 Dec 6. PMID: 30169236.

[52] Lönnerdal B, Excess iron intake as a factor in growth, infections, and development of infants and young children, The American Journal of Clinical Nutrition, Volume 106, Issue suppl_6, December 2017, Pages 1681S–1687S, https://doi.org/10.3945/ajcn.117.156042

[53] Oti-Boateng P, Seshadri R, Petrick S, Gibson RA, Simmer K. Iron status and dietary iron intake of 6-24-month-old children in Adelaide. J Paediatr Child Health. 1998 Jun;34(3):250-3. doi: 10.1046/j.1440-1754.1998.00205.x. PMID: 9633972.

[54] Karr M, Alperstein G, Causer J, Mira M, Lammi A, Fett MJ. Iron status and anaemia in preschool children in Sydney. Aust N Z J Public Health. 1996 Dec;20(6):618-22. doi: 10.1111/j.1467-842x.1996.tb01076.x. PMID: 9117969.

[55] 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.

[56] Björmsjö M, Hernell O, Lönnerdal B, Berglund SK. Reducing Iron Content in Infant Formula from 8 to 2 mg/L Does Not Increase the Risk of Iron Deficiency at 4 or 6 Months of Age: A Randomized Controlled Trial. Nutrients. 2020 Dec 22;13(1):3. doi: 10.3390/nu13010003. PMID: 33374970; PMCID: PMC7821997.

for 7 to 12month olds, of which 10% would be bioavailable. This is in comparison to breastmilk which provides 1.5% of the EAR, based on the average iron content of 0.013mg/100kJ, intakes of 600mL of breastmilk providing 0.21mg iron /day, of which only 50% is absorbed. This results in formula providing three to eight times the amount of absorbable iron than breastmilk. EFSA also noted literature from the U.S and U.K. indicating that food provides the majority of iron in the second six months and can feasibly make up the difference if formula contains 0.14mg/100kJ[57]. This indicates it is not necessary for formula to meet 50% of iron requirements of this age group.

- Supplementing infant formula well above the nutritional reference of breastmilk and breastfed infants to reduce iron deficiency anaemia in a minority of infant populations risks undermining breastmilk as the ideal and preferred source of nutrition and may not be in the best interests of infant health. Breastmilk has sufficient iron to meet the needs of infants until around 6 months of age, and as part of a progressive diversified diet that includes solid foods rich in iron, until 12 months and beyond.

The departments support higher provisions for iron in soy-based formula, consistent with EU 2016/127 to account for the reduced absorption from phytic acid content. The departments note FSANZ and industry submissions report that it is possible to reduce phytic acid content of soy formula to improve absorption of nutrients, but also that there is no requirement or recognised method to do this in the Code and therefore removal of phytic acid cannot be assured.

Selenium

Summary position: The departments support FSANZ's proposed approach for selenium.

The departments note selenium compositional requirements are currently 0.25-1.19 µg/100 kJ in the Code, 0.24-2.2 µg/100 kJ in Codex and 0.72-2.0 µg/100 kJ in the EU. **The departments support FSANZ's proposed approach to increase the compositional requirements for selenium from 0.25 – 1.19 µg/100 kJ to 0.48 – 2 µg/100 kJ.** The minimum is lower than the level set by the EU (0.72 µg/100 kJ) but consistent with a more recent US FDA 2015 rule and also that for the draft Codex for follow-up formula. The minimum better reflects the selenium content of Australian and New Zealand breastmilk (0.4 – 0.5 µg/100 kJ) and is closer to the NHMRC AI of 12 µg/day (at 10.5 µg/day) noting the uncertainty around this AI level and whether Australian and New Zealand infants are considered to be selenium replete with current levels in breastmilk. We note the maximum results in intakes are below the NHMRC UL and reflect levels found in breastmilk.

7.4 Other ratios, equivalents and nutrient interactions

Calcium/ phosphorous

Summary position: The departments support FSANZ's proposed approach to align the calcium to phosphorous ratio with Codex and the EU. The departments also support separate provisions for soy-based formula.

The departments note that Standard 2.9.1, Codex STAN 72-1981 and EU 2016/127 are generally aligned for the minimum and maximum amounts of calcium and phosphorus and ratios of the two. **The departments support amending the lower minimum calcium to phosphorus ratio from 1.2:1 to 1: 1 to align with Codex STAN 72-1981 (this is also consistent with the EU regulations).**

The maximum phosphorus amount listed in Standard 2.9.1 (and Codex STAN 72-1981) is set higher than is needed (25mg/100kJ) to allow for the lower availability of phosphorus from soy-based

[57] EFSA (EFSA Panel on Dietetic Products Nutrition and Allergies), Scientific opinion on the essential composition of infant and follow-on formulae. EFSA Journal, 2014. 12(7): p. 3760-3866

formulas. We note that European regulations set separate minimum and maximum levels of phosphorus for soy-based formulas, to account for the reduced availability, rather than have these levels apply to all formulas. **As soy-based formulas present a very small minority of the infant formulas on the market, a separate phosphorus range for soy formulas should be provided. The departments do not support a single provision to cover cow and soy milk, but separate provisions to make it clear to regulators and manufacturers that soy products have lower bioavailability of nutrients and therefore require higher levels**. The departments note this is the proposed approach in the Chinese infant formula standards as well as the EU, so should have limited impact on trade.

Vit E: fatty acids ratio

Summary position: The departments support FSANZ's proposed approach for vitamin E to fatty acids ratio.

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

The departments support FSANZ's proposed approach to retain the current permission for vitamin E requirements relating to the PUFA content of infant formula within Standard 2.9.1 rather than adopting Codex STAN 72-1981 factors of equivalence as this has little effect on the levels.

Copper/vitamin C/iron

The departments note that Standard 2.9.1, Codex STAN 72-1981 and EU 2016/127 do not comment on the nutrient interactions between copper, vitamin C and iron, and that FSANZ's 2021 nutrition assessment did not evaluate this nutrient interaction but did note that nutrient interactions between copper, vitamin C and iron may be of relevance if the vitamin C maximum amount currently permitted in Standard 2.9.1 is increased. This is based on high intakes of iron and ascorbic acid potentially having a synergistic negative effect on copper metabolism. We note that despite the lack of assessment FSANZ considers the proposed approaches for copper, vitamin C, and iron to be appropriate in regard to the potential interactions between these nutrients. **The departments support lower levels than FSANZ proposes for iron, vitamin C and a higher minimum copper on the basis of infant health and safety, and these should also help address this potential nutrient interaction.**

7.5 Permitted forms of micronutrients

β -carotene

As discussed above, **the departments do not support retaining β-carotene as a form of vitamin A** given it is not permitted to be included in calculation of vitamin A activity and there is therefore no purpose for its addition as a nutritive substance.

Vitamin D

Summary position: The departments do not support FSANZ's proposed approach to retain vitamin D_2 as a form of vitamin D at this stage.

The departments note that FSANZ proposes to retain vitamin D_2 as a form of vitamin D, noting it is not permitted in Codex STAN 1981-72 due to concerns about effectiveness compared to vitamin D_3. In 2016 our departments indicated there needed to be clear evidence that vitamin D_2 and D_3 were

equivalent in order to support an ongoing permission for D_2.. FSANZ notes in its consultation paper that no further nutrition risk assessment was considered on this issue.

A brief review of the literature indicates **the majority of reviews on this topic indicate that D_3 is more effective than D_2 in its ability to raise 25-hydroxyvitamin D status**, both with supplementation and at lower levels in multiple food fortification vehicles[58,59,60]. However we also note one study in infants found supplementation with D_2 and D_3 produced similar effects[61]. Given the majority of evidence indicates that vitamin D_2 and D_3 are not equivalent in their ability to raise 25-hydroxyvitamin D status, **the departments do not support FSANZ's proposed approach to retain vitamin D_2 as a form of vitamin D at this stage.** The departments consider that further assessment should be conducted before the First Call for Submissions if vitamin D_2 is to be permitted.

Fluoride

Summary position: The departments support removing the warning statement and the setting of a compositional maximum limit for fluoride, however further assessment is required given use of tap water to reconstitute formula will exceed the limit.

The departments support in principle FSANZ's proposed approach to align with Codex and EU 2016/127 and adopt a maximum limit for fluoride in infant formula prepared ready for consumption and remove the warning statement.

The departments request that FSANZ give this issue further consideration. It would be useful to understand compliance overseas in jurisdictions who are using the 24 µg/100 kJ maximum limit.

The departments note that this maximum provides 0.52mg/day for 0-6 mth olds, which is below the recently revised NHMRC ULs of 1.2 mg/day for 0-6 mths and 1.8 mg/day for 7-12 month olds.

However, optimal fluoridation of water in Australia is 1mg F/L. If carers use fluoridated water to reconstitute formula (likely the case in the majority of Australia), fluoride in the water alone would exceed the Codex maximum (fluoridated water at 1mg F/L would contribute 33 µg/100kJ to formula, assuming 90% of formula is water).

While a set compositional limit for fluoride would be preferred, setting a voluntary GUL for fluoride could ensure products are not considered non-compliant if they exceed the 24 µg/100 kJ when prepared. However, we consider it not ideal to set a maximum that cannot be met. If a GUL is set, the departments are also concerned about the potential for prepared formula to contain fluoride at or above the NHMRC UL of 1.2mg/day. While FSANZ has indicated median levels of fluoride in

[58] Tripkovic L, Lambert H, Hart K, Smith CP, Bucca G, Penson S, Chope G, Hyppönen E, Berry J, Vieth R, Lanham-New S. Comparison of vitamin D2 and vitamin D3 supplementation in raising serum 25-hydroxyvitamin D status: a systematic review and meta-analysis. Am J Clin Nutr. 2012 Jun;95(6):1357-64. doi: 10.3945/ajcn.111.031070. Epub 2012 May 2. PMID: 22552031; PMCID: PMC3349454.

[59] Tripkovic L, Wilson LR, Hart K, Johnsen S, de Lusignan S, Smith CP, Bucca G, Penson S, Chope G, Elliott R, Hyppönen E, Berry JL, Lanham-New SA. Daily supplementation with 15 µg vitamin D_2 compared with vitamin D_3 to increase wintertime 25-hydroxyvitamin D status in healthy South Asian and white European women: a 12-wk randomized, placebo-controlled food-fortification trial. Am J Clin Nutr. 2017 Aug;106(2):481-490. doi: 10.3945/ajcn.116.138693. Epub 2017 Jul 5. PMID: 28679555.

[60] Wilson LR, Tripkovic L, Hart KH, Lanham-New SA. Vitamin D deficiency as a public health issue: using vitamin D2 or vitamin D3 in future fortification strategies. Proc Nutr Soc. 2017 Aug;76(3):392-399. doi: 10.1017/S0029665117000349. Epub 2017 Mar 28. PMID: 28347378.

[61] Gallo S, Phan A, Vanstone CA, Rodd C, Weiler HA. The change in plasma 25-hydroxyvitamin D did not differ between breast-fed infants that received a daily supplement of ergocalciferol or cholecalciferol for 3 months. J Nutr. 2013 Feb;143(2):148-53. doi: 10.3945/jn.112.167858. Epub 2012 Dec 19. PMID: 23256143; PMCID: PMC3969107.

formula are currently low, manufacturers have been requesting of the Department of Health a dedicated non-fluoridated water source, presumably to remain under the current warning statement trigger of 17µg/100 kJ fluoride. If manufacturers are currently unable to keep powdered formula under 17µg/100 kJ, this raises concerns that when this is reconstituted with fluoridated water infants will consume fluoride at the UL (0.4 mg/day from formula and 0.8mg from water).

Section 8 – Other optional substances

General comments

The departments recognise that the permission for addition of optional ingredients is intended to encourage industry to innovate to improve infant formula and reduce the adverse health outcomes experienced by formula-fed infants relative to breastfed infants. The development of the Policy Guideline for the Regulation of Infant Formula Products included principles to ensure the aim of innovation was to benefit infants. The current regulatory framework for optional ingredients in Standard 2.9.1 needs revision to ensure formula-fed infants do actually benefit from industry innovation.

Currently, when voluntary permissions are granted for nutritive substances, there is no mechanism to review these permissions to determine whether they should be made available in all infant formula or, if not, removed to avoid placing unnecessary burden on infants' systems. This has resulted in permissions for optional ingredients that have continued for 20 years or more, and the situation where some nutrients now considered essential for more than 14 years, have remained voluntary (e.g. choline). **Continuing voluntary permissions for essential nutrients is not consistent with FSANZ's primary objective to protect infant health and safety and does not ensure equitable access for all infants**. Similarly, where the evidence indicates that optional ingredients are not needed in a breastmilk substitute for optimal growth and development, the continuation of these in formula, which are labelled as 'premium' at a higher cost to carers, could mislead carers into believing there is a benefit. **The departments note that FSANZ has not reviewed either taurine (voluntary for 20 years and considered by many to be conditionally essential for infants[62,63]) or lutein (a voluntary permission since 2009). The departments consider that all optional ingredients need to be reviewed as part of P1028 (with the exception of 2'-FL and LNnT permitted in 2021) and that FSANZ needs to commit to reviewing these at regular periods, such as every 5 years.**

8.1 Choline

Summary position: The departments support FSANZ's proposed approach to mandate choline, with a maximum level of 12mg/100kJ.

The departments do not support retaining the current minimum level and instead support a level of 6mg/100kJ, in line with EU 2016/127.

The departments support FSANZ's proposal to make choline a mandatory ingredient on the basis that it has been long recognised as an essential nutrient. This will align with the position in Codex STAN 72-1981 and EU 2016/127 and other international regulations.

[62] Ripps H., Shen W. Review: Taurine: a "very essential" amino acid. *Molecular Vision.* 2012;18:2673–2686.
[63] Almeida CC, Mendonça Pereira BF, Leandro KC, Costa MP, Spisso BF, Conte-Junior CA. Bioactive Compounds in Infant Formula and Their Effects on Infant Nutrition and Health: A Systematic Literature Review. Int J Food Sci. 2021 May 14;2021:8850080. doi: 10.1155/2021/8850080. PMID: 34095293; PMCID: PMC8140835.

The departments note that the maximum levels of 12mg/100kJ are consistent across regulations and we support this proposed level for the Code, noting there is no Upper Level for infants but it results in intakes well below the UL for 1-3 year olds of 1000mg/day[64].

Minimum levels

The departments note there is inconsistency between regulatory minimums for choline. Codex STAN 72-1981 and the Code currently have the lowest minimums of 1.7mg/100kJ of choline, while the EU 2016/127 requires 6mg/100kJ, based on all sources of choline; i.e. choline, phosphocholine, glycerophosphocholine, phosphatidylcholine and sphingomyelin. Chinese infant formula standards appear to be proposing a minimum closer to the EU of 4.8mg/100kJ[65].

The EU raised its minimum from the Codex level in 2016 in order to meet infant requirements it established to be 130mg/day, which is similar to the NHMRC Adequate Intake of 125mg/day[66]. The current proposed minimum of 1.7mg/100kJ would provide 37mg/day, which is significantly lower than accepted infant requirements. This is also significantly lower than levels found in breastmilk, which are on average 160mg/L or ~6mg/100kJ. **The departments are concerned that a minimum level of choline is being proposed that is well below infant requirements.**

The departments note that FSANZ states there are multiple forms of choline in breastmilk, but only free choline is permitted to be added to infant formula, therefore the minimum level would not be based on the total choline content or infant requirement. This is not consistent with FSANZ's approach to other nutrients with multiple forms.

The departments support setting a limit that meets total choline requirements. Choline is an essential nutrient, with accumulating evidence for its importance in early neurodevelopment during the first 1000 days of life. Infants can synthesize choline but not in sufficient amounts to meet requirements[67]. Strong evidence from animal studies have demonstrated that deficiency in infancy leads to cognitive impairments such as permanent long term impaired memory function[68],[69]. It is also critical for maintaining structural integrity of cells, is a precursor for neurotransmitters, is involved in lipid and cholesterol transport and metabolism and is a source of methyl groups for many metabolic processes, including folate-dependent one-carbon metabolism[70]. Neonates and infants require large amounts of choline to support a rapid growth rate and optimal development[71].

Choline exists in both water-soluble (e.g., free choline, phosphocholine, and glycerophosphocholine) and lipid-soluble (e.g., phosphatidylcholine and sphingomyelin). In infancy, the predominant forms of choline via breastmilk are the water-soluble forms, including free choline, which are more readily absorbed than the lipid-soluble forms of choline (phosphatidylcholine and sphingomyelin), which are

[64] NHMRC Nutrient Reference Values for Australia and New Zealand 2006
[65] USDA Foreign Agricultural Service Global Agricultrural Information 2018 China Notifies Measure on Infant Formula for Young Infants (as SPS 1082)
[66] EFSA (EFSA Panel on Dietetic Products Nutrition and Allergies), Scientific opinion on the essential composition of infant and follow-on formulae. EFSA Journal, 2014. 12(7): p. 3760-3866
[67] Mun JG, Legette LL, Ikonte CJ, Mitmesser SH. Choline and DHA in Maternal and Infant Nutrition: Synergistic Implications in Brain and Eye Health. Nutrients. 2019;11(5):1125. Published 2019 May 21. doi:10.3390/nu11051125
[68] Schwarzenberg, S.J.; Georgieff, M.K. Advocacy for improving nutrition in the first 1000 days to support childhood development and adult health. *Pediatrics* 2018, *141*, doi:10.1542/peds.2017-3716.
[69] Zeisel, S.H.; Carolina, N.; Hill, C.; Carolina, N.; Blusztajn, J.K. Choline and human nutrition. Annu Rev Nutr 1994, 14, 269–96.
[70] Zeisel, S.H.; Klatt, K.C.; Caudill, M.A. Choline. *Adv. Nutr.* 2018, *9*, 58–60, doi:10.1093/advances/nmx004.
[71] *Zeisel SH, Wurtman RJ* Developmental changes in rat blood choline concentration. *Biochem J. 1981 Sep 15; 198(3):565-70.*

mainly present as a minor component of the milk fat globule membrane, and thus make up a relatively small fraction of the total choline in human milk[72], [73]. Free choline is converted to these other forms. The provision of free choline therefore may be sufficient to meet total choline requirements.

The departments also note that cow's milk is a source of all forms of choline and studies indicate it is possible to manufacture infant formula that more closely matches these metabolites' profile in human milk[74, 75]. Therefore while other forms of choline are not permitted to be added to infant formula at this time, they are permitted to be present from cow's milk and will contribute to total choline.

The departments consider that the total choline in infant formula should meet infant requirements of at least 125mg/day and should encompass both free choline added as an ingredient as well as the free choline and other forms naturally present from cow's milk, in line with the total nutrient content of the final product for other nutrients. Given the essential nature of choline, the water-soluble nature of free choline and the presence of other forms of choline in infant formula, the departments consider it prudent to align the minimum with the EU 2016/127 level of 6mg/100kJ of total choline to meet infants' total choline requirements.

8.2 L-carnitine

Summary position: The departments support FSANZ's proposed approach to mandate L-carnitine at 0.3 – 0.8 mg/100kJ.

The departments note that the Code permits the addition of L-carnitine as an optional substance at 0.21–0.8 mg/100 kJ. However, Codex STAN 72-1981 has set a mandatory higher minimum amount of 0.3 mg/100 kJ but has set no maximum amount. The EU 2016/127 also states that L-carnitine content shall be at least equal to 0.3 mg/100 kJ. EU 2016/127 does not specify a maximum level for L-carnitine.

The departments support FSANZ's proposed approach to mandate L-carnitine with a range of 0.3 to 0.8 (GUL)mg/100kJ on the basis that this best meets infant requirements, is similar to the range found in breastmilk and there is a theoretical risk at higher amounts which warrants a maximum level. The voluntary guideline maximum allows industry some flexibility given there are variable levels in infant formula ingredients.

8.3 Inositol

Summary position: The departments support FSANZ's proposed approach to mandate inositol, and the proposed maximum, but request FSANZ provides further scientific justification for setting a minimum that is five times lower than breastmilk.

The departments support FSANZ's proposed approach to mandate inositol, which is currently voluntary, in line with the approach in the EU and Codex. Current compositional requirements when

[72] Zeisel S.H., Char D., Sheard N.F. Choline, phosphatidylcholine and sphingomyelin in human and bovine milk and infant formulas. *J. Nutr.* 1986;116:50–58. doi: 10.1093/jn/116.1.50.
[73] Wiedeman, A.M.; Barr, S.I.; Green, T.J.; Xu, Z.; Innis, S.M.; Kitts, D.D. Dietary choline intake: Current state of knowledge across the life cycle. *Nutrients* 2018, *10*, doi:10.3390/nu10101513.
[74] Artegoitia VM, Middleton JL, Harte FM, Campagna SR, de Veth MJ. Choline and choline metabolite patterns and associations in blood and milk during lactation in dairy cows. *PLoS One*. 2014;9(8):e103412. Published 2014 Aug 26. doi:10.1371/journal.pone.0103412
[75] Zeisel S.H., Char D., Sheard N.F. Choline, phosphatidylcholine and sphingomyelin in human and bovine milk and infant formulas. *J. Nutr.* 1986;116:50–58. doi: 10.1093/jn/116.1.50.

added are very similar across regulations at 1-9.5mg/100kJ in the Code and Codex STAN 72-1981 and 0.96 to 9.6mg/100kJ in EU 2016/127. FSANZ is proposing retaining the current levels. We note FSANZ has not done further nutrition risk assessment on this issue. **The departments support the proposed maximum (GUL).**

In terms of the minimum level required, FSANZ identified the departments' 2016 comment that the minimum levels were well below the lower levels present in mature breastmilk but did not address this. The departments note that inositol is considered essential in cells and is found in high amounts in breastmilk[76] and there is some endogenous synthesis of inositol in newborns, however **the First Call for Submissions should consider whether a minimum level in formula that is five times lower than the lower level in breastmilk is sufficient**.

8.4 Nucleotides

Summary position: The departments do not support FSANZ's proposed approach to maintain a voluntary permission for nucleotides. Further assessment is required on whether a source of nucleotides in breastmilk substitutes is required for optimal infant growth. If so, these should be mandated to make them available to all infants to protect health. If not, the permission should be removed.

The departments note that Schedule 29 permits the optional addition of five nucleotides to infant formula, Codex STAN 72-1981 permits the addition of nucleotides at the discretion of national authorities. EU 2016/127 permits the optional addition of five specific nucleotides to infant formula. FSANZ has not conducted any nutrition risk assessment on this issue and proposes retaining both the current permission in Schedule 29 and the maximum total limit of nucleotides prescribed in Standard 2.9.1.

Twenty years ago, *P93 – standard for infant formula products* included a voluntary permission for nucleotides. FSANZ has not assessed since then whether nucleotides in infant formula contribute to optimal infant growth and development. **The departments consider that it is not appropriate to maintain a voluntary permission, made available in only some formula and therefore to some infants, for 20 years. In the First Call for Submissions, as for other optional ingredients, there needs to be a reassessment of nucleotides to determine whether an external supply (through breastmilk and formula) is important for infant growth and development. If so, these substances should be mandated to be in all formula to ensure equitable access by all infants. If a benefit is unable to be established for infants, the voluntary permission should be withdrawn** on the basis that retaining it would imply a benefit to infants and therefore could be misleading for carers.

[76] Howlett A, Ohlsson A, Plakkal N. Inositol in preterm infants at risk for or having respiratory distress syndrome. Cochrane Database of Systematic Reviews 2019, Issue 7. Art. No.: CD000366. DOI: 10.1002/14651858.CD000366.pub4