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PROPOSAL P93 – REVIEW OF INFANT FORMULA

SUPPLEMENTARY FINAL ASSESSMENT (Inquiry – s.24) REPORT

EXECUTIVE SUMMARY

This Proposal makes recommendations on draft standard (Standard 2.9.1 - Infant Formula Products) for adoption into Volume 2 of the *Food Standards Code* (Volume 2) and a variation to Standard A11 of Volume 1 of the *Food Standards Code* (Volume 1).

The specific **objectives** of the review of infant formula regulation are to:

- protect the health and safety of formula fed infants;
- provide carers with sufficient information about infant formula products to enable them to make appropriate choices in feeding their infant and in the safe use of products;
- develop unambiguous food regulations that reflect contemporary scientific knowledge; and
- harmonise the food regulations applying to infant formula products in Australia and New Zealand.

The review of the standard for infant formula (Proposal P93) has been in progress since 1993. Public submissions were received in the preparation of the Proposal in 1993, at Full Assessment in 1995 and at Preliminary Inquiry in May 1999. The Australia New Zealand Food Authority (ANZFA) completed an Inquiry into the proposed draft standard in November 1999. However, Industry requested further consultation on the draft standard as proposed at Inquiry (Nov 1999).

Therefore, this Supplementary Final Assessment (Inquiry - s.24) Report (Feb 2002) consolidates ANZFA's assessment of all issues raised following Preliminary Inquiry (May 1999), including those issues raised by Industry following Inquiry (Nov 1999) and recommends the draft standard to the Ministerial Council (ANZFSC) for adoption into Volume 2, and an amendment to Standard A11 of Volume 1. An assessment of the issues raised since Preliminary Inquiry is given at Attachment 1, and a summary of changes to the draft standard since Full Assessment (1995) and the rationale for these changes is provided in the Statement of Reasons at Attachment 5.

This report also includes at Attachment 2, a safety assessment of certain microbial oils (DHASCO and ARASCO) that are currently added to infant formula as sources of long chain polyunsaturated fatty acids (LCPUFA). The regulation impact statement as assessed at Preliminary Inquiry (May 1999) has been revised in recognition of the significant time delay and changes that have been made to the draft standard as proposed at Preliminary Inquiry and is at Attachment 3.

In conclusion, ANZFA proposes that draft Standard 2.9.1 – Infant Formula Products, as proposed at Supplementary Final Assessment (Inquiry – s.24) (Attachment 4), be adopted into Volume 2 and that Standard 1.3.4 of Volume 2 and Standard A11 of Volume 1 be amended to include specifications for DHASCO and ARASCO oils.

1. INTRODUCTION

This Proposal makes recommendations on a draft standard (Standard 2.9.1 - Infant Formula Products) for adoption into Volume 2 of the *Food Standards Code* (Volume 2). It is part of the Review of Food Standards, which aims to reduce prescriptiveness and simplify food regulations, and as such reviews the Australian infant formula standard (Standard R7) of the *Food Standards Code* (Volume 1) and Regulation 242 - Infant Formula of the New Zealand *Food Regulations 1984.*

This Proposal has been progressed with regard to the Australia New Zealand Food Authority (ANZFA) objectives as outlined in section 10 of the ANZFA Act 1991. However, the specific **objectives** of the review of infant formula regulation are to:

- protect the health and safety of formula fed infants;
- provide carers with sufficient information about infant formula products to enable them to make appropriate choices in feeding their infant and in the safe use of products;
- develop unambiguous food regulations that reflect contemporary scientific knowledge; and
- harmonise the food regulations applying to infant formula in Australia and New Zealand.

Infant formula products provide for the sole or principal source of nutrition for a very vulnerable population group and in accordance with the level of risk, necessitates a more prescriptive regulation than for other foods. This review has not only considered the needs of healthy infants but also the needs of infants requiring specialised infant formula products. These types of infant formula products have been included in Proposal P93, although in acknowledgement of the specialised nature of these products ANZFA proposes to develop more specific provisions for infant formula products for special dietary uses under a new proposal in the next five years.

This Supplementary Final Assessment (Inquiry – s.24) (Feb 2002) consolidates ANZFA's assessment of all issues raised by stakeholders following both Preliminary Inquiry (May 1999) and Inquiry (Nov 1999), and makes recommendations on the draft standard as proposed at Preliminary Inquiry (May 1999).

2. BACKGROUND

2.1 Draft Standard 2.9.1 – Infant Formula Products

ANZFA prepared a Proposal (P93) to review the Australian infant formula standard (Standard R7) in 1993. Public submissions were requested after the preparation of the Proposal in 1993, and at Full Assessment in 1995.

In 1998, the Proposal was included as a part of the Review of Food Standards and the development of Volume 2 of the *Food Standards Code*. A further round of public consultation at Preliminary Inquiry (May 1999) was included, additional to the usual process, to provide an opportunity for consultation in New Zealand. ANZFA completed an Inquiry into the draft standard in November 1999.

However, prior to the draft standard being recommended to the Ministerial Council for adoption, the infant formula industry requested further consultation on the draft standard, claiming some provisions in the standard would affect the affordability and availability of products on the local market. A large number of issues were raised at the time. These issues were considered at a Stakeholders Forum in May 2000, and by the members of the External Advisory Group at a meeting in June 2000. Subsequent meetings between ANZFA staff and industry representatives were also held in August 2000 and in October 2001 to discuss outstanding issues.

2.2 DHASCO and ARASCO oils as sources of long chain polyunsaturated fatty acids (LCPUFA) in infant formula.

DHASCO and ARASCO are microbial oils rich in the long-chain polyunsaturated fatty acids (LCPUFA) docosahexaenoic acid (DHA) and arachidonic acid (ARA), respectively. DHASCO is extracted from the algae *Crypthecodinium cohnii* and ARASCO is extracted from the fungus *Mortierella alpina*. Infant formula products containing these oils have been available for sale in Australia and New Zealand for approximately the last three years, and elsewhere for up to seven years.

ANZFA had previously indicated at Preliminary Inquiry (May 1999), as well as at Inquiry (Nov 1999), that these substances were likely to be considered "novel" ingredients, and as such would require assessment and approval under the Novel Food Standard (Standard 1.5.1), which was not due to come into effect until 16 June 2001.

ANZFA subsequently received an application, in March 2001, from the Infant Formula Manufacturers' Association of Australia (IFMAA), the New Zealand Infant Formula Marketers' Association (NZIFMA) and Martek Biosciences Corporation to amend Standard 1.5.1 to permit the addition of DHASCO and ARASCO to infant formula. During early consideration of this application by ANZFA it became apparent that, while DHASCO and ARASCO oils would be regarded as non-traditional foods (i.e. food that does not have a history of significant human consumption by the broad community) and thus satisfy the first criterion for consideration as a novel food, they did not satisfy the second criterion. That is, ANZFA considered that because infant formula containing such substances had been

available for at least the last three years, that the majority of infants receiving such formula did so under medical supervision (i.e., in the case of pre-term infants) and that considerable evidence existed (from clinical studies) for the safe use of such formula, it could be argued that sufficient knowledge already existed in the community to enable their safe use when added to infant formula. Thus, the oils could not be regarded as novel food ingredients when added to infant formula.

The applicants subsequently withdrew their application but were invited to re-submit the data package as a submission to the review of infant formula, under which a safety assessment was undertaken for the purpose of confirming that the substances are safe sources of DHA and ARA for infant feeding.

3. ISSUES RAISED SINCE PRELIMINARY INQUIRY (MAY 1999)

3.1 Summary of Issues raised during public consultation

Fifty-eight submissions were received to the Inquiry of draft Standard 2.9.1 during the public consultation period May to June 1999 from infant formula manufacturers, pharmaceutical companies, health professionals, governments, community organisations and individuals. A summary of these submissions is at Attachment 7. Below is the list of issues raised in submissions.

In addition Industry stakeholders, namely the Infant Formula Manufacturers' Association of Australia (IFMAA) and the New Zealand Infant Formula Marketers' Association (NZIFMA), prior to the formal adoption of the draft standard requested further consultation on the standard as proposed at Inquiry (Nov 1999). Industry provided a submission detailing a large number of issues in April 2000. The issues raised by Industry's submission are indicated by **bolded** text in the following list of issues. The specific details of these issues are summarised at Attachment 6.

ISSUES

<u>General</u>

- Title of and inclusion of Follow on formula within the draft Standard

<u>PART 1 – GENERAL PROVISIONS</u>

<u>Division 1 – Interpretation</u>
<u>Definitions</u>

- Infant formula product
- Infant formula
- **Follow on formula**
- Infant
- Lactose free and low lactose
- Pre-term formula
- Protein substitute
- Soy protein formula
- Fat modified.

Division 2 – Calculations

- Potential Renal Solute Load (PRSL)
- Calculation of PRSL
- Calculation of amino acid score
- **Protein Quality – Amino acid reference profile**

Division 3 – General Composition Requirements

- Restrictions and prohibitions
- Permitted optional nutritive substances
  - Error in drafting for carnitine, choline and inositol
  - Carnitine
  - Choline

- Nucleotides
- Food Additives
  - Carrageenan
  - Citric esters of mono- and di- glycerides of fatty acids
  - Mono- and di-glycerides of fatty acids
  - Diacetyl tartaric acid esters of mono- and di-glycerides (DATEM)
  - **Locust bean gum**

- Aluminium

Division 4 – General labelling and packaging requirements

- General comments
- Requirement for a measuring scoop
- **Required statements**
  - **Use of the term 'very' ill'**
  - Instructions on the preparation of bottle
  - **Statement about additional foods**

- **Print and package size.**
- **Declaration of nutrition information**
- Date marking and storage instructions
- Statement on the source of protein
- Statement on dental fluorosis
- Labelling of lactose free and low lactose formula
- **Prohibited representations – 'added iron' claims**

Division 5 – General Microbiological Requirements

PART 2 – INFANT FORMULA AND FOLLOW ON FORMULA

- Composition
- Protein content
- Potential renal solute load (PRSL) of follow on formula (and special purpose formula)
- Fat

- **Units of expression for linoleic acid (LA) and alpha-linolenic (ALA) acid**
- **Alpha linolenic acid (ALA)**
- Trans fatty acids
- Long Chain Polyunsaturated Fatty Acids (LCPUFA)

The regulation of LCPUFA
Levels of addition of series-6 fatty acids
LCPUFA in follow on formula

- Vitamins and minerals
  - Policy for safety of vitamins and minerals
  - Specific levels in the Table to Clause 31

Selenium
Copper
Zinc to copper ratio
Chromium and molybdenum
Pyridoxine
Riboflavin
Iron
Phosphorus

- Schedule 1 – Permitted forms of nutrients
  - General
  - Cupric carbonate
  - Nicotinic acid
  - Selenium
  - Choline and carnitine forms

PART 3 – INFANT FORMULA PRODUCTS FOR SPECIAL DIETARY USE
Division 1 – Pre-term formula

- Fat content
- MCT content of pre-term formula
- Vitamin and mineral content of pre-term formula
- Use of pre-term formula
- Labelling statement on pre-term formula

Division 2 – Infant formula products formulated for metabolic and immunological conditions

- Scope
- Availability
- **Claims on thickened formula**
- **Composition and labelling of special purpose formula**

Issues not in draft standard

- Soy formula
- Novel foods
- Cadmium
- **Innovation**

3.2 Other

Other issues relevant to the proposed infant formula standard and the (then draft) joint *Australia New Zealand Food Standards Code* were also identified following Inquiry (Nov 1999). These are:

- Percentage labelling (Standard 1.2.10)
- Declaration of source of protein
- Composition of lactose free and low lactose formula

In addition, the safety of microbial oils (DHASCO and ARASCO) as sources of LCPUFA was included for consideration as part of Proposal P93 - Review of Infant Formula.

4. ASSESSMENT OF ISSUES RAISED

4.1 Issues raised since Preliminary Inquiry (May 1999)

A full discussion of ANZFA's assessment and recommendations on all issues raised by submissions following both Preliminary Inquiry (May 1999) and Inquiry (Nov 1999) is at Attachment 1.

4.2 Safety of DHASCO and ARASCO oils as sources of LCPUFAs

ANZFA has undertaken a safety assessment of DHASCO and ARASCO oils, which are microbial-derived oils currently added to infant formula as sources of DHA and ARA. The full safety assessment report is at **Attachment 2** to this report. The safety assessment considered the safety of the source organisms, the composition of the oils, bioavailability studies in animals and human infants, animal toxicity studies as well as clinical studies with human infants fed DHASCO and ARASCO-containing formula.

Neither of the source organisms are known to be pathogenic to humans nor other mammals and specific studies with the biomass from both organisms have confirmed the absence of any toxin production.

The extracted oils are free flowing triglyceride oils with a fatty acid profile that is comparable to that of a number of other edible oils. No unusual fatty acids are present and there are no detectable (< 0.1%) cyclic or *trans* fatty acids present in either oil. Bioavailability studies indicate that the efficiency of intestinal absorption of ARA and DHA from ARASCO- and DHASCO-supplemented infant formula is similar to that from breast milk with the oils being able to support maximal tissue accretion of ARA and DHA.

There is no evidence of toxicity associated with the administration of ARASCO and DHASCO to laboratory animals at dose levels up to 2500 mg and 1250 mg/kg bw/day, respectively. These dose levels are approximately 18 – 35 fold greater than the maximum levels being added to infant formula. Clinical studies with human infants also indicate that

formula supplemented with DHASCO and ARASCO is well tolerated by human infants and is not associated with any apparent adverse effects.

Overall, the evidence does not indicate any safety concerns regarding the addition of ARASCO and DHASCO oils to infant formula as sources of LCPUFA.

Recommendation

To permit the addition of DHASCO and ARASCO oils as sources of LCPUFA in infant formula products and include their respective specifications in Standard 1.3.4 – Identity and Purity of Volume 2 and in Standard A11 of Volume 1.

5. CHANGES TO PRELIMINARY INQUIRY (MAY 1999) RESULTING FROM SUPPLEMENTARY FINAL ASSESSMENT (INQUIRY - s.24) (FEB 2002)

The following changes are recommended to the draft standard as prepared at Preliminary Inquiry (May 1999). This is following consideration of issues and consultation with stakeholders. The rationale for these changes is detailed in this Supplementary Final Assessment (Inquiry – s.24) Report (see Section 4.1 above). Details of all changes proposed for the draft standard since Full Assessment (1995) and the justification for these changes is provided in the Statement of Reasons at Attachment 5 of this report.

Clause Number at Preliminary Inquiry	**Proposed at Preliminary Inquiry (May 99)**	**Recommended at Supplementary Final Assessment (Inquiry – s.24) (Feb 02)**
Purpose	First paragraph includes the words 'This Standard provides for the compositional, microbiological and labelling requirements…'	**Deletion** of the word 'microbiological'. **Inclusion** of reference to Standard 1.3.1 Food Additives and Standard 1.6.1 Microbiological Limits for Food. **Inclusion** of a reference to specifications in Standard 1.3.4 of **'permitted nucleotides and added nutrients'**
1. Definitions		**Inclusion of subclause 1(1)** This subclause reads "The definitions in clauses 1 and 2 of Standard 1.2.8 apply to this Standard".
	'follow-on formula' means infant formula product represented as being suitable as the **principal source of food for infants aged over six months**.	**'follow-on formula'** means: an infant formula product represented as either **a breast-milk substitute or replacement for infant formula and which constitutes the principal liquid source of nourishment in a progressively diversified diet for infants aged from six months.**

Clause Number at Preliminary Inquiry	Proposed at Preliminary Inquiry (May 99)	Recommended at Supplementary Final Assessment (Inquiry – s.24) (Feb 02)
	'infant formula' means an infant formula product that is represented as being suitable as the **principal source of food for infants.**	**'infant formula'** means an infant formula product represented as a breast- milk substitute for infants and which **satisfies the nutritional requirements of infants aged up to four to six months.**
	'infant formula product' is a product based on milk or other edible food constituents of animal or plant origin and which is intended to be, and is suitable for use as, the principal source of nourishment for infants.	**'infant formula product'** means a product based on milk or other edible food constituents of animal or plant origin and which is nutritionally adequate to serve as, the principal liquid source of nourishment for infants.
	'pre-term formula' means an infant formula product represented as being suitable as the **principal source of food** for infants born prematurely or of low birth weight	**'pre-term formula'** means an infant formula product specifically **formulated to satisfy particular needs** of infants born prematurely or of low birth weight
	'Lactose free' and **'low lactose formula'** mean infant formula products represented as being the **principal source of food** for lactose intolerant infants.	**'lactose free'** and **'low lactose formula'** mean infant formula products which **satisfy the needs of lactose intolerant infants**.
	Clause 1 includes a definition for "protein equivalent"	The **removal** of the definition for protein equivalent from Clause 1.
4. Calculation of protein		This clause has been re-formatted to be consistent with the Food Standard Code in general.
5.Calculation of potential renal solute load	The calculation for the potential renal solute load is stated as: Potential renal solute load in mOsm/100 kJ = [Na (mg/100 kJ) /23] + [Cl (mg/100 kJ) /35] + [K (mg/100 kJ) /39] + [**P** (mg/100 kJ)/31] + [protein (mg/100 kJ)/175].	The calculation now reads: Potential renal solute load in mOsm/100 kJ = [Na (mg/100 kJ) /23] + [Cl (mg/100 kJ) /35] + [K (mg/100 kJ) /39] + [$\mathbf{P_{avail}}$(mg/100 kJ)/31] + [N (mg/100 kJ)/28]. **Where P_{avail} is P of milk- based formula + 2/3 of P of soy- based formulas.** This clause has been re-formatted to be consistent with the Food Standard Code in general.
6. Calculation of amino acid score	Contains a definition of an amino score and the Table to Clause 6 (provides amino acid reference values expressed as g/100g protein).	**Clause removed**. Table to clause 6 transferred to Clauses 22 and 32.

Clause Number at Preliminary Inquiry	Proposed at Preliminary Inquiry (May 99)	Recommended at Supplementary Final Assessment (Inquiry – s.24) (Feb 02)
Due to the removal of Clause 6, the clause numbering is reduced by one and Tables to Clauses re-numbered accordingly		
8. Permitted optional nutritional substances		**Now Clause 7** **The title is now** 'Permitted nutritive substances'.
	The Table to Clause 8 contains maximum levels per 100kJ for the following nutrients: • Choline **5.4** mg • Inositol **5.4** mg • L- Carnitine **0.42** mg	The values in the Table / 100kJ have been changed as follows: • Choline **7.1** mg • Inositol **9.5** mg • L- Carnitine **0.8** mg
9. Limit on nucleotide 5'-monophosphates	This clause states that an infant formula product must not contain more than a total amount of **1.2** mg of nucleotide 5'-monophosphates per 100 kJ.	**Now Clause 8** The clause has been changed to read that an infant formula product must not contain more than a total amount of **3.8** mg of nucleotide 5'-monophosphates per 100 kJ.
10. Lactic acid cultures	This clause reads: 'L(+) producing lactic acid cultures may be added to infant formula products **subject to Standard 1.6.1**'	**Now Clause 9** **Removal** of 'subject to Standard 1.6.1'.
11. Food Additives	General food additive permissions	**Transferred** to Standard 1.3.1 Food Additives.
12. Carry-over of food additives	Carry-over permissions for food additives in ingredients.	**Transferred** to Standard 1.3.1 "Food Additives".
Due to the removal of Clauses 11 and 12, the clause numbering is reduced by a total of three clauses and the Tables to Clauses re-numbered accordingly.		
13. Limit on Aluminium		**Now Clause 10**
14. Limit on Lead	This clause states that an infant formula product must not contain more than 2 μg of lead per 100 mL	**This Clause has been replaced by an Editorial Note** stating that 'The maximum level (ML) of lead in infant formula products is specified in Standard 1.4.1'.
15. Composition of lactose free and low lactose formulas	Subclause (3) states 'Low lactose formula must not contain more than **0.24g** per 100mL of lactose'.	**Now Clause 29** Subclause (3) now states 'Low lactose formula must not contain more than **0.3g** per 100mL of lactose'.
		This clause has been moved to the section 'Infant Formula Products for Special Dietary Uses' (Division 3).
Due to the removal of Clauses 14 and transferral of Clause 15 to another part of the Standard, the clause numbering is reduced by a total of five clauses and the Tables to Clauses re-numbered accordingly.		

Clause Number at Preliminary Inquiry	Proposed at Preliminary Inquiry (May 99)	Recommended at Supplementary Final Assessment (Inquiry – s.24) (Feb 02)
Clause 18 – Requirement for a measuring scoop	A package, other than a single serve sachet, containing infant formula product in a powdered form, must contain a scoop, which facilitates the use of the infant formula product in accordance with the directions contained in the label on the package.	**Now Clause 13** (1) a package of infant formula product in a powdered form must contain a scoop to enable the use of the infant formula product in accordance with the directions contained in the label on the package. (2) Subclause 1 does not apply to single serve sachets, or packages containing single serve sachets containing infant formula product in a powdered form.
19. Required statements		**Now Clause 14** **The title is now** 'Required warnings directions and statements'.
	Subclause (1) requires the statement '**Inappropriate** use or preparation can make your baby very ill'. This statement is contained in parts (a), (b) and (c) of this subclause.	The statement is now '**Incorrect preparation** can make your baby very ill'.

Clause Number at Preliminary Inquiry	Proposed at Preliminary Inquiry (May 99)	Recommended at Supplementary Final Assessment (Inquiry – s.24) (Feb 02)
	Subclause (3) reads; Subject to subclause (4) the label on an infant formula product must contain statements indicating that: (a) breastfeeding is superior to the use of infant formula product in the feeding of infants; (b) the infant formula product should only be used on the advice of a medical practitioner or health worker as to the need for its use and the proper method of its use; (c) the infant formula product may be used from birth, in the case of infant formula; (d) the infant formula product should not be used for infants aged under 6 months in the case of follow-on formula; (e) except in the case of packages of pre-term formula, **infants over the age of 6 months should receive foods** in addition to the infant formula product. The statements required by subclause (3) must occur under a heading that reads 'Important Notice' or any word or words having the same or similar effect	Subclause (3) now reads: Subject to subclause (4) the label on an infant formula product must contain the following statement: **'Breast milk is best for babies. Before you decide to use this product, consult your doctor or health worker for advice'** under a heading that reads **'Important notice'** or any word or words having the same or similar effect. Subclause (4) now is; **Sub clause (3) does not apply to infant formula products for metabolic, immunological, renal, hepatic or malabsorptive conditions.** Subclause (5) is now; The label on an infant formula product must contain statements indicating that: (a) the infant formula product may be used from birth, in the case of infant formula; (b) the infant formula product should not be used for infants aged under 6 months in the case of follow-on formula; (c) except in the case of packages of pre-term formula, **it is recommended that infants over the age of 6 months should receive foods** in addition to the infant formula product.
20. Print and Package Size	(1) Where infant formula product is in a package having a net weight of more than 1 kg, the statements required by clauses 19(1) and 36(1) must be in size of type of not less than 3 mm.	**Now Clause 15** Product weight has been decreased to **500g or more**.
	(2) Where infant formula product is in a package having a net weight of 450g or less than 1 kg, the statements required by clauses 19(1) and 36(1) must be in size of type of not less than 1.5 mm.	**Now Clause 15** Product weight has been increased to **500g or less**.

Clause Number at Preliminary Inquiry	Proposed at Preliminary Inquiry (May 99)	Recommended at Supplementary Final Assessment (Inquiry – s.24) (Feb 02)
	The minimum print sizes specified in both subclauses only applied to the warning statements under Subclauses 19(1) and 36(1).	**The scope of the minimum print size requirement has been extended** to the newly formed advisory statement in Subclause 14(3) (see above).
21. Declaration of Nutrition Information	For subclauses (1), (2) and (3), part (b)(ii) required that nutrients are expressed as **units per 100g** for a powdered infant formula product, or units per 100mL prior to reconstitution in the case of a liquid concentrated infant formula product.	**Now Clause 16** Reference to **"units per 100g" has been deleted** from part (b)(ii). The clause has been re-formatted to improve clarity – it now contains only two subclauses.
		A new subclause 16(2)(d) has been added requiring the declaration of the weight of one measuring scoop and the proportion of the product on a weight / volume basis.
22. Date marking and storage instructions	Subclause 22(1) states: 'Notwithstanding the provisions in subclause 2(1) of Standard 1.2.5, the label on an infant formula product must include a statement of the best before date'.	**Now Clause 17** As a means of maintaining consistency with other Standards in Volume 2, **subclause (1) has been changed to read:** 'Paragraphs 2(1)(c) and (d) of Standard 1.2.5 do not apply to this Standard'.
23. Statement of protein source	This clause states that "…a package of infant formula product must contain a statement of the source of protein…"	**Now Clause 18** **This clause now reads**: '…a package of infant formula must contain a statement of the **specific** source, **or sources,** of protein…'
25. Labelling of Lactose free and low lactose formulas		**Now Clause 30** This clause has been moved to the section 'Infant Formula Products for Special Dietary Uses'. **The title is now** 'Claims relating to lactose free and low lactose formulas'.

Clause Number at Preliminary Inquiry	Proposed at Preliminary Inquiry (May 99)	Recommended at Supplementary Final Assessment (Inquiry – s.24) (Feb 02)
	Subclause (1) The words 'lactose free' must appear as part of the appropriate designation of lactose free formula. (2) The words 'low lactose' must appear as part of the appropriate designation of low lactose formula. (3) The label on a package containing a lactose free formula or a low lactose formula must include the following statements: (a) The amount of lactose expressed in g per 100 mL; and (b) The amount of galactose expressed in g per 100 mL.	The drafting has been changed to: **'Where a label contains a claim that the infant formula product is lactose free, low lactose or words of similar import, the label on a package of lactose free or a low lactose formula product must include** (a) the words 'lactose free' as part of the name of lactose free formula; and (b) the words 'low lactose' as part of the name of low lactose formula; and (c) the following statements - (i) the amount of lactose expressed in g per 100 mL; and (ii) the amount of galactose expressed in g per 100 mL.
27. Microbiological standards		**Transferred** to Standard 1.6.1 Microbiological Limits for Food
Due to the removal of Clause 27, and the transferral of Clause 25 to Clause 30, clause numbering has reduced by a total of seven and the Tables to Clauses re-numbered accordingly.		
29. Protein	Subclause (1) requires "The protein in infant formula and follow-on formula must have an amino acid score of no less than **0.8**".	**Now Clause 22** Subclause (1) has been **removed.**
	In the Table to Clause 6, amino acids are expressed as **g/100g**.	The **Table to Clause 6 has been transferred to this clause** with minimum amino acids expressed as **mg/100kJ**.
	Separate values for methionine and cysteine, and phenylalanine and tyrosine, in the Table to Clause 6.	A single value for the respective **summation** of [methionine and cysteine] and [phenylalanine and tyrosine] is included in the Table to Clause 22

Clause Number at Preliminary Inquiry	Proposed at Preliminary Inquiry (May 99)	Recommended at Supplementary Final Assessment (Inquiry – s.24) (Feb 02)
	Subclause (2) 'L-amino acids may be added solely for the purpose of achieving the amino acid score specified in subclause (1)'	Subclause (2) has been added to provide the requirement: **'Infant formula or follow-on formula must provide no less than 6mg cysteine per 100kJ and 17mg phenylalanine per 100kJ'** **Subclause (3) is now** 'L-amino acid may be added to infant formula or follow-on formula only in an amount necessary to improve protein quality'.
30. Fat	Subclause 30(d) contains the statement '…a ratio of total long chain omega 6 series fatty acids (C>= 20) to total long chain omega 3 series fatty acids (C>= 20) **of 2**…'	**Now Clause 23** The statement now reads '…a ratio of total long chain omega 6 series fatty acids (C>= 20) to total long chain omega 3 series fatty acids (C>= 20) **of approximately 2**…'
	Column 2 of the Table to Clause 26 specifies a maximum level of **1.75%** of total fatty acids for alpha-linolenic acid.	Column 2 of the Table to Clause 24 specifies a maximum level of **1.1%** of total fatty acids for alpha-linolenic acid.
		Inclusion of an Editorial note that contains reference to specifications for docosahexanoic acid (DHA) rich oil and arachidonic acid (ARA) rich oil derived from algal or fungal sources in Standard 1.3.4.
31 Vitamins and Minerals	In the Table to Clause 31, selenium content is listed per 100kJ as • a minimum of **0.36**µg • a maximum of **0.9**µg	**Now Clause 24** In the Table to Clause 24, selenium content is now listed per 100kJ as • a minimum of **0.25**µg • a maximum of **1.19**µg
	Subclause (4) requires the ratio of zinc to copper in infant formula and follow-on formula must be no more than **12 to 1**.	Subclause (4) has been changed to require that the ratio of zinc to copper: (a) in infant formula must be no more than **15 to 1**; and (b) in follow-on formula must be no more than **20 to 1**.
	The Editorial Note below this clause contains the statement **'While there are no maximum levels specified in relation to a number of the vitamins and minerals in this table the Australia New Zealand Food Authority has recommended** guidelines…'	The Editorial Note now reads **'The standard contains** guidelines…'

Clause Number at Preliminary Inquiry	Proposed at Preliminary Inquiry (May 99)	Recommended at Supplementary Final Assessment (Inquiry – s.24) (Feb 02)
Schedule 1 to Clause 31 – Vitamins and minerals		The following forms were added to the list of permitted forms at Preliminary Inquiry (now **Schedule 1, Clause 24)** • Retinyl propionate as a source of vitamin A • Cholecalciferol-cholesterol as a source of vitamin D • dl – alpha- tocopheryl succinate as a source of vitamin E • Phytylmenoquinone as a source of vitamin K • Sodium chloride iodized as a source of sodium • Cupric citrate as a source of copper. • Manganese carbonate and manganese citrate as sources of manganese • Sodium selenate
32-35. Pre-term formula	Clauses 32 – 35 contained detailed compositional requirements for pre-term formula.	**Now Clause 25** **Clauses 32-35 have been replaced with a single clause titled "Composition and Labelling".** Clause 25 states: 'Infant formula products may be specifically formulated for premature or low birthweight infants provided that in all other respects they comply with this Standard'.
Due to the changes to clauses 32-35, the clause numbering is reduced by a total of ten clauses and the Tables to Clauses re-numbered accordingly.		

Clause Number at Preliminary Inquiry	Proposed at Preliminary Inquiry (May 99)	Recommended at Supplementary Final Assessment (Inquiry – s.24) (Feb 02)
37. Composition (Division 2)	Subclause (1) states that infant formula products may be specifically formulated to satisfy particular **metabolic or immunological** conditions and must comply with; (a) this division (b) with all the other requirements of this standard that are not inconsistent with this division	**Now Clause 27 (Division 3, Subdivision 2) Title changed to Infant Formula Products for metabolic, immunological, renal, hepatic and malabsorptive conditions** Subclause (1) states that infant formula products may be specifically formulated to satisfy particular **metabolic, immunological, renal or malabsorptive** conditions. (2) The permission in subclause (1) only applies where the infant formula products comply with – (a) this Division; and (b) all the other requirements of this Standard that are not inconsistent with this Division. **Subclause (3) has been added** stating that 'Subclause (2) takes effect 5 years after the announcement of this Standard'.

Clause Number at Preliminary Inquiry	Proposed at Preliminary Inquiry (May 99)	Recommended at Supplementary Final Assessment (Inquiry – s.24) (Feb 02)
38. Additional Labelling (Division 2)	(1) The label on a package containing an infant formula product formulated for **metabolic or immunological conditions** must include a statement indicating that the product is not suitable for general use and should be used under medical supervision. (2) The appropriate designation of a food standardised in this division must include a statement indicating (a) the condition, disease or disorder for which the food has been specially formulated; and (b) the nutritional modifications which have been made to the infant formula product.	**Now Clause 28** **The title is now 'Claims'** and has been re-formatted to improve clarity; 'Where a claim is made that an infant formula product is suitable for infants with metabolic, immunological, renal, hepatic or malabsorptive conditions, then the label on a package containing the infant formula product must include a statement indicating: (a)that the product is not suitable for general use and should be used under medical supervision; (b) the condition, disease or disorder for which the food has been specially formulated; and (c) the nutritional modifications, if any, which have been made to the infant formula product.'
Two clauses relating to lactose free and low lactose formula (Clauses 15 and 25 at Preliminary Inquiry) have **now changed to Clauses 29 and 30**. Therefore clause numbers have reduced by a total of eight for the following clauses and the Tables to clauses re-numbered accordingly.		
40. Protein	Subclause (2) requires that 'The protein in infant formula product based upon protein substitutes must have an amino acid score of no less than **0.8**'.	**Now Clause 32** Subclause (2) has been **removed.**
	In the Table to Clause 6, amino acids are expressed as **g/100g**.	The **Table to Clause 6 has been transferred into this clause** with minimum amino acids expressed as **mg/100kJ**.
	Separate values for methionine and cysteine, and phenylalanine and tyrosine, in the Table to Clause 6.	A single value for the respective **summation** of [methionine and cysteine] and [phenylalanine and tyrosine] is included in the Table to Clause 32.
		Subclause (3) now provides the requirement: 'Infant formula for specific dietary use based upon protein substitutes must provide no less than 6mg cysteine per 100kJ and 17mg phenylalanine per 100kJ'.
		Subclause (4) has been added, 'L-amino acid may be added to infant formula or follow-on formula only in an amount necessary to improve protein quality.'

Clause Number at Preliminary Inquiry	Proposed at Preliminary Inquiry (May 99)	Recommended at Supplementary Final Assessment (Inquiry – s.24) (Feb 02)
42. Additional permitted additions		**Now Clause 34** **The title is now** 'Additional permitted triglycerides'
	Subclause (2) specified levels for permitted food additives that could be added to infant formula products for specific dietary use based on protein substitutes.	**Subclause (2) has been removed and the provisions contained therein transferred** to Standard 1.3.1 Food Additives.
	The Table to Clause 42 specified the following: • DATEM – maximum amount **0.4** g/ 100 mL • **No permission** for Citric acid esters of mono- and di-glycerides of fatty acids (E472c) • Mono-and di-glycerides	These changes have been transferred to Standard 1.3.1: • DATEM (E472e) – maximum amount **0.04** g/100 mL • **Permission** for citric acid esters of mono- and di-glycerides of fatty acids (E472c) **up to a maximum amount 0.9g /100 mL** • Mono-and di-glycerides **of fatty acids (E471)**
Nutrition information table	All features of the Nutrition Information Table are mandatory	Includes Editorial Note **"The information in column 2 is not mandatory".**
Table of Contents to Volume 2 of the Food Standards Code	Previous drafting did not include an amendment to the Table of Contents for Volume 2 as this had not been adopted and gazetted at the time of Preliminary Inquiry (May 99).	The Table of Contents as gazetted 20th December 2000 included a reference to "Standard 2.9.1 Reserved (Infant Formula Products)". The Table of Contents is amended under Part 2.9 Special Purpose Foods to read **"Standard 2.9.1 Infant Formula Products"**.

6. OTHER CONSIDERATIONS

6.1 Regulation Impact Statement

In meeting the objectives of this Proposal, ANZFA is required to assess the relative costs and benefits of regulatory options and their respective impacts on identified affected parties. As part of Preliminary Inquiry (May 1999), ANZFA undertook a regulation impact analysis. In recognition of the significant time delay and changes that have been made to the draft standard as proposed at Inquiry (Nov 1999), the previous draft regulation impact statement as assessed at Preliminary Inquiry has been revised and updated as part of this Supplementary Final Assessment (Inquiry – s.24) (Attachment 3). The Office of Regulation Review has assessed this revised regulation impact statement as adequate.

6.2 International and World Trade Organization obligations

Australia and New Zealand are members of the World Trade Organization (WTO) and are bound as parties to WTO agreements. In Australia, an agreement developed by the Council of Australian Governments (COAG) requires States and Territories to be bound as parties to those WTO agreements to which the Commonwealth is a signatory. Under the Treaty between the Governments of Australia and New Zealand on joint Food Standards, ANZFA is required to ensure that food standards are consistent with the obligations of both countries as members of the WTO.

In certain circumstances Australia and New Zealand have an obligation to notify the WTO of changes to food standards to enable other member countries of the WTO to make comment. Notification is required in the case of any new or changed standards which may have a significant trade effect and which depart from the relevant international standard (or where no international standard exists).

Following Preliminary Inquiry (May 1999), this matter was notified to the WTO as a technical barrier to trade matter as the proposed revisions to the existing infant formula standards are more prescriptive than other standards internationally. One submission from the United States of America was received on this matter.

6.3 Transition Arrangements

Proposal P252 currently at Draft Assessment, proposes a 2-year transition period from the commencement of Standard 2.9.1, which involves concurrent operation of the existing regulations (Standard R7) as Transitional Standard 1.1A.1 Infant Formula Products and Standard 2.9.1. When Standard 2.9.1 becomes the sole standard, the proposed general stock-in-trade provisions (Proposal P248) will apply for a further 12 months.

7. CONCLUSION

This Supplementary Final Assessment (Inquiry – s.24) Report (Feb 2002) has assessed all issues raised since Preliminary Inquiry (May 1999) and made recommendations on the draft standard to address stakeholder concerns.

Therefore, ANZFA having undertaken a long and comprehensive review of infant formula, recommends to ANZFSC that draft Standard 2.9.1 – Infant Formula Products, as proposed in this Supplementary Final Assessment (Inquiry – s.24) Report (Attachment 4), be adopted in Volume 2 of the *Food Standards Code* (Volume 2) and that Standard 1.3.4 (Volume 2) and Standard A11 (Volume 1) be amended to include specifications for DHASCO and ARASCO oils.

8. ATTACHMENTS

1. Assessment of issues raised following Preliminary Inquiry (May 1999)
2. Safety assessment report - DHASCO and ARASCO as sources of long-chain polyunsaturated fatty acids in infant formula.
3. Revised regulation impact statement
4. Proposed draft Standard 2.9.1 - Infant Formula Products and amendments to Standard 1.3.4 – Identity and Purity, and to Standard A11, Volume1
5. Statement of Reasons
6. Summary of issues raised in Industry submission following Inquiry (Nov 1999)
7. Summary of Submissions following Preliminary Inquiry (May 1999)

ATTACHMENT 1

PROPOSAL P93 – REVIEW OF INFANT FORMULA

ASSESSMENT OF ISSUES RAISED FOLLOWING PRELIMINARY INQUIRY (MAY 1999)

The issues, as listed below, were raised in submissions to the Inquiry of draft Standard 2.9.1 – Infant Formula Products during public consultation in May to June 1999.

An assessment of these issues was completed and changes to the draft standard recommended at Inquiry (Nov 1999). However Industry, namely the Infant Formula Manufacturers' Association of Australia (IFMAA) and the New Zealand Infant Formula Marketers' Association (NZIFMA), prior to formal adoption of the draft standard requested further consultation claiming some provisions in the standard would affect the affordability and availability of products on the local market. Industry provided a submission detailing a large number of issues with the draft standard as proposed at Inquiry (Nov 1999). The issues raised by Industry are indicated in the following list by **bolded** text.

ANZFA has now consolidated its assessment of all issues raised at Inquiry (June 1999 – February 2002) and makes recommendations on changes to the draft standard as proposed at Preliminary Inquiry (May 1999) and at Inquiry (Nov 1999).

ISSUES

PART 1 – GENERAL PROVISIONS

Division 1 – Interpretation

1. Definitions

    1.1. Title of and inclusion of Follow on formula within the draft Standard
    1.2. Infant formula product
    1.3. Infant formula
    1.4. Follow–on formula
    1.5. Infant
    1.6. Lactose free and low lactose
    1.7. Pre–term formula
    1.8. Protein substitute
    1.9. Soy protein formula
    1.10. Fat modified.

2. Division 2 – Calculations

    2.1. Potential Renal Solute Load (PRSL)
    2.2. Calculation of PRSL
    2.3. Protein Quality – Amino acid reference profile

3. Division 3 – General Composition Requirements

3.1. Restrictions and prohibitions
3.2. Permitted optional nutritive substances
3.2.1. Error in drafting for carnitine, choline and inositol
3.2.2. Carnitine
3.2.3. Choline

3.3. Nucleotides
3.4. Food Additives

3.4.1. Carrageenan
3.4.2. Citric esters of mono– and di– glycerides of fatty acids
3.4.3. Mono– and di–glycerides of fatty acids
3.4.4. Diacetyl tartaric acid esters of mono– and di–glycerides (DATEM)
3.4.5. Locust bean gum

3.5. Aluminium
3.6. Composition of lactose free and low lactose formula

4. Division 4 – General labelling and packaging requirements

4.1. General comments
4.2. Clause 18 Requirement for a measuring scoop
4.3. Clause 19 Required statements

4.3.1. Clause 19 (3) (a) and (b)
4.3.2. Statement about additional foods
4.3.3. Clause 19 (1) Use of the term 'very ill'
4.3.4. Clause 19 Ready to drink formula
4.3.5. Clause 19 Instructions on the preparation of bottle

4.4. **Clause 20 Print and package size**.
4.5. Clause 21 Declaration of nutrition information
4.6. Clause 22 Date marking and storage instructions
4.7. Clause 23 Statement on the source of protein
4.8. Clause 24 Statement on dental fluorosis
4.9. Clause 25 Labelling of lactose free and low lactose formula
4.10. Prohibited representations – 'added iron' claims

5. Division 5 – General Microbiological Requirements

6. PART 2 – INFANT FORMULA AND FOLLOW ON FORMULA

Composition

6.1. Protein content
6.2. Potential renal solute load (PRSL) of follow on formula (and special purpose formula)

8. ISSUES NOT IN DRAFT STANDARD

8.1 Soy formula
8.2 Novel foods
8.3 Cadmium
8.4 Percentage labelling
8.5 Innovation

ASSESSMENT OF ISSUES

NOTE: The clause numbers referred to in this assessment are those proposed at Preliminary Inquiry (May 1999) and may not coincide with the clause numbers in the draft Standard as proposed at Inquiry (Nov 1999) and Supplementary Final Assessment (Feb 2002). A summary of the changes (including clause numbering) to the draft standard as proposed at Preliminary Inquiry (May 1999) is included in the Supplementary Final Assessment (Inquiry – s.24) Report (Feb 2002) (see Section 5).

DIVISION 1 INTERPRETATION

1. DEFINITIONS

1.1 Title of, and inclusion of Follow–on Formula within, the draft Standard

Very few submissions addressed issues relating to the title of the draft Standard, or the proposed definitions of infant formula product, infant formula, and follow–on formula.

Proposed at Preliminary Inquiry

The title of the draft standard was proposed as "*Infant formula products*" and follow–on formula was included within the draft Standard.

Issue

The New Zealand Infant Formula Marketers' Association (NZIFMA) objected to follow–on formula being included within the scope of the draft standard.

Assessment

The NZIFMA specifically, was concerned that the proposed title "*Infant formula products*" and scope of the draft Standard may potentially imply that *all* formula covered by this standard, including follow–on formula, should be considered within the category of infant formula (which is specifically defined as a breast–milk substitute in the WHO International Code of Marketing Breast–Milk Substitutes (WHO Code)). The NZIFMA was further concerned that this implied the need for follow–on formula to conform to the present definition of infant formula in the draft standard as the principal source of food/nourishment for infants. The NZIFMA based their objection on the articles of the WHO Code, which they contend, exclude follow–on formula unless it is presented as a breast–milk substitute.

[*Ed note: It is not proposed to discuss in detail the interpretation of the WHO Code in this report other than to point out that the Code is interpreted and given effect differently in Australia and in New Zealand such that New Zealand manufacturers have agreed that advertising of follow–on formula could occur, but that Australian manufacturers have agreed not to advertise follow–on formula. The Authority reiterates its acceptance of the status quo in relation to the interpretation of the WHO Code in each country.]*

Recommendation

At Full Assessment (1995) the name of the standard was proposed as *'Human milk substitutes*'. This name was highly unpopular and '*infant formula*' as proposed at Preliminary Inquiry was much preferred. Therefore no change to the name of the standard is recommended. It is also proposed to maintain the inclusion of follow–on formula, but to amend the definition of follow–on formula (refer to Item 1.4 below).

1.2 Definition of infant formula product

Proposed at Preliminary Inquiry

The definition given at Preliminary Inquiry was "*a product based on milk or other edible food constituents of animal or plant origin and which is intended to be, and is suitable for use as, the principal source of nourishment for infants*".

Issues

One manufacturer found the definition too prescriptive stating that it did not allow for any innovative modifications. Some support was given to the current and draft Codex definition for infant formula, especially the last part of the definition "*which has been proved for infant feeding*", partly as a means to ensure safety of products. A contrary view was that the latter part of the definition should read, "*which is intended as the principal source of food for infants who are not breastfed*". The **NZ Ministry of Health** pointed out that some formula categories within the draft standard would not necessarily be *the principal* source of food/nourishment.

Assessment

To address concerns and to include an explicit nutritional outcome, it is proposed to modify the definition to "a product based on milk or other edible food constituents of animal or plant origin and which is ***nutritionally adequate to serve as****, the principal* ***liquid*** *source of nourishment for infants"*

Recommendation

To modify the definition to "*a product based on milk or other edible food constituents of animal or plant origin and which is* ***nutritionally adequate to serve as****, the principal* ***liquid*** *source of nourishment for infants"*

1.3 Definition of infant formula

Proposed at Preliminary Inquiry
The definition given at Preliminary Inquiry was "*an infant formula product that is represented as being suitable as the principal source of food for infants*".

Issues

Comments focused on criticising use of the term 'suitable as'; on including reference to infants who are not breastfed; suggesting the latter part of the Codex definition for infant formula; and strengthening *principal* source to *sole* source for infants in the first 4 to 6 months of life.

Assessment

It is proposed to modify the definition consistent with the direction of the draft Codex standard for Infant Formula to become: "an infant formula product represented as *a breast milk substitute for infants and which satisfies the nutritional requirements of infants aged up to four to six months"*.

Recommendation

To modify the definition to: *"an infant formula product represented as a breast milk substitute for infants and which satisfies the nutritional requirements of infants aged up to four to six months"*.

1.4 Definition of follow–on formula

Proposed at Preliminary Inquiry

The definition given at Preliminary Inquiry was "*an infant formula product represented as being suitable as the principal source of food for infants aged over six months*".

Issues

Most comments criticised the use of the term 'the principal source' as being inappropriate for infants from six months. There was general support for the Codex definition that refers to "liquid part of the weaning diet". One contrary comment suggested "intended as a suitable source of food in conjunction with complementary foods, only for infants older than six months who are not being breast fed".

Assessment

While not explicitly discussed at Preliminary Inquiry, it is reasonable to extend the applicability of follow–on formula to young children to align with current market practice (which sometimes provides guidance on the intake for children over 12 months), and the Codex standard for follow–on formula. However, it is not necessary to include specific provisions to do this, as there is no impediment to manufacturers providing additional information about a product, including information about ideal use and target population.

Recommendation at Inquiry

It is proposed to modify the definition consistent with the direction of the Codex standard for Follow–up Formula to become: "an infant formula product represented as *either a breast–milk substitute or replacement for infant formula and which constitutes the principal liquid source of nourishment in a progressively diversified diet for infants aged from six months"*.

Industry issue at Inquiry

That follow–on formula be defined as being intended as 'part of progressively diversified diet for an infant beyond six months of age' and not as a breast milk substitute.

Assessment

Health professionals advise that the Australian and New Zealand practice is different to that in Europe, since Australian and New Zealand mothers breastfeed their babies beyond the age of 6 months, whilst in Europe this is not common. It was noted that the current Codex standard is a European standard. Health professionals advise that locally 'follow–on formula' is perceived and used as a breast milk replacement for babies over 6 months of age. It was also noted that presentation of these products promotes their use as a replacement for infant formula, by use of:

- similar pack design;
- proprietary names that signify 'second stage';
- similar bottle preparation instructions; and
- adjacent placement on supermarket shelves.

Recommendation at Supplementary Final Assessment.

The definition in the proposed standard be retained.

1.5 Definition of Infant

Proposed at Preliminary Inquiry

The definition given at Preliminary Inquiry was "*Infant means child under the age of 12 months"*.

Issue

Maureen Minchin (IBCLC) suggests that a definition for infant should be included in the standard. She suggests the following definition.

"An infant is a person under 12 months of age."

Assessment

The standard already contains a definition of an infant in Clause 1. The definition in the standard has the same intent as the definition suggested by Maureen Minchin.

Recommendation

The drafting should remain as proposed at Preliminary Inquiry.

1.6 Lactose Free and Low Lactose

Proposed at Preliminary Inquiry

The definition given at Preliminary Inquiry was *"'Lactose–free formula' and 'low lactose formula' mean infant formula products represented as being the principal source of food for lactose intolerant infants*".

Issue

Maureen Minchin (IBCLC) suggests that the definition for 'lactose–free' or 'low lactose' formula should highlight the temporary nature of the condition and the short–term nature of the formula use. 'Lactose –free' or 'low lactose' formula means infant formula products with reduced lactose content for short–term use by infants with medically diagnosed problems with lactose malabsorption.

Assessment

The reasoning **Maureen Minchin (IBCLC)** has given for inclusion of the temporary nature of lactose malabsorption in the definition of 'lactose–free' and 'low lactose' formula, is to educate consumers about the temporary nature of the condition. However, the definition of 'lactose–free' and 'low lactose' formula will not appear in the label of 'lactose–free' and 'low lactose' products. It only appears in the Food Standards Code in order for manufacturers and enforcement agencies to correctly name and identify the product. Therefore, there is no need for a statement on the temporary nature of lactose malabsorption in the definition of 'lactose–free' and 'low lactose' formula. Medical practitioners and/or health workers could supply this information to consumers.

Changes recommended for other definitions in this standard mean the definition for lactose free and low lactose formulas should also be amended for consistency.

Recommendation

The definition of 'lactose–free' and 'low lactose' formula is amended to *"lactose free and low lactose formulas mean infant formula products which satisfy the needs of lactose intolerant infant"*.

1.7 Pre–term Formula

Proposed at Preliminary Inquiry

The definition given at Preliminary Inquiry was " '*Pre–term formula' means infant formula product represented as suitable, as the principal source of food, for infants of less than 37 weeks gestation*".

Issues

Bristol–Myers Squibb Australia Pty Ltd, Wyeth Australia Pty Ltd and Nestle Australia Ltd state that in regard to 'pre–term formula' they recommend a more appropriate definition would be based upon the weight of the infant or at least include the weight of the infant. The amount of pre–term formula given to an infant is determined by the weight of the baby. Suggested categorisation:

- extremely low birth weight infant (ELBW) as less than 1000 g; and
- pre–term as 1000 g – 1750 g in weight.

InforMed Systems Ltd suggest the definition of a pre term formula should be for infants less than 38 weeks gestation, since 38 – 42 completed weeks is defined as a term infant.

Maureen Minchin (IBCLC) states pre–term formula means infant formula products specially modified / intended for use by infants of less than 36 weeks gestation.

Assessment

The type and amount of infant formula product given to a pre–term baby is determined by the weight of the baby and biomedical parameters rather than the gestational age. The pre–term category was intended to provide for infants with special needs due to prematurity or low birth weight whilst providing scope for a range of formulations.

Weight for height tables for normal infants start at 2500 g for the 5th percentile weight at birth. Therefore, it seems reasonable to define a low birth weight infant as an infant below 2500g at birth. However for the purposes of setting a food standard category for infants born prematurely or who are of low birth weight where the choice of formula is decided by medical specialists, it is not necessary to include specifics about age or weight in the definition. Manufacturers would also be in the best position to state the most appropriate use for the formula. Therefore it is recommended that the definition be amended to refer in a general way to prematurity and birth weight.

Recommendation

Amend the drafting to define the age and weight in general terms such as "*a pre–term formula means an infant formula product specially formulated to satisfy particular needs of infants born prematurely or of low birthweight*".

1.8 Protein substitute

Proposed at Preliminary Inquiry

The definition given at Preliminary Inquiry was " '*Protein substitute' means L–amino acids and / or the hydrolysate of one or more of the proteins on which infant formula product are normally based*".

Issue

Abbott Australasia Pty Ltd suggest the use of specific terms such as hydrolysates or amino acids instead of the proposed term protein substitutes.

Assessment

The term 'protein substitutes' covers a range of protein extracts. It would be difficult to list them all. Using the class name is the best option for use in the standard.

Recommendation

The drafting remain as proposed at Preliminary Inquiry.

1.9 Soy–based Formula

Proposed at Preliminary Inquiry

The definition given at Preliminary Inquiry was " '*Soy–based formula' means infant formula product in which soy protein isolate is the sole source of protein*".

Issue

Maureen Minchin (IBCLC) suggests that it may limit the definition of soy protein formula if it only mentions soy protein isolate.

Assessment

Soy protein isolate is the only fraction of soy that is permitted in soy formula.

Recommendation

The drafting remain as proposed at Preliminary Inquiry.

1.10 Fat Modified

Proposed at Preliminary Inquiry

A definition of 'fat modified' was not included in the draft standard at Preliminary Inquiry.

Issues

The International Formula Council expressed concern about the term 'fat modified' and wish to clarify that this term has been dropped.

Abbott Australasia Pty Ltd indicate that they believe the definition 'fat–modified' is still inappropriate due to the fact the there are other means of modifying the lipid component than through the use of medium chain triglycerides.

Assessment

The term ‘fat modified’ is no longer used in the standard.

2. DIVISION 2 – CALCULATIONS

2.1 Potential Renal Solute Load (PRSL)

Proposed at Preliminary Inquiry

It was proposed at Preliminary Inquiry to control the PRSL of formula instead of prescribing the ‘osmolality’. PRSL is a more suitable parameter of formula to indicate risk to infants for dehydration illness in certain relatively common adverse circumstances to which infants are prone. Submissions were received about the prescribed calculation method, the PRSL values and also the justification for the prescription of the PRSL given it is not prescribed by the Codex standard (see also Item 6.3).

2.2 Calculation of Potential Renal Solute Load

Proposed at Preliminary Inquiry

5. The potential renal solute load must be calculated as follows:

Potential renal solute load in mOsm/100 kJ
= [Na (mg/100 kJ) /23] + [Cl (mg/100 kJ) /35] + [K (mg/100 kJ) /39] + [P(mg/100 kJ)/31] + [protein (mg/100 kJ)/175].

Issue

The calculation for estimating the PRSL provides for total phosphorus content. Fomon and Ziegler (1999), the original authors of this calculation, have recently revised it to exclude ‘unavailable phosphorus’[1].

Assessment

Unavailable phosphorus is that part of the phosphorus content of an infant formula likely to be bound to phytate. Phytate–phosphorus is excreted in the faeces rather than absorbed into the blood supply and thus does not contribute to the renal excretion load.

Fomon and Ziegler (1999) have estimated that one third of the total phosphate content of a soy–based formula is likely to be bound to phytate and hence unavailable for metabolic use. Therefore they claim 1/3 of the total phosphorus of a soy–based formula will not contribute to renal excretion load. Phytate is present in cereals, legumes and some nuts. These foods could be potential ingredients for infant formula and therefore may also impact on available phosphorus content.

[1] Fomon AJ and Ziegler EE (1999) Renal solute load and potential renal solute load in infancy. J Pediatr 134: 11–4.

Currently these foods are not significant ingredients of infant formula and hence will not be factored into the estimation of 'unavailable phosphorus' for the calculation of PRSL at this time. It is accepted that the unavailable phosphorus content of formula should be excluded from the estimation of PRSL for infant formula products.

The Fomon and Ziegler calculation uses nitrogen rather than protein. The protein value was included at Preliminary Inquiry as it was thought to be easier for manufacturers but it seems nitrogen is the more useful for analytical purposes. Therefore, it is recommended that the nitrogen value be included in the calculation instead of the protein value.

Recommendation

That the equation for calculation of PRSL be amended to exclude the unavailable phosphorus content of infant formula products and to substitute nitrogen for protein. The calculation recommended is

Potential renal solute load in mOsm/100 kJ
= [Na (mg/100 kJ) /23] + [Cl (mg/100 kJ) /35] + [K (mg/100 kJ) /39] + [P_{avail} (mg/100 kJ)/31] + [N (mg/100 kJ)/28].
Where P_{avail} is P of milk–based formulas + 2/3 P of soy– based formulas.

2.3 Protein Quality

Proposed at Inquiry

At Full Assessment (1995) it was proposed that the protein in infant formula be the same quality as that in human milk. Human milk amino acid levels were referenced in the draft standard for use in complying with this requirement. The values proposed were those recommended by the FAO/WHO in 1985 and again in the 1991 report on Protein Quality Evaluation[2]. These protein quality values are reported in the standard way as 'g amino acid per 100g protein' (g/100g).

The FAO/WHO reference values summed the values for cysteine and methionine as well as for phenylalanine and tyrosine, however submissions from health professionals indicated it was necessary to include a minimum value for cysteine as this amino acid is considered essential for very young infants. At Preliminary Inquiry (May 1999), in response to this advised potential health need for cysteine, ANZFA included values for these four individual amino acids as reported by Sarwar et al[3]. In addition, an amino acid score of 0.8 was proposed, as it was believed this would allow manufacturers to meet the recommended protein quality levels within the minimum protein content. This approach was consistently maintained and was included in the draft standard as proposed at Inquiry (Nov 1999).

Issues at Preliminary Inquiry

Wyeth Australia Pty Ltd submit that they would need to reformulate to meet the amino acids levels which are set in the standard and that these levels are unsubstantiated.

[2] Protein Quality Evaluation (1991) Report of the Joint FAO/WHO Expert Consultation. FAO Rome
[3] Sarwar G at al (1996) Use of amino acid profiles of pre–term and term human milks in evaluating scoring patterns for routine protein quality assessment of infant formulas. J AOAC Int 79 N 2 p 498.

Abbott Australasia Pty Ltd submitted that the valine content of 5.5 g/100 g of protein is still much higher than the reference cited by the European Union (4.5 g /100 kJ).

Industry issue at Inquiry

Industry argued that to allow for manufacturing practicalities the amino acid reference values should be expressed per 100 kJ of energy rather than per 100g protein. In addition, industry disagreed with the proposed amino acid profile specified (i.e. FAO/WHO 1991), particularly the values for cysteine, histidine, phenylalanine, tryptophan and tyrosine. Industry suggested that the amino acid profile from the European Commission (EC) Directive (91/321/EEC), including being able to sum cysteine and methionine, be used in Standard 2.9.1.

Assessment

The issue of protein quality has been the most contentious and difficult to resolve. Industry has argued strongly against the proposed breast milk reference values for a number of reasons namely, inconsistency with international regulations, significant reformulation of current products required to meet the proposed values and the lack of evidence to support the safety of the proposed values versus the current regulations that have a history of promoting normal growth and development in formula fed infants.

Industry commissioned Makrides et al [4] to conduct *inter alia* a review of amino acid profiles, which in addition to favouring a lower reference value for cysteine, concluded that '*the standard of clinical trials in the area of protein quality and growth is poor and offers little guidance for recommendations for infant diets'*.

This lack of clear scientific evidence is an inherent difficulty in resolving this issue as health professionals have indicated support for the expression of protein as g/100g protein because of concerns of the potential health risks associated with higher levels of poorer quality protein in infant formula.

Reference Amino Acid Profile

The amino acid profile of human milk has been studied by a number of researchers in the last 30 years. In 1991 the FAO/WHO commissioned an Expert Consultation on Protein Quality Evaluation. This consultation reaffirmed the amino acid profile for breast–milk as determined by FAO/WHO in 1985. ANZFA recommended this profile as expressed as g/100g protein (Schedule 1) for inclusion in the draft standard at Full Assessment.

The EC has also used human milk protein quality (expressed in mg/100 kJ) as the basis for its Directive but set the levels using data from the 1970s. The 1991 FAO/WHO Expert Consultation noted that the review of a 1970 FAO publication on amino acid content of foods revealed considerable shortcomings in the FAO data especially for cysteine, tryptophan and methionine and concluded these earlier recommendations needed revision.

[4] Makrides M et al (2000) Report to the Infant Formula Manufacturers Association of Australia – "Review of amino acid profiles, zinc to copper ratios and essential fatty acid composition of infant formulas

Additionally Dr Sarwar Gilani [5] recently compared literature reports on the amino acid composition of human milk with the amino acid values reported by FAO/WHO (1991) and EC (1991). This comparison indicated that the literature supports the use of the FAO/WHO values for assessing protein quality in foods for infants less than one year of age.

These values were considered by a range of stakeholders at a forum to consider industry issues in May 2000 and again by members of the ANZFA External Team in June 2000. Schedule 1 from the Full Assessment was re–tabled at the External Team meeting. This schedule which uses the values recommended by the WHO in 1991 summed cysteine and methionine and also summed phenylalanine and tyrosine. It was agreed that this Schedule would be recommended for re–inclusion in the standard.

Cysteine needs of infants

The enzyme cystathionase facilitates the conversion of methionine to cysteine. Many researchers report that cystathionase activity is insufficient in premature infants and some term infants. Atkinson and Lonnerdal[6] note that cystathionase levels appear to reach mature levels when infants are about 3 months of age. Therefore, cysteine is considered to be 'essential' for some infants such as premature or low birth weight infants. Therefore it is important to ensure a cysteine content of formula, especially those prepared for very young or premature infants as the need for cysteine may not be as crucial for full term infants.

Cysteine level in human milk for the setting of a reference value

A minimum cysteine level, based upon the level in human milk, is proposed for the standard to ensure infant formula products meet the needs of very young infants.

The WHO/FAO recommendations provide for cysteine in combination with methionine and therefore do not provide an individual recommendation for cysteine. The level of cysteine proposed at Preliminary Inquiry (2.45g cysteine /100g protein) was that reported by Sarwar to be the level in transitional human milk i.e. milk from mothers who had given birth in the previous few weeks. Industry challenged this value on the basis that it was from transitional milk rather than from mature milk for older infants. Given the public health interest in relation to very young babies for whom cysteine may well be considered an 'essential' nutrient, this choice was justified.

Industry submitted an assessment of literature reports on the cysteine value of human milk and claimed the mean value from that literature review was 1.7 g /100g protein[7]. However this report failed to report on key papers which assessed human milk amino acid content such as the Sarwar paper (cysteine of 2.45± 0.15 g/100g protein for transitional milk, 2.51 ± 0.42 for pre–term milk g/100g protein), the Darragh and Moughan[8] paper (8. g protein/L and 310 mg cysteine /L) and Davis TA et al [9] (cysteine of 20.2± 2.6 mg/g total amino acid).

[5] Dr Sarwar, personal communication, 2001
[6] Atkinson SA and Lonnerdal B. (1989) Protein and non–protein nitrogen in human milk. CRC Press Inc Boca Raton, Florida, USA
[7] Makrides M et al (2000) Report to the Infant Formula Manufacturers Association of Australia – "Review of amino acid profiles, zinc to copper ratios and essential fatty acid composition of infant formulas.
[8] Darragh AJ and Moughan PJ. (1998) The amino acid composition of human milk corrected for amino acid digestibility. Br J Nutr 80: 25–34.
[9] Davis et al Amino acid composition of human milk is not unique. (1994) J Nutr 124: 1126–1132

These recent papers generally had assessed the cysteine content to be higher than the mean derived by the Makrides team for the submission by industry.

Darragh and Moughan analysed human milk from New Zealand women in their 10–14th weeks of lactation. They found the cysteine content to be 20% higher that previously reported values and attributed this higher level to the correction for losses due to acid hydrolysis before the amino acid analysis. The Darragh and Moughan values when calculated to g/100g protein show cysteine content of the order of 3.5 g/100g protein or higher than the Sarwar transitional milk values from Canadian women. It is not proposed to incorporate the Darragh and Moughan values into the standard but they indicate that Sarwar values are not 'outliers' as claimed by industry.

Methods of analysis for cysteine

Industry claim that the values considered above are reported from non–standard methods of analysis. The method of analysis used to estimate cysteine content has been fairly standard for about 15 years (personal communication with Mr C Rayner, Agriculture Victoria). This method requires pre–oxidation, hydrolysis and measurement of free amino acid (cysteine) using HPLC. Whilst as with all analytical methods there will be variation in results reported from laboratory to laboratory, the method is sufficiently well used for there to be no need to prescribe a method of analysis in the Food Standards Code for cysteine.

Cysteine level in current formulations

The level of cysteine proposed at Preliminary Inquiry (2.45g cysteine /100g protein) was able to be met by some manufacturers of Spanish infant formulas[10] and was therefore considered achievable as some formula are currently complying with the proposed level.

Industry did not provide ANZFA with data about the amino acid content of formula on the Australian or New Zealand market, so ANZFA was not able to assess the real extent of the problem for industry. Therefore ANZFA requested a Professor of Biochemistry from the External Advisory Group to review the amino acid content of the source ingredients (whey and casein) using amino acid sequence data and data supplied by industry on whey:casein ratios and total protein content of various products. This assessment indicated formula prepared to 60:40 whey: casein ratios met the minimum proposed amino acid content for all prescribed amino acids, including cysteine. The high casein based products, such as follow–on–formula varieties met the proposed minimum amino acid contents for all amino acids, except cysteine. Cysteine is not considered to be an essential amino acid for infants 6 months and over.

[10] Alegria A et al (1999) Amino acid contents of infant formulas. J Food Comp Anal 12: 137–146.

Cysteine level for the reference value in the standard

The 1998 Life Sciences Research Office (LSRO)[11] report commissioned by the US Food and Drug Administration, stated that although they made recommendation that the sulphur containing amino acids (i.e. cysteine and methionine) could be summed, '*it should be noted that in no case should the requirement be met with only one of the respective constituents. Because the ratio of each of these combinations of amino acids is approximately 1:1 in human milk, ratios that exceed 2:1 or 1:2 are probably unbalanced and should not be used without appropriate testing for adequacy'.*

The ANZFA External Advisory Group agreed that a minimum level of 1.9 g cysteine per 100g protein be provided for infants under 6 months. This would adjust to a reference value for human milk of 2.4g cysteine per 100g protein (using an amino acid score of 0.8) if one should be included. This level is consistent with the recommendations of the LSRO report in relation to the ratio of sulphur containing amino acids as given the reference value for the sulphur containing amino acids (i.e. sum of cysteine and methionine) of 4.2g/100g protein the minimum ratio would be 1.2.

At a further meeting with industry in August 2000, evidence was presented that the Zlotkins group[12] showed that pre–term infants given parenteral nutrition lacking in cysteine grew well and that the addition of cysteine to the infants' regimen did not improve growth or nitrogen retention. Attention was also drawn to the LSRO report's recommendation on combining the cysteine and methionine values and the recommended ratio. The stakeholders considered, on the basis of industry data, that by adopting this additional parameter, it might be possible to retain the current form of protein expression and not shift to expression of amino acids/100 kJ.

Therefore, new industry data and previously provided average values for formula products were re–examined to test the ratio approach. This was shown not to be feasible unless the ratio was lowered to 1:4, cysteine to methionine. Rather than introduce a new approach, the absolute minimum value for cysteine was reduced to 1.1 mg /100g protein to apply to infant formula products suitable from birth. On the basis of submitted industry data, this level does not require manufacturers to add cysteine but provides infants with a source of cysteine.

Units of expression

The protein content permissions proposed for the draft standard are consistent with those of Codex, that is, a protein range of 0.45– 0.7 g protein/100 kJ for formulas prepared for the youngest infants and 0.45– 1.3 g protein/100 kJ for infants over 6 months of age.

Protein content and protein quality are interrelated in determining the biological use of a food protein source. Whilst the amino acid components are utilised for growth and maintenance of tissues, any excess is required to be partially metabolised and excreted. Therefore, the protein content and protein quality of an infant formula contributes to the load on the infant's kidneys.

[11] Raitrn DJ et al (1998) Assessment of nutrient requirements for infant formulas. J Nutr Supplement Vol 128 no 15–Report prepared for the Centre for Food Safety and Applied Nutrition, Food and Drug Administration, Department of Health and Human Services, Washington DC

[12] Zlotkin SH et al (1981) Cysteine supplementation to cysteine – free intravenous feeding regimes in new born infants. Am J Clin Nutr 34: 914–923

Protein quality is traditionally expressed in units of amino acids per total protein content i.e. g/100g protein and Schedule 1 from Full Assessment is expressed in this way and allows for the summation of cysteine and methionine, and phenylalanine and tyrosine levels. Expression as g amino acids per 100 g protein was accompanied by a requirement that all of the protein in the formula be at least 80% of the quality of the reference human milk profile (i.e. Schedule 1). ANZFA maintained the opinion that the needs of formula fed infants were best served by a protein profile expressed in g/100g protein that closely follows that of human milk.

Industry however stated that to meet these values, free amino acids would need to be added to some lower quality formula, which would potentially incur risks if not first subjected to clinical trial. ANZFA disputed this generalised claim. The current Standard R7 and the international standard (Codex), and most international regulations permit the addition of L–amino acids to improve the quality of the protein in the formula. Safety is determined by the quality and amounts of amino acids added and Industry are expected to use only amino acids in safe forms. It was noted that free amino acids are already used in special purpose formulas and these are apparently safe in that context.

However in acknowledging that this approach was different to existing international standards, ANZFA sought the assistance of Dr Sarwar Gilani (Health Canada). Dr Sarwar, having expertise in the area of protein quality and infant formula, was chairing one of the FAO/WHO/UNU Working groups on reviewing protein and energy requirements in Rome in July 2001. Dr Sarwar kindly agreed to raise the issue of infant formula and the expression of protein quality at the working group meetings as a means of establishing a consensus from working group participants.

Following the meetings, Dr Sarwar reported that discussions, albeit limited, provided no conclusive evidence to support the expression of protein quality by grams amino acid / 100 grams of protein (g/100g protein) over the more common expression by energy value (mg amino acid / 100 kJ) for regulatory purposes.

Consequently, due to the apparent lack of conclusive evidence to favour the expression of protein quality as g amino acid / 100 grams protein and the lack of precedent for this requirement in other international regulations, ANZFA believes it is no longer able to maintain its position on the expression of protein quality. It is therefore recommended that the amino acid reference values as proposed at Full Assessment (Schedule 1) be expressed as mg / 100 kJ and including the summation of cysteine and methionine and phenylalanine and tyrosine.

Following the decision to change the expression of protein quality to milligrams amino aicd/100 kJ, a minimum level of cysteine was still considered important. Based on the conversion of the proposed level of 1.1g/100g protein to 4.95 mg /100 kJ, ANZFA is proposing a minimum level of cysteine of 6 mg/100 kJ, which corresponds to the level required by the EC and equates to an approximate minimum ratio of cysteine to methionine of 1:2 in line with LSRO.

Recommendation at Supplementary Final Assessment

It is recommended that:

1. the values proposed at Full Assessment, i.e. Schedule 1 that provide reference values for human milk, be expressed as mg amino acid/100 kJ and be reinstated in the draft standard;

2. the standard no longer permits deviation from reference values as per an amino acid score because an absolute minimum has been set instead; and

3. in allowing the summation of cysteine and methionine, and phenylalanine and tyrosine, infant formula products should provide a minimum cysteine content (6 mg/100 kJ) and a minimum level for phenylalanine (17 mg/100 kJ).

The future

Refinement to regulations for protein quality will be desirable in the future to capture the evolving knowledge about the protein profile of human milk, the bioavailabilities of amino acids from these human milk proteins and the technological advances in the development of the proteins that mimic the bioactivity of the human milk proteins.

It is anticipated that ANZFA will review the issue of protein quality following the outcomes of the joint FAO/WHO Expert Consultation on Human Protein Requirements scheduled to take place in April 2002 and developments in the Codex draft standard for infant formula.

3. DIVISION 3 – GENERAL COMPOSITIONAL REQUIREMENTS

3.1 Restrictions and prohibitions – Clause 7

Proposed at Preliminary Inquiry

A vitamin, mineral, food additive or nutritional substance must not be added to infant formula unless:

(a) expressly permitted by this standard; or
(b) it is included in the infant formula as naturally present in an ingredient of the infant formula product.

An infant formula product must not contain any detectable gluten.

Issues

InforMed Systems Ltd queried if the proposed list of 'additives' at Clause 7 to be permitted in infant formula was more restrictive than Codex, as Codex does not specify precise forms of additives in their draft standard.

Assessment

This issue was addressed at Preliminary Inquiry. Specification of forms of vitamins, minerals, food additives and nutritive substances is intended to ensure substances other than 'foods' which are added to formula are safe and suitable.

This clause also controls the use of potential novel ingredients by ensuring independent safety assessments are carried out before these substances are used in formula sold in Australia and New Zealand (refer to Item 8.2 – Novel Foods).

Recommendation

Clause 7 be retained as prepared at Preliminary Inquiry.

3.2 Permitted optional nutritive substances – Clause 8

The term *'nutritive substance'* has been defined in the Preliminary Provisions (Standard 1.1.1) of the joint Food Standards Code (Volume 2), therefore the term *'nutritional substance'* used at Preliminary Inquiry has been changed at Inquiry to *'nutritive substance'*.

Proposed at Preliminary Inquiry

The draft standard provides for certain nutritive substances to be added to infant formula, in one or more of the forms specified, on a voluntary basis. Maximum permitted amounts of these nutritive substances are provided and a minimum specified level, which must be met in order to make a claim.

3.2.1 Error in draft standard for Carnitine, Choline and Inositol.

The maximum level included in the table to Clause 8 for carnitine, choline and inositol were incorrect as the values set at Full Assessment were included in the draft standard rather than the revised levels agreed at Preliminary Inquiry. Therefore, the following correct recommended maximum levels as reflected in the Preliminary Inquiry report are recommended for the standard.

	Maximum permitted amount per 100 kJ
Choline	7.1 mg per 100 kJ
Carnitine	0.8 mg per 100 kJ
Inositol	9.5 mg per 100 kJ

3.2.2 Carnitine

Proposed at Preliminary Inquiry
The range of carnitine permitted to be added to an infant formula product is 0.21–0.42 mg per 100 kJ.

Issues

The **Dairy Goat Co–Operative (NZ) Ltd** submitted that the maximum level should be deleted or raised to accommodate the innate carnitine level of goat milk. **Nestlé Australia Ltd** also submitted that the range for carnitine is too narrow to provide for the innate carnitine levels of the base milk ingredients.

Assessment

The draft standard only regulates carnitine in the circumstance when carnitine is 'added' as an ingredient to the formula. In that case, the regulation provides for 'total carnitine'. The regulation is intended to provide for the addition of carnitine to formula such as soy–based or amino acid based which do not have innate carnitine levels. As there is no need and hence no justification for adding carnitine to a milk–based formula, this provision should not apply to formula based upon either cow or goat milk.

Recommendation

An editorial note be included in the relevant clause to the effect that "*it is not the intent of the standard to regulate the maximum nutritive substance level of formula in the case when the nutritive substance is not added as an ingredient to the formula*".

3.2.3 Choline

Proposed at Preliminary Inquiry

The range of choline permitted to be added to an infant formula product is 1.7–5.4 mg per 100 kJ.

Issue

InforMed Systems Ltd submits that choline is classified as an essential nutrient and therefore should be listed under 'vitamins'.

Assessment

This issue was addressed at Preliminary Inquiry where it was noted that the dietary use for choline is still inconclusive and as it has not been declared an essential nutrient would be regulated as an optional ingredient.

Recommendation

It is recommended choline continue to be regulated as an optional ingredient.

3.3 Nucleotides – Clauses 8 and 9

Proposed at Preliminary Inquiry

The draft standard provides for 5 nucleotides not previously permitted in infant formula to be added on a voluntary basis. Maximum total and individual levels of nucleotides are provided and a minimum specified level must be met in order to make a claim.

Issues

A lack of standardised methodologies for the analysis of nucleotides has resulted in wide ranges of values being reported for the individual nucleotide content of human milk.

Bristol Myers Squibb Australia Pty Ltd commented that the permissions to add nucleotides should be included in the additive standard and cross–referenced for use in infant formula. This includes any necessary purity standards. **Wyeth Australia Pty Ltd** commented that the moisture specification and bacteriological profile might be redundant, as they are included under Division 5–General Microbiological Requirements. **Abbott Laboratories (NZ) Ltd** and **Abbott Australasia Pty Ltd** asked that the specifications for the 5 nucleotides be increased to those proposed in the most recent LSRO report. The **Nursing Mothers' Association of Australia** commented that the safety of all optional ingredients should be established before being permitted in infant formula.

Assessment

The levels of nucleotides permitted in the draft standard have been based on the European Commission (EC) Directive. However more recent research would seem to support that the levels in the EC Directive actually underestimate the levels of nucleotides in breast milk. The recent LSRO report recommended a maximum content of [nucleotides and nucleotide precursors] of 16 mg/100 kcal (3.8 mg/100 kJ), a value similar to the upper level reported for human milk. The current draft standard permits up to a maximum total nucleotide level of 1.2 mg /100 kJ.

There are currently believed to be 13 different nucleotides present in human breast milk. At Preliminary Inquiry it was suggested that until further evidence of safety and efficacy was available, only 5 of the 13 nucleotides be permitted for use in infant formula. Therefore it is recommended that the level proposed at Full Assessment and at Preliminary Inquiry for the 5 specified nucleotides be retained. The maximum total nucleotide content could be raised to the level the LSRO of 3.8 mg/100 kJ.

It was commented that nucleotide specifications should not be contained in an infant formula products standard. It was never intended that these specifications would be in the infant formula standard. As outlined at Preliminary Inquiry, these specifications for nucleotides will be included in Standard 1.3.4 – Identity and Purity. In addition, the microbiological specifications will be deleted from this standard, as these are incorporated under general microbiological requirements (Standard 1.6.1) with which infant formula must comply.

Recommendation

That the proposed maximum permitted total nucleotide content in infant formula be increased to 3.8 mg/100 kJ as recommended by the LSRO report.

3.4 Food Additives

Proposed at Preliminary Inquiry

At Preliminary Inquiry, ANZFA proposed to include the Codex provisions for food additive use in infant formula, with adjustment for the recommendations by the European Commission's Scientific Committee on Food (SCF).

3.4.1 Carrageenan

Issues

The Victorian Food Safety Council Food Standards Sub–committee and **the NZ Ministry of Health** expressed some concerns regarding the safety of the food additive carrageenan. Both submissions requested that further consideration be given, especially as the additive is still under review internationally.

The **International Formula Council** supported the proposal. **InforMed Systems Ltd** suggested that the proposed levels of carrageenan in hydrolysed and amino acid based formula were more restrictive than Codex; and that the standard for infant formula should align with Codex recommendations.

Assessment

Carrageenan is currently permitted in infant formula in New Zealand, with no maximum limit prescribed. Under the current standard R7, infant formula may contain not more than 0.3g per litre (0.03%) of carrageenan, in the case of liquid milk–based and soy–based varieties, and not more than 1.0 g per litre of carrageenan in the case of liquid hydrolysed protein–based and amino acid–based types.

At Full Assessment, ANZFA proposed not to permit the addition of carrageenan in infant formula. At Preliminary Inquiry, ANZFA undertook an assessment of carrageenan. Since the Preliminary Inquiry report was written, no new evidence has been presented. As concluded at Preliminary Inquiry, there is not considered to be sufficient evidence of potential adverse effects of carrageenan to restrict its use in infant formula.

ANZFA proposes to permit no more than 0.03g of carrageenan per 100 mL of liquid infant formula product, and no more than 0.1g of carrageenan per 100 mL of infant formula product based upon protein substitutes for a specific dietary use.

Recommendation

The provisions proposed at Preliminary Inquiry be retained.

Permission to add carrageenan

Issue

Nestle Australia Ltd commented that the drafting at Clause 11(3) does not give permission for the addition of carrageenan.

Assessment

ANZFA has amended the drafting to '… *may contain not more than* …' to ensure permission for addition of carrageenan to infant formula is provided.

Recommendation

The permission for the use of carrageenan in liquid infant formula products should remain as proposed at Preliminary Inquiry. However, the words 'must not contain more than' in Clause 11 Subclause 3 should be amended to '*may contain not more than*'.

3.4.2 Citric esters of mono– and di–glycerides of fatty acids (E472c)

Issue

Nestle Australia Ltd requested the inclusion of the food additive citric esters of mono– and di–glycerides of fatty acids for the preparation of formula based on extensively hydrolysed protein, as this was included in the European Commission (EC) Directive for Infant Formula in November 1998.

Assessment

The Scientific Committee on Food (SCF) of the European Commission considered citric acid esters of mono– and di–glycerides of fatty acids (E472c) to be safe for use in infant formula based on extensively hydrolysed protein at a level of 0.9 g/100 mL.

Recommendation

Therefore it is recommended that citric acid esters of mono– and di–glycerides of fatty acids (E472c) be permitted up to a level of 0.9 g/100 mL in formula based on extensively hydrolysed protein.

3.4.3 Mono– and di–glycerides of fatty acids (E471)

The names of the mono– and di– glycerides listed in the Tables at Clauses 11 and 42 are class names rather than the specific food additives included under INS number 471. The appropriate food additives numbers have been added to the table for clarification.

3.4.4 Diacetyl tartaric acid esters of mono and diglycerides (DATEM) (E472e)

The value for DATEM in the Table to Clause 42 proposed at Preliminary Inquiry included a typographical error that created an error of a factor of 10 in the table. The figure in the table was to be that recommended by the SCF for infant formula based upon protein substitutes. The SCF recommended 0.4 g/L, which should have been included in the Table as 0.04 g/100 mL.

Recommendation:

The correct figure of 0.04 g/100 mL for DATEM be included in the Table to Clause 42. The food additive number E472e should also be included in the Table to Clause 42.

3.4.5 Locust bean gum

Proposed at Preliminary Inquiry and Inquiry

Permission to use locust bean gum to a maximum level of 0.1 g/100 mL.

Industry issue

Industry proposes the maximum locust bean gum level be increased from 0.1 to 0.7 g/100 mL.

Assessment

ANZFA has relied on reports from the Scientific Committee on Food (SCF) of the European Commission for its assessment of food additives. The term of reference for this committee is:

'To consider the safety–in–use of certain additives in infant formulae, follow–on formulae and weaning foods for infants and young children in good health and in foods for special medical purposes (FSMP) for infants and young children.'

Locust bean gum (E410)

In respect of the use of locust bean gum, the SCF[13] reported that locust bean gum, also called carob bean gum, is refined from the endosperm of the carob tree, *Ceratonia siliqua*. It contains tannins and the carbohydrate component is a galactomannan polymer consisting of linked D–mannose units with side chains of D–galactose. It is used as a stabiliser and thickening agent

Locust bean gum was evaluated by JECFA in 1981. An Acceptable Daily Intake was not specified due to lack of toxicity known. However, in considering a request to increase the permission for locust bean gum in infant formula products from 0.1 to 1 g/100 mL, the SCF considered:

- there are indications of growth depression in animals fed locust bean gum, although these are equivocal;
- bean gum preparations are fermented in the colon, providing a small energetic gain. They can cause abdominal pain and diarrhoea;
- absorption of minerals and trace elements may be reduced by dietary fibre and tannins. Although a study on adults ingesting locust bean gum has shown no evidence of impaired absorption of minerals and trace elements, it is not always appropriate to use results from adults when evaluating health effects in infants in cases where growth may be affected. In rapidly growing healthy infants, even minor effects on gastro–intestinal absorption of trace elements and minerals may have growth retarding effects; and
- studies on growth in healthy infants chronically exposed to locust bean gum are lacking.

[13] Opinion on certain additives for use in foods for infants and young children and in foods for special medical purposes– adopted 106th meeting of SCF (March 1997).

The SCF concluded it was not persuaded that it is necessary to give thickened infant formula to infants in good health. It therefore recommended that the use of locust bean gum is not acceptable, at the doses requested, for use in infant formula and follow–on formula intended for infants in good health.

Gastro–oesophageal reflux (GOR).

The SCF noted '*that some medical specialists recommend that thickening of foods is useful in the treatment of GOR, and that in cases of uncomplicated GOR, treatment with thickening agents may be started without complementary investigations.'*

Clinical observations have shown that the clinical efficacy is best when locust bean gum is added to infant formula in the concentration range 4–10 g/L. However, there are few controlled studies of the efficacy of use of thickened infant formula in reducing GOR. It is believed that the increased viscosity of thickened feed will reduce the episodes of reflux, but it has been shown that the effects are unpredictable. Thickeners added to infant formula may reduce the number of reflux episodes, but may also prolong the duration of remaining episodes. Increased coughing in infants after thickened feedings compared with after unthickened feedings has also been reported.

Nonetheless the SCF accepted that the use in food for special medical purposes up to 10g/L is acceptable.

ANZFA has already stated its concerns about the use of claims about physiological conditions. ANZFA has requested, but not been provided with data to show that the marketing of products with these claims does not reduce breastfeeding rates (see Item 7.2.3). Therefore the standard does not provide for claims about physiological conditions such as 'anti–reflux', and there is no provision for 'anti–reflux' formula in Division 3 of the standard.

The SCF raised a number of concerns about the efficacy of these formulations. Therefore it is considered appropriate that an increase in the use of a food additive, which has the potential to impact adversely on the health of infants, be subjected to a full assessment as required under the food standard setting process.

Recommendation:

The proposed provisions for locust bean gum be retained.

Summary of recommendations for Section 3.4

Clause 11 should be varied at Subclause (3) to read "liquid infant formula product may contain not more than 0.03 g carrageenan per 100 mL".

The Table to Clause 42 be amended to include permission for the use of citric acid esters of mono– and di–glycerides of fatty acids (E472c) up to level of 0.9 g/100 mL in formula based on extensively hydrolysed protein.

The entry for mono– and di– glycerides listed in the Tables at Clauses 11 and 42 be amended to mono– and di–glycerides of fatty acids (E471).

Permission to use locust bean gum to a maximum level of 0.1 g/100 mL is retained.

3.5 Clause 13 – Limit on aluminium

Proposed at Preliminary Inquiry

(1) Infant formula product, other than a soy–based formula product or pre–term formula, must not contain more than 0.05 mg of aluminium per 100 mL.

(2) Pre–term formula must not contain more than 0.02 mg of aluminium per 100 mL.

(3) Soy–based formula must not contain more than 0.1 mg of aluminium per 100 mL.

Issues

Several industry groups supported this proposal although the **NZ Dairy Marketing and Customer Services** submitted additional costs would be incurred by this provision. The **NZ Ministry of Health** submitted that the toxicological assessment does not provide a robust argument demonstrating safety at this level; **Maureen Minchin (IBCLC)** submitted that the lower level should be universal, not the higher. **Nestle Australia Ltd** submitted that the prescription of a level is consistent with international regulations but submit that there should only one limit, which should be a guideline level to meet WTO obligations and if there is no health or safety issue with the level of aluminium in soy–based infant formula, then this level should apply to all formula.

Assessment

At Full Assessment, ANZFA consulted experts on the levels that would be adequate to protect public health and safety. Available data at that time on aluminium levels in infant formula, from the Australian Market Basket Survey and from industry, showed that in general the levels in soy–based products were higher than those in milk–based products.

Consequently, the levels at Preliminary Inquiry were proposed not only to protect public health and safety but also from the advice received at levels which were also achievable from sound manufacturing processes. No new evidence was provided about the safety of aluminium levels in infant formula, therefore the level proposed at Preliminary Inquiry should be retained.

Recommendation

Retain levels proposed at Preliminary Inquiry.

3.6 Composition of lactose free and low lactose formula

Proposed at Preliminary Inquiry and Inquiry

An infant formula product that makes a claim that it is ‘low lactose’ must not contain more than 0.24 g lactose per 100 mL.

Issue

The lactose content of low lactose infant formula product was specified before the provisions were set for low lactose foods. The level set for a claim for a low lactose food (general purpose) is not more than 0.3g per 100g of the food (Standard 1.2.8 (14)). An infant formula product that makes a claim that it is 'low lactose' must not contain more than 0.24 g lactose per 100 mL.

Assessment

At Preliminary Inquiry and Inquiry, it was proposed to revise the provisions for low lactose formula such that low lactose formula regardless of base ingredient should not contain more than 2.4 g/L but it was noted this maximum level might be revised when Standard R1 (5) is reviewed in the Review of Food Standards to ensure consistency.

Given the Nutrition Information Table will provide information on the lactose content of a low lactose formula, it is considered that increasing the maximum permission to 0.3g per 100g will not create problems for lactose intolerant infants.

Recommendation at Supplementary Final Assessment

Drafting is revised to specify that low lactose formula must contain no more than 0.3 g lactose per 100 mL infant formula product.

4. DIVISION 4 – GENERAL LABELLING AND PACKAGING REQUIREMENTS

4.1 General Comments

Issues

The Victorian Food Safety Council Food Standards Sub–Committee suggest that there should be specific education material to inform health professionals and users of the product about the rationale for the content of the new standard.

Nestlé Australia Ltd states that the required statements specified are listed in the labelling requirements of the International Code of Marketing of Breast–milk Substitutes that Australia has agreed to comply with. The inclusion of specific statements for the labelling these products will create a difficulty for our WTO obligations with respect to the importation of infant formula.

Assessment

The WHO International Code of Marketing of Breast milk Substitutes is a voluntary Code. Inclusion of requirements for specific labelling statements in the Food Standards Code is essential to ensure compliance and enforcement. Only those sections of the WHO Code essential to protect public health and safety are included in the standard.

Recommendation.

No changes to the drafting are required. A communication / education strategy will be developed to inform health professionals and consumers of the changes to the standard for infant formula.

4.2 Clause 18 – Requirement for a measuring scoop

Proposed at Preliminary Inquiry

A package, other than a single serve sachet, containing infant formula product in a powdered form, must contain a scoop, which facilitates the use of the infant formula product in accordance with the directions contained in the label on the package.

Issues

Wyeth Australia Pty Ltd suggest that Clause 18 should read "A package, other than a single serve sachet or a package containing single serve sachets, must contain a scoop which facilitates the use of the infant formula product in accordance with directions contained in the label on the package."

InforMed Systems Ltd states that Codex has no statement on scoops.

The Department of Nutrition and Dietetics and the James Fairfax Institute of Paediatric Clinical Nutrition state that in regard to the measuring scoop it would have been preferable to have a standard scoop for measuring infant formula, e.g. 1 scoop to 30 mL or 1 scoop to 60 mL. This would reduce consumer confusion when changing brands.

Assessment

No information has been presented in submissions concerning the need for a statement about the 'scoop' that was not discussed at Preliminary Inquiry. The wording should be amended to take into account the suggestion of Wyeth Australia Pty Ltd.

Recommendation

The drafting will now read "*A package, other than a single serve sachet or a package containing single serve sachets, must contain a scoop which facilitates the use of the infant formula product in accordance with directions contained in the label on the package."*

4.3 Clause 19 – Required statements

Proposed at Preliminary Inquiry

Several mandatory advisory statements and one mandatory warning statement were proposed to be required in the label of infant formula products.

4.3.1 Clause 19 (3)(a) and (b)

Proposed at Preliminary Inquiry

Statements are required to indicate that:

- breast feeding is superior to the use of infant formula product in the feeding of infants; and

- infant formula products should only be used on the advice of a medical practitioner or health worker as to the need for its use and proper method of use.

Issues

There is concern from consumers and public health organisations that the proposed information to be provided in the label of infant formula is not sufficient to advise consumers that breastfeeding is the best method of feeding for infants. Some submissions commented that consumers should be warned that infant formula might be dangerous to infants and mothers.

Consumers and Public Health representatives submitted that they felt there should be stronger warning statements. Comments made included the following:

- this proposal would weaken current labelling provisions by downgrading the prescribed statements into advisory statements;

- a warning statement in 6 mm type to the effect that artificial formula feeding can be dangerous to the health of the infant should be mandatory on all infant formula;

- the labelling requirements do not warn consumers of the health risks to the child or mother of using artificial formula;

- consumers will not generally seek information from health professionals and advice from health professionals may be incorrect;

- the required statement that “breast is best” is ambiguous. It may maintain the misconception that feeding infants artificial formula is ‘standard’ or normal. It does not convey that there are adverse health risks associated with use of the formula; and

- the labelling requirements do not require information to be on the product that would enable consumers to avoid being deceived about the relative merits of formula and human milk.

Mr Dunstone had made an application (A376) to require the statement 'this formula may harm your baby' on the label of the formula in addition to specific label statements targeted to health professionals. ANZFA considers that there are two main issues arising from Mr Dunstone’s application. These issues are:

- should messages targeted to health professionals be on the labels of infant formula? ; and

- will the warning statements and explanatory messages in the application from Mr Dunstone increase the incidence of breastfeeding in Australia and New Zealand?

Assessment

Breastfeeding is the preferred method of feeding for infants. Government supported public health initiatives strive to promote breast–feeding to all new mothers. Limitations in scientific knowledge mean that formula prepared for infants does not support the nutrition of infants as well as human milk. However, infant formula is intended to be a substitute for breast milk when breastfeeding is not possible. The food standard sets provisions for the safest and healthiest formula for babies. Infant formula available in Australia and New Zealand are safe products and are the best alternative to breast milk when breastfeeding is not medically possible.

Mothers and carers of infants, who cannot breastfeed, should not be made to feel guilty about the fact that they use infant formula. Warning statements in the label of infant formula stating that infant formula is dangerous, are not only false and misleading, but might also cause carers to use other less suitable alternatives.

The proposed labelling provisions encourage the use of breast milk rather than infant formula and the required statements are intended to fulfill this task. Comments received from submitters suggested that these required statements are not strong enough because manufacturers will be permitted to use their own words as long as the intent of the statement is correct. Currently the required statement in Australia reads:

'ATTENTION – BREAST MILK IS BEST FOR BABIES. BEFORE YOU DECIDE TO USE AN INFANT FORMULA, CONSULT YOUR DOCTOR OR CLINIC FOR ADVICE'

In the light of public concern, ANZFA considers that the words of the statement should be mandated. The current statement has been amended slightly to;

- Cover the inclusion of follow–on formula in addition to infant formula
- The term health worker was considered more appropriate than clinic.

The mandated statement will be;

'Breast milk is best for babies. Before you decide to use this product, consult your doctor or health worker for advice.'

Mr Dunstone suggested that requiring the statement "this formula may harm your baby" on the labelling of the formula in addition to specific label statements targeted to health professionals will increase the rates of breastfeeding in Australia and New Zealand. **Mr Dunstone** did not present ANZFA with specific evidence to indicate that implementation of the specific statements on all infant formula would increase breastfeeding rates in Australia and New Zealand. There are a number of complex, social, physiological and cultural factors, which could affect the rate of breast–feeding.

It is therefore unlikely that breast–feeding targets can be achieved through implementing the warning statements and explanatory messages proposed in the application by **Mr Dunstone** alone.

Advice to health professionals

There is no evidence that health professionals view these particular food labels at retail level. Therefore there is no justification for label messages targeted to these particular non–purchasers. Health professionals who advise carers of infants are more effectively reached with direct information dissemination strategies. It is considered that the most appropriate way to communicate to health professionals is using specific education campaigns directed through professional associations.

However, ANZFA considers that education in conjunction with labelling can be an effective means of communicating public health messages to consumers. There are a number of education initiatives planned or being undertaken in Australia and New Zealand to improve breastfeeding rates in both countries. These initiatives differ in both countries but may include family education, education of health professionals, development of national accreditation standards for health care services, training for indigenous health workers, workplace support and monitoring.

Use of unprescribed text and print size

Advisory statements and other mandatory information, except warning statements, are not required to have a specified print size. Mandatory information, with the exception of warning statements, is simply required to be legible. Warning statements are required to be in 3 mm type and on small packages in 1.5 mm type. Submitters did not think that this was appropriate.

The mandatory labelling statements required in the label of infant formula are necessary to ensure that products are used as they are intended to be used. Therefore ensuring that the statements are noticed by users of the product and are prominent is essential. In addition ensuring the words presented on all infant formula products are the same will ensure that the messages being sent to consumers are consistent.

It is proposed that the drafting be changed to require all mandatory warning and advisory statements on the label of infant formula to appear in 3 mm type, or in the case of small packages, in 1.5 mm type. The wording of advisory statements should be mandated as is the case for warning statements.

<u>Recommendations</u>

The following amendments to the draft standard are recommended.

Clause 19 (3) – Infant formula product must contain the following statement under the heading of ‘Important Notice’:

“*Breast milk is best for babies. Before you decide to use this product, consult your doctor or health worker for advice*” in a minimum print size of 3 mm.

4.3.2 Statement about additional foods

Proposed at Inquiry

'*except in the case of packages of pre–term formula, infants over the age of 6 months should receive foods in addition to the infant formula product'.*

Industry issue at Inquiry

Industry submit that the requirement for a statement indicating that infants over 6 months should receive foods as well as formula should be removed.

Assessment

Standard R7 currently requires a similar statement and it is also required by Codex for infant formula and follow–on formula. Stakeholders and members of the External Advisory Group considered this statement and it was agreed that the intent of this statement be retained but the drafting be amended to *'… it is recommended that infants over 6 months be offered foods as well as the infant formula product'.*

Recommendation at Supplementary Final Assessment

The drafting is amended to'*… it is recommended that infants over 6 months be offered foods as well as the infant formula product'.*

4.3.3 Clause 19 (1) Use of the term 'very ill'

Proposed at Preliminary Inquiry

The following warning statement should appear in the label of infant formula in type of 3 mm.

"*Warning – Follow instructions exactly. Prepare bottles and teats as directed. Do not change proportions of powder or concentrate (–use whichever is applicable) except on medical advice. Inappropriate use or preparation can make your baby very ill*."

Issues

Nestlé Australia Ltd, Wyeth Australia Pty Ltd, InforMed Systems Ltd and Bristol–Myers Squibb Australia Pty Ltd state that the reference to 'very ill' in the warning statements of Clause 19(1) needs to be changed to 'ill' as the use of the term 'very' is too extreme and could cause unnecessary anxiety to carers, which is not justified.

Maureen Minchin (IBCLC) submitted that the following statement should be required:

'WARNING
Follow the instructions below. Infant formula can harm your baby if you do not. Always read the instructions on every can of formula you use, as they may be different. Never use more or less powder or water or a different measuring scoop and use only shrink proof bottles with reliable markings. DO not overheat infant formula, as you can destroy important ingredients. Do not heat infant formula in a microwave.'

Assessment

The intent of the proposed statement is to warn users of infant formula that if the product is not prepared correctly it could cause serious harm to the infant. Deleting the term 'very' but retaining the word 'ill' does not convey the potential seriousness of the health risk to infants if formula is made incorrectly. The use of the term 'very ill' was used as a softer alternative than the terms 'seriously ill' or 'fatally ill'. Industry has not given significant justification for the deletion of the word 'very' and there was no opposition to the use of this word from consumers or most public health organisations. Therefore the word 'very' should remain in the drafting of the proposed warning statement.

Industry issue at Inquiry

The term 'inappropriate use' should be changed to 'incorrect use' and the term 'very ill' is too alarmist.

Assessment

Representatives at a Stakeholder forum agreed this should be revised to: delete the words 'use or' in the last sentence; and replace the word 'inappropriate' with 'incorrect ', thus to read 'incorrect preparation'.

Again it was not agreed to alter the term 'very ill' as non–industry participants believed this to be an accurate representation of the consequences of incorrect preparation and they did not agree this would stop carers purchasing these products.

Recommendation at Supplementary Final Assessment

The clause be amended to:
'Warning –…. Incorrect preparation can make your baby very ill'.

4.3.4 Clause 19 – Ready to drink formula

Proposed at Preliminary Inquiry

The following statement is required in the label of ready to drink formula:

'Warning – follow instructions exactly. Prepare bottles and teats as directed. Do not dilute or concentrate this ready to drink formula except on medical advice. Inappropriate use or preparation can make your baby ill'.

Issue

Wyeth Australia Pty Ltd state that it is difficult to concentrate ready to drink formula so in Clause 19 it may be more appropriate to say 'do not dilute this ready to drink formula except on medical advice.'

Assessment

Ready to drink formula may be concentrated by the addition of powdered formula or milk powder. Such practices should be discouraged except under medical or dietetic advice. Therefore, the intent of the provision should be retained but the wording should be amended to clarify that nothing should be added to the ready to drink formula.

Recommendation

The clause be amended to "Warning….. do not dilute or add anything to this 'ready to drink' formula…..".

4.3.5 Clause 19 – Instructions on the preparation of bottles

Proposed at Preliminary Inquiry

The label on an infant formula product must contain directions for the preparation and use of the infant formula product, which include words and pictures that instruct:

(a) that each bottle should be prepared individually;

(b) that if a bottle of made up formula is to be stored prior to use, it must be refrigerated and used within 24 hours;

(c) that potable, previously boiled water should be used;

(d) where a package contains a measuring scoop, that only the enclosed scoop should be used; and

(e) that formula left in the bottle after a feed must be discarded.

Issue

InforMed Systems Ltd state that Clause 19(2) should be deleted or amended to state 'that each bottle should preferably be prepared individually.' This is commonly ignored and they have seen no problems arising if it is made up and stored correctly.

Assessment

This issue was discussed at length at Full Assessment and Preliminary Inquiry. The requirement has been misinterpreted by InforMed Systems. Infant formula may be made in advance and stored as long as each bottle is made up individually rather than in bulk.

Recommendation

No changes to the drafting are required.

4.4 Clause 20 Print and package size

Proposed at Preliminary Inquiry

Mandatory information must be clear, legible and noticeable; warning statements required on infant formula products should be in 3 mm standard type (legibility being the key criteria) or in the case of packages of less than 1 kg, 1.5 mm standard type.

Issues

Wyeth Australia Pty Ltd, Nestlé Australia Ltd and InforMed Systems Ltd suggest that Clause 20(2) be redrafted to state that a package having a net weight of 1 kg or less should have standard type of not less 1.5 mm. Codex requires that the print size must be 'easily readable'. They question whether specifying an actual size could be more restrictive.

Maureen Minchin (IBCLC) suggests a net weight of 450g of formula rather than the 1 kg tin for a small package of infant formula.

Assessment

At Preliminary Inquiry a 1 kg tin was considered to be a small package in terms of infant formula products. However, on further investigation the majority of packages sold at retail are less than 1 kg in weight. This means that any warning statements would be in small type of 1.5 mm on almost all retail tins of formula. This is not considered to be appropriate. There is ample space on a 1 kg tin of formula for the required mandatory labelling statements in type of 3 mm.

The size of a small package of infant formula is therefore recommended to be considerably smaller than the 1 kg tin. On investigation of tin weights available it seems that the 450g tin, as suggested by Maureen Minchin, should be classed as a small package. Manufacturers would have difficulty fitting all the required information on this size tin if type had to be 3 mm. Inclusion of all the prescribed information is still required despite the size of the package. However, for a small package the mandatory warning statements may be in 1.5 mm type rather than 3 mm. All other type simply needs to be legible. The print size for warning statements should be consistent with the requirements for warning statements on the label of other food products.

Recommendation at Inquiry

A small package for infant formula products should be 450 g or less. The print size for mandatory warning statements in the label of small packages of infant formula products should be 1.5 mm or more.

Industry issue at Inquiry

Many imported products come in one pound [454g] cans, which have the same sized cans as smaller amounts, for example a can height of 121 mm compared to a height of 163 mm for a 900 g can; yet both require the same type size on the label. Using a break point of 500g for this requirement could obviate this problem. Since there is an overall requirement that label information be legible, it is debatable whether specifying type size actually benefits anyone. This should conform only to general labelling requirements for legibility.

Assessment

It was necessary to define a small package of infant formula product for the purpose of specifying the print size of mandatory label information. The 450g was chosen as it represented the small pack sizes in the market. However, it appears some imported products are packaged in 454g packs. Therefore there is a case to increase the 'cut–off' from 450 g to 500 g for 1.5 mm versus 3.0 mm print size for warning statements as requested by industry.

Recommendation at Supplementary Final Assessment

Drafting is amended to replace the package size '450g' with '500g'.

4.5 Clause 21 Declaration of nutrition information

Use of 100g in the Nutrition Information Panel (NIP) / Reconstitution

Proposed at Preliminary Inquiry

Clause 21 (2)

(a) The average amount of each of protein, fat and carbohydrate expressed in g per 100 mL in the case of ready to drink formula;

(b) In the case of powdered or concentrated infant formula products

(i) the average amount of each of protein, fat and carbohydrate expressed in g per 100 mL of infant formula products that has been reconstituted according to directions; and

(ii) the amount of each of protein, fat and carbohydrate expressed in g per 100g of infant formula product prior to reconstitution in the case of powdered infant formula product or g per 100 mL prior to reconstitution in the case of liquid concentrated infant formula products.

Issues

Nestlé Australia Ltd, Wyeth Australia Pty Ltd and Bristol–Myers Squibb Australia Pty Ltd state that it is not necessary to include the average amount of product on a per 100g basis. The relevant information is as per the made up product. They state that a product that is to be reconstituted with water should only be labeled as the reconstituted amount not as the dehydrated or concentrated amount. All products have different densities and require different amounts of powder to be reconstituted so it does not allow consumers to compare products

Nestlé Australia Ltd also state that Clause 21(2)(b)(ii) needs to state 'the average amount of' rather than 'the amount of' for consistency.

Assessment

It was recommended at Preliminary Inquiry that the NIP include nutrients and nutritive substances as purchased as well as per 100 mL ready to consume formula.

Codex required declaration of the nutrients in infant formula products per serve when reconstituted and per 100 g as sold. Therefore the requirement proposed at Preliminary Inquiry is consistent with Codex.

It is noted that the 'per 100g' declaration may not be useful for consumers to compare products as every product has a different density. However, specialist health professionals often use the 'per 100g' readings to calculate any necessary concentrations or dilutions of infant formula that they may require for particular medical or dietetic reasons.

Recommendation at Inquiry

The 'per 100g' declaration is consistent with Codex and may be useful to health professionals, therefore, the requirement proposed above should be retained.

Industry issue at Inquiry

That the requirement for an NIP for nutrients expressed as per 100g as sold is deleted as industry argued that it crowds the label, leads to confusion in the general public and is only necessary for health professional use.

Assessment

As stated, this provision was included to provide consistency with the Codex standard (and proposed Codex standard) which requires the declaration of both types of information. Health professionals had also advised that information about nutrients per product as sold was necessary for some purposes. However, the External Advisory Group members considered that provided information about the weight of the product per scoop and the percentage solution on a weight/volume basis for the product was provided on the label, health professionals would be able to calculate nutrients per 100 g product as sold from the information provided on an 'as consumed' basis. Therefore it is agreed that the requirement for a NIP to express nutrients per 100g of product (as sold) be deleted.

Recommendation at Supplementary Final Assessment

Drafting be amended to only require nutrient declaration per 100 mL as consumed and to require the declaration of the weight of product per scoop (if included) and the percentage solution on a weight/volume basis for the product.

4.6 Clause 22 Date marking and storage instructions

Proposed at Preliminary Inquiry

The label on an infant formula product must include a statement of the best before date and must contain storage instructions covering the period after it is opened.

Issues

Nestlé Australia Ltd, Wyeth Australia Pty Ltd, InforMed Systems Ltd and Bristol–Myers Squibb Australia Pty Ltd state that a use by date must be permitted as well as a best before date otherwise they will not be permitted to sell a product with a use by date. A use by date would prohibit the sale of goods after that date.

Assessment

At Preliminary Inquiry it was decided that a 'best before' date is suitable for infant formula as it is safe for an infant to consume the formula after this date. There may be some degradation of nutrients, but the formula will not harm the infant. Codex recommends a best before date.

In general, a 'use by' date will only be used in the future where a food is unsafe to consume after the use by date has expired. Such food will not be permitted for sale.
However, manufacturers believe a 'use by' date which prohibits sale after the date may be necessary in some circumstances to provide for losses in nutrient stability particularly, vitamin stability. Therefore to accommodate the concerns of industry the label of an infant formula product should include a statement of the 'best before' date or a 'use by' date. This requirement is consistent with the generic provisions for the date marking of foods (Standard 1.2.5) and hence special provision is not in the standard for infant formula products.

It is proposed that the label of an infant formula product must provide advice about storage of the product after it is opened. It was intended that this provision would also cover advice about correct handling of the remaining product to ensure it is safe for the infant when used. The drafting may not reflect this intent; therefore it is recommended that the drafting be amended to expressly require advice about correct handing of the remaining unused food in the container.

Recommendations

1. The label of an infant formula product should include a statement of the 'best before' date or a 'use by' date. The date marking requirements proposed at Preliminary Inquiry should be deleted from the standard for infant formula products as the generic provisions for the date marking of foods provide the appropriate cover.

2. The label should also expressly provide information about safe handling of the remaining infant formula product to ensure it is safe and healthy for infants when used.

4.7 Clause 23 Statement on source of protein

Proposed at Preliminary Inquiry

The label on an infant formula product must contain a statement of the source of protein in an infant formula product immediately adjacent to the name of the infant formula product.

Issues

Bristol–Myers Squibb Australia Pty Ltd and **Nestlé Australia Ltd** state that the requirement to declare the source of protein appears to be overly prescriptive, particularly when manufacturers include the ingredients in the ingredient list. Where cow's milk is used as the protein source the ingredient statement will claim this as a milk ingredient. Where a different protein source other then cow's milk is used manufacturers would declare this in the name of the food anyway. The proposal for the naming of foods requires manufacturers to name their products so consumers are not misled. The information provided by manufacturers on labels must not be false, misleading or deceptive.

Wyeth Australia Pty Ltd state that this requirement should only apply to products that do not have cow's milk as a source, as other cow's milk products do not need to state that the source is from a cow.

Maureen Minchin (IBCLC) agrees there should be a statement of protein source.

Assessment

The declaration of the protein source of infant formula is necessary for consumer information. It is true that a product must not be represented in a manner that is false, misleading or deceptive and that the protein source would be declared in the ingredient list. It is also apparent that if manufacturers used a product other than cow's milk they would advertise the fact.

However, specific declaration of the protein source adjacent to the name of the product is considered to be necessary to ensure that consumers are aware of the protein source of the food at the time of purchase. The protein source will be noticeable and not hidden in the label. Codex requires the protein source of the formula to be in the label in close proximity to the name of the food. Such a requirement is difficult to regulate because 'close proximity to the name' is subjective. The proposed requirement is consistent with Codex recommendations and provides an easily enforceable requirement.

Recommendation

Retain the requirement to declare the protein source of the formula in the label immediately adjacent to the name of the food.

Further Issue at Inquiry

Infant formula products are required to include a statement of protein source on the label. It is intended that this information should be specific rather than general.

This specificity is not clear from the current drafting and there is a need to clarify the intent. Manufactures are uncertain how to comply with this provision where more than one source of protein is used.

Assessment

It is important carers are aware of the specific protein used in an infant formula product. Therefore the drafting should be amended to clarify that the declaration of source or sources of protein be specific rather than as class names.

Recommendation at Supplementary Final Assessment

That the drafting be amended to clarify that the declaration of source or sources of protein be specific rather than as class names.

4.8 Clause 24 Statement on dental fluorosis

Proposed at Preliminary Inquiry

(*1) An infant formula product that:*

> *(a) contains more than 17 mcg of fluoride per 100 kJ prior to reconstitution, in the case of powdered or concentrated infant formula product; or*
> *(b) contains more than 0.15 mg of fluoride per 100 mL, in the case of ready to drink formula;*

must contain the statements:

> *(a) indicating that consumption of formula has the potential to cause dental fluorosis; and*
> *(b) recommending that the risks of dental fluorosis should be discussed with a medical practitioner or other health professional.*

Issues

Nestlé Australia Ltd, InforMed Systems Ltd and Wyeth Australia Pty Ltd do not agree with the need to include advisory statement on products regarding fluoride and dental fluorosis. They state that:

- there is no international equivalent legislation, it would constitute a technical barrier to trade; and
- there is no firm scientific evidence to suggest fluorosis occurs strictly from high fluoride levels in reconstituted infant formula products.

The National Council of Women of New Zealand (NCWNZ) state that a required maximum fluoride level should be determined if a warning statement is required on the label.

Assessment

At Preliminary Inquiry ANZFA stated that the toxicology assessment concludes that the issue of fluoride in infant formula products is adequately covered by the current water quality guidelines. Therefore, it is proposed not to specify a maximum level for fluoride in infant formula products.

Whilst ANZFA does not dispute that at high fluoride levels dental fluorosis may occur, from the available information manufacturers of infant formula products are already taking steps to reduce fluoride content in formula. This combined with the existing water quality guidelines and proposed advisory statements (below) is sufficient to maintain protection of public health and safety.

However, due to the possibility of dental fluorosis from the use of some formula, ANZFA proposed that products with high fluoride contents should have an advisory statement on the label to advise carers of this potential risk. This statement was proposed for infant formula product powders containing fluoride levels >0.5 mg/L when reconstituted with fluorine free water (formulas with approx. 17 microgram fluoride /100 kJ) and ready–to–drink formulas containing fluoride > 1.5 mg/litre. These levels were also proposed to accommodate the higher levels in soy–based products (cited in published literature and surveys) arising from current manufacturing processes yet still retain protection of public health and safety.

Some water in Australia and New Zealand contains fluoride and some does not, therefore, regulation of a maximum level of fluoride in infant formula is difficult. At the levels given above the formula may not cause fluorosis if prepared with water that has been distilled. However, if used with fluoridated water it may cause fluorosis. It is impossible to regulate the water used by carers of infants when they prepare the infant formula products.

A warning statement on the label of infant formula products that contain the above levels of fluoride should warn consumers that the formula might cause fluorosis. Such a warning statement may reduce sales of infant formula products that contain fluoride and may encourage manufacturers to decrease the level of fluoride in such formula.

Doctors and health professionals may not be aware of the potential for dental fluorosis from formula consumption. Therefore it may be prudent to provide education on this issue.

Recommendation.

That the labelling provision for fluoride be retained.

4.9 Clause 25 Labelling of lactose free and low lactose formula

Proposed at Preliminary Inquiry

The words 'lactose free' must appear as part of the appropriate designation of lactose free formula. The words ‘low lactose’ must appear as a part of the appropriate designation of low lactose formula and the label on a package containing a lactose free formula or a low lactose formula must include the following statements:

(a) the amount of lactose expressed in g per 100 mL; and
(b) the amount of galactose expressed in g per 100 mL.

Issues

Wyeth Australia Pty Ltd state that if a product is lactose free there is no benefit gained by including the amount of lactose expressed in g/100 mL**. Wyeth Australia Pty Ltd and Bristol–Myers Squibb Australia Pty Ltd** state that they do no routinely test for galactose and question the relevance of a statement of the amount of galactose present when the small proportion of infants who have galactosaemia are under strict medical supervision.

The Department of Nutrition and Dietetics and the James Fairfax Institute of Paediatric Clinical Nutrition state that the provisions for labelling of low lactose and lactose free formula appears adequate for galactosaemia.

Assessment

The declaration of lactose in g/100 mL in the label of lactose free formula is consistent with Standard 1.2.8 – Nutrition Information Requirements for declaration of lactose in lactose free foods. Gluten free foods are also required to have a declaration in the label of the gluten content of the food, even though the reading would be zero.

The intent is to educate consumers that a product with a 'free' declaration will not contain any of the nutrients that are declared to be free. In the past gluten free foods were permitted to contain some gluten; this was not considered acceptable, just as it is not acceptable for lactose free products to contain lactose.

At Preliminary Inquiry it was determined that lactose is the major dietary source of galactose. Information suggesting a reduction in lactose content may be misconstrued to imply a reduction in galactose content when this may not be true. Low lactose, reduced lactose and lactose free foods based upon milk, including infant formula products are therefore currently required to provide information about the galactose content of the food. This information enables carers of children or infants with galactosaemia to determine how much of the food, if any, is suitable for galactosaemics. It was recommended that this provision be included in the standard for infant formula.

The current provision requires all 'lactose free' or 'low lactose' formulas to carry this labelling regardless of whether or not a claim is made about lactose content. Therefore the provision has been amended to be triggered only if a claim is made about the lactose content of the formula. This amendment allows formula not specifically formulated for lactose mal–digesters but which are inherently lactose free e.g. soy–based formulas, not to be required to make a claim about lactose content.

Recommendation

To be consistent with the requirements for lactose free and low lactose foods, the requirement for declaration of the lactose and galactose content of lactose free and low lactose infant formula, in g/100 mL, be retained and apply if a claim is made about the lactose content of the formula.

4.10 Clause 26 – Prohibited representations

Proposed at Preliminary Inquiry

Clause 26 contains the following list of prohibited representations on the label of an infant formula product:

(a) a picture of an infant;
(b) a picture that idealises the use of infant formula product;
(c) the word 'humanised' or 'maternalised' or any words or words having the same or similar effect;
(d) words claiming that the formula is suitable for all infants;
(e) information relating to the nutritional content of human milk;
(f) a reference to the presence of any nutrient or nutritive substance except for a reference to a nutrient or nutritive substance in:

(i) the name of a lactose free formula or low lactose formula
(ii) a statement of ingredients; or
(iii) a nutritional information statement;

(g) Representation that the food is suitable for a particular condition, disease or disorder.

Issues

Wyeth Australia Pty Ltd suggest that the prohibited representation in Clause 26 (a)(b) and (c) should be removed from the proposal because they are under the jurisdiction of the MAIF agreement as they are not health and safety issues.
They state that without a firm definition of what 'a picture that idealises the use of infant formula product' is this clause has little relevance to infant health and safety.

Wyeth Australia Pty Ltd and **Bristol–Myers Squibb Australia Pty Ltd** state that Clause 26(f), the prohibition on declaration of nutrients should be removed because it effectively removes information to the consumer about infant formula. They are unable to educate the consumer about the presence of new ingredients. They request that some sort of information be allowed with respect to new or novel ingredients such as nucleotides.

The **New Zealand Infant Formula Marketers' Association (NZIFMA)** submitted that follow–on formula should be permitted to make a claim for added iron to discourage carers from using cows milk instead of an infant formula product for their infant.

Assessment

No new information has been presented by submitters that has not already considered at the Preliminary Inquiry stage. The only reason for manufacturers to want to include any of these representations or declarations of nutrients in the label of an infant formula product is as a marketing tool. ANZFA does not consider it appropriate to use such information to market infant formula products.

The prohibition of representations of infant formula products is consistent with the requirements of the WHO International Code of Marketing of Breast Milk Substitutes and with the requirements of the MAIF agreement. Inclusion of these provision in the Food Standards Code makes them mandatory requirements and enforceable by law.

"With added iron" claim

All infant formula products (infant formula and follow–on formula) have added iron and all are required to provide for the iron needs of infants to 12 months. Therefore such a claim is true for all infant products for the nutrient 'iron' and as well as for all other essential nutrients. The flexibility provided by the proposed standard would permit an infant formula product represented as suitable for infants from birth to have an iron level higher than a follow on formula product represented as suitable for infant from 6 months of age, if so formulated by a manufacturer. It is not consistent with the objectives of ANZFA or fair trade law in Australia or New Zealand to create provisions for a specified range of products when the same provisions apply to other products in the range.

ANZFA is currently reviewing the issue of labelling statements on reduced fat milk products (Proposal P240) to address public health and safety concerns on the use of such milks or milk alternatives in the diet of children under two years of age. The unsuitability of cow's milk as the sole dietary liquid source for infants is also under consideration. It is considered that a direct message on the specific product of concern is more useful for carers than is a declaration of a nutritional modification on an infant formula product. Carers may not link the statement about 'added iron' on an infant formula to the importance of not introducing other beverages as the principal liquid source of nourishment.

Recommendation at Inquiry
The proposed requirements for prohibitions on representations of infant formula and the declaration of nutrients be retained.

Industry Issue at Inquiry

Following Inquiry (Nov 1999), Industry again raised the issue of a claim of 'added iron' for follow–on formula.

ANZFA has several times requested evidence to show that the label statement 'added iron' on specific infant formula products such as follow–on formula will improve the iron intake of infants aged 6–12 months. Data to show this labelling will impact positively to reduce infant iron deficiency has not been provided.

Consumer representatives and health professionals at the Stakeholder forum also did not support this proposal by Industry. Therefore, an application supported by data to show such a label statement will reduce the incidence of iron deficiency anaemia is necessary to assess the claimed public health benefit.

Recommendation at Supplementary Final Assessment

No change to the provisions on 'added iron' claims.

5. DIVISION 5 – GENERAL MICROBIOLOGICAL REQUIREMENTS

The microbiological standards for infant formula products are regulated in Standard 1.6.1 – Microbiological Limits for Food. Issues raised in the submissions to P93 have been referred to the review of the micro standards. Therefore Division 5 – General Microbiological Requirements will be deleted from Standard 2.9.1.

Industry issue at Inquiry

The Standard plate count (SPC) (Standard 1.6.1) has been made more restrictive to the current Standard R7.

Assessment

It was necessary to correct an error in interpreting the current Code when transforming to ICMSF format for SPC and Coliform levels where the intention was to retain the existing limits. For Bacillus cereus, the current NZMRC levels were considered to provide an adequate level of protection. The following proposed amendments have been incorporated into Standard 1.6.1.

Standard plate count/g
n=5, c=2, m=1000, M=10,000

Coliforms/g
n=5, c=2, m=<3, M=10
Bacillus cereus/g
n=5, c=2, m=10, M=100.

6. PART 2 – INFANT FORMULA AND FOLLOW–ON FORMULA

COMPOSITION

6.1 Protein content

Proposed at Preliminary Inquiry

That the protein content of infant formula have a minimum level of 0.45 g /100 kJ and a maximum levels of 0.7 g/100g for infant formula and 1.3 g/100 kJ for follow–on formula.

Issue

Nestlé Australia Ltd submit that the minimum protein level proposed by Codex of 0.43 g /100 kJ be adopted rather than 0.45 g/100 kJ. There were no other submissions about this value.

Assessment

The proposed Codex standard ‘rounds’ the minimum protein content of formula expressed in metric values to 0.45 g/100 kJ as does the EC Directive. It is therefore recommended that this figure be retained.

Recommendation

The drafting should remain as proposed at Preliminary Inquiry.

6.2 PRSL of Follow on Formula (and Special Purpose Formula Clause)

Proposed at Preliminary Inquiry

Clause (28) (2) – Follow–on formula must have a potential renal solute load value of not more than 8 mOsm/100 kJ.

Clause (39) (1b) —An infant formula product for specific dietary use based upon protein substitutes must have a potential renal solute load of not more than 8 mOsm per 100 kJ

Issue

Submissions was received to the effect that this parameter is more prescriptive than some international regulations and some imported formula may not comply.

Assessment

It is now well accepted that health outcomes for infants have improved since the PRSL of alternatives to human milk have been reduced. Infant formula that unnecessarily increases risks to infants is not desirable, even if sold overseas. Infant formula products are formulated to supply the total diet of the infant.
The wider range proposed for nutrient contents would permit the sale of a formula with an unnecessarily high PRSL but which complies with the standard, if the PRSL was not prescribed. To protect the health and safety of formula fed infants in Australia and New Zealand, it is recommended that the PRSL be prescribed where formula with high levels of permitted nutrient levels could be given to infants. No new data was provided to justify alteration to the current proposed levels for follow on formula or infant formula product for specific dietary use based upon protein substitutes.

Recommendation

Retain the provision that follow–on formula or an infant formula product for special dietary use based upon protein substitutes must have a potential renal solute load value of not more than 8 mOsm/100 kJ.

6.3 Fat content

6.3.1 Units of expression for linoleic (LA) and alpha–linolenic (ALA) acids

Proposed at Inquiry

	Minimum % total fatty acids	**Maximum % total fatty acids**
Linoleic Acid	9	26
Alpha– linolenic acid	1.75	4

Industry issue at Inquiry

That the levels of linoleic and alpha–linolenic acid be expressed as absolute values per 100 kJ of energy and not in terms of proportion of total fatty acids.

Assessment

It was noted that most relevant scientific reports about the requirements of infants refer to the fatty acid levels as a percentage of total fats rather than absolute values or per 100 kJ. For example, the International Society for the Study of Fatty Acids and Lipids (ISSFAL)[14] in 1999 made a recommendation for the adequate intake of fatty acids for infants from formula (this has not yet passed the ISSFAL procedure to be a considered a 'policy statement from ISSFAL'). ISSFAL also recommended a level for each fatty acid, expressed as a percentage of total fatty acids.

The complexity of essential fatty acid metabolism and its potential intermediary metabolites plus the link to eicosanoid systems suggest that a system of expression where fats are interrelated seems prudent.

Additionally, the setting of a specific value per unit of energy is problematic where a range (1.05–1.5 g /100 kJ) is permitted for the fat content of formula and the problem is confounded by the influence of protein and carbohydrate levels.

Recommendation at Supplementary Final Assessment

That the provision on the method of expression in the standard is retained as proposed.

6.3.2 Alpha Linoleic Acid (ALA)

Current provisions and proposed provisions

	Infant formula	**Follow–on formula**
current R7	not specified	as per infant formula
proposed at Full Assessment	2 – 4% total fatty acids	as per infant formula
Codex	not specified	not specified
proposed Codex standard	>or = 12 mg/100 kJ	Not applicable
LSRO Recommendations	1.75 – 4.0 % total fatty acids	as per infant formula
Proposed at Preliminary Inquiry	1.75 – 4.0 % total fatty acids	as per infant formula
Recommendation at Inquiry	As proposed at Preliminary Inquiry	As proposed at Preliminary Inquiry
RECOMMENDATION AT SUPPLEMENTARY FINAL ASSESSMENT	1.1 – 4.0 % total fatty acids	As per infant formula

[14]Report from a workshop on Essentiality of and recommended Dietary intakes for Omega – 6 and Omega–3 Fatty Acids, (1999) ISSFAL <http://www.issfal.org.uk.adequateintakes.htm>

Issues

The **International Formula Council** endorses the decision to reduce the proposed minimum ALA content to 1.75% of total fatty acids. However **Nestlé Australia Ltd** submits that the EC Directive and proposed draft Codex standard specify the minimum ALA at 12 mg/100 kJ which is approximately 1% of the total fatty acids. Therefore **Nestlé Australia Ltd** states consideration needs to be given to harmonising with these standards to ensure that the obligations under WTO are met.

Assessment

The LSRO have noted that several studies have suggested that formula that provides ALA at less than the 1.75% of total fatty acids may be associated with delayed visual development and other adverse effect in infants. Therefore, should the Codex standard ALA content be reduced to 1% of total fatty acids, the safety of such formulations would need rigorous assessment before a similar permission could be agreed for Australia or New Zealand. There is no justification to reduce the ALA permissions proposed at Preliminary Inquiry.

Recommendation at Inquiry

Retain the ALA permissions proposed at Preliminary Inquiry.

Industry issue at Inquiry

The minimum alpha linolenic acid be 1.1% of total fatty acids or 12 mg/100 kJ.

Assessment

Industry representatives claimed that the literature research by Makrides et al. undertaken on behalf of industry showed a minimum alpha linolenic level of 1.1% total fat is safe citing a trial by Lucas et al [15]. This recent, large (n = 447) randomised control trial by Lucas and others, compared development, growth, and safety outcomes at baseline, 6, 9 and 18 months of age between randomised formula–fed groups with and without LCPUFAs (ALA 1.1% total fatty acids without LCPUFA; and ALA 1.4% with LCPUFA), and found no statistical differences in overall cognitive and motor developmental scores, growth or safety outcomes of infection rates, atopy and gastrointestinal tolerance between the formula–fed groups. When compared with breast fed infants, the same outcomes were observed except that the breast fed group at 18 months had larger head circumferences than both formula–fed groups.

The EC Directive for infant formula has set a minimum of 50 mg ALA/100 kcal (=1.1% ALA at minimum fat 1.05 g/100 kJ), which corresponds to the amount in the control formula in the Lucas study. Breast milk content of ALA is influenced by dietary intake and is reported to range between 0.5– 1.0% although breast milk also contains LCPUFA.

[15] Lucas A et al (1999) Efficacy and safety of long chain polyunsaturated fatty acids supplementation of infant formula milk: a randomised trial. The Lancet 345: 1948.

A workshop convened by the ISSFAL recommended intakes for omega–3 and omega–6 fatty acids in 1999 recommended an alpha–linolenic acid content of 1.5% of fatty acids as an adequate intake for infant formula /diet[16].

Due to the lack of clear guidelines internationally on the most appropriate level of ALA, ANZFA believes that there is sufficient evidence from the Lucas study and Makrides review to warrant a reconsideration of the issue.

Recommendation at Supplementary Final Assessment

That the minimum level of alpha–linolenic acid be reduced from 1.75% to 1.1% of total fatty acids.

6.3.3 Trans fatty acid content

Proposed at Preliminary Inquiry

It was proposed at Preliminary Inquiry that the fats in infant formula and follow–on formula must not contain more than 4% total trans fatty acids as a percentage of total fatty acids.

Issues

Two submissions were received from industry groups pertaining to this issue. One submitter suggested that the maximum level of trans fatty acids be increased to 8% of total fatty acids. The other submitter suggested that the level of a maximum of 4% trans fatty acids would require modification of some oil blends currently in use, therefore a maximum level of 8% total fatty acids be allowed for an intervening period of 2 years. This would allow any required modifications to oil blend compositions to be introduced with sufficient time to enable clinical trials and evaluations of stability to be completed.

Assessment

The current EC Directive allows a maximum level of 4% trans fatty acids as a percentage of total fatty acids. Therefore this level is achievable by industry and harmonises with a major international standard. There was no new evidence provided in the submissions to justify higher levels of trans fatty acids in infant formula.

Recommendation

The level of 4% proposed at Preliminary Inquiry be retained in the standard.

[16] Workshop on the essentiality of and Recommended Dietary Intakes from omega–6 and Omega –3 fatty acids. http://www.issfal.org.uk/adequate intakes.htm

6.3.4 Long chain polyunsaturated fatty acids (LCPUFA)

6.3.4.1 The regulation of LCPUFA

Proposed at Preliminary Inquiry

At Preliminary Inquiry, it was noted that there was no consensus about the public health benefit of the addition of LCPUFA to infant formula and that there are safety concerns about the potential sources of LCPUFA and inappropriate levels of these fatty acids. The following three options were proposed for the addition of LCPUFA to formula.

Option 1: Do not provide express permission

The efficacy of the addition of these LCPUFA is not proven and there are safety concerns about the effects of imbalance of the different LCPUFA but insufficient data to determine suitable levels for a regulation. Removal of express permission would leave the LCPUFA content regulated by the general permissions for the addition of other foods, the safety assessment of novel foods or ingredients from novel foods and the due care of manufacturers.

Option 2: Align permissions with those of the EC and UK

There is emerging evidence that some LCPUFA may be beneficial for visual and neurodevelopment in infants. However, there is also evidence to suggest that different LCPUFAs of the 3– and 6–series may interfere with each other's metabolisms to varying extents. Therefore it is proposed as at Full Assessment to given a broad permission for a LCPUFA content similar to that found in human milk, sourced from food ingredients (subject to the novel food standard requirements) rather than individual fatty acids and control the maximum levels as per the EC and UK since these are currently in force.

Option 3: Align permissions with those of the EC and UK but require a series 6 to series 3 ratio of 2 as in human milk.

As proposed at Option 2 but the ratio of series 6 to series 3 LCPUFA should be regulated at the level reported to be in human milk i.e. 2.

ANZFA's preferred option was Option 3 as this was consistent with known international regulations but afforded an extra safety measure of aligning the series 6 to series 3 LCPUFA ratio to that in human milk.

Therefore the draft standard includes the following provisions:

Long chain polyunsaturated fatty acids	**% Maximum Total fatty acids**
Long chain omega 6 series fatty acids (C>= 20)	2
Arachidonic acid (20:4)	1
Long chain omega 3 series fatty acids (C>= 20)	1

If LCPUFA are added to the formula then:

- total long chain omega 6 series fatty acids (C>= 20) to total long chain omega 3 series fatty acids (C>= 20) must be 2; and

- the eicosapentaenoic acid (20:5 n–3) content should not exceed the docosahexanoic acid (22:6 n–3) content.

Issues

Comments were made on this issue in 11 submissions. Options 1 and 2 were supported by 2 submitters each, and Option 3 by 6 submitters. One submitter did not indicate which option they supported but questioned the safety of the addition of LCPUFA since there would be addition of un–purified constituents. A number of submissions expressed an interest in why ANZFA was proposing to include a ratio of omega 6 to omega 3 fatty acids.

Assessment

This issue was addressed at Preliminary Inquiry. There is evidence to suggest that the series–6 and series–3 LCPUFA can interfere with each other's metabolism to varying extents, therefore regulating this ratio to the level found in human milk affords an extra measure of safety. Additionally, LCPUFA substrates are expensive. ANZFA had anecdotal information that at least one overseas manufacturer was to release a formula which has only one of the series of LCPUFA added due to cost concerns. This formulation would comply with the provisions at Option 2. The regulation to maintain the LCPUFA ratio to that of human milk series would not permit this formulation, which has the potential to be harmful to infants. Therefore it is recommended that if these fats are added to infant formula then their addition should be at levels as close to those known to be in human milk. Forsyth (1998)[17] reports that the series 6 to series 3 LCPUFA ratio in breast milk remains relatively constant at 2. There was significant support for this additional safety measure.

Submissions were made that the ratio in human milk is not always exactly 2 and making the ratio exactly 2 is extremely prescriptive. It was the intent at Preliminary Inquiry, that the series 6 to series 3 LCPUFA ratio in formula should be approximately 2 or as close to 2 as possible. Therefore it is recommended that the draft standard be amended to reflect this intent.

Safety of substrates

The safety of substrates used to add LCPUFA to infant formula will be required to be assessed if these are 'novel' ingredients for infants. ANZFA as part of Proposal P93 has recently conducted a safety assessment of certain algal and fungal sources of these fatty acids (refer to Supplementary Final Assessment Report – Attachment 2). Additionally ANZFA is aware of herbal oils being used overseas as substrates for the addition of LCPUFA to formula for infants. ANZFA would require a safety assessment of the use of such a substance before sale in Australia or New Zealand.

[17] Forsyth JS (1998) Lipids in infant formulas Nutr Res Revs 11: 255–278.

Recommendation at Inquiry

The provisions proposed at Preliminary Inquiry should be retained with an amendment to clause 30(d) to effect the intent that the ratio of the different series of LCPUFA be changed to "the fats in infant formula and follow–on formula must have a ratio of total long chain omega 6 series to total long chain omega 3 series fatty acids of **approximately** 2.

Industry issue at Inquiry

That the specification for the ratio of series 3 fatty acids to series 6 fatty acids be abandoned on the basis that it does not exist elsewhere.

Assessment

There is a high degree of interrelationship between these sets of fatty acids as well as incomplete knowledge of metabolic pathways. Although the levels of some of these fatty acids may be lower in human milk, given the proposed levels harmonise with those of the EC Directive and the uncertainties around absorption rates and bioavailability of the source materials, the levels of LCPUFA prescribed in the proposed standard should be retained.

Recommendation at Supplementary Final Assessment

That the provisions proposed at Inquiry be retained.

6.3.4.2 Levels of addition of the series–6 fatty acids

Proposed at Preliminary Inquiry

That series –6 LCPUFA and arachidonic acid be not more than 2% and 1% respectively of total fatty acids.

Issue

InforMed Systems Ltd and **Wyeth Australia Pty Ltd** pointed out that under Options 2 and 3, only up to 1% arachidonic acid is allowed to be added but a total of 2% long chain omega 6 fatty acids. They felt this was nonsensical to only allow the addition of 1% arachidonic but 2% total omega 6 fatty acids.

Assessment

Arachidonic acid is only one of several series–6 fatty acids. Therefore, there are other minor series–6 fatty acids that could also contribute to the total series–6 content of the formula. There is not sufficient scientific data to support any more detailed regulation for these fatty acids. What has been proposed in terms of levels of arachidonic acid and total series–6 fatty acids is consistent with the approach by the EC.

Recommendation

The levels proposed at Preliminary Inquiry be retained.

6.3.4.3 LCPUFA in 'follow–on–formula'

Issue

Nestle Australia Ltd. has submitted that LCPUFA should not be permitted to be added to 'follow–on formula' as they are not permitted by the EC Directive.

Assessment

There is no consensus about the public health benefit of the addition of LCPUFA to infant formula although there is greater evidence that such fatty acids may be more useful for infants born prematurely than for infants born at term or older infants. The permissions given for the addition of LCPUFA in the standard approximate the levels found in human milk as best as is possible with current scientific knowledge.

Recommendation

There is no case to prohibit the addition of these LCPUFA to 'follow–on formula'.

6.4 Vitamins and minerals

6.4.1. Policy for the safety of vitamin and mineral contents of formula

Proposed at Preliminary Inquiry

It was proposed at Preliminary Inquiry to prescribe mandatory maximum levels for vitamins and minerals classified as of ‘significant risk’ to infants when consumed at excess intakes. Advisory maximum levels were recommended for other nutrients whose risk classification was provisionally assessed as ‘not of significance on the basis of current scientific knowledge’.

Issues

Although industry preferred neither prescribed levels nor recommended guideline levels for maximum nutrient content and consumers supported prescribed levels for maximum contents, there is reasonable support for the proposed approach. However, this support was provisional. In the case of industry submissions, support was indicated provided that these levels don’t become ‘pseudo–regulation’ and in the case of the consumer representatives, support was indicated provided that there is effective monitoring of Good Manufacturing Practice (GMP) and levels of nutrients.

Assessment

Consumer representatives note that GMP guidelines were insufficient in the 1970s to protect infants from unsafe formula in the USA and the resultant harm to infants lead to the introduction of regulation for infant formula by the US government. Industry consider a ‘guideline’ may become a pseudo–regulation’ and one industry submission was not in favour of nutrient levels being recommended in the guidelines as this would imply that compliance be expected to be monitored.

ANZFA recommends maximum levels of nutrients in infant formula as whilst not all nutrients are toxic in excess, an excess of one nutrient can sometimes interact adversely with other nutrients.

Manufacturers are believed and expected by carers or consumers to be aware of the levels of nutrients in formula. Whilst maximum levels were not stipulated for some specific nutrients, ANZFA has recommended a guideline level. This guideline level was stipulated to assist industry improve formulations to those considered safer by health professionals. It is generally accepted that the current health outcome of formula fed infants is not as good as those who are fed human milk; the causation being multifactorial. ANZFA has not been provided with data about the maximum levels of nutrients in infant formula sold in Australia or New Zealand. Therefore ANZFA is not able to exclude the current levels as implicated in the less positive outcome for formula fed infants. Until such time as current levels are specifically excluded from implication in reducing health outcome to consumers, ANZFA expects infant formula manufacturers to monitor formula nutrient levels regularly and work towards achieving the recommended level for their formula.

Consumers note that the EC Directive for foods for special medical purposes, which prescribes maximum levels for all nutrients, has recently been adopted. Industry contributed to the development of this Directive, which suggests that it is well within the capacity of industry to meet prescribed maximum levels.

Recommendation

ANZFA will maintain the current guideline levels unless evidence is provided that it is in the interest of infants to amend these levels.

6.4.2 Specific levels in the Table to Clause 31

Only those levels where a specific request for amendment has been received are discussed below. There were submissions of support for many nutrient levels.

6.4.2.1 Selenium

Current and proposed provisions

	Infant formula mcg/100 kJ	**Follow–on formula mcg/100 kJ**
current R7	not specified	as per infant formula
proposed at Full Assessment	0.42–0.89	0.79–0.89
Codex	not specified	not specified
proposed Codex standard	not specified – 0.7	Not applicable
LSRO Recommendations	0.36–1.19	as per infant formula
Proposed at Preliminary Inquiry	0.36– 0.9	as per infant formula
RECOMMENDATION AT INQUIRY	0.25–1.19	as per infant formula

Issues

No new data was supplied about the safety of the levels of selenium.
Abbott Australasia Pty Ltd, Abbott Laboratories (NZ) Ltd and **the International Formula Council** submitted for the maximum level to be increased to 1.1–1.19 mcg/100 kJ as per the LSRO recommendation for a maximum level. **Dr Simmer**, **Neonatologist and Associate Professor** submitted that lower levels of selenium may meet the needs of infants.

Assessment

Minimum level

The minimum level set at Preliminary Inquiry was assessed against the recommended dietary intake (RDI) and would meet the needs of most infants. Given the variation in individual requirements and daily consumption levels, a lower level may also meet the needs of most infants. The EC has recently adopted a standard which includes a minimum selenium level of 0.25 mcg/100 kJ for foods for special medical purposes prepared for infants. Adoption of this minimum level would provide 60–70% of the RDI for infant to 6 months and the needs of older infants. The RDI is a population based recommendation rather than an indicator of the need for a particular individual. The minimum level of 0.25 mcg selenium /100 kJ is consistent with a safe formulation for infants. Hence it is recommended that the minimum level be reduced to 0.25 mcg/100 kJ which is consistent with the recent EC foods for special medical purposes standard level.

Maximum level

The LSRO has recommended a maximum of 1.19 mcg selenium/100 kJ based on the upper limits of selenium in breast milk. Manufacturers have requested the maximum level be raised to that recommended by the LSRO. This upper level would provide 2–3 times the RDI for an infant from formula. Additional selenium would also be contributed from other foods consumed by older infants but the contribution from formula intakes would therefore be reduced in this case. There is no evidence that this level would pose a risk to infants and therefore it is recommended that the limit recommended by the LSRO be adopted.

Recommendation

The selenium values in the Table to Clause 31 of the draft standard be amended to 0.25–1.19 mcg/100 kJ.

6.4.2.2 Copper

Current provisions and proposed provisions

	Infant formula mcg/100 kJ	**Follow–on formula mcg/100 kJ**
current R7	14– not specified	as per infant formula
proposed at Full Assessment	14–36 (non soy based formula) 21–43 (soy based formula)	as per infant formula
Codex	14– not specified	not specified
proposed Codex standard	4.8–19	Not applicable

	Infant formula mcg/100 kJ	Follow–on formula mcg/100 kJ
LSRO Recommendations	14.3–38.1	as per infant formula
Proposed at Preliminary Inquiry	14–43	as per infant formula
RECOMMENDATION AT INQUIRY	As proposed at Preliminary Inquiry	As proposed at Preliminary Inquiry

Issue

Nestlé Australia Ltd argues that as the EC permits a minimum copper content of 4.8 mcg per 100 kJ, some formulas manufactured to EC formulations will not comply with the proposed standard. The implication is that the minimum level should be reduced to meet the EC level.

Assessment

The copper content of human milk ranges from 7–25 mcg/100 kJ. A formula made to the minimum level of copper would not provide the necessary copper to meet the estimated safe and adequate daily dietary intakes (ESADDI) set for infants. The minimum level recommended at Preliminary Inquiry is consistent with the LSRO recommendation and also the recommendation from the American Academy of Paediatrics in 1985. The recommended level in the standard may constitute a technical barrier to trade but a formula made to the minimum copper level in the EC standard would not meet minimum nutritional requirements for copper and therefore would be considered a risk to infants.

Although the level in pre–term formula are not under discussion in this section, pre–term babies have a greater need for copper than term babies. It should be noted that the Canadian minimum recommended level for pre–term formula is 23.8 mcg/100 kJ, i.e. well above the EC prescribed minimum level.

Recommendation

No change to proposed minimum copper level.

6.4.2.3 Zinc to copper ratio

Current and proposed levels

	Infant formula & Follow–on Formula Max Zn:Cu Ratio (mcg/100 kJ)
Current R7	*NS
Proposed at Full Assessment	10:1
Codex	*NS
Proposed Codex standard	*NS
LSRO Recommendations	20:1
Proposed at Preliminary Inquiry	12:1
Recommendation at Inquiry	As proposed at Preliminary Inquiry
RECOMMENDATION AT SUPPLEMENTARY FINAL ASSESSMENT	15:1 (Infant formula) 20:1 (Follow–on formula)

*NS – Not Specified

Issues

International Formula Council endorses the level of 12:1 recommended at Preliminary Inquiry. However, **Nestlé Australia Ltd** submits that the majority of **Nestlé Australia Ltd** products would not meet this maximum ratio. **Wyeth Australia Pty** also submits the need to considerable reformulation to meet the 12:1 ratio and support a ratio of 22:1. **Wyeth Australia Pty Ltd** also submitted that the Codex levels are 19–25:1

Assessment

Clarification of Codex levels

The current Codex standards for infant formula and follow–on–formula do not specify maximum levels for zinc or copper and therefore there is no Zn:Cu ratio specified.
The proposed draft Codex standard for infant formula was returned to Step 3 of the 8–step process in September 1998, as consensus could not be reached. That proposed standard currently includes maximum limits for both zinc and copper and also a different set of limits for the zinc content of soy–based formula as shown in the following table.

Proposed draft Codex Infant Formula Standard	**Minimum amount per 100 kJ**	**Maximum amount per 100 kJ**
Zinc	0.12 mg	NS*
Zinc content in soy–based or soy &milk based formulas	0.18 mg	0.6 mg
Copper	4.8 mcg	19 mcg
Zn:Cu (ANZFA calculation)		
Milk–based formulas	6.3:1	High given the max Zn is NS
Soy–based formula and soy &milk –based formulas	9.4:1	125:1

*NS – Not Specified

The Zn:Cu ratio in the draft proposed Codex standard ranges from 6 – high:1.
Therefore harmonisation with the Codex or proposed Codex standards is not in the interest of infants as this could legitimize unsafe levels.

Ratio

The threshold for adverse effects ascribed to copper deficiency caused by zinc excess needs to be defined. When the zinc: copper intake exceeds 10, retention of copper is decreased leading to copper deficiency and changes in copper dependent metabolism have been observed at ratios above 20:1 (Langley and Mangas, 1997)[18]. The Zn:Cu ratio of human milk is 10:1.

[18] Langley A and Mangas S (1997) Zinc. *National Environmental Health Forum Monographs.* Metal Series No. 2.

At a recent international meeting it was concluded that preparations intended to increase the zinc intake above that provided by the diet should not exceed the dietary reference values, and should contain sufficient copper to ensure a ratio of zinc and copper of approximately 7, as found in human milk (WHO, 1996)[19]. LSRO suggests on the basis of adult studies that the ratio should not exceed 20:1.

The basic premise for aligning mineral and vitamin level to those of human milk is that in general, formula–fed infants do not have the same positive health outcome as those fed on human milk. Whilst current scientific knowledge is not able to attribute the specific compositional parameters that may be involved in reducing the health outcome for infants, nutrient interactions may be one such cause. Manufacturers are advised to modify formulations where possible to bring nutrient levels as close to those of human milk as possible whilst accounting for the bioavailability of the specific nutrient forms.

Recommendation at Inquiry

Maintain the ratio of 12:1 proposed at Inquiry until further data on infants is available.

Industry issue at Inquiry

That the value be raised to 20:1, as studies have indicated that a ratio up to 25:1 is safe.

Assessment

The zinc to copper (Zn:Cu) ratio is a new concept in infant public health and is a separate issue from the minimum and maximum limits of zinc and copper. The Zn:Cu ratio of human milk is 10:1 but there are no studies in infants to indicate the appropriate or optimal Zn:Cu ratio for formula. However, effects on copper status have been noted at ratios of above 100:1. Given that infants have immature systems (absorption, metabolism, excretion), that infant formula is the sole source of nutrition, that infants are at a stage of development characterised by intense growth (which may make infants more vulnerable to factors such as copper deficiency) and that data on adverse effects is limited, a cautious approach was considered the best option in recommending the appropriate Zn:Cu ratios for formula.

Industry provided a literature search of papers on the zinc/copper interactions arising from 5 clinical trials from 1982 to 1994. All trials assessed healthy term infants and had an infant formula Zn:Cu ratio of 20:1 or greater. Given the inherent limitations of the design of the trials cited by the reviewer (Makrides *et al*[20]) the studies all reported no adverse effects of an altered Zn:Cu ratio.

Professor Bo Lonnerdal, Professor of Nutrition and Internal Medicine, Department of Nutrition, University of California provided a summary and opinion on the ratio. Professor Lonnerdal stated that animal studies show that zinc can interfere with copper absorption; however, in these studies high levels of zinc were used, often with low copper levels.

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[19] WHO (1996) *Environmental Health Criteria for Zinc*. International Program on Chemical Safety. In preparation.

[20] Makrides M et al (2000) Report to the Infant Formula Manufacturers association of Australia – "Review of amino acid profiles, zinc to copper ratios and essential fatty acid composition of infant formulas.

The ensuing Zn:Cu ratio was frequently unphysiological and beyond what can be assumed to be consumed by humans. He also noted there are few studies in human infants that have focused on Zn:Cu ratio. However, Lonnerdal and Hernell (1994)[21] have reported a study of healthy Swedish babies fed formula with a Zn:Cu ratio of 37:1 from 6 weeks to 6 months age that indicated no adverse effects or impairment of copper status.

Therefore in an attempt to achieve a ratio that is as close as possible to that of breast milk but which can be readily achieved by industry, a ratio of 15:1 was considered suitable for infant formula products intended for infants under 6 months.
As older babies are consuming an increasingly varied diet with infant formula contributing less of the total intake the maximum level could be increased to 20:1.

Recommendation at Supplementary Final Assessment

That the maximum Zn:Cu ratio in the draft standard be increased to 15:1 for infant formula intended for infants less than 6 months of age, and to 20:1 for follow–on formula based on no evidence of harm to infants in the data submitted by Industry.

6.4.2.4 Chromium and Molybdenum

Current provisions and proposed provisions

	CHROMIUM		**MOLYBDENUM**	
	Infant formula mcg/100 kJ	Follow–on formula mcg/100 kJ	**Infant formula mcg /100 kJ**	**Follow–on formula mcg /100 kJ**
Current R7	NS	as per infant formula	NS	as per infant formula
Proposed at Full Assessment	NS (for prox Mod Formula 3.5 mcg to 15 mcg)	as per infant formula	NS (for prox Mod Formula 0.36 mcg to 0.71 mcg*)	as per infant formula
Codex	NS	NS	NS	NS
Proposed Codex standard	NS	NA	NA	NA
LSRO Recommendations	did not re–commend Min or max levels	as per infant formula	did not re–commend a Min or max	as per infant formula
Proposed at Preliminary Inquiry	[Advisory guideline max:15] prox mod formulas: 0.35– 15.0	as per infant formula	[Advisory guideline max 3.0] Prox mod formulas: 0.36 – 3.0	as per infant formula

[21] Lonnerdal B, Hernell O (1994) Iron, zinc, copper and selenium status of breast–fed infants and infants fed trace element fortified milk–based infant formula. Acta Paediatr, 83, 367–73.

Recommendation at Inquiry	As proposed at Preliminary Inquiry	As proposed at Preliminary Inquiry	As proposed at Preliminary Inquiry	As proposed at Preliminary Inquiry
RECOMMENDATION AT SUPPLEMENTARY FINAL ASSESSMENT	As proposed at Inquiry	As proposed at Inquiry	As proposed at Inquiry	As proposed at Inquiry

NA – Not applicable; NS – Not Specified

Issues

InforMed Systems Ltd questioned why chromium and molybdenum must be added in this case (assumed to be in relation to Clause 41) but not for similar ordinary formula as these nutrients are essential for all infants.

Assessment

This issue was addressed at Preliminary Inquiry. It was noted that as these nutrients are ubiquitous in nature a formula based on usual food ingredients does not need any added chromium or molybdenum. Provision was made in the draft standard for the addition of these nutrients to infant formula products based upon protein substitutes as in some cases these formula may be elemental i.e. not based upon food constituents. Therefore without the addition of these nutrients these formula would be devoid of chromium or molybdenum and unsuitable for infants.

Recommendation at Inquiry

Retain the proposed standard.

Industry issue at Inquiry

That the addition of chromium and molybdenum be permitted for all formula such as resulting in a requirement to the levels currently specified for special purpose formula.

Assessment

No new data was provided by industry to show how this provision affects the affordability or availability of infant formula products. As stated previously, chromium and molybdenum are ubiquitous in nature. Formula based upon food ingredients will provide sufficient chromium and molybdenum for the requirements of infants. Therefore there is no need for the addition of these nutrients to formula made from food ingredients.

Stakeholders at a forum agreed permission could be given in the standard to add chromium and molybdenum to formula for healthy infants, provided this supplementation was reviewed long term. Additionally it was anticipated industry would supply data about base levels of chromium and molybdenum in base ingredients and any supplementation undertaken for monitoring of the intakes of infants for these two nutrients. The issue was later withdrawn by industry.

Recommendation at Supplementary Final Assessment

The provisions for chromium and molybdenum be retained.

6.4.2.5 Pyridoxine (Vitamin B6)

Current provisions and proposed provisions

	Infant formula mcg/100 kJ	**Follow–on formula mcg/100 kJ**
current R7	9– not specified (> 15 mcg/g protein for form with 0.6 mg/100 kJ)	as per infant formula
proposed at Full Assessment	8.9–36	as per infant formula
Codex	9–not specified	11– not specified
proposed Codex standard	15– not specified mcg/g protein but not less than 9– not specified)	Not applicable
LSRO Recommendations	7.14–30.95	as per infant formula
Proposed at Preliminary Inquiry	9–36 mcg/100 kJ	as per infant formula
RECOMMENDATION AT INQUIRY	As proposed at Preliminary Inquiry	As proposed at Preliminary Inquiry

Issue

Nestlé Australia Ltd has submitted that the inclusion of a maximum for vitamin B6 has the potential to provide a technical barrier to trade.

Assessment

At Preliminary Inquiry ANZFA stated that the retention of maximum level for vitamin B6 was unlikely to cause any trade restriction based on the LSRO conclusion. The maximum prescribed for the proposed standard is 36 mcg/100 kJ and the LSRO maximum level was based on 31 mcg pyridoxine /100 kJ which was the 90th percentile of analyses of infant formula.

Whilst ANZFA is not aware of any reports of pyridoxine toxicity in infants, there have been reports of toxicity in adults with excess pyridoxine intake. The EC has recently limited the maximum pyridoxine content of special purpose formula to 75 mcg/100 kJ.

The proposed maximum level is 4 times the RDI for infants (to 6 months). A review of the formula available in Australia whose pyridoxine content ANZFA was aware of, indicted they are well below the maximum level set. Justification for excessive content should be provided if manufacturers have a need to exceed this level to assist healthy infants attain their nutritional requirements.

Recommendation

Retain the proposed maximum level.

6.4.2.6 Riboflavin (Vitamin B_2)

Current provisions and proposed provisions

	Infant formula mcg/100 kJ	**Follow–on formula mcg/100 kJ**
current R7	14– not specified	as per infant formula
proposed at Full Assessment	14 – 86	as per infant formula
Codex	14– not specified	14– not specified
proposed Codex standard	14– not specified	Not applicable
LSRO Recommendations	19.0 – 71.4	as per infant formula
Proposed at Preliminary Inquiry	14 mcg/100 kJ – not specified [Advisory guideline maximum of 86 mcg/100 kJ]	as per infant formula
RECOMMENDATION AT INQUIRY	As proposed at Preliminary Inquiry	As proposed at Preliminary Inquiry

Issue

The NZ Dairy Board submits that the maximum level of riboflavin at 86 mcg is set too low. The Board states that some products can have naturally occurring levels of riboflavin as high as 86.5 mcg and recommends that level be increased to 87 mcg to accommodate the variability of the naturally occurring nutrient.

Assessment

The EC has prescribed a maximum level of 100 mcg/100 kJ for foods for special medical purposes. The maximum level is recommended as a guideline level rather than as a mandatory level. ANZFA's policy is to maintain guideline levels unless evidence is provided that it is in the interest of infants to vary a guideline level. This guideline level provides 5 times the RDI for infants. In accordance with ANZFA's policy, it is recommended the guideline level be maintained. Manufacturers are encouraged to moderate nutrient levels where possible.

Recommendation

Retain current guideline level.

6.4.2.7 Iron

Current provisions and proposed provisions

	Infant formula mg/100 kJ	**Follow–on formula mg/100 kJ**
current R7	0.1 – 0.48	as per infant formula
proposed at Full Assessment	0.2 – 0.5	as per infant formula
Codex	min 0.04 or 0.25 (added iron claim) max. NS	0.25 – 0.50
proposed Codex standard	0.12 – 0.36	N/A
Proposed at Preliminary Inquiry	0.2 – 0.5	as per infant formula

	Infant formula mg/100 kJ	Follow–on formula mg/100 kJ
Recommendation at Inquiry	As proposed at Preliminary Inquiry	As proposed at Preliminary Inquiry
RECOMMENDATION AT SUPPLEMENTARY FINAL ASSESSMENT	As proposed at Inquiry	As proposed at Inquiry

NS – Not specified

Industry issue at Inquiry

That the permitted level of iron be reviewed in light of the discrepancy with Codex values. Industry proposed a reduction in the minimum iron content from 0.2 mg/100 kJ to 0.12 mg/100 kJ.

Assessment

Levels in other relevant standards

The rationale for the lower level proposed by industry is that this level is the minimum level in the EC Directive for infant formula. Codex currently sets a level of 0.04 mg/100 kJ for a low iron infant formula product, although the current draft revised Codex standard proposes a minimum level consistent with the level in the EC Directive.

Infant iron deficiency

The Australian and New Zealand governments consider the issue of infant iron deficiency a public health issue. For the prevention of iron deficiency the National Health and Medical Research Council (NHMRC)[22] recommends iron–fortified cereals as one of the first solid foods to be introduced to infants between 4 to 6 months of age. Therefore, Standard 2.9.2 – Foods for Infants mandates the iron fortification of cereals for infants.

In 1995, health authorities on the Authority's Expert Panel recommended prescribed iron levels in the standard for infant formula products to provide an iron fortification to infants. Therefore, the iron level proposed in draft Standard 2.9.1, which is set for all formula regardless of base ingredients, provides a mild degree of iron fortification for infants. It is not considered necessary to set different nutrient levels for different base ingredient contents in the standard as manufacturers are expected to address issues of bio–availability of the base ingredients in their formula. The levels are set at higher than the level in human milk because the iron added to infant formula is of lower bio–availability. This proposal for iron fortification has been supported in submissions, including those from industry, to the development of this standard since 1995.

The proposal by industry to reduce the proposed minimum iron level was discussed by a range of stakeholders. Consumer representatives and health professionals favoured the degree of iron fortification required by the proposed levels because iron deficiency anaemia is a public health concern in Australia and New Zealand and noted the benefits of iron supplemented formula are well established.

[22] NHMRC 1995 Dietary guidelines for children and adolescents

Recommendation at Supplementary Final Assessment

It is recommended that the proposed draft standard for infant formula products retain the proposed minimum iron level of 0.2 mg iron/100 kJ to address concerns of iron deficiency in infants in Australia and New Zealand

6.4.2.8 Phosphorus

Proposed at Inquiry

Phosphorus levels of 6–25 mg/100 kJ were prescribed and an advisory guideline maximum of 22 mg/100 kJ was also included in the standard to encourage industry to reduce phosphorus levels of infant formula products.

Industry issue

That the maximum phosphorus content of formula be increased to 40 mg/100 kJ. Industry stated that for follow–on formula, protein limits are increased to 0.45 to 1.3 g/100kJ. Typical cow's milk phosphorus levels are shown as 28 mg phosphorus/g protein in the Annex VII of the EC Directive for infants/follow on formulas. Therefore, as an example, if a follow–on formula contained the maximum 1.3 g protein/100 kJ, the average phosphorus level would be 36 mg phosphorus/100 kJ, which would exceed the maximum permission.

Support for a level of 37 mg phosphorus /100 kJ was later expressed by the industry representative from Wyeth.

Assessment

Significant interactions that affect bioavailability and utilisation of other nutrients have been reported for phosphorus. Phosphorus makes a significant contribution to renal solute load, as excess intake is required to be excreted by the kidneys. Therefore it is considered high intakes of phosphorus pose a significant risk for infants and the maximum level of phosphorus should be regulated in the standard. The maximum phosphorus level recommended by the LSRO Report[23] is 16.7 mg/100 kJ.

The levels proposed in the standard will provide for the needs of infants to 12 months of age and the maximum aligns with that in the EC, the UK regulations and those currently proposed for use in the revised Codex standard for infant formula (not follow up formula).

As previously noted in the discussion on the definition of follow–on formula, Australian and New Zealand usage of follow–on formula is different to the usage in Europe where it is not used as a 'formula' but rather a drink. Therefore the maximum level should be safe for infants who are fed this formula in the quantities that provide for the sole source of nutrition.

[23] Raiten DJ et al (1998) Assessment of nutrient requirements for infant formulas. JON Supplement Vol 128 N 15 – Report prepared for the Centre for Food Safety and Applied Nutrition, Food and Drug Administration, Department of Health and Human Services, Washington DC

At Preliminary Inquiry, the maximum level proposed for phosphorus at Full Assessment was increased to 25 mg/100 kJ to provide for seasonal variation of ingredients. However to encourage industry to reduce the maximum phosphorus content of infant formula to 22 mg/100 kJ the level consistent with the Codex level, a guideline level of 22 mg/100 kJ was incorporated into the standard.

Members of the External Advisory Group noted that the phosphorus in milk is linked to the casein fraction and industry endeavours to limit the casein content, hence the high level of phosphorus, is not likely. Health professionals are also concerned about the high protein levels permitted by the standard and manufacturers are not expected to use the maximum levels in the standard other than for exceptional circumstances. The External Advisory Group agreed that the level proposed in the standard be retained.

Recommendation at Supplementary Final Assessment

That the levels in the proposed standard be retained.

6.4.3 Schedule 1–Permitted forms of vitamins & minerals

Proposed at Preliminary Inquiry

Infant formula and follow–on formula must contain the vitamins and minerals specified in Clause 31 in the forms permitted in Schedule 1. The amount of vitamins and minerals in infant formula and follow–on formula must contain more than the minimum amount per 100 kJ specified in Clause 31 and no more than the maximum amount per 100 kJ specified in Clause 31.

6.4.3.1 General

Issue

Only manufacturers of infant formula products addressed this issue, claiming a list was unnecessary and may impede innovation. No new information was provided. Manufacturers called for permission to use any nutrient form permitted elsewhere.

Assessment

To protect the health and safety of infants, new forms of nutrients should be assessed before use in infant formula in Australia and New Zealand. **Nestlé Australia Ltd** has submitted that several specific forms of nutrients should be permitted because they were permitted in the EC or New Zealand Food Regulations (NZFR). Forms permitted by other agencies for many years may not necessarily still be considered safe in the light of more recent evidence. For example, nicotinic acid is permitted by a number of regulations, including the Codex standard. Recent evidence suggests this form may cause adverse effects in high amounts, whilst other forms of niacin do not.

Recommendation

Codex has stated its intention to review its list of permitted forms of nutrients for addition to foods for infants. ANZFA will maintain a watching brief on the Codex developments. ANZFA has proposed a much broader range of permitted forms than currently permitted by Codex. However, there are some substances permitted to be used in infant formula by Codex which were not included at Preliminary Inquiry. The trade obligations of Australia and New Zealand impose a requirement to include all forms permitted by Codex if there is no health or safety concern. Therefore, with the exception of nicotinic acid (refer below for discussion), forms permitted by the Codex standard have been added to the list of permitted forms of nutrients for use in infant formula products.

6.4.3.2 Cupric carbonate

Issue

Nestlé Australia Ltd has submitted that cupric carbonate should be permitted as it is permitted by Codex.

Assessment

Whilst Codex provides permission for cupric carbonate for use in baked products and protein hydrolysate and meat based formula no permission is provided for infant formula based upon cows milk.

Recommendation

That cupric carbonate not be added to the list of suitable permitted forms of nutrients for infant formula.

6.4.3.3 Nicotinic acid

Issue

Nestlé Australia Ltd has submitted that nicotinic acid should be permitted as it is permitted by Codex, the NZFR and the EC.

Assessment

Nicotinic acid is permitted as a vitamin compound for use in infant formula by some international food regulations including Codex. However, the LSRO has reported adverse effects with large doses of nicotinic acid. The potential risks to the health and safety of infants from nicotinic acid should be assessed before use in infant formula. Therefore as alternatives are available, e.g. niacinamide, manufacturers wishing to use nicotinic acid should make an application for permission including the necessary scientific data to justify with the application.

Recommendation

Nicotinic acid should be reassessed for safety before being permitted for use in infant formula.

6.4.3.4 Selenium

Proposed at Preliminary Inquiry

Codex does not give permission for the use of specific forms of selenium. At Preliminary Inquiry ANZFA requested data about the bioavailability of sodium selenate so as to consider its inclusion as a source of selenium in infant formula products.

Issues

Dr L Daniels, Flinders Medical Centre supplied data relating to selenium supplementation of infant formula to ANZFA. **Dr Daniels** provided information on reports which conclude that infant consumption of formula unsupplemented with selenium does not produce the same blood levels as in breastfed infants. **Dr Daniels** also notes whilst there is insufficient evidence to define the optimal form of selenium for supplementation, recent studies have concluded that 'fortification of foods with either selenate or selenite would be equally efficient in providing 'bioavailable selenium'.

Recommendation

Sodium selenate be added to Schedule 1 in Standard 2.9.1 – Permitted forms of vitamins and minerals in infant formula products.

6.4.3.5 Choline and carnitine forms

Issue

Nestlé Australia Ltd has also requested permission for choline (per se), choline citrate and the hydrochloride of L–carnitine claiming the EC permits the use of these forms.

Assessment

At Preliminary Inquiry it was stated that requests to extend the list of permitted forms would need to be accompanied by data suitable for safety assessment or an application should be made after the standard is gazetted. Data has not been provided to assess the safety of these forms of carnitine and choline.

Recommendation

These forms should not be added to the list of permitted forms of vitamins and minerals until such time as a full assessment has been made.

Summary recommendation for Section 6.4.3

The following substances be added to Schedule 1 in Standard 2.9.1 – Permitted forms of vitamins and minerals in infant formula products:

- Retinyl propionate as a source of vitamin A;
- Cholecalciferol–cholesterol as a source of vitamin D;
- Dl–alpha– tocopheryl succinate as a source of vitamin E;
- Phytylmenoquinone as a source of vitamin K;
- Sodium chloride iodized as a source of sodium;
- Cupric citrate as a source of copper;
- Manganese carbonate and manganese citrate as sources of manganese; and
- Sodium Selenate as a source of selenium.

7. PART 3 – INFANT FORMULA PRODUCTS FOR SPECIAL DIETARY USE

7.1 Division 1 – Pre–term formula

Refer to definition of pre–term formula at Item 1.7.

Proposed at Preliminary Inquiry

Regulation of pre–term prescribes energy and nutrient content of formula.

Issues

Some submitters claimed the regulation of pre–term formula would result in unnecessary delay of new products. The proposed standard will mean that some product currently on the market will be illegal in Australia and New Zealand.
Concern was raised that there was no international regulation for pre term formula
ANZFA requested data to assist with the safety assessment of the inclusion of Medium Chain Triglycerides in formula for pre–term infants.

Assessment

It has been claimed that the field of nutrition in pre–term or low birth weight (LBW) is rapidly changing and needs to respond to scientific advances. ANZFA has noted the highly variable compositions of the vitamin, mineral and medium chain triglyceride (MCT) contents of pre–term formula currently available and is concerned that the efficacy of these formula has not been reviewed independently from industry evaluations. Independent assessment of these formula is necessary for the health and safety of pre–term infants.

Recommendation

ANZFA prepare a proposal to review the provisions for safe formula for pre–term and low birth weight infants within 5 years of draft Standard 2.9.1 being adopted.

7.1.1 Fat content of Pre–term formula

Issue

Dr Robert Gibson, Director, Child Nutrition Research Centre and Maria Makrides, Research Dietitian and NHMRC fellow submitted that the requirement for fats in formula for pre–term infants to comply with the fats in formula for term infants is not based on scientific evidence. **Dr Gibson** and **Ms Makrides** stated there is little known about the fat requirement for term infants. Therefore, it is incongruous to be basing the fat composition of formula for pre–term infants on the fats that are in breast milk of mothers who gave birth to term infants

Assessment

There are now concerns being raised that the type and levels of fatty acids added to pre–term formula by manufacturers are not ideal for pre–term babies, therefore there appears to be a need for some regulatory control. Whilst it is acknowledged that the usual nourishment for infants 'in utero' is not human milk but rather transfused nutrients via the placenta, there is insufficient data to base nutrient levels on transfused nutrient levels. Hence the current most appropriate model in this case would be the human milk nutrient contents with modifications for 'known' safe variations to nutrients. This is the model proposed at Full Assessment (and unchanged at Preliminary Inquiry).

Recommendation

ANZFA prepare a proposal to review the provisions for safe formula for pre–term and low birth weight infants within 5 years of draft Standard 2.9.1 being adopted.

7.1.2 Medium Chain Triglyceride (MCT) content of pre–term formula

Issue

At Full Assessment it was proposed to prohibit MCTs in formula for healthy infants and pre–term infants. However, strong opposition was raised by industry in relation to banning MCTs in pre–term formula. Pre–term formulas with high levels of MCTs are already in use in Australia and New Zealand and this provision would disadvantage pre–term infants in these countries. Pre–term formula is such a small market in Australia and New Zealand that banning MCTs in formula in these countries may mean that companies withdraw their products from this market rather than reformulate them. At Preliminary Inquiry, ANZFA asked for assistance in resolving the requirements for the MCT content of pre–term formula. It was proposed that data at Inquiry would be used to determine a potential MCT content of formula prepares for pre–term infants.

Assessment

Data was provided at Preliminary Inquiry by industry submitters as to the current levels of MCTs in pre–term formula and levels of usage. Levels of MCTs in pre–term formula currently used in Australia and New Zealand vary from 15% to 40% of total fatty acids as MCTs.

The predominant formula used in New Zealand has levels of about 15% MCTs as a percentage of total fatty acids. The predominant formula used in Australia have 40% or less MCTs as a percentage of total fatty acids. Submitters were also asked to provide information that MCTs at currently used levels are safe and efficacious as recent reports have questioned the efficacy and safety of high MCT fat intake by premature infants.

Evidence was provided that MCTs may be more readily absorbed than other fats in pre–term babies. However, no new information was presented to ANZFA that high levels of MCTs are safe and efficacious in pre–term formula. ANZFA needs to evaluate the toxicological safety of MCT content of pre–term formulas but does not have sufficient resources to do this within the scope of this Inquiry into the draft Standard 2.9.1.

Recommendation

ANZFA prepare a proposal to review the provisions for safe formula for pre–term and low birth weight infants within 5 years of draft Standard 2.9.1 being adopted.

7.1.3 Vitamin and mineral content of pre–term formula.

Issue

The ranges of vitamins and minerals proposed at Full Assessment was not reviewed at Preliminary Inquiry due to insufficient resources.

Assessment

ANZFA's initial review of generally available data about the micronutrient levels of pre–term formula reveals highly variable nutrient contents from brand to brand. Pre–term formula manufactured by some manufacturers do not comply with the proposed standard and would have to be withdrawn from the market if the proposed standard proceeds. The highly variable micronutrient content of the available different brands of pre–term formula needs safety and efficacy evaluation.

Supplies are generally determined by tendering process in hospitals.
Variable compositions in these formula may inadvertently create difficulties for medical specialists when hospital supplies change due to tendering outcomes.

There are also significant differences exist between the levels proposed at Full Assessment and those recommended by a Canadian expert panel[24]. ANZFA wishes to consult with technical experts in the feeding of premature infants for recommendations as to the most appropriate regulation for these micronutrients.

Recommendation

ANZFA prepare a proposal to review the provisions for safe formulas for pre–term and low birth weight infants within 5 years of draft Standard 2.9.1 being adopted.

[24] Guidelines for the composition and clinical testing of formulas for preterm infants (1995) Report of an ad hoc expert consultation to the Health Protectorate Branch, Health Canada, Canada.

7.1.4 Use of pre–term formula

There is a clear need for a degree of regulation in the compositions of pre–term formula as unsafe or less than ideal formulations are able to be marketed for use by pre–term infants without independent review. The trend overseas is for pre–term infants who are stabilised on a pre–term formula at discharge to continue the use of the same formula at home. It is noted that at least one major Australian manufacturer includes instructions to doctors on making up pre–term formula at home in the MIMS. Therefore the use of these infant formula may increase and may not necessarily be under hospital care.

An alternative to a food standard such as a 'pre–market clearance' program may be more appropriate for Australia and New Zealand. Such options need further consideration. Issues arise for the implementation of the Australian Quarantine Inspection Service duties where no food standard exists, particularly for so called 'foods for special medical purposes'. Therefore a provision is required within the Food Standards Code to assist in the assessment of imported foods categorised as 'pre–term formula'. Therefore it is recommended that proposed standard be replaced by a generic permission for pre–term formula within the standard and the detailed provisions be assessed in a separate project.

Conclusion

ANZFA intends to undertake an assessment of the compositional requirements for pre–term formula however, insufficient resources are available to do this assessment within this Inquiry into draft Standard 2.9.1. It is recommended that a new proposal be prepared to assess the safety and efficacy of formula prepared for pre–term babies and the current specific regulation be replaced by a temporary general provision.

7.1.5 Clause 36 –Labelling statement on pre–term formula

Proposed at Preliminary Inquiry

The label of pre–term formula must include the statement, *'Suitable only for pre–term infants under specialist medical supervision'*.

Issue

Nestlé Australia Ltd believe the statement on pre–term formula, that the product is suitable only for pre–term infants under specialist medical supervision, is not needed because these products are only available in hospitals for babies under specialist medical supervision.

Assessment

If pre–term formula is only permitted to be used in hospitals and are not available for general sale then the statement is superfluous. However, ANZFA is unaware of any restriction on their sale, therefore there is a potential that they may be sold in a retail outlet. As noted above advice is available to all doctors on how to prepare these formula at home. In such a case the statement is necessary.

Recommendation

That the labelling requirement be retained as proposed at Preliminary Inquiry.

Summary recommendations for Section 7.1

1. Clauses 32–35 be deleted from Standard 2.9.1 and replaced by a clause to the effect that infant formula product may be specifically formulated to satisfy the needs of pre–term or low birth weight infants but in all other respects must comply with the standard for infant formula products. This provision will provide temporary regulatory status for these foods and require manufacturers to be able to justify their variations from the general standard.

2. ANZFA prepare a proposal to review the provisions for safe formula for pre–term and low birth weight infants within 5 years of draft Standard 2.9.1 being adopted.

7.2 Division 2 – Infant formula products formulated for metabolic and immunological conditions

Proposed at Preliminary Inquiry

Infant formula product may be specifically formulated to satisfy particular metabolic or immunological conditions but otherwise need to comply with the standard.

Issues

Issues were raised in relation to the scope of the standard, position of special purpose formula within the general standard for infant formula, suitable availability, and claims on thickened formula. These issues are addressed separately below.

7.2.1 Scope

Patricia McVeagh, **a consultant pediatrician**, states that the definition of special purpose formula refers to metabolic and immunological conditions but needs to be broader to include other infants requiring special purpose formula such as malabsorptive disorders including pancreatic deficiency, cholestasis, short bowel etc. She states that soy formula should be included in special purpose formula. Appropriate indication for their use would be galactosaemia, proven cow protein allergy or cow milk protein intolerance.

Two submissions did not believe that the draft regulation was broad enough to cater for special purpose formula for conditions such as gastrointestinal or renal diseases.

Assessment

ANZFA intended a wide interpretation of the descriptor 'metabolic' as it was considered that mal–absorptive disorders, other than disaccharide mal–digestion, e.g. lactose mal–digestion, are frequently merely a symptom of an underlying immunological or metabolic condition. However, it seems necessary to provide more specifically for renal, hepatic or mal–absorptive disorders.

Therefore it is recommended that this category be expanded to include renal, hepatic and mal–absorptive conditions. This will have the effect of capturing the formula specially prepared for lactose mal–digesters within this category.

Soy–based formula are used for both medical and non–medical purposes. Claims about nutrient content or about a special medical purpose for a soy–based product should trigger labelling consistent with that required of 'other' special purpose formula. This would allow a soy–based formula to be positioned as a standard infant formula product if no nutrient claims are made and if no special medical purpose is claimed; or alternatively to be positioned as a special purpose product if certain claims are made. Specifically, if a claim is made about lactose content then the same labelling provisions required for dairy–based lactose free or low lactose formula should apply. Equally a statement about 'suitability for infants with lactose intolerance' on a soy–based infant formula product should trigger the same labelling provisions as are required for dairy–based formula making the same claim.

Recommendations

This clause be expanded to the effect that infant formula product may be specifically formulated to satisfy particular metabolic, immunological, renal, hepatic or mal–absorptive conditions but otherwise need to comply with the standard.

The drafting should be amended to require the Division 2 composition and labelling provisions to apply where applicable for soy–based formula for which a special medical purpose claim or nutrient claim is made.

Position of special purpose in the general standard.

Submissions questioned the inclusion of special purpose formula in the general standard and recommended that they should be regulated either in a separate standard or as part of a 'foods for special medical purpose' standard.

Assessment

At Preliminary Inquiry, it was noted that there is confusion about the regulatory status of these foods and provision in the standard even if on an interim basis would provide clearer regulatory status for these products. Presently these formula are largely confined to use under medical or dietetic care. However, with the trend for more pharmacy items to be available in supermarkets, more specific labelling is warranted such as that proposed in Clause 38.

Recommendation

It is proposed to retain this provision within this standard with the additional labelling requirement. This does not preclude this category being reassessed within any proposal to review a 'foods for special medical purpose' standard category.

7.2.2 Availability

One submission suggested that formula based on hydrolysed protein and nutritionally complete would be suitable for general use.

Assessment

A designed formula based on non–food ingredients cannot be considered 'nutritionally complete' for infants whose organs are still undergoing maturation, as current nutritional requirements are not fully known. Intact proteins impact on the bioavailability of micronutrients and this factor will not be in action in these formula e.g. folate– binding proteins. Elemental formula is still experimental and should not be available for general use.

These formula have been tested in babies for a shorter time than soy based formula. There are no provisions for restricted sale of foods therefore reliance is placed upon the additional labelling to inform that this product is not for general use and should be used under medical supervision.

Recommendation

This should remain as proposed at Preliminary Inquiry.

7.2.3 Claims on thickened formula

Proposed at Preliminary Inquiry

ANZFA proposed not to provide specific permission for claims in relation to physiological conditions (e.g. gastric reflux) until evidence is presented to show that thickened formula are not detrimental to breastfeeding rates in Australia and New Zealand.

Issues

The **Gastric Reflux Association for Support of Parents/Babies of New Zealand** and some industry submissions supported having "anti–reflux" products on the market and did not believe that use of thickened formula is detrimental to breastfeeding. Industry commented that thickened formula is "marketed" to health professionals, not consumers e.g. the decision is based upon recommendation by a professional. **Bristol–Myers Squibb Australia Pty Ltd** stated that the fact that the Advisory Panel on the Marketing in Australia (APMAIF) finds the use of thickened formula problematic reflects a limited view. **Bristol–Myers Squibb Australia Pty Ltd** questioned whether this view has been presented in a scientific, peer–reviewed article. **Wyeth Australia Pty Ltd** commented that if claims about physiological conditions are not permitted on formula for gastric reflux then the use of thickeners should be banned.

The **Department of Nutrition and Dietetics at the James Fairfax Institute** commented that the proposal would not prevent the term "anti–reflux" from being used**. Maureen Minchin (IBCLC), the National Council of Women of New Zealand, the Department of Nutrition and Dietetics at the James Fairfax Institute** all commented that the availability of thickened formula should be restricted e.g. prescription only, only on medical advice.

Assessment

No new scientific evidence was submitted to indicate that thickened formula are not detrimental to breastfeeding rates in Australia and New Zealand. ANZFA does not agree that APMAIF represents a limited view.

APMAIF comprises a diverse range of views and includes an independent chair, a community representative appointed by the relevant Minister, and a member nominated by the infant formula industry. The Panel undertakes rigorous debate and examination of issues before making decisions on interpretation of the WHO Code. The same concerns about the marketing of formula making claims of 'anti–reflux' have been raised in New Zealand.

ANZFA considers that not providing specific permission for claims in relation to physiological conditions has many advantages. The prohibition would help to ensure that carers do not unnecessarily switch their infants from breastfeeding to thickened formula to treat regurgitation. It is also likely that carers will only use these products when directed under medical advice, which will enable correct use.

ANZFA does not consider that manufacturers will be disadvantaged under the proposed standard as carbohydrate thickeners such as rice and cornstarch can continue to be used in thickened formula. Furthermore, these products can be described as "thickened" to ensure adequate identification by carers. Terms such as "anti–reflux" will not be permitted under the proposed standard. ANZFA does not consider that that the availability of thickened formula should be restricted as the proposed prohibition aims to prevent its unwarranted use by carers.

Recommendation

As proposed at Preliminary Inquiry, ANZFA proposes not to provide permissions for claims relating to physiological conditions in infant formula (e.g. gastric reflux).

7.2.4 Composition and labelling of special purpose formula

Proposed at Inquiry

That infant formula products may be specifically formulated to satisfy particular metabolic, immunological, renal, hepatic or malabsorptive conditions provided they comply with the requirements of the standard that are not inconsistent with the division. Specific labelling is required for these products to advise that the product is not suitable for general use and should be used under medical supervision; the condition, disease or disorder for which the food has been formulated and the nutritional modifications made to the product.

Industry issue at Inquiry

That formula for specific clinical purposes, including those for pre–term and low birth weight infants and infants with specific metabolic disorders be required to adhere with accepted international norms for those purposes.

Issues

Some special purpose infant formula for infants with highly specialised needs may not comply with the existing standard. These are made in very small quantities for nil or minimal profit by manufacturers. As these products are made offshore manufacturers have signalled that they will not be reformulating these for to meet Australian or New Zealand standards.

Many of these products are manufactured overseas and hence are imported into Australia and New Zealand. In Australia, AQIS monitor imported products against the prevailing standard and AQIS might need to place holding orders on these products to assess compliance and although unlikely, States and Territory health officials may need to request these products to be withdrawn from the market to the detriment of infants.

Assessment

The proposed standard requires these formulations to comply with the base formulation for healthy infants whilst permitting modification of the specific nutrient or nutrients necessary for the specific condition or disorder. Health professionals have stated that it may be even more important for the base formula of the product to comply with the new standard, as these consumers are the more vulnerable infants.

Currently marketed products do not comply with the proposed base formulation and manufacturers have stated that given the small volume of this market they will not be modifying these formulations to comply with the standard, and are likely to withdraw supply of these formulations to sick babies. The supply of approved products for these infants needs to be guaranteed for obvious health and safety reasons.

Therefore, although it is proposed that special purpose products are expected to conform to the base standard for healthy infants except where necessary to met the particular needs of the infant with the special condition, ANZFA is proposing to include a temporary exemption for the compositional requirements of the standard to permit the supply of these products. The exemption is recommended for a period of five years from the adoption of the standard. This period will allow ANZFA to develop a special standard for 'foods for special medical purposes' that could include these highly specialised infant formula products. This will ensure that the particular needs of these infants are protected.

Labelling requirements.

It is also proposed to exempt these products from requiring the following statement;

'Breast milk is best for babies. Before you decide to use this product, consult your doctor or health worker for advice;'

as it is considered for most of these infants breast milk is not appropriate and the advice of a doctor is already being provided.

Recommendation at Supplementary Final Assessment

The standard is amended to include an exemption for a period of five years on the compositional requirements for special purpose formula and that these products are exempted from requiring the statement as detailed above.

8. ISSUES NOT COVERED BY PROVISIONS IN THE DRAFT STANDARD

8.1 Soy Formula

Proposed at Preliminary Inquiry

There was no drafting in the Preliminary Inquiry regarding soy formula specifically. Submitters raised concern about the safety of soy formula.

Phytoestrogen content

The Preliminary Inquiry carried out an investigation into the safety of soy formula and concluded that *"while phytoestrogens at the levels found in soy–based infant formula have the potential to cause adverse effects, there is no evidence that exposure of healthy infants to soy–based infant formula over some 30 years of use has been associated with any demonstrated harm"*.

Issues

Consumer submitters provided strong opposition to soy–based formula being allowed on the market. Some consumers and public health groups provided support for an appropriate warning statement on it. Industry submitters supported keeping soy–based formula on the market and were opposed to a warning statement on these products.

Assessment

No new evidence has been presented since Preliminary Inquiry. It is noted however, that submissions provide even stronger support for an appropriate warning statement on soy–based formula. Nevertheless, ANZFA considers it more appropriate to support education initiatives that reduce the indiscriminate and inappropriate use of soy formula and which promulgate the public health policy that infants should be breast–fed where possible, and that where breast–feeding is not an option, modified cow's milk formula be recommended as the preferred feeding choice.

Recommendation

As no new evidence has been presented, it is recommended that the approach specified at Preliminary Inquiry remain.

Levels of trypsin in soy formula.

Issue

Mr James raised concerns about the levels of trypsin in soy formula. **The New Zealand Ministry of Health** pointed out that there are trypsin inhibitors in soy formula and these compounds cause mal–absorption of proteins. It was suggested that maximum levels of trypsin allowable or a denaturation process be considered.

Assessment

An infant formula product is required to be suitable for infants, therefore a product which contains trypsin inhibitors at levels, which impacted adversely on the digestive process would not be considered suitable for infants

Recommendation

No special provision is required.

8.2 Novel Food and novel ingredient use in infant formula

Proposed at Preliminary Inquiry

ANZFA proposed that novel foods should be assessed for safety before use in infant formula in Australia and New Zealand by virtue of the proposed Standard A19 – Novel Foods (now Standard 1.5.1 Novel Foods). ANZFA called for information to identify the use of potential novel foods or ingredients from novel sources.

Issues

Some industry submissions did not agree that novel foods accepted elsewhere in the world should be required to undergo a safety assessment in Australia or New Zealand, particularly when trade is involved.

Safety concerns, relating to the use of novel foods in infant formula were raised by **Fiona Compston, the Australian College of Midwives Incorporated, Mark Dunstone, Julie Smith and Maureen Minchin (IBCLC**). Submitters indicated that proof of benefit and absence of long–term harm in childhood must be demonstrated (e.g. in independent clinical trials) before widespread use of novel products are permitted in infant formula. **Wyeth Australia Pty Ltd** stated that safety assessments of such novel nutrients in infant formula should not be unfairly constrained by the safety standards that apply for novel food additives as novel nutrients are added for nutritional benefit. **Mark Dunstone and Julie Smith** commented that they do not support use of novel foods based on safe consumption of similar foods by adults and that the proposed standard is contrary to the objectives in the Food Act.

Fiona Compston and the **Australian College of Midwives Incorporated** stated that infant formula containing "novel ingredients" should contain large warning messages. **Maureen Minchin (IBCLC)** commented that misleading advertising about the benefits of infant formula containing novel foods should be prevented. **Nestle Australia Ltd** indicated that there be a maximum time of three months for the approval of novel foods.

Only **Maureen Minchin (IBCLC)** responded to ANZFA's request for submitters to identify the use of potential novel, foods or ingredients. **Maureen Minchin (IBCLC)** stated that **Wyeth Australia Pty Ltd's** S26 brand contains marine oils that are triglycerides manufactured by genetically or environmentally engineered marine algae. Other examples of novel ingredients of concern were synthetic analogues of 5 of the 13 nucleotides in breast milk and egg phospholipids.

Assessment

Standard 1.5.1 – Novel Food, which came into effect on the 16 June 2001, requires a safety assessment of novel foods and novel food ingredients before these foods can be offered for sale in Australia and New Zealand.

Standard 1.5.1 defines novel foods as below:

> *novel food means a non–traditional food for which there is insufficient knowledge in the broad community to enable safe use in the form or context in which it is presented, taking into account:*
>
> *(a) the composition or structure of the product; or*
> *(b) levels of undesirable substances in the product; or*
> *(c) known potential for adverse effects in humans; or*
> *(d) traditional preparation and cooking methods; or*
> (f) *patterns and levels of consumption of the product.*
>
> *non–traditional food means a food which does not have a history of significant human consumption by the broad community in Australia or New Zealand.*

The intent of the novel food standard is to have ANZFA conduct a formal safety assessment only on those foods that have features or characteristics that raise safety concerns. The definition of a novel food in the proposed standard indicates the issues that need to be taken into account in identifying such foods. Foods regarded as novel are likely, but do not necessarily, fall into one of the following classes:

- dietary macro–components;
- extracts of plants, animals or microorganisms;
- single ingredient foods; and
- viable microorganisms.

The extent of the safety assessment necessary on a novel food will depend on the nature of the food and its proposed use. In many cases, there will be data available in relation to the use of the food in other countries. For those foods for which there has been no human exposure, or exposure at much lower dose levels, more extensive data will be required.

In relation to the use of novel foods or novel food ingredients in infant formula, there is no reason to make any exemption from the requirement for a safety assessment for these foods. Indeed, there is a strong argument that infants represent a vulnerable sector of the community and that a safety assessment of all new ingredients in infant formula is more appropriate for this group. For novel ingredients in infant formula, it is not expected that any additional studies would be required in the first instance but the applicant should provide ANZFA with all of the data that has been generated to ensure the safety of the product. ANZFA will also conduct its own research to ensure all appropriate data has been used in the safety assessment. This should not impose a significant additional regulatory burden on industry since such data should be readily available.

ANZFA does not support a three–month time frame for approval of novel foods in infant formula. This is not consistent with the statutory processes of ANZFA in relation to applications. Section 35(1) of the ANZFA Act 1991 requires that applications are processed within 12 months of receipt of the application. There is a significant lead–in time for the development of new ingredients for infant formula and this is unlikely to be disrupted by the need to make an application to ANZFA.

Recommendation

Novel foods or novel food ingredients used in infant formula should be assessed for safety before use in Australia and New Zealand. Standard 1.5.1 –Novel Foods provides an appropriate mechanism for the safety assessment of all novel foods and novel food ingredients, including those to be used in infant formula. Therefore no change is required to the draft Standard 2.9.1 to provide for the safe use of novel foods.

8.3 Cadmium

Recommendation at Preliminary Inquiry

ANZFA's toxicological assessment of specific contaminants indicated that there was no reason to specifically restrict the level of cadmium in infant formula.

Issue

Maureen Minchin (IBCLC) was concerned that a level is not proposed for cadmium. The submission suggested that there is a potential risk for contamination with cadmium in heavily processed products e.g. high levels of cadmium have been found in Belgian and Canadian infant formula.

Assessment

A review of the Australian standards for cadmium in foods has been conducted over five years. Health Ministers accepted revised standards for all foods, except peanuts, in July 1997. A revised standard for cadmium in peanuts was accepted by Health Ministers, in August 1999. Data on exposure to cadmium from all sources was considered in this review and standards have been established for all of the major sources of cadmium in the diet. The major dietary sources of cadmium are potatoes, wheat, meat and cocoa.

Cadmium is a cumulative contaminant that can cause renal toxicity in humans following a lifetime of high dietary exposure. The levels normally found in food, even highly contaminated food, would be unlikely to cause any immediate adverse effects. Long–term exposure is required for manifestation of any adverse effects. The relatively short period of use of infant formula means this is unlikely to be regarded as a significant source of dietary cadmium over a lifetime.

Recent research on cadmium content in a range of infant formula for sale in Australia and New Zealand[25] indicates that the levels are generally similar to or lower than those found in comparable overseas products.

Recommendation

As proposed at Preliminary Inquiry, ANZFA does not propose to establish a maximum level for cadmium in infant formula.

8.4 Percentage Labelling

Issue

The joint *Australia New Zealand Food Standards Code* (Volume 2) includes provisions for foods to be labelled with the percentage of the characterising ingredient or component of that food. These are set out in Standard 1.2.10.

Assessment

It is difficult to identify the characterising ingredient or component in infant formula. The mandatory labelling requirements are far more stringent than for other foods. For example, infant formula products are already required to include a statement of protein source on the label.

The objective of percentage labelling is to provide consumers with an additional information tool for comparing like products to assist them in making an informed choice. In the case of infant formula, consumers are already well informed from the label and it is unlikely that a small variation in the quantity of a particular ingredient or component will influence choice of purchase. Therefore infant formula products could be exempted from the provisions of Standard 1.2.10.

Recommendation

That infant formula products are exempt from the percentage labelling requirements in Standard 1.2.10 of Volume 2.

8.5 Innovation

Industry issue

Industry made a request for a new clause to be added to the standard to the effect that nutritive substances may be added to infant formula to the levels found in human milk. Industry claim the usual ANZFA application process to vary a standard is unacceptable because this would then be assessed in the public domain and this removes any exclusivity rights to the company that has made significant resource investment.

[25] Assessment of Selected Pesticides and the Elements Cadmium, Lead, Tin, Iodine and Fluoride in Infant Formulae and Weaning Foods, ESR report for Ministry of Health, 1997.

Assessment

The current international and local regulatory systems for infant formula has led to the addition of some ingredients to formula without rigorous, objective safety assessments which are required for other food ingredients eg, food additives. Some constituents are added at unregulated levels or as unpurified forms with associated uncharacterised constituents and the safety of such ingredients may be of concern.

The food standards setting process is an open and transparent process that involves public consultation into proposed amendments to the food standards. The industry proposal is inconsistent with the ANZFA Act requirements for the setting of food standards. Members of the External Advisory Group were consulted on this matter and there was no agreement from non–industry representatives for such a provision in the proposed standard.

Recommendation at Supplementary Final Assessment

That no new 'innovation' clause be included in the draft standard.

ATTACHMENT 2

SAFETY ASSESSMENT REPORT

DHASCO AND ARASCO AS SOURCES OF LONG-CHAIN POLYUNSATURATED FATTY ACIDS IN INFANT FORMULA

SUMMARY

DHASCO and ARASCO are microbial oils rich in the long-chain polyunsaturated fatty acids (LCPUFAs) docosahexaenoic acid (DHA) and arachidonic acid (ARA), respectively. DHA and ARA are the major fatty acids present in the structural phospholipids of the human brain and retina and accumulate rapidly in foetal and infant neural tissue during the last months of gestation and the first months of postnatal life. Although both term and pre-term infants are capable of endogenous synthesis of DHA and ARA from precursor fatty acids, this capacity appears to be sub-optimal to meet the demands of the developing tissues in pre-term infants. The evidence indicates that pre-term infants in particular benefit from a dietary supply of pre-formed LCPUFAs. While breast-fed pre-term infants can obtain this dietary supply from breast milk, which naturally contains pre-formed DHA and ARA, for the formula-fed pre-term infant a dietary supply can only be obtained by supplementation of the formula. Hence, oils, such as DHASCO and ARASCO, which contain high levels of DHA and ARA, are being used to supplement a number of pre-term infant formula products and increasingly are also being used to supplement formula for term infants, although the evidence for benefit for this group is equivocal.

Intake and extent of use

DHASCO and ARASCO have been added to infant formula products in Australia and New Zealand for about the last three years. They are currently added to about 17% of formulae intended for term infants up to 6 months of age, and about 87% of pre-term formulae. The extracted oils are being added to infant formula up to a maximum level of 1.25 % each of formula fat, which corresponds to a maximum level of 0.5% each of ARA and DHA. This level of supplementation would equate to a maximum intake of about 70 – 85 mg each of DHASCO and ARASCO/kg bw/day.

Safety of the source organisms

DHASCO is extracted from the non-photosynthetic marine micro-algae *Crypthecodinium cohnii* and ARASCO is extracted from the common soil fungus *Mortierella alpina*. Neither *C. cohnii* nor *M. alpina* are known to be pathogenic to humans or other mammals and specific studies with the biomass from both organisms have confirmed the absence of any toxin production.

Composition of the oils

ARASCO and DHASCO are free flowing triglyceride oils with a fatty acid profile that is comparable to that of a number of other edible oils. No unusual fatty acids are present and there are no detectable (< 1%) cyclic or *trans* fatty acids present in either oil. The oils also contain no or only very low levels of eicosapentaenoic acid (EPA), which has been associated with reduced growth in infants.

The sterol fraction of the oils constitutes about 9.5 mg/g dry weight of DHASCO and 7.9 mg/g dry weight of ARASCO (i.e., less than 1% by weight of the oil). The most common sterol in DHASCO is dinosterol, which is unique to algae and possesses an unusual chemical structure. In contrast, the sterols found in ARASCO are commonly found in plants and edible fungi, e.g., mushrooms.

The DHA and ARA-containing triacylglycerols in DHASCO and ARASCO are different to those found in breast milk. In breast milk, ARA and DHA are primarily esterified at the *sn*-2 and *sn*-3 positions, whereas in DHASCO and ARASCO they are esterified at all three positions of the triacylglycerol. Also, in contrast to breast milk, ARASCO and DHASCO contain significant amounts of triacylglycerol with two or more molecules of either DHA or ARA.

Absorption, distribution, metabolism and excretion

A number of studies, in both animals and humans, including human infants, have been done on the absorption, distribution, metabolism and excretion of the LCPUFAs from ARASCO and DHASCO. These studies indicate that the efficiency of intestinal absorption of ARA and DHA from ARASCO- and DHASCO-supplemented infant formula is similar to that from breast milk, this is despite some differences between breast milk and the microbial oils in positional specificities of the LCPUFAs in the triacylglycerol molecule. In the pre-term infant about 80% of ingested ARA and DHA (either from breast milk or DHASCO/ARASCO-supplemented formula) is absorbed. Efficient levels of absorption (i.e., >95%) are also seen in neonatal animal models, even at very high levels of dietary incorporation. Non-absorbed DHA and ARA are excreted via the faeces. Once absorbed, DHA and ARA are largely unavailable for oxidation, and are instead preferentially channelled into the phospholipid pool where they are rapidly incorporated into the cell membranes of the developing brain and retina. Studies with neonatal rats and pigs, as well as pre-term infants, indicate that the LCPUFAs in ARASCO and DHASCO are able to support maximal tissue accretion of ARA and DHA by the retina and other membrane phospholipids.

Toxicology studies

A number of toxicology studies have been done with ARASCO and DHASCO administered either singly or in combination. Acute dosing studies in rats with the oils using levels up to the maximum dose level attainable (20 g/kg body weight) yielded no adverse findings. Three short-term (4 week and 9 week) studies and three sub-chronic (13 week) studies in rats were evaluated, one of which included a full neurological and neurohistological assessment. In one of the sub-chronic studies some of the findings point to an impaired concentrating ability of the kidneys at the highest dose levels tested (4900 mg ARASCO/kg bw/day alone or in combination with 3650 mg DHASCO/kg bw/day), however, the vast majority of the treatment related findings were generally not accompanied with any associated histopathological, biochemical or haematological changes that would be indicative of toxicity at doses up to 2500 mg ARASCO/kg bw/day and 1250 mg DHASCO/kg bw/day. The most frequent changes observed (e.g. increased liver weights, decreased serum cholesterol and triglycerides) are entirely consistent with the physiological changes observed in response to the administration of high levels of LCPUFAs, irrespective of source, and are not a manifestation of toxicity specific to the administration of either ARASCO or DHASCO.

A single developmental study, where ARASCO and DHASCO were administered to pregnant rats during organogenesis at dose levels up to 2500 mg ARASCO/kg bw/day and 1250 mg DHASCO/kg bw/day, likewise did not produce any treatment-related adverse developmental effects. The oils were also found to be negative in a number of bacterial and mammalian genotoxicity test systems at concentrations *in vitro* up to 5000 μg/ml, suggesting the oils are non-genotoxic (both with and without metabolic activation).

Overall, there is no evidence of toxicity associated with the administration of ARASCO and DHASCO at dose levels up to 2500 mg and 1250 mg/kg bw/day, respectively. These dose levels are approximately 18 – 35 fold greater than the maximum levels being added to infant formula.

Human studies

A large number of clinical studies with pre-term and term infants have been undertaken with infant formula supplemented with DHASCO and ARASCO at levels producing ARA and DHA concentrations approximating those found in human milk. These were primarily undertaken for the purposes of establishing efficacy, however a number also examined how well the supplemented formulae were tolerated and whether its use was correlated with any adverse effects (e.g., reduced growth, changes in serological markers of spleen and liver function). These studies all indicate that formula supplemented with DHASCO and ARASCO is well tolerated by human infants and is not associated with any apparent adverse effects.

Conclusions

Neither of the source organisms exhibit any signs of either pathogenicity or toxicity and the extracted oils do not demonstrate any consistent evidence for toxicity in animal studies or adverse effects in the studies with human infants conducted to date. This indicates there are no components of the extracted oils that raise any specific concerns and supports the conclusion that DHASCO and ARASCO are safe sources of LCPUFAs for supplementation of infant formula.

1. INTRODUCTION

DHASCO® (DHA-rich Single Cell Oil) and ARASCO® (ARA-rich Single Cell Oil) are microbial-derived triglyceride oils that are rich in the long-chain polyunsaturated fatty acids (LCPUFAs) known as docosahexaenoic acid (DHA) and arachidonic acid (ARA). The extracted oils contain between 40 and 55 % DHA or ARA.

DHASCO is extracted from the algae *Crypthecodinium cohnii* and ARASCO is extracted from the fungus *Mortierella alpina*. Both oils are standardised with high oleic sunflower oil to contain 40 % by weight of DHA or ARA prior to being added to infant formula.

DHASCO and ARASCO have been added to infant formula products (both term and pre-term formulae) in Australia and New Zealand for about the last three years and in a number of other (primarily European) countries for about seven years. They are currently added to about 17% of formulae intended for term infants up to 6 months of age, and about 87% of pre-term formulae.

DHASCO and ARASCO are currently being added to infant formula at levels that provide ARA and DHA levels up to 0.5% each of formula fat. These levels are therefore consistent with those specified in Draft Standard 2.9.1 Infant Formula which prescribes a maximum level of ARA and long chain omega-3 series fatty acids of 1.0% each of formula fat. Draft Standard 2.9.1 also specifies that when added to formulas the ratio of total long chain omega 6 series fatty acids (C>= 20) to total long chain omega 3 series fatty acids (C>= 20) should be approximately 2.

Assuming human infants consume about 420 – 500 kJ/kg bw/day (100 to 120 kcal/kg bw/day), of which fat comprises about 50 %, an infant will consume about 210 – 250 kJ/kg bw/day of fat, or about 5.6 – 6.7 g of fat/kg body weight/day (1 g fat = 37 kJ). As the ARA and DHA in the oils are standardised to a concentration of 40%, the amount of DHASCO and ARASCO being added to formula equates to a maximum of 1.25% each of total formula fat. This level of incorporation would therefore correspond to a DHASCO and ARASCO intake of 70 – 85 mg each of DHASCO and ARASCO/kg bw/day.

The purpose of the assessment is to confirm that DHASCO and ARASCO, when added to infant formula at the levels specified above, are safe sources of DHA and ARA for infant feeding.

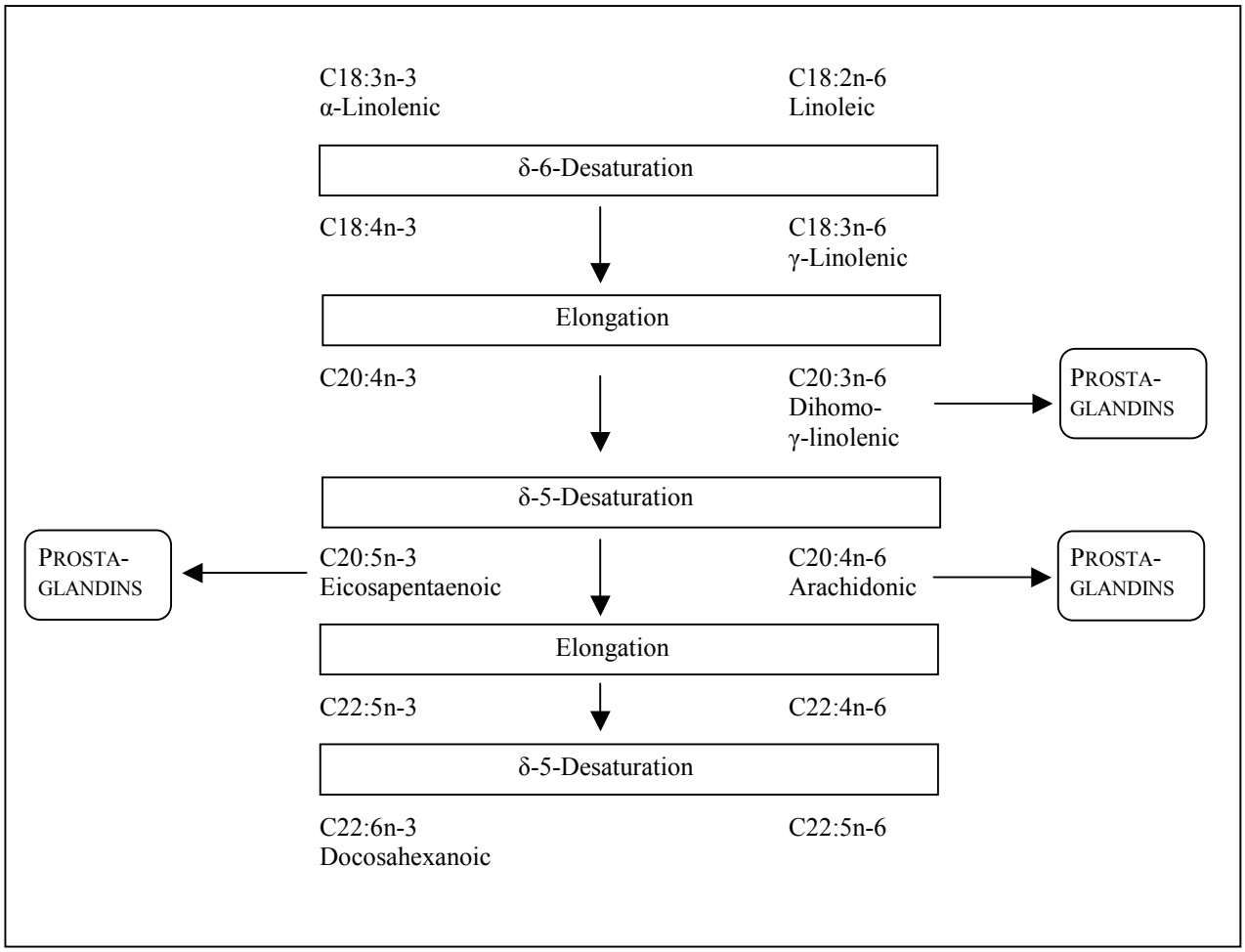
2. BACKGROUND

2.1 The role of LCPUFAs in early development

DHA (C22:6n-3) and ARA (C20:4n-6) are the predominant fatty acids in the structural phospholipids of the human brain and retina (Innis 1991, Martinez 1992) and accumulate rapidly in foetal and infant neural tissue during periods of most rapid growth and development, that is, during the last months of gestation and the first months of postnatal life (Martinez 1992, Makrides 1994).

Unlike term infants, pre-term infants cannot benefit from the placental LCPUFA supply during the last trimester of pregnancy. Instead, they are dependent on their own dietary supply through human milk, which contains small but significant quantities of DHA and ARA, as well as other LCPUFAs. Studies of breastfed pre-term infants have shown that the LCPUFA content in pre-term human milk provides adequate DHA and ARA to support normal neural tissue growth and development (Carlson *et al* 1986, Martinez 1992). For formula-fed pre-term infants, however, a large number of studies have shown that conventional formulae, even when it contains substantial amounts of linoleic and α-linolenic acid, which are the precursors for endogenous synthesis of ARA and DHA (see Figure 1), are unable to maintain postnatal DHA and ARA levels in plasma and erythrocyte lipids to levels observed after feeding human milk (Carlson *et al* 1986, Pita *et al* 1988, Koletzko *et al* 1989, Clandinin *et al* 1992). Although both term and pre-term infants are capable of endogenous synthesis of LCPUFAs from precursors (Salem *et al* 1996), this capacity appears to be sub-optimal and inadequate to maintain DHA and ARA at levels comparable to those found in breastfed infants (Carlson *et al* 1986, Koletzko *et al* 1989).

FIGURE 1. Major pathway for the synthesis of LCPUFAs from linoleic and α-linolenic acids.



It has been suggested that the higher tissue levels of DHA and ARA in breastfed infants is an important causative factor in the correlation between breastfeeding and better cognitive and visual function, particularly in the pre-term infant (Heird 2001). On the basis of these observations, and on the basis that breastfed infants are naturally supplied with pre-formed LCPUFAs in breast milk, it has been suggested that formula-fed pre-term infants could benefit from supplementation with LCPUFAs, particularly DHA and ARA. This had led to recommendations from various expert bodies, including the FAO/WHO (FAO 1994), for the inclusion of pre-formed LCPUFAs in infant formulae, for both term and pre-term infants. While a recently conducted study has demonstrated that pre-term infants fed a formula supplemented with ARA and DHA showed improved visual development (O'Connor *et al* 2001), the same was not seen in a similar study conducted with term infants (Auestad *et al* 2001). This suggests that term infants are better able to meet their DHA and ARA needs from essential fatty acids in their diet – either from breast milk, or from infant formula containing an appropriate fat blend providing linoleic and α-linolenic acid – the precursors of ARA and DHA, respectively.

2.2 Sources of LCPUFAs for formula supplementation

In formulas for infants, LCPUFAs are added to the fat blend by using relatively highly unsaturated lipids. Three main sources are used: fish oil, which is mainly triacylglycerol (TAG); egg yolk lipid and phospholipids; or oils from algae and fungi (mainly TAG).

Fish oil contains large amounts of the omega-3 LCPUFAs but minimal amounts of omega-6 LCPUFAs, therefore, fish oil is typically used in combination with another LCPUFA source to supply the ARA. Some fish oils contain at least 1.5-fold as much eicosapentaenoic acid (EPA; 20:5n-3) as DHA and high EPA content has been associated with adverse effects on growth in infants (Carlson *et al* 1992, Carlson *et al* 1994, Montalto *et al* 1996). Fish oils with low EPA content are now available, although these have also been shown to have an adverse effect on the growth of pre-term infants (Carlson *et al* 1999), although a smaller effect than that observed with high-EPA fish oil occurred. It is speculated that supplementation with EPA (and/or DHA), results in feedback inhibition of the elongation and desaturation of the C18 essential fatty acids, leading to a decrease in ARA synthesis (Diersen-Schade *et al* 1999).

Egg yolk lipid contains large amounts of cholesterol. For this reason, egg phospholipids are preferred to egg yolk lipid (Heird 2001). Although egg phospholipids contain both ARA and DHA, the proportions of the two are not necessarily the same as the proportions found in human milk. These proportions can however be modified by altering the diet of the hens (Heird 2001).

The third source of LCPUFAs for addition to infant formula is single cell organisms, principally algae and fungi. TAG containing relatively high concentrations of DHA or ARA, but without any other LCPUFAs, such as EPA, can be produced from these organisms. For this reason, these oils are preferred for addition to infant formula.

2.3 Source organisms

2.3.1 Crypthecodinium cohnii

C. cohnii is a member of the Dinophyta (dinoflagellates). This is a distinct phylum of unicellular eukaryotic micro algae comprising an estimated 2000 species (van der Hoek *et al* 1995). Most species of the Dinophyta are photosynthetic; of which a small number are known to produce a group of closely related toxins (Steidinger and Baden 1987). There are also several heterotrophic species, of which *C. cohnii* is one. None of the heterotrophic species are known toxin producers or pathogenic to either humans or other mammalian species (van der Hoek 1995). *C. cohnii* has a long history of laboratory cultivation dating back to 1908 (Kyle 1996), but has not previously been used for human food.

The *C. cohnii* strain used for the production of DHASCO is proprietary to Martek Biosciences Corporation (US Patents 5,397,591, 5,407,957 and 5,492,938). The strain originated from the University of Texas culture collection and was selected for rapid growth and high levels of production of the specific oil. The specific strain of *C. cohnii* has been deposited with the American Type Culture Collection (ATCC # 40750) under the obligations of the US patent relating to its use. Master seed stocks of the production strain are maintained under liquid nitrogen at the ATCC.

2.3.2 Mortierella alpina

M. alpina is a member of the Phycomycetes group of fungi, which are common inhabitants of soil. Although some fungal species have been reported to produce mycotoxins, the mycotoxin-producing fungi belong to the class of Basidiomycetes, which differ from the Phycomycetes group of fungi, to which *M. alpina* belongs (Jay 1992).

A number of fungal species are also human pathogens, but the vast majority of these belong to the Deuteromycetes group of fungi (Davis *et al* 1980).

The *M. alpina* strain used for the production of ARASCO originates from the ATCC (ATCC # 32222) and was selected for rapid growth and high levels of production of the specific oil. Master seed stocks of this strain are maintained cryogenically at the ATCC.

2.4 Production of DHASCO and ARASCO

2.4.1 DHASCO

DHASCO is produced from *C. cohnii* using fermentation techniques. Cultures of the organism are grown up in liquid medium in shaker flasks and are transferred to progressively larger vessels. When the culture reaches a specified cell density and fatty acid content, the cells are harvested by centrifugation and spray dried. The process for extraction of the oil is basically the same as that used in conventional vegetable oil processing plants. The oil is extracted from the biomass by blending the biomass with hexane in a continuous extraction process. The extracted oil is separated from the de-oiled solids and the clarified miscella is desolventised under vacuum and winterised to remove the more highly saturated oil fractions. The winterised oil is then refined, bleached and deodorised using standard procedures. The deodorised DHASCO is then diluted to a standard 40% DHA concentration by the addition of high oleic sunflower oil and mixed with antioxidants – tocopherols (0.025%) and ascorbyl palmitate (0.025%). The DHA-rich oil produced is free-flowing liquid, which is orange in colour as a result of carotenes co-extracting with the oil.

2.4.2 ARASCO

One specific strain of *M. alpina* was selected to produce ARASCO because it produced oil that was not only rich in ARA, but which contains no EPA or other unusual components (Kyle 1997). *M. alpina* is a psychrotrophic, non-photosynthetic organism, which requires a reduced carbon source for growth. The fermentation process for the production of ARASCO-containing biomass starts with inoculation of liquid culture medium in a shaker flask with seed stock. The growing culture is transferred to successively larger vessels based on pre-defined criteria and when the culture reaches maximum productivity it is harvested by centrifugation and then dried. The dried biomass is then subject to oil extraction similar to that described for DHASCO. The deodorised ARASCO is then diluted to a standard 40% ARA concentration by the addition of high oleic sunflower oil and mixed with antioxidants – tocopherols (0.025%) and ascorbyl palmitate (0.025%). The ARA-rich oil that is produced is free-flowing liquid oil which is slightly yellow in colour.

2.5 Composition and triglyceride structure of DHASCO and ARASCO

ARASCO and DHASCO are free flowing oils, which are predominantly triglyceride (>95%) with some diglyceride and non-saponifiable material (<5%).

2.5.1 Triglyceride structure

In breast milk, ARA and DHA are mainly in TAG, although they also occur in phospholipids in breast milk (Jensen 1989). In breast milk TAG they are primarily esterified at the *sn*-2 and *sn*-3 positions (Breckenridge 1969, Innis 1992, Martin *et al* 1993), with the *sn*-1 position being relatively deficient in these acids (Martin *et al* 1993). The ARA and DHA, however, actually only make up a very small proportion of the total fatty acids found esterified into TAG. ARA makes up 0.4% of fatty acids at the *sn*-2 position and 0.37% at the *sn*-3 position, whereas DHA makes up 0.26% of fatty acids at the *sn*-2 position and 0.13% at the *sn*-3 position (Martin *et al* 1993). The predominant fatty acids found in the breast milk TAG are oleic acid (18:1) predominantly in the *sn*-1 and *sn*-3 positions, and palmitic acid (16:0) predominantly in the *sn*-2 position.

The DHA and ARA in DHASCO and ARASCO, respectively, do not display as clear a positional specificity, with the fatty acids being found in all three positions (Myher *et al* 1996). In ARASCO, about 50% of the ARA is found in the *sn*-1 position, 30% in the *sn*-2 position and 20% in the *sn*-3 position. In DHASCO, between 40 and 50% of DHA is found in the *sn*-2 position, with about 30% in the *sn*-3 position and between 20 to 30% in the *sn*-1 position. ARASCO and DHASCO also possess the unusual feature of containing significant amounts of TAG with two or more polyunsaturated long-chain fatty acids per molecule (Myher *et al* 1996).

2.5.2 Oil composition

The composition of both oils is given in Table 1. No unusual fatty acids are present and there are no detectable (< 1%) cyclic or *trans* fatty acids. Minor fatty acid components of DHASCO, listed as "other" in Table 1 generally constitute about 1% of the total fatty acid composition. Small amounts of C28:8 (n-3) has been reported in DHASCO oil (VanPelt *et al* 1999). This fatty acid is the next expected omega-3 end product of the Sprecher biochemical pathway beyond DHA and is one of the minor components of both DHASCO, as well as fish oils (Luthria *et al* 1996).

2.5.3 Sterol composition

The 1.5% by weight nonsaponifiable fraction of DHASCO and ARASCO is made up primarily of sterols, which constitute 9.5 mg /g dry weight of DHASCO, and 7.9 mg/g dry weight ARASCO. The sterol fraction of both oils have been independently analysed and the results are summarised in Table 2.

The sterols of algae are of interest because they appear to be structurally different to those of higher plants (Patterson 1991). By far the most common sterol found in *C. cohnii* is the 4α-methyl sterol, dinosterol. The next most common sterol is the 4-demethyl sterol, dehydrocholesterol. Dinosterol is unique in that it has a saturated ring system and an unusual side chain alkylation pattern.

The principle component of the sterol fraction of ARASCO is desmosterol, with smaller amounts of two 24-methyl sterols. These sterols are commonly found in plants and fungi, including edible fungi such as mushrooms (Nes and Le 1990).

In addition to these common sterols, *M. alpina* strain 1S-4 has been reported to contain the sterol 24,25-methylene cholesta-5-en-3β-ol, which has not been reported previously to exist in nature (Shimizu *et al* 1992). This novel sterol, however, could not be detected in the batches of ARASCO analysed for their sterol content (Table 2).

TABLE 1. Chemical composition of ARASCO and DHASCO

ARASCO		**DHASCO**	
Fatty acids	**% total**	**Fatty acids**	**% total**
Myristic acid (14:0)	0-2	Myristic acid (14:0)	10-20
Palmitic acid (16:0)	3-15	Palmitic acid (16:0)	10-20
Palmitoleic acid (16:1)	0-2	Palmitoleic acid (16:1)	0-2
Stearic acid (18:0)	5-20	Stearic acid (18:0)	0-2
Oleic acid (18:1)	5-38	Oleic acid (18:1)	10-30
Linoleic acid (18:2)	4-15	Linoleic acid (18:2)	0-5
Linolenic acid (18:3)	1-5	Arachidic acid (20:0)	0-1
Arachidic acid (20:0)	0-1	Behenic acid (22:0)	0-1
Eicosatrienoic acid (20:3)	1-5	Docosapentaenoic acid (22:5)	0-1
Arachidonic acid (20:4)	**38-44**	**Docosahexanoic acid (22:6)**	**40 -45**
Behenic acid (22:0)	0-3	Nervonic acid (24:1)	0-2
Docosapentaenoic acid (22:5)	0-3	Others	0-3
Lignoceric acid (24:0)	0-3		
Chemical analysis		**Chemical analysis**	
DPA	<0.1%	DPA	<0.1%
EPA	<0.1 – 0.16%	EPA	<0.1%
Free fatty acid	0.10 – 0.27%	Free fatty acid	0.14 – 0.22%
Peroxide value	0.12 – 1.51 meq/kg	Peroxide value	<0.1 – 0.24 meq/kg
Volatiles	<0.01 – 0.03%	Volatiles	<0.01%
Non-saponifiables	1.18 – 1.73%	Non-saponifiables	1.36 – 1.85%
Insoluables	<0.01%	Insoluables	<0.01%
Trans fats	<1.0%	Trans fats	<1.0%
Elemental analysis	**ppm**	**Elemental analysis**	**ppm**
Arsenic	<0.5	Arsenic	<0.5
Cadmium	<0.1	Cadmium	<0.1
Chromium	<0.1	Chromium	<0.1
Copper	<0.02	Copper	<0.02
Iron	<0.02	Iron	<0.02
Lead	<0.1	Lead	<0.1
Manganese	<0.01	Manganese	<0.01
Mercury	<0.04	Mercury	<0.04
Molybdenum	<0.05	Molybdenum	<0.05
Nickel	<0.1	Nickel	<0.1
Phosphorous	<1	Phosphorous	<1
Silicon	280 – 350	Silicon	18 – 135
Sulphur	3 – 6	Sulphur	18 – 80

TABLE 2. Sterols identified in DHASCO and ARASCO

Sterol fraction		Common name	% total sterols
DHASCO:			
4α,23,24-trimethyl cholesta-22-en-3β-ol	C30:1	dinosterol	31.5
Cholesta-5,7-dien-3β-ol	C27:2	dehydrocholesterol	9.6
4α,24-dimethyl cholestan-3β-ol	C29:0		9.2
4α,23,24-trimethyl cholesta-5,22-dien-3β-ol	C30:2	dehydrodinosterol	8.2
Cholesta-7-en-3β-ol	C27:1	lathosterol	7.5
4α,24-dimethyl cholesta-22-en-3β-ol	C29:1		6.4
4α,23,24-trimethyl cholesta-22-en-3β-ol	C30:1	dinosterone	6.0
4α,23,24-dimethyl cholesta-5-en-3β-ol	C29:1		4.6
4α,23,24-trimethyl cholesta-24(28)-ene-3β-ol	C30:1		4.2
Cholesta-*x*,*x*-dien-3β-ol*	C27:2		3.6
Cholesta-5,24-dien-3β-ol	C27:2	desmosterol	2.4
Cholesta-5-en-3β-ol	C27:1	cholesterol	1.7
23 or 24-methyl cholesta-5,7-dien-3β-ol	C28:2		1.9
	C27:3		1.3
a 5,7-dien sterol	C29:2		
ARASCO:			
Cholesta-5,24-dien-3β-ol	C27:2	desmosterol	67.3
24-methyl cholesta-5,24(25 or 28)-dien-3β-ol	C28:2		14.0
24-methyl cholesta-5,25-dien-3β-ol	C28:2		12.3
	C28:2		2.1
4α,4β,14-trimethyl-8,24-dien-3β-ol	C30:2	lanosterol	1.1
Cholesta-5,25-dien-3β-ol	C27:2		2.0
24,25-methylene cholesta-5-en-3β-ol	C28:1		Not detected

* The *x* refers to unassigned double bond placement

3. ABSORPTION, DISTRIBUTION, METABOLISM AND EXCRETION

3.1 General overview

The general physiological processes for digestion/absorption, distribution, metabolism and excretion of lipids and fatty acids are well described in the general literature (e.g., Lehninger 1982, Eckert and Randall 1983).

3.1.1 Absorption

Most of the fat ingested by humans is in the form of TAG so in this respect DHASCO and ARASCO are no different to other types of dietary fat. The ingested TAG must be hydrolysed by lipases to fatty acids and monoacylglycerols before they can be absorbed by the small intestine. Digestion of TAG actually commences in the stomach, where the churning action helps to create an emulsion (FAO 1994) and also where a small amount of lipid hydrolysis occurs mediated by both lingual lipase (secreted by glands of the tongue) and gastric lipase. In the infant, the amount of gastric hydrolysis can be quite significant with as much as 30% of ingested TAG being digested during the one- to three-hour period that fat remains in the stomach (Watkins 1985).

The further emulsification and digestion of TAG in the small intestine is facilitated by bile salts, which are secreted into the upper portion of the small intestine (duodenum). Emulsification serves to stabilise the TAG molecule and to maximise the area of oil-water interface, where lipase activity occurs (Watkins 1985).

Intestinal hydrolysis of TAG is mediated by pancreatic lipase which catalyses the hydrolysis of fatty acids at the *sn*-1 and *sn*-3 positions (i.e., the outer positions) to yield free fatty acids and 2-monoacylglycerols (Tso 1985).

After hydrolysis of the ingested TAG, those fatty acids containing less than 14 carbons enter into the circulation directly via the portal vein and from there are transported to the liver, whereas larger fatty acids are taken up into intestinal cells by passive diffusion where they are re-esterified into TAG and incorporated, along with small amounts of cholesterol and phospholipid, into chylomicrons. The chylomicrons are coated with a layer of lipoproteins, are loosely contained in vesicles formed by the Golgi apparatus, and are expelled from the cell by exocytosis into the interstitial fluid of the villus. From there they enter into the lymph through the thoracic duct and are delivered into the circulation via the subclavian vein. Once in the bloodstream, chylomicrons are acted upon by vascular lipoprotein lipase, which hydrolyses the TAG, releasing individual fatty acids, which are then available for distribution, in various forms, to particular tissues. The liver clears the remnants of chylomicrons within a few hours of the ingestion of a fat-containing meal.

In children and adults, fat digestion is efficient and is nearly completed in the small intestine. In the neonate, however, secretion of pancreatic lipase is low (Norman *et al* 1972) and its levels probably do not become adequate until 4 to 6 months of age (Watkins 1975). The digestion of fat in infants is thus augmented by lingual lipase, gastric lipase and a lipase present in human breast milk (FAO 1994). Human milk lipase is a non-specific lipase that is activated by bile salt conjugates (Watkins 1985). It is stable at pH 3.5 for one hour and so can resist passage through the stomach. The enzyme hydrolyses dispersed, water-insoluble substrates (TAG, lipovitamins, and cholesterol esters) as well as water-soluble substrates (short chain and medium chain monoglycerides). When human milk fat is used as the lipid source, it is estimated that human milk lipase concentrations are sufficient to hydrolyse 30 to 40% of available TAG in two hours. Alternative enzymatic mechanisms such as these serve to maximise lipid adsorption and to circumvent the relative immaturity or inefficiency of the pancreatic, intestinal, and hepatic system. One-week-old term infants have been determined to readily absorb more than 90% of the fat from human breast milk (Widdowson 1965).

In breast milk, about half of the ARA and DHA content of TAG are found at the *sn*-2 position; the other half is esterified to the *sn*-3 position (Martin *et al* 1993). Although the presence of some LCPUFAs, including DHA and ARA, at outer positions of the TAG is reported to induce resistance to pancreatic lipase (Bottino *et al* 1967), the non-specific lipases, such as gastric lipase, lingual lipase and human milk lipase, appear able to circumvent this resistance. Therefore, after intestinal hydrolysis of human milk TAG by the neonate, a similar proportion of ARA and DHA are absorbed as 2-monoacylglycerol and as free fatty acid (Martin *et al* 1993).

The positional differences of LCPUFAs among TAG from different sources was studied by Carnielli *et al* (1998) to determine what affect this had on their absorption by pre-term infants. The dietary intakes, faecal output and percentages of intestinal absorption of n-6 and n-3 LCPUFAs were studied in healthy pre-term infants fed exclusively pre-term breast milk, formula without LCPUFA supplementation, formula with LCPUFAs derived from phospholipids, or formula with LCPUFAs derived from DHASCO and ARASCO.

The study showed that in pre-term infants fed pre-term breast milk, LCPUFAs are not absorbed completely (about 80% of ARA and DHA is absorbed) and that LCPUFAs bound to phospholipids are better absorbed (88% DHA absorbed, 85% ARA absorbed) than LCPUFAs from ARASCO- and DHASCO-supplemented formula (about 80% of ARA and DHA absorbed), or breast milk. This indicates that intestinal absorption of ARA and DHA from ARASCO- and DHASCO-supplemented infant formula is similar to that from breast milk. This was considered an important finding because, unlike in breast milk TAG, DHA and ARA in DHASCO and ARASCO do not have a strong positional specificity (see Section 2.5). On the basis of previous work by Bottino *et al* (1967) on the resistance of certain LCPUFAs of fish oils to hydrolysis by pancreatic lipase, relatively low absorption might have been expected with the LCPUFAs from DHASCO and ARASCO. However, the results of the Carnielli study indicate that LCPUFAs from these sources are absorbed as efficiently as those from breast milk.

3.1.2 Distribution

Once fatty acids are absorbed they are distributed into various lipid pools, i.e., phospholipids, TAG, sterol esters and free fatty acids, all of which have important physiological roles. The pools into which they are distributed, and their relative proportions, depend very much on the individual fatty acid concerned.

For example, studies in rats with radio-labelled linoleic acid and α-linolenic acid have shown that 50 – 60% of the label can be recovered from expired CO_2 within 24 hours (Leyton *et al* 1987), indicating that the majority of the linoleic and α-linolenic acids are oxidised to provide energy to the cells. In contrast, only 15% of administered ARA and DHA are oxidised in rats, the rest being spared from oxidation and preferentially channelled into the structural lipids, i.e., the phospholipids (Sinclair 1975, Leyton *et al* 1987). This appears to be the case also with human infants where relatively small concentrations of dietary LCPUFA have marked effects on plasma lipid composition, particularly the phospholipid pool (Koletzko *et al* 1989). A dietary LCPUFA (ARA and DHA) supply of only 1.7% with human milk and 0.5% with LCPUFA-supplemented formula led to LCPUFA values in plasma phospholipids that were 8% and 3% higher, respectively, than those of the control formula (containing no detectable ARA or DHA), indicating preferential incorporation into the phospholipid pool.

Phospholipids are the most abundant membrane lipid, where they serve primarily as structural elements of membranes and, unlike TAG, are never stored to any great extent. Phospholipids make up about a quarter of the solid matter of the brain (Farquharson *et al* 1992) and ARA and DHA are by far the most abundant fatty acids present in brain cell membranes, with particularly high concentrations in the membranes of neuronal synapses and the retina (British Nutrition Foundation 1992). During the last trimester of pregnancy, the human foetal brain experiences a rapid growth spurt where it increases in size by four to five fold (Clandinin *et al* 1980). This rapid increase in size coincides with the rapid accumulation of DHA and ARA by neural tissue (Martinez 1992, Makrides *et al* 1994).

3.1.3 Metabolism

Fatty acids are metabolised by a process known as β–oxidation, which takes place primarily in the mitochondria. Transport into the mitochondria is a carrier–dependent process using carnitine.

Fatty acid molecules are degraded in the mitochondria by progressive release of two–carbon segments in the form of acetyl coenzyme A, which are then used by the citric acid cycle, producing CO_2 and NADPH, which is then oxidised to produce ATP.

It is apparent however, both from studies in rats as well as humans, including infants, that the majority of dietary ARA and DHA is unavailable for oxidation, particularly in the infant, and is instead preferentially channelled into the phospholipid pool.

3.1.4 Excretion

The lipids that are metabolised are excreted as carbon dioxide and water. Various amounts of lipid may also be excreted in the faeces and this is generally a reflection of the efficiency of intestinal absorption. In cases of malabsorption due to certain pathologies (e.g., pancreatic insufficiency, short bowel etc) lipids can be excreted in large amounts in the stools. Also, in specific studies with pre-term infants (Carnielli *et al* 1998) it appears as though between 20 – 25% of ingested LCPUFAs (either from DHASCO/ARASCO-supplemented formula or human milk) can be lost in the faeces, that is, not absorbed by the intestine. Term infants, however, exhibit more efficient absorption, readily absorbing greater than 90% of human milk fat (Widdowson 1965), therefore the proportion of ingested LCPUFAs in the faeces is likely to be considerably less than that found in pre-term infants. Studies with weanling rats (see Section 3.2 below), using DHASCO and ARASCO, indicate that less than 2% of ARA and DHA are actually excreted in the faeces, even at very high levels of diet incorporation.

3.2 Specific studies with ARASCO and DHASCO in animals and humans

A number of studies with neonatal and weanling animals were submitted, as well as a single human study using pre-term infants. The studies are listed below.

3.2.1 Animal studies

(i) Absorption of ARASCO and DHASCO in rats. Mason, S. and Yuhas, R. (1994**)** Wyeth-Ayerst Research. Study GTR-20407.

(ii) Tissue accretion of fatty acids in rat pups. Boyle, *et al*. (1995**)** Wyeth-Ayerst Research. Study GTR-24592.

(iii) Diets varying in n-3 and n-6 fatty acid content produce differences in phosphotidylethanolamine and phosphotidylcholine fatty acid composition during development of neuronal and glial cells. Jumpsen *et al*. (1995**)**. Department of Agricultural, Food and Nutritional Science, University of Alberta, Canada. Study GTR-26223.

(iv) Relationship between dietary supply of long chain fatty acids and membrane composition of long and very long chain fatty acids in developing rat photoreceptors. Suh, M. *et al* (1995). Nutrition and Metabolism Research Group, University of Alberta, Canada. Study GTR-26222.

(v) Retinal fatty acids or piglets fed microbial sources of DHA and ARA. Craig-Schmidt, M.C. *et al* (1995). Department of Nutrition and Food Science, Auburn University, Alabama, USA. GTR-26221.

(vi) Plasma and erythrocyte lipids of piglets fed formula containing microbial sources of DHA and ARA. Craig-Schmidt, M. *et al* (1995). Department of Nutrition and Food Science, Auburn University, Alabama, USA. GTR-26532.

The animal studies above examined both the absorption and tissue accretion of LCPUFAs from DHASCO and ARASCO in weanling rat, neonatal rat or neonatal pig models. The studies were all well prepared, performed and presented, although no declarations were included with any of the above studies to indicate that they have been conducted in accordance with good laboratory practice.

The absorption study with DHASCO and ARASCO in weanling rats (study (i) above) indicates that DHA and ARA are well absorbed (> 98%) when incorporated at low levels (1.7% DHASCO, 2.1% ARASCO) in a formula fat blend and at higher levels (24 % DHASCO, 29% ARASCO) with soybean oil.

The tissue accretion studies in neonatal rats indicate there is a complex interaction between n-6 and n-3 fatty acids and that even small dietary amounts of DHA and ARA can readily influence the fatty acid composition of phospholipids, reflected in the plasma, brain and retina fatty acid levels. Similar results were also obtained using the neonatal pig model.

The above studies indicate that both ARASCO and DHASCO are bioavailable and that they are able to support maximal tissue accretion of ARA and DHA by the retina and other membrane phospholipids.

3.2.2 Human studies

Bioavailability of arachidonic and docosahexanoic acids from Preemie SMA supplemented with long chain polyunsaturated fatty acids. Clandinin, M.T. *et al* (1995). Nutrition and Metabolism Research Group, Department of Food Science and Nutrition, University of Alberta, Canada. [Published as Clandinin *et al* (1997)].

Study objective

The purpose of the above study was two-fold: (i) to measure the blood lipid responses of pre-term infants fed human milk or infant formula supplemented with four different levels of ARA and DHA; and (ii) to determine the quantity of LCPUFAs in infant formula that will promote blood lipid profiles in formula-fed pre-term infants that are similar to that of human milk-fed infants.

Study conduct

The study was an open (non-blinded), sequential, prospective design. Healthy, pre-term infants whose birth weight was less than 2200 g were enrolled in the study. All study infants were receiving 100% of their daily fluid and energy requirements enterally by 14 days of age. Infants were assigned to one of four feeding groups based on the mother's decision to breast-feed or feed infant formula to their infant.

Infants were thus assigned to one of four diet groups: human milk (33 infants); pre-term formula with no added ARA and DHA (15 infants); pre-term formula with 0.4% ARA and 0.25% DHA (22 infants); and pre-term formula with 0.6% ARA and 0.45% DHA (21 infants). The different pre-term formulas varied only with respect to their ARA and DHA content. The source of ARA was ARASCO and the source of DHA was DHASCO. Between the groups, infants were matched for gestational age, postnatal age and birth weight.

Body weight was measured daily, and body length and head circumference were measured weekly. Human milk or formula intake was estimated daily. Occurrence of vomiting was used to assess study formula tolerance. Venous blood samples were obtained at approximately 12 to 14 days of age (week 0 of the study) and after an additional 4 weeks of feeding (week 4). Blood samples were analysed for total plasma and red cell membrane phospholipid fatty acid composition, complete blood count, differential white count, platelet count and serum creatinine. Routine urinalysis was done at weeks 0 and 4. Total plasma phospholipid (TPL), erythrocyte-phosphatidylcholine (RBC-PC), and erthyrocyte-phosphatidylethanolamine (RBC-PE) fatty acid compositions were also determined.

Results

There were no differences between the groups with respect to weight, length and head circumference at week 0 and week 4. There was also no difference between the groups with respect to feeding tolerance. The average daily intake of human milk or infant formula exceeded 150 ml/kg/day by 12-14 days of age.

Human milk or LCPUFA-supplemented formula feedings were associated with increases in ARA and DHA in TPL and RBC-PC relative to those fed unsupplemented formula. RBC-PE DHA levels were similar in the human milk and 0.6% ARA/0.4% DHA supplemented groups, and both were significantly different from the unsupplemented group, while RBC-PE ARA levels were not detectably different among the various groups. Supplementation with 0.6% ARA/0.4% DHA or 0.4% ARA/0.25% DHA resulted in ARA and DHA concentrations in TPL and RBC-PC that were not significantly different from each other or from the human milk-fed group.

There were no consistent effects of ARA or DHA supplementation on non-essential fatty acid concentrations in plasma or erythrocyte phospholipids regardless of the supplementation level.

No significant differences were noted in any of the haematological parameters measured. The formula fed infants all had significantly higher urine pH values at 4 weeks than the human milk-fed group but this is an expected finding related to infant formula feeding. No other differences in urine parameters were noted.

Conclusions

The DHASCO/ARASCO supplemented formula was well tolerated by the infants. Supplementation of the pre-term formula supplemented 0.6% ARA and 0.4% DHA produced ARA and DHA concentrations in TPL and erythrocyte phospholipids that match those of human milk-fed pre-term infants. These levels of supplementation also approximate the levels of DHA and ARA found naturally in human pre-term milk and thus suggest that the LCPUFAs in DHASCO and ARASCO are as well absorbed and assimilated as those in human milk.

4. TOXICOLOGY

4.1 Acute studies

4.1.1 Acute oral toxicity study of DHASCO (oil) in rats. Glaza, S.M. (1990) Hazleton Wisconsin Inc, Wisconsin, USA on behalf of Martek Corporation. Study GTR 26203. December 1990. [Published as Boswell *et al* 1996]

Study conduct

Test material:	DHASCO oil, described as a cloudy, viscous, amber liquid.
Test species:	Albino rats, Crl:CD®BR (Charles River Laboratories, Inc., Portage MI).
Dose:	20 g/kg body weight administered orally by gavage to 5/sex.
GLP:	US Code of Federal Regulations for Non-clinical Laboratory Studies, 21 CFR 58.
Guidelines:	US FDA Toxicological Guidelines (Redbook I).

Five male and five female rats, weighing from 202 to 260g, were administered with a single dose level of 20 g/kg body weight of the test material. Food and water were available *ad libitum* throughout the study, except for approximately 17 to 20 hours before test material administration when food, but not water, was withheld. An individual dose of the undiluted test material was calculated for each animal based on its fasted body weight and administered by gavage. The test material was administered in a volume of 22.73 ml/kg body weight, based upon an average bulk density of 0.88 g/ml. Clinical signs and mortality checks were done at 1, 2.5 and 4 hours after dosing. The animals were observed daily thereafter for 14 days for clinical signs and twice daily (morning and afternoon) for mortality. Body weights were determined before test material administration (Day 0), at Day 7, and at termination of the study (Day 14). Before initiation of treatment (Day –1), at Day 7, and at termination of the experimental phase (Day 14), all animals (not fasted) were anaesthetised with ketamine and 2 ml of whole blood was collected from the retro-orbital plexus. The samples were sent frozen to the Sponsor (Martek Corporation) after termination of the study. At termination of the study, all animals were killed, subjected to gross necropsy examination and all abnormalities were recorded. After necropsy, animals were discarded and no tissues were saved. No statistical analysis was performed.

Results

No deaths were recorded during the study and all animals exhibited increased weight gain over the course of the study. Clinical signs observed were soft stools and dark stained urogenital area. All animals returned to a normal appearance within three days of test material administration. Gross necropsy examination of the animals at study termination revealed no visible lesions. The estimated LD_{50} for males and females was determined to be greater than 20 g/kg body weight.

Comment

The appearance of soft stools and stained urogenital areas are expected and normal consequences of a large single dose of a fatty substance and are thus not considered to be an adverse effect.

4.1.2 Acute oral toxicity study of ARASCO (oil) in rats. Glaza, S.M. (1992) Hazleton Wisconsin Inc, Wisconsin, USA. Study GTR 26204. January 1992.

Study conduct

Test material:	ARASCO oil, described as a yellow liquid.
Test species:	Albino rats, Crl:CD®BR (Charles River Laboratories, Inc., Portage MI).
Dose:	20g/kg body weight administered orally by gavage to 5/sex.
GLP:	US Code of Federal Regulations for Non-clinical Laboratory Studies, 21 CFR 58.
Guidelines:	US FDA Toxicological Guidelines (Redbook I).

Study conduct as described for 4.1.1 above.

Results

No deaths were recorded during the study and all animals exhibited increased weight gain over the course of the study. Clinical signs observed were oily soft stools and oily hair coat (males only). All animals returned to a normal appearance within two days of test material administration. Gross necropsy examination of the animals at study termination revealed no visible lesions. The estimated LD_{50} for males and females was determined to be greater than 20 g/kg body weight.

4.1.3 Acute oral toxicity study of Microencapsulated Formulaid® in rats. Glaza, S.M. (1997) Corning Hazleton Inc, Wisconsin, USA. Study . January 1992.

Study conduct

Test material:	Microencapsulated Formulaid®, Lot No. RBD28-03612 (a 2:1 mixture of ARASCO and DHASCO), described as tan granules.
Test species:	Young adult albino rats, Crl:CD®BR (Charles River Laboratories, Inc., Portage MI).
Dose:	5 g/kg body weight administered orally by gavage to 5/sex.
GLP:	US Code of Federal Regulations for Non-clinical Laboratory Studies, 21 CFR 58 with the exception that analysis of the test material mixture for concentration, homogeneity/ solubility and stability was not conducted.

Five male and five female rats, weighing from 225 to 299 g, and approximately 8 to 16 weeks of age, were administered with a single dose level of 5 g/kg body weight of the test material. Food and water were available *ad libitum* throughout the study, except for approximately 17 to 20 hours before test material administration when food, but not water, was withheld. Clinical signs were done at 1, 2.5 and 4 hours after dosing and daily thereafter for 14 days. The animals were observed twice daily (morning and afternoon) for mortality. Body weights were determined before test material administration (Day 0), at Day 7, and at termination of the study (Day 14). At termination of the study, all animals were killed, subjected to gross necropsy examination and all abnormalities were recorded. After necropsy, animals were discarded and no tissues were saved. No statistical analysis was performed.

Results

No deaths were recorded during the study and all animals, with the exception of one female, exhibited increased weight gain over the course of the study. None of the animals exhibited any clinical signs during the course of the study and no lesions were observed at necropsy.

The estimated LD_{50} for males and females was determined to be greater than 5 g/kg body weight.

4.2 Short-term studies

4.2.1 4-week oral gavage toxicity study with ARASCO, DHASCO, and Formulaid (ARASCO and DHASCO) in rats.

Williams, K.D. (1994). Hazleton Wisconsin Inc., Wisconsin, USA. Study HWI 6539-100. 29 June 1994. [Published as Boswell *et al* 1996]

Study conduct

Test material:	ARASCO (Lot No. A011-DS-2, yellow-tan liquid), DHASCO (Lot No. DD004-WS, yellow-red liquid), and Formulaid (Lot No. F011-DS-2, a 2:1 mixture of ARASCO and DHASCO, yellow-tan liquid)
Test species:	Male and female Crl:CD®(SD)BR VAF/Plus® rats (Charles River Laboratories, Inc., Portage, Michigan)
Dose:	ARASCO: 50 (5/sex), 1000 (5/sex), 2500 mg/kg bw/day (10/sex); DHASCO: 25 (5/sex), 500 (5/sex), 1250 mg/kg bw/day (10/sex); Formulaid: 1500 (5/sex), 3750 mg/kg bw/day (10/sex). Each animal received a total of 3.75 g oil/kg bw/day, vehicle was high oleic sunflower oil.
GLP:	US Code of Federal Regulations for Non-clinical Laboratory Studies, 21 CFR 58.

After 11 days acclimatisation, male and female rats were assigned at random to nine groups and were dosed according to the following:

Group	No. of animals	High oleic sunflower oil (mg/kg bw/day)	ARASCO (mg/kg bw/day)	DHASCO (mg/kg bw/day)	Formulaid (mg/kg bw/day)
1	10/sex	3750			
2	5/sex		50		
3	5/sex		1000		
4	10/sex		2500		
5	5/sex			25	
6	5/sex			500	
7	10/sex			1250	
8	5/sex				1500
9	10/sex				3750

Each animal received dose preparations containing the carrier (high oleic sunflower oil), test materials, or a combination of both at a dose volume of 4.17 ml/kg. Each animal received a total 3.75g oil/kg bw/day.

Food and water were provided *ad libitum*. Animals were observed twice daily for mortality and clinical signs and at least once each week, each animal was removed from its cage and examined for abnormalities and signs of toxicity. Individual body weight and food consumption data were collected weekly for 4 weeks.

Blood samples were collected for haematology and clinical chemistry tests from 5 animals/sex/group during Week 5 of the study (i.e., prior to termination of the study). Blood samples were also collected from 5 animals/sex before treatment and during Weeks 2 and 5; serum was collected and sent to the Sponsor for possible future analyses. During Week 5, animals were anaesthetised, weighed, exsanguinated, and necropsied.

At necropsy, macroscopic observations were recorded, selected organs were weighed, and selected tissues were collected and preserved. The brain, heart, liver (representative sample), and right testis (where present) were collected from 5 animals/sex/group, frozen in liquid nitrogen and stored at -70˚C until shipped to the Sponsor. Microscopic examinations were done on tissues from 5 animals/sex/group from all high dose groups plus the high oleic sunflower oil control. Data were analysed by appropriate statistical techniques.

Results

Antemortem observations and survival: All animals survived to the end of the study. No test material-related antemortem observations were noted during the study.

Body weight and food consumption: No significant differences in body weights, cumulative body weight gain or food consumption between the treated and control groups were noted during the study.

Clinical chemistry: Some females in the mid dose ARASCO group and the high dose DHASCO group had a significantly lower total protein value than the control group. Albumin was also significantly lower for females in the mid and high dose ARASCO groups and the high dose DHASCO group. These occurrences appear to be sporadic and do not exhibit any apparent dose-response relationship. In addition, these affects are not observed in the low or high dose Formulaid groups. The males also were not similarly affected. High serum potassium levels were observed in several animals, including those in the control group, and thus do not appear to be related to the test material.

Postmortem observations: The only significant organ weight finding was higher absolute liver weights for males in the high dose Formulaid group compared to the controls and those of males in the high dose DHASCO group. The change in liver weight was also reflected in the organ-to-body weight and organ-to-brain weight ratios for males in the high dose Formulaid group. The increased liver weights were not however correlated with any histopathologic finding or clinical chemistry finding therefore is most likely to represent an adaptive change to the high concentrations of LCPUFAs in the diet.

Histopathological observations: A few histopathological changes were evident, however the incidence of the changes was similar in control and treated animals.

Conclusions

No evidence of toxicity was observed at doses of ARASCO up to 2500 mg/kg body weight/day and DHASCO up to 1250 mg/kg body weight/day, administered either individually or in combination (as Formulaid).

Comment

The high serum potassium levels observed in several animals, including those in the control group, have been attributed to an excessively deep plane of anaesthesia before blood collection because if the levels observed had been present before anaesthesia they would have seriously affected the animals (Boswell *et al* 1996).

4.2.2 Sub-acute (4-wk) oral toxicity study with polyunsaturated fatty acids in rats. Lina, B.A.R. (1996). TNO Nutrition and Food Research Institute, The Netherlands. Study No.1751. March 1996.

Study conduct

Test material:	ARASCO (Batch No. PU 506HD/KA070) and DHASCO (Batch No. 50150)
Test species:	Young male and female Wistar outbred rats (Crl:(WI)WU BR) (Charles River Wiga GmbH, Sulzfeld, Germany)
Dose:	Administered by gavage daily to 5/sex/group at the following doses: 100- 3000 mg ARASCO/kg bw/day; 50- 1500 mg DHASCO/kg bw/day; 2000 mg ARASCO/1000 mg DHASCO/kg bw/day; 3000 mg ARASCO/1500 mg DHASCO/kg bw/day.
GLP:	OECD Principles of Good Laboratory Practice.
Guidelines:	OECD Guideline for Testing of Chemicals 407 and EC Guideline 84/449/EC

After acclimatisation, rats were assigned to various groups proportionately by weight class by a computer randomisation program and were dosed according to the following.

Group	Treatment	Dose (mg/kg bw/day)	No. of animals
A (control)	Vehicle only	-	10/sex
B	ARASCO	100	5/sex
C	ARASCO	600	5/sex
D	ARASCO	2000	5/sex
E	ARASCO	3000	5/sex
F	DHASCO	50	5/sex
G	DHASCO	300	5/sex
H	DHASCO	1000	5/sex
I	DHASCO	1500	5/sex
J	ARASCO / DHASCO	2000/1000	5/sex
K	ARASCO / DHASCO	3000/1500	5/sex

The test substances were administered daily by gavage for 4 weeks. Each animal received dose preparations containing the vehicle (corn oil) at a constant volume of 5 ml/kg body weight. The vehicle control group received 5 ml corn oil/kg body weight only.

Food and water were provided *ad libitum*. Animals were observed twice daily for mortality and clinical signs. All abnormalities, clinical signs or reactions to treatment were recorded. The body weight of each animal was recorded at the beginning of the study (Day 0) and twice weekly thereafter. In addition, terminal body weights were recorded in order to determine the organ to body weight ratios. Food consumption was measured on a weekly basis. At necropsy, blood samples were taken from the abdominal aorta and tested for haematology parameters and clinical chemistry parameters. At necropsy, animals were killed by exsanguination under ether anaesthesia and then examined macroscopically for pathological changes.

Selected organs were weighed and selected tissues (adrenals, bone marrow, brain, fatty tissue, heart, kidneys, large intestine, liver, lungs, lymph nodes, ovaries, pancreas, spleen, small intestine, stomach, testes, thyroid with parathyroids, uterus and all gross lesions) were preserved for microscopic examination. Data were analysed by appropriate statistical techniques.

Results

Antemortem observations and survival: No animals died during the study. A number of animals exhibited areas of sparsely haired skin and/or focal alopecia but this was also observed among control animals. No other abnormal clinical signs or behaviour were observed among any of the animals.

Body weight and food consumption: There were no apparent differences in food consumption between the various groups and the controls and the only statistically significant difference in mean body weights between groups was an increase in males of the DHASCO 1000 group on Day 7.

Clinical chemistry: A number of changes in clinical chemistry were observed. Alanine aminotransferase (ALAT) and aspartate aminotransferase (ASAT) activities were significantly increased in females of the ARASCO/DHASCO high dose group and alanine aminotransferase activity was also significantly increased in males of the DHASCO 1500 group. The changes were only slight and were well within historical control ranges.

A tendency towards decreased levels of phospholipids was observed in males of the DHASCO 1000 group, in both sexes of the DHASCO 1500 group and in both sexes of the ARA/DHA low and high dose groups. These changes reached the statistical significance in males of the DHASCO 1000 group, in both sexes of the ARASCO/DHASCO low dose group and in females of the ARASCO/DHASCO high dose group. These changes were not clearly within the range of historical control data.

In males, triglyceride levels were relatively low in the ARASCO 2000 and ARASCO 3000 groups, the DHASCO 1500 group and the ARASCO/DHASCO low dose and high dose groups, both in comparison to the controls and in comparison to the historical control data. These changes reached statistical significance in males of the ARASCO/DHASCO low dose group.

An increased creatinine level was observed in males of the ARASCO 100 group but was not seen at any of the higher dose levels.

Haematology: Values obtained for red blood cell variables and clotting potential did not show any statistically significant changes, apart from slight increases in mean corpuscular haemoglobin concentration (MCHC) in males of the ARASCO/DHASCO low dose and high dose groups. This slight increase was well within the normal range and not associated with any other changes in red blood cell variables.

There were no statistically significant changes in total white blood cell counts or in differential white blood cell counts in any group, apart from a decrease in the absolute number of lymphocytes in females of the DHASCO 50 group. This appears to be a sporadic finding, as this effect was not observed at any of the higher dose levels.

Post-mortem observations: The relative weight of the spleen was significantly increased in males of the ARASCO 3000 group and in females of the ARASCO/DHASCO high dose group. The absolute weight of the spleen was increased in males of the ARASCO 2000 group but this change was not reflected in a significant increase in the relative weight of this organ.

A few other organ weight changes were noted (decreased relative testes weight and increased relative liver weights in males of the DHASCO 50 group, and increased relative heart weight in females of the DHASCO 50 group and the ARASCO/DHASCO low dose group) but these changes were not observed at any of the higher doses and were thus considered to be spurious findings.

A number of gross changes were observed at necropsy however these occurred sporadically among both test and control groups and are common for animals of this strain and age. The only exception was the occurrence of local peritonitis (indicated by ascites and white deposition on the spleen – see Histopathologic observations) in one male of the DHASCO 1500 group. As this condition was not observed in any other animals it was considered to be a sporadic finding, unrelated to treatment.

Histopathologic observations: Microscopic examination did not reveal any treatment related histopathological changes. All changes observed were randomly distributed among the groups or occurred in a single animal only and are common for rats of this strain and age, except for local peritonitis (ascites with splenic capsular and serosal inflammation) observed in one DHASCO 1500 male.

Conclusion

The administration of ARASCO and DHASCO to Wistar rats at doses up to 3000 and 1500 mg/kg bw/day, respectively, for 4 weeks, either singly or in combination, was not associated with any evidence of toxicity.

Comment

The increases in ALAT and ASAT observed in some of the high dose groups were not accompanied by changes in liver weight or associated with any histopathological findings therefore they are not of toxicological significance.

The decreases in phospholipid and triglyceride levels were not always statistically significant and also did not always show a clear dose-response relationship however they appear to be definitely treatment related. These findings however are not considered to be toxic effects but rather are normal consequences of the feeding of long chain polyunsaturated fatty acids. Similar changes are also observed with the feeding of fish oils (see Appendix 1 for further discussion).

The increases in spleen weight were not accompanied by any relevant histopathological changes or change in haematology parameters and thus are not considered to be of toxicological significance (see Appendix 1).

4.2.3 Martek oil: Nine week oral (diet) safety study in rats. Anon. (1994). Wyeth-Ayerst Research, New York, USA. Study No. 06288. 9 February 1994.

Study conduct

Test material:	Martek oil (Lot Nos. 17798 and 17799) containing a 1.5:1 blend of ARASCO:DHASCO produced using Martek Manufacturing Standard Operating Procedure 1.
Test species:	Male and female Charles River CD VAF rats (Charles River Laboratories, Inc., Portage, Michigan)
Dose:	129mg ARASCO + 91.9mg DHASCO (low dose), and 1044mg ARASCO + 720mg DHASCO (high dose)/kg bw/day to 15/sex/group.
GLP:	US Code of Federal Regulations for Non-clinical Laboratory Studies, 21 CFR 58

After 12 days acclimatisation, male and female rats were assigned to four treatment groups (15/sex/group) and dosed via the diet according to the following:

Treatment Group	Diet/dose	% total fat component
1 (Control)	Purina certified rodent chow	-
2 (Positive control)	Soybean oil (basal diet)	100%
3 (Low)	129 mg ARASCO/kg bw/day 92 mg DHASCO/kg bw/day	2.9 % 2.0%
4 (High)	1044 mg ARASCO/kg bw/day 720 mg DHASCO/kg bw/day	23.2% 16.0%

The synthetic diets fed to Groups 2, 3 and 4 contained 5% total dietary fat and 20% protein. The total fat content of the rodent chow diet was not specified. The doses of ARASCO and DHASCO administered to Group 3 were intended to approximate the expected clinical consumption and the dose administered to Group 4 was a 8-fold excess of this amount.

The appropriate diet and water were provided *ad libitum*. All animals were observed at least twice daily for mortality. Individual body weights and group mean food consumption was recorded weekly. All animals were observed daily for changes in gross motor and behavioural activity and in appearance and were observed weekly for alterations of teeth, nose, eyes, pelage, perineum, and body orifices and to detect the onset and progression of tissue masses. Ophthalmoscopic examinations were performed on all rats 1 week prior to study initiation and during week 9. Blood samples were collected for haematology and clinical chemistry tests from 10/sex/group 1 week prior to study initiation and during weeks 4 and 9. Additional haematology parameters were also examined at termination on samples collected at necropsy during week 10. All rats surviving the 9 weeks treatment and a single animal that was killed *in extremis* received a complete necropsy. At necropsy, macroscopic observations were recorded, selected organs were weighed, and selected tissues were collected and preserved for histological examination.

Results

Antemortem observations and survival: One Group 3 male was killed *in extremis* during study week 8 due to a swollen left hind leg. No evidence of any treatment-related changes was seen in this rat. All other animals survived until the end of the study.

Body weight and food consumption: No differences were observed in body weight gain between groups throughout the study and food consumption of rats fed ARASCO and DHASCO (Group 3 and Group 4 rats) were comparable to those fed the high fat (soybean oil) control diet (Group 2 rats). Slight decreases in food consumption, with concomitant decreases in body weight gain, were observed during the first week of the study in female rats in Groups 2, 3 and 4 and in male rats in Group 3 and 4, compared to the rats in Group 1 (rodent chow diet). Sporadic decreases in food consumption, but without any corresponding changes in body weight gain, continued to occur throughout the study in male and female rats in Groups 2, 3 and 4. These differences are most likely be attributed to differences in diet composition of Groups 2, 3 and 4, compared to Group 1, although details of the specific diet formulations were not provided in the study report.

Clinical observations: No treatment-related differences were observed following physical and ophthalmologic examination.

Haematology: During week 4, slight decreases in haematocrit values occurred in male Group 3 and 4 rats and in female Group 4 rats, compared to Group 1 and 2 rats. Slight decreases in reticulocyte counts were also evident in male and female rats in Groups 2, 3 and 4 at weeks 4 and 9. The magnitude of this change was greatest in Group 3 and 4 rats. These changes appear to be treatment (i.e. DHASCO/ARASCO) related, however they do not clearly correlate with any specific histopathologic changes therefore they may not be toxicologically significant.

Clinical chemistry: Variations in several clinical chemistry parameters were observed. These included slight to moderate increases in cholesterol and the HDL fraction and decreases of the same magnitude in triglyceride values in male and female rats in Groups 2, 3 and 4 throughout the treatment. Some fluctuations also occurred in the LDL fraction, with slight decreases noted in Group 3 male rats and Group 4 male and female rats at week 4, and slight decreases in this fraction seen in Group 2 females during week 4 and 9, with Group 2 males also similarly affected at week 9 only. Changes in Groups 3 and 4 were generally equivalent to or less severe than changes observed in Group 2. As these effects were also noted in the high fat control (Group 2) rats, they do not appear to be test-material related, and are more likely attributed to the fat load in the diet fed to Groups 2, 3 and 4.

Slight decreases in potassium values occurred at week 4 in male and female rats in Groups 2, 3 and 4. At week 9, similar decreases were still evident in male Group 3 and 4 rats, as well as in female Group 2 rats. Individual female rats in Groups 2, 3 and 4 also exhibited slight increases in blood urea nitrogen values during weeks 4 and 9. Because the changes in potassium the blood urea nitrogen values were also noted in Group 2 rats, they do not appear to be treatment related.

Postmortem observations: Mean absolute and adjusted female ovarian weights were mildly increased in Group 4 rats, and mean absolute and adjusted male testicular weights were slightly increased in Group 4 rats, compared to Group 2 rats. Mean absolute and adjusted liver weights were slightly increased in Group 4 female rats compared to Group 2 rats. Mean absolute and adjusted brain weights were slightly decreased in Group 3 and 4 female rats, compared to Group 2 rats. These changes appear to be treatment related although the magnitude of the changes is quite small and, with the exception of hepatic fatty change, they also do not correlate with any specific histopathologic finding therefore they may have no biological or toxicological significance. Organ-to-brain weight ratios are not reported.

Gross pathologic lesions consisted of radial streaks in the kidneys from one Group 4 male, two Group 3 and two Group 4 females and hepatic discoloration in one Group 2 female and one Group 3 female. These lesions appear to correlate with some of the histopathologic findings (see below). The remaining gross pathologic lesions encountered in the tissues were consistent with spontaneous lesions encountered in control animals.

Histopathologic observations: Histopathologic lesions observed consisted of increased incidence of tubular mineralisation, tubular basophilia and hepatic fatty change in females from Group 2, 3 and 4 and an increased incidence of eosinophilic gastritis and gastric gland mucification in both males and females from Groups 2, 3, and 4. The renal histopathological findings appear to correlate with the slight increases in blood urea nitrogen values observed in females of Groups 2, 3 and 4 and the renal tubular mineralisation was also found to correlate well with the occurrence of radial streaks in the kidneys of Group 3 and 4 animals. The hepatic fatty change correlated with the occurrence of hepatic discoloration observed in one Group 2 and one Group 3 female. There is no clear indication from the data that these effects are treatment related as they were also frequently observed in Group 2 animals. The only effects that might be treatment related are eosinophilic gastritis and gastric gland mucification, the incidence of which appears to be slightly increased in Group 4 males, compared to Group 2 males. The incidence and severity (slight, mild, moderate, marked) of these lesions are summarised in the following table.

	GROUP (FEMALES)							
	1		**2**		**3**		**4**	
EFFECT	**Tot.**	**Severity**	**Tot.**	**Severity**	**Tot.**	**Severity**	**Tot.**	**Severity**
Tubular mineralisation	**6**	6,0,0,0	**14**	5,5,4,0	**14**	1,5,8,0	**15**	3,6,4,2
Tubular basophilia	**0**		**8**	4,3,1,0	**11**	6,3,2,0	**12**	3,7,2,0
Hepatic fatty change	**0**		**9**	7,1,1,0	**11**	8,2,1,0	**14**	7,5,1,0
Eosinophilic gastritis	**0**		**9**	6,3,0,0	**5**	4,1,0,0	**5**	1,3,1,0
Gastric gland mucification	**0**		**8**	0,5,3,0	**4**	2,2,0,0	**7**	1,4,2,0
	GROUP (MALES)							
	1		**2**		**3**		**4**	
EFFECT	**Tot.**	**Severity**	**Tot.**	**Severity**	**Tot.**	**Severity**	**Tot.**	**Severity**
Tubular mineralisation	**2**	2,0,0,0	**1**	1,0,0,0	**3**	3,0,0,0	**1**	0,1,0,0
Tubular basophilia	**5**	4,1,0,0	**2**	2,0,0,0	**4**	2,1,1,0	**7**	4,3,0,0
Hepatic fatty change	**0**		**2**	2,0,0,0	**1**	1,0,0,0	**3**	3,0,0,0
Eosinophilic gastritis	**0**		**6**	2,4,0,0	**4**	2,2,0,0	**12**	6,5,1,0
Gastric gland mucification	**0**		**9**	3,5,1,0	**3**	2,1,0,0	**15**	1,6,8,0

Conclusion

A number of changes were observed, many of which occurred in both the high fat control group (Group 2), as well as the low and high dose ARASCO/DHASCO groups (Groups 3 and 4), therefore they could not be specifically attributed to ARASCO and DHASCO administration.

Effects that may be related to DHASCO and ARASCO administration were slightly decreased haematocrit values and reticulocyte counts, slightly increased ovarian and testicular weights in female and males, respectively, slightly increased liver weights in females, slightly decreased brain weights in females, and an increased incidence of eosinophilic gastritis and gastric gland mucification in males. The magnitude of these changes, however, was quite small and likely to be within historical control ranges, and therefore, these effects do not appear to have any toxicological significance.

Therefore, doses of ARASCO up to 1044 mg/kg bw/day and of DHASCO up to 720 mg/kg bw/day administered for a period of 9 weeks to rats do not appear to be associated with any toxicologically significant effects.

Comments

The performing laboratory attributed the majority of the effects seen to the synthetic diet being fed to Groups 2, 3 and 4. They reported that the renal lesions are similar to those in previous reports from studies feeding synthetic diets to rats and are thought to result from improper calcium to phosphorous rations. The hepatic fatty change was considered minor and reversible and was interpreted to result from high levels of carbohydrates in the synthetic diets. Similar lesions in the stomach to those described in this study have also apparently been reported in previous studies with rats fed synthetic diets. Apart from the fat and protein content of the synthetic diet fed to Groups 2, 3 and 4, no other information was provided in the report regarding the diet formulation.

4.3 Sub-chronic studies

4.3.1 Subchronic (3-month) combined neurotoxicity and toxicity study of ARASCO and DHASCO in the rat via oral gavage. Boswell, K. (1995). Pharmaco LSR, New Jersey, USA. Study No. 94-2352. 17 August 1995.

Study conduct

Test material:	ARASCO (Lot No. A013-DS) and DHASCO (Lot No. D015-DS)
Test species:	Male and female CD® (Sprague-Dawley derived) (Charles River Laboratories, Inc., Portage, Michigan)
Dose:	1000 and 2500 mg ARASCO/kg bw/day and 500 and 1250 mg DHASCO/kg bw/day to 20/sex/group by gavage. Each animal received a total of 3ml oil/kg bw/day; vehicle was high oleic sunflower oil.
GLP:	US Code of Federal Regulations for Non-clinical Laboratory Studies, 21 CFR 58.

Animals were randomly assigned to six groups of 20 animals per sex and were acclimatised for approximately two weeks prior to dosing by gavage according to the following:

Treatment group	Test material	Dose (mg/kg bw/day)
1 (untreated control)	-	0
2 (vehicle control)	High oleic sunflower oil	0
3 (low)	ARASCO	1000
4 (high)	ARASCO	2500
5 (low)	DHASCO	500
6 (high)	DHASCO	1250

Control Group 1 received standard laboratory diet only. The dose volume for the oils was 3 ml/kg. Animals were observed twice daily for mortality and gross signs of toxicological effects. In addition, animals were given detailed physical examinations for signs of local or systemic toxicity and tissue masses twice pre-treatment and weekly thereafter. Ophthalmoscopic examinations were performed prior to treatment and at termination of the study. Body weight measurements were taken twice prior to treatment and weekly thereafter during treatment and also at termination. Food consumption was measured weekly, beginning one week prior to treatment.

In addition to above, 10/sex/group were examined pre-test, Week 5, 9 and 13 for motor activity, signs of autonomic function (ranking and degree of lacrimation and salivation, presence or absence of piloerection and exophthalmos, count of urination and defecation), description, incidence and severity of any convulsions, tremors or abnormal movements, reactions to general stimuli, posture and gait evaluations, forelimb and hind limb grip strength, landing foot splay, and ranking or righting ability.

Blood was collected by venipuncture of the orbital sinus from 10/sex/group, selected at random, at termination of treatment and was tested for haematology parameters and clinical chemistry parameters. Organ weights were measured and histology was performed. Neuropathology was also performed on tissues from 5/sex/group at necropsy. The tissues examined were brain (forebrain, cerebral cortex, hippocampus, basal ganglia, midbrain, cerebellum and pons, medulla), spinal cord (cervical, thoracic and lumbar – cross and longitudinal sections), sciatic, tibial and sural nerves (cross and longitudinal sections). Data were analysed by appropriate statistical techniques.

Results

Antemortem observations and survival: One male and one female from the high dose ARASCO group and one male from the low dose DHASCO group died during the study. The death of the male from the high dose ARASCO group was due to gavage error. The cause of death of the other two animals could not be established on either macroscopic or microscopic examination. As there were no morphological changes and clinical signs of toxicity, the deaths of one animal each in the low dose DHASCO and the high dose ARASCO groups were not attributed to the test material. All other animals survived until the end of the study.

The majority of animals were free of any unusual signs throughout the study. The abnormalities that did occur did so sporadically in individual animals. All animals received ocular examinations pre-test and at termination of the study. There was no indication of dose or compound related ocular disease and none of the ocular abnormalities observed could be attributed to the test material.

Body weight and food consumption: Mean body weights and body weight gains of ARASCO and DHASCO-treated groups were comparable or slightly lower than body weights of animals in the vehicle control group throughout the study. All values were within 5% of concurrent control values. Mean food consumption of the vehicle control group were lower than those of the untreated control group due most likely to the fat content of the vehicle (high oleic sunflower oil). Mean food consumption values for the ARASCO and DHASCO-treated groups were comparable to that of the vehicle control group.

Haematology: There was no indication of any effect on mean haematology values at termination of the study. A few statistically significant differences between the control and treated groups were observed (e.g., increased white blood cell count in high dose ARASCO males and females, decreased mean corpuscular volume in high dose ARASCO males, and increased prothrombin time in high dose DHASCO females) but were not considered to be toxicologically significant.

Clinical chemistry: Mean alkaline phosphatase values were elevated for males and females in the low and high dose DHASCO groups compared to the control mean values. Differences were generally statistically significant but were not dose-related. No other changes in serum enzymes were seen and no morphological changes were seen upon microscopic examination. These differences may represent metabolic changes associated with DHASCO administration but do not appear to be toxic effects. All other parameters evaluated were comparable between the control and treated groups.

Neurological observations: Administration of ARASCO and DHASCO was not associated with changes in motor activity for either sex during the periods tested and also did not affect the overall neurological condition of the animals as measured by a battery of functional assessments.

Postmortem observations: A number of statistically significant differences in organ weights between control and treated groups were seen. These included: increased liver weights in high dose ARASCO females; increased kidney weights in high dose DHASCO males and females; and increased spleen weights in high dose ARASCO males. However, these differences were generally slight and were also not reflected in the organ-to-body or organ-to-brain weight ratios. Therefore, no consistent pattern of changes, indicative of an effect of either test material, was seen. There were also no histopathologic findings that were considered to be treatment related or that correlated with any of the organ weight findings.

Histopathologic observations: No histopathologic findings appear to be treatment related. They occurred with comparable incidence and severities in rats from the treatment and control groups (e.g., an increased incidence of chronic progressive nephropathy in males of the vehicle control and high dose DHASCO and ARASCO groups, increased incidence of lymphocytic infiltration in the liver of males and females from the vehicle control and high dose ARASCO and DHASCO groups) or they occurred sporadically and have been seen in rats of similar strain and age previously used in the testing laboratory.

Conclusion

None of the changes observed appear to be toxicological effects related to the administration of either DHASCO or ARASCO. All the changes observed were slight and were not indicative of a consistent pattern of effects. They are most likely to be metabolic or adaptive changes to the administration of high dose of LCPUFAs. Therefore it can be concluded that the administration of 2500 mg ARASCO/kg bw/day or 1250 mg DHASCO/kg bw/day to rats for three months is not associated with any toxicologically significant effects.

4.3.2 Martek oil: thirteen week oral (diet) safety study in rats. Wren, J.M. (1995). Hazleton Wisconsin Inc.. Study No. 9430-102. 11 August 1995

Study conduct

Test material:	Martek Oil (Lot Nos. unspecified) produced using Martek Manufacturing Standard Operating Procedure 2.
Test species:	Male and female Charles River CD VAF rats (Charles River Canada, Quebec, Canada).
Dose:	88.2 mg ARASCO + 58.3mg DHASCO (low dose), 441 mg ARASCO + 291.5 mg DHASCO (mid dose), 1764 mg ARASCO + 1166 mg DHASCO (high dose)/kg bw/day to 20/sex/group. Vehicle was soybean oil.
GLP:	US Code of Federal Regulations for Non-clinical Laboratory Studies, 21 CFR 58.

After 18 days acclimatisation, male and female rats were assigned to six groups (20/sex/group) and were dosed with a total of 50g/kg fat (5%) in their diet according to the following:

Group	Description	Fat blend	Estimated dose
1	Vehicle control	100% soybean oil	-
2	Low dose	2.0% ARASCO, 1.3% DHASCO, 96.7% soybean oil	90 mg ARASCO/kg bw/day, 59 mg DHASCO/kg bw/day
3	Mid dose	10% ARASCO, 6.5% DHASCO, 83.5% soybean oil	450 mg ARASCO/kg bw/day, 293 mg DHASCO/kg bw/day
4	High dose	40% ARASCO, 26% DHASCO, 34% soybean oil	1800 mg ARASCO/kg bw/day, 1170 mg DHASCO/kg bw/day
5	Untreated control	-	

The untreated control group received standard laboratory diet only. The low dose treatment group was given ARASCO and DHASCO at the proposed clinical concentration. The middle and high dose groups received 5 fold and 20 fold multiples of the proposed clinical concentration. Drinking water and the appropriate diets (prepared fresh daily) were available *ad libitum*. Animals were observed twice daily for mortality and at least once per day for general clinical observations including general appearance and behaviour. Body weight was measured once per week (twice pre-test) and food consumption was recorded weekly. Detailed clinical observations were made weekly and ophthalmologic examinations were performed once pre-test and immediately prior to termination.

Blood was collected from 10/sex/group prior to commencement of the study and during weeks 4 and 13 and was tested for haematology parameters and clinical chemistry parameters. Additional blood samples were taken from the last 5/sex/group in order to supply adequate plasma for fatty acid analysis.

Necropsies were performed during week 14 and included external examination with gross evaluation of tissues from every animal. Organ weights were measured and histology was performed. Additional liver sections from all rats were stained with Oil Red O and examined. Data were analysed by appropriate statistical techniques.

Results

Antemortem observations and survival: All animals survived until the end of the treatment period. No changes were evident in clinical observations or in ophthalmologic examinations between the groups.

Body weight and food consumption: No changes in body weight or food consumption was observed between the groups.

Haematology: During week 4, slightly decreased total red blood cell count and haematocrit values and slightly increased platelet and reticulocyte values occurred in Groups 2, 3 and 4, compared to Group 1. These changes were not considered biologically relevant because of the magnitude and transitory nature of the changes and their lack of correlation with specific histopathological changes.

Clinical chemistry: Slightly decreased cholesterol (week 4 only in Group 4 males), LDL (week 4 and 13 in Group 4 males and females) and triglyceride values (week 4 only in Group 3 and 4 males, week 4 and 13 in Group 4 females) were seen throughout treatment and are likely to reflect secondary metabolic changes associated with the consumption of high levels of LCPUFAs, rather than toxicological changes. Slightly increased blood urea nitrogen values occurred in individual female rats in Groups 1 – 4 and generally correlated with the histopathological renal findings in these groups.

Postmortem observations: Organ weight changes consisted of slightly higher absolute mean kidney weight in male rats, mildly higher absolute and adjusted mean thyroid weights in female rats, and slightly higher adjusted mean liver weight in female rats in Group 4 (high dose DHASCO + ARASCO), compared to Group 1 (vehicle control). These observations did not correlate with any histopathological findings and therefore do not appear to be toxicologically significant. Gross pathological observations included radial streaks in the kidneys in low numbers of female rats in Groups 1, 2, 3 and 4, which correlated with the occurrence of renal tubular mineralisation.

Histopathologic observations: A number of histopathological lesions were observed and consisted of increased incidences of renal tubular mineralisation and renal tubular basophilia (females only), hepatic fatty change, eosinophilic gastritis, gastric gland mucification, and eosinophilic chief cells in male and female rats. These lesions were found to occur in treatment as well as vehicle control groups and were thus attributed to the synthetic diet, which was not fed to the untreated control group.

Conclusions

No treatment-related toxicological effects were observed in the study at doses of ARASCO up to 1800 mg/kg bw/day combined with doses of DHASCO up to 1170 mg/kg bw/day.

4.3.3 Sub-chronic (13-week) oral toxicity study, preceded by an *in utero* phase, with polyunsaturated fatty acids in rats. Lina, B.A.R. and Waalkens-Berendsen, D.H. (1997). TNO Nutrition and Food Research Institute, The Netherlands. Study No.450588. May 1997 [Published as Hempenius *et al* 2000]

Study conduct

Test material:	ARASCO (Batch No. PU 512 HG 1) and DHASCO (Batch No. 50150), both having the appearance of clear, light yellow oil.
Test species:	Male and female Wistar outbred rats (Crl:(WI)WU BR) (Charles River Wiga GmbH, Sulzfeld, Germany).
Dose:	3 g – 75 g ARA oil/kg diet, 75 g ARA oil + 55 g DHA oil/diet. Vehicle was corn oil.
GLP:	US Code of Federal Regulations for Non-clinical Laboratory Studies, 21 CFR 58.

From the start of the pre-mating period (F0 rats), throughout mating, gestation and lactation, until termination of treatment of the F1 animals, the test substances were administered at a constant concentration in the diet. A standard cereal based rodent diet was used and the total level of fat in each test diet and in the corn oil control diet was kept constant by adding the appropriate amounts of corn oil. The various levels of diet incorporation are indicated in the table below.

Group	Treatment	Treatment level (g/kg diet)	Corn oil level (g/kg diet)	No. of F1 rats/sex
A (control)	Rodent diet	-	-	10
B (control)	Corn oil	0	130	20
C (low dose ARA)	ARASCO	3	127	20
D (mid dose ARA)	ARASCO	15	115	20
E (high dose ARA)	ARASCO	75	55	20
F (high dose ARA/DHA)	ARASCO /DHASCO	75 + 55	0	20

Parental animals (F0) received the above test diets and control diets from 4 weeks prior to mating, and treatment was continued throughout mating, gestation, lactation and weaning of the F1 pups. Subsequently the sub-chronic study was started and the above test and control diets were fed to randomly selected male and female F1 rats for a period of 13 weeks. Feed and drinking water were provided *ad libitum*.

In utero phase: For the F0 animals, the general condition and behaviour of animals were checked daily and all abnormalities were recorded. The body weight of each animal was recorded at the commencement of the study and weekly thereafter until the parental rats were discarded. Mated females were weighed on Days 0, 7, 14 and 21 of gestation and on Days 1, 4, 7, 14 and 21 of lactation. Food consumption was measured on a weekly basis, during the pre-mating period in both males and females. Food consumption of mated females was recorded during pregnancy on Days 7, 14, 21 and during lactation on Days 4, 7, 14 and 21.

A number of observations were made with respect to fertility and reproductive performance for each group. These included: number of females placed with males; pre-coital time, number of successful copulations; number of males that became sires; number of pregnant females; number of females surviving delivery; number of females with live born; number of females with stillborn pups; duration of gestation; number of pups delivered number of pups lost; number of litters lost; mating index (no. of females mated/no. of females place with males X 100); male fertility index (no. of sires/no. of males placed with females X 100); female fertility index (no. pregnant females/no. females mated X 100); gestation index (no. females with live foetuses/no. of pregnant females X 100); live birth index (no. live pups/total no. pups born X 100).

For the pups the following observations were made: daily viability checks; observation of appears of pups on Days 1, 4, 7, 14 and 21 of lactation; the number of live pups per litter on Days 1, 4, 7, 14 and 21 of lactation; the number of pups per sex on Days 1, 4, 7, 14 and 21; the number of male pups at Day 1 and 21; the sex ratio at Day 1 and 21; the weight of the litters as a whole on Days 1, 4, 7 and 14 post partum; the weight of individual pups was recorded on Day 21.

Sub-chronic study with the F1 animals: all animals were checked daily for clinical signs and any abnormalities recorded. Ophthalmoscopic observations were made prior to the start of the study and towards the end of the treatment period (on Day 84) in all rats on the corn-oil control group (B), the ARA high dose group (E) and the ARA/DHA group (F). Body weights of each animal were recorded at the start of the study (Day 0) and weekly thereafter, including at necropsy. Food consumption was measured weekly. In addition to these observations, a functional evaluation battery of observations and tests selected to detect signs of neurological, behavioural and physiological dysfunctions were undertaken in Week 1 and Week 12 of the study in 10 animals/sex of each group.

These observations, in combination with histopathological examination of tissue samples representative of major areas of brain, spinal cord and peripheral nerves, were used to assess neurotoxicity.

For each test group, the intake of ARASCO and/or DHASCO/kg bw/day, as calculated on the basis of food intake, body weight and nominal dietary incorporation of the test substance is provided below.

Prior to necropsy, blood samples were taken from the abdominal aorta of 10 rats/sex/group and were tested for various haematology parameters and clinical chemistry parameters. Blood glucose was measured in blood taken from the tip of the tail shortly before the termination of the study (Day 88) and was taken from the same animals from which blood was taken just prior to necropsy.

On Day 87 – 88 of the study, the same 10 rats/sex/group that were used for haematology were deprived of water for 24 hours and of food during the last 16 hours of this period. The rats were kept in metabolism cages and urine was collected. The concentration ability of the kidneys was investigated by measuring urinary volume and density in individual samples. The same urine was also subjected to urinalysis as follows: appearance; glucose; pH; occult blood; ketones; protein; bilirubin; urobilinogen; and microscopy of sediment.

At necropsy the animals were examined macroscopically for pathological changes. A full necropsy was also performed on a single male rat belonging to the ARA high dose group (E162) that was killed unscheduled on day 67. Selected organs were examined and weighed and selected tissues were preserved for microscopic examination. Histopathological examination was performed for all animals of the corn-oil control group (B) and the ARA high dose group (E). The kidneys, liver, lungs, small intestines, Peyer's patches, mesenteric lymph nodes and gross lesions were also examined microscopically in all rats of the ARA low and mid dose groups and the ARA/DHA high dose group. Histopathological examination was not conducted in rats of the rodent diet group (A), except for examination of brain, spinal cord, small intestines, Peyer's patches, and mesenteric lymph nodes in both sexes and of the liver in females. Data were analysed by appropriate statistical techniques.

Results for the in-utero phase

All F0 animals survived until the end of the treatment period. No changes were evident in clinical observations between groups. Body weight gain in F0 females was lower than in the corn oil control during the pre-mating and mating period in the ARA/DHA high dose group, and during the first week of the gestation period in the ARA high dose group and the ARA/DHA high dose group. At the end of the lactation period however parental body weights were comparable in all groups. Mean body weights of F0 males were comparable in all groups.

There were no treatment related differences in fertility or reproductive performance among the ARA groups, the ARA/DHA high dose group and the corn oil control. All of the reproduction variables measured were normal for rats of this strain and none of the pregnant females died.

There were no treatment related differences in the general condition of pups, viability, sex ratio or number of pups per litter. Pup weight gain in the ARA/DHA high dose group was lower than in corn oil controls from Day 7 of lactation.

Results for sub-chronic study

Antemortem observations and survival: General condition and behaviour were not adversely affected by treatment in any of the groups and the functional observation battery and motor activity assessment did not reveal any unusual findings. Alopecic areas were frequently observed but the incidence of this finding was similar in test and control groups. One male rat of the ARA high dose group (E162) was killed on Day 67 of the study because of conditional decline. Microscopic examination revealed severe pyelonephritis. Similar findings were not observed in any of the other rats therefore the death of this rat was not considered to be treatment related. Ophthalmoscopic examination did not reveal any treatment related changes. The few changes that were observed are a common finding in rats of this strain and age.

Body weight and food consumption: At the start of the study mean body weight in the ARA/DHA high dose groups tended to be lower than in the corn oil controls but the differences were not statistically significant. There were no dose-related differences in body weight gain between the test groups and the corn oil controls. Males of the rodent diet group showed statistically significantly increased body weights as compared to the corn oil controls throughout the study. A similar tendency was observed in females of this group in the first few weeks of the study. Mean food consumption did not show any consistent differences between the test groups and the corn oil controls. The food consumption data, along with the body weight data, were used to calculate the dietary intake of ARASCO and DHASCO, which is presented below.

	Mean dietary intake (mg/kg bw/day)				
	ARA low ARASCO	**ARA mid ARASCO**	**ARA high ARASCO**	**ARA/DHA high ARASCO**	**DHASCO**
Males (average over 13 weeks)	190	958	4738	4883	3581
Females (average over 13 weeks)	192	984	4860	4997	3665

Haematology: Haematocrit was slightly decreased in males of the ARA/DHA high dose groups and mean corpuscular haemoglobin concentration was slightly increased in males of the ARA high dose and the ARA/DHA high dose group as compared to the corn oil controls. No other differences were observed.

Clinical chemistry: A number of differences in clinical chemistry parameters were observed between the test groups and the corn oil control group. These consisted of: decreased alkaline phosphatase activity in males and females of the ARA high dose group; decreased cholesterol in females of the ARA high dose group and in both sexes of the ARA/DHA high dose group; decreased triglycerides and phospholipids in males and females of the ARA high dose group and the ARA/DHA high dose group; increased creatinine concentration in males of the ARA high dose group and the ARA/DHA high dose group; increased urea concentration in males of the ARA/DHA high dose group.

These changes however do not appear to be treatment related as similar changes were also seen in the rodent diet control group, compared to the corn oil group.

The renal concentration test showed an increased volume and a decreased density in the ARA high dose group in both sexes and in the ARA/DHA high dose group in males as compared to the corn oil controls. Urinary volume was also higher in males and females of the rodent diet control group, but was not accompanied by a decrease in density. There were no differences in semi-quantitative observations in the urine or in the microscopy of the urinary sediment among groups.

Postmortem observations: A number of differences in organ weights between the corn oil controls and the ARA high dose group or the ARA/DHA high dose group were evident. These comprised: increased absolute and relative spleen weights in both sexes of the ARA high dose group and the ARA/DHA high dose group (the increase in relative weight was not statistically significant in males of the ARA high dose group); increased absolute and relative liver in females of the ARA high dose group and the ARA/DHA high dose group (the increase in absolute liver weight was not statistically significant in the ARA high dose group); increased absolute and relative adrenal weight in females of the ARA/DHA high dose group; increased absolute and relative testes weights in males of the ARA high dose group (the increase in relative weight was not statistically significant); and increased absolute thymus weight in males of the ARA/DHA high dose group, although this was not reflected in the relative weight of this organ. In females of the rodent diet group (A), the weights of the kidneys and liver were increased compared to the corn oil controls (B). Other significant changes in organ weights in the rodent diet group were ascribed to the higher terminal body weights in this group.

Macroscopic examination at necropsy did not reveal any treatment related findings. The abnormalities observed are all common findings in this strain of rat and occurred sporadically in both control and treatment groups. A number of male animals exhibited a pale liver however no dose response was evident and there was an equal incidence of this finding in males of the corn oil control group, therefore this change was not considered treatment related.

Observations in the male rat of the ARA high dose group (E162) that was killed on Day 67 of the study included unilateral hydronephrosis, dilatation of ureter and urinary bladder and bladder calculi.

Histopathologic observations: Microscopic examination revealed a number of changes, a number of which appear to be treatment related. The mesenteric lymph nodes of most males and several females of the ARA high dose group and the ARA/DHA high dose group contained focal aggregates of oil droplets. Oil droplets were also present in the tips of the villi of the small intestine of many animals of the ARA and ARA/DHA high dose groups. This histopathological change was not present in any animal of the other groups, except for one male in the corn oil control group. In addition, lipogranulomas were observed in the mesenteric lymph nodes in a number of rats in these groups. These changes were not present in any animals of any of the other groups. Oil droplets were also observed in the Peyer's patches of the small intestine of several rats in all groups including the corn oil controls, but not in the rodent diet control group. The incidence did not differ significantly between the test groups and the corn oil control group therefore this finding does not appear to be treatment related.

Several males and females of the corn oil group and the ARA high dose group exhibit vacuoles in the brain, especially in the white matter of the cerebellum, and in the spinal cord. The vacuoles did not contain any fat. These findings were not observed in the rodent diet control group. As the vacuoles occurred in both the ARA high dose group and in the corn oil controls, and their incidence was lower in the ARA high dose group, they do not appear to be treatment related.

In females, a dose-dependent increase in hepatocellular vacuolation in the liver was observed and reached statistical significance in the ARA high dose and ARA/DHA high dose groups. Hepatocellular vacuolation was not present in any female of the rodent diet control group. In males, vacuolation was also present in the liver of about one third of the males of all ARA groups and the corn oil control group but was absent in the ARA/DHA high dose group. The incidence of mononuclear cell infiltrate in the liver was slightly increased in males of the ARA/DHA high dose group.

In all test groups as well as the corn oil controls, several males showed increased hyaline droplet nephropathy. This change is commonly found in male rats and its incidence is reported to vary considerably (Hempenius *et al* 2000). In this study, the incidence was statistically significantly increased in the ARA high dose and ARA/DHA high dose groups. Signs of cell damage and regenerative features did not accompany these changes.

All other histopathological changes are common findings in rats of this strain and age and were equally distributed among the various groups or occurred in one or a few animals only, therefore they could not be related to the treatment. Microscopic examination of the male rat killed on Day 67 (E162) revealed the presence of severe pyelonephritis.

Discussion and conclusion

The administration of ARA-oil or DHA-oil to parental (F0) rats did not affect the health, fertility, reproductive performance or pup characteristics. The only change observed was growth retardation in parental females of the ARA and/or ARA/DHA high dose groups during the pre-mating, mating and gestation period, accompanied by a decrease in pup weight in the ARA/DHA high dose group. These lower pup weights were not however reflected in significant effects on body weights of F1 rats in the sub-chronic study.

The slight increase in mean corpuscular haemoglobin concentration in males of the ARA and ARA/DHA high dose groups may be treatment related. Similar changes were also observed in males in a 4-week study following administration of high levels of ARASCO + DHASCO (see (ii) in Section 4.2). These changes were only slight and, apart from a slight decrease in haematocrit values in males of the ARA/DHA high dose group, are not accompanied by any other changes in red blood cell parameters. For this reason, the increase in mean corpuscular haemoglobin concentration has doubtful toxicological significance.

The decreases in cholesterol, triglycerides and phospholipid concentrations in the plasma of rats of the ARA and/or ARA/DHA high dose groups are a well-documented and normal consequence of the incorporation of high levels of long chain polyunsaturated fatty acids in the diet. These changes are not considered to have any toxicological significance.

The increased volume and decreased density of urine observed in the renal concentration test in the ARA and ARA/DHA high dose groups may point to an impaired concentrating ability of the kidneys. Other findings that may be associated with this finding were increased plasma creatinine concentration and increased hyaline droplet nephropathy in males of the ARA and ARA/DHA high dose groups. In a similar study, using doses of ARASCO of 5900 mg/kg bw/day and DHASCO of 3000 mg/kg bw/day administered in combination, no such findings were reported (Burns *et al* 1999), although a renal concentration test appears not to have been performed.

The increases in spleen weight (both sexes) and in liver weight (females) in the ARA and ARA/DHA high dose groups appear to be treatment related and have been noted in a number of other short term and sub-chronic studies (see Section 4.2 and other sub-chronic studies above). This appears to be a recurrent finding associated with the feeding of diets high in long chain polyunsaturated fatty acids (refer to Appendix 1 for further discussion). Such effects are generally not regarded as toxic *per se* as they are typically not accompanied by biochemical or morphological changes that would be indicative of toxicity. In this particular study the increased liver weight in females of the ARA and ARA/DHA high dose groups was accompanied with an increased incidence of hepatocellular vacuolation and is a finding that has been observed in similar studies (Duthie *et al* 1988, Burns *et al* 1999). In Burns *et al* (1999), where even higher doses of ARASCO and DHASCO were used (up to a total of 8900 mg/kg bw/day), hepatic vacuolation was found to occur in both the high fat control as well as the high dose groups. It is speculated that the finding of hepatic vacuolation in animals fed high levels of LCPUFAs indicates that the fat level of the diets is close to that which may impede normal physiological functions in rats. While this finding may be regarded as an adverse effect associated with a diet high in LCPUFAs, it does not appear to be an adverse effect specific to either ARASCO or DHASCO.

The presence of oil droplets in the mesenteric lymph nodes and in the intestinal villi in the ARA and ARA/DHA high dose groups, as well as the appearance of lipogranulomas, is clearly treatment related, as these lesions did not occur in any other groups. These findings however do not appear to be associated with any adverse physiological effects, as determined from the absence of significant abnormalities such as inflammation. These findings are probably related to the absorption of high levels of certain fats from the intestine and their passage into the lacteals and mesenteric lymph vessels and are regarded as a harmless finding (Hempenius *et al* 2000).

In conclusion, the administration of 4738 – 4997 mg ARASCO/kg bw/day alone or in combination with 3581 – 3665 mg DHASCO/kg bw/day to rats for a period of 3 months is associated with a number of treatment related changes. Some of these findings point to an impaired concentrating ability of the kidneys at the highest dose levels tested, however, the vast majority of these changes appear to be a physiological adaptation to high dietary levels of LCPUFAs and not a manifestation of toxicity specific to the administration of either ARASCO or DHASCO. No treatment related changes were observed at the mid dose level of ARASCO. This dose level is equivalent to an intake of 958 mg ARASCO/kg bw/day.

4.4 Chronic studies

No chronic studies were submitted.

4.5 Reproduction studies

No reproduction studies were submitted.

4.6 Developmental studies

4.6.1 Developmental toxicity study with ARASCO and DHASCO in rats. Henwood, S.M. (1995). Hazleton Wisconsin, Inc., Wisconsin, USA. Study No. HWI 6539-103. 16 August 1995. [Published as Arterburn *et al* 2000]

Study conduct

Test material:	ARASCO (Lot No. A013-DS) and DHASCO (Lot No. D015-DS)
Test species:	Female Crl:CD® (SD) BR VAF/Plus® rats (Charles River Laboratories, Inc., Portage, Michigan)
Dose:	1000 and 2500 mg ARASCO/kg bw/day and 500 and 1250 mg DHASCO/kg bw/day to 25 mated females/group by gavage. Each animal received a total of 2.5g oil/kg bw/day; vehicle was high oleic sunflower oil.
GLP:	US Code of Federal Regulations for Non-clinical Laboratory Studies, 21 CFR 58

Mated female rats were assigned at random to five groups of 25 animals/group and were dosed by gavage according to the following:

Group	ARASCO (mg/kg)	DHASCO (mg/kg)	High oleic sunflower oil (mg/kg)
1 (control)	-	-	2500
2 (low)	1000	-	1500
3 (high)	2500	-	-
4 (low)	-	500	2000
5 (high)	-	1250	1250

Doses were administered in a total volume of 2.78 ml/kg bw on days 6 through 15 of gestation. Animals in Group 1 received the carrier according to the same dosing regimen as the test groups.

Food and water were provided *ad libitum*. Animals were observed twice daily for mortality and moribundity and for indications of toxic effects. Detailed clinical observations were made and body weights recorded on days 0 and 6 through 20 of gestation. Individual food consumption data were recorded during days 0 to 6, 6 to 9, 9 to 12, 12 to 16, and 16 to 20 of gestation. Necropsies were done on day 20 of gestation. Uteri with visible implantations were excised, weighed and the number and placement of implantation sites, live and dead foetuses, early and late resorptions, and any abnormalities were recorded. Each live foetus was sexed, weighed and examined for external abnormalities. Approximately one half of all live foetuses from each litter were processed and examined for soft tissue development and the remaining foetuses were eviscerated, processed and examined for skeletal abnormalities. The maternal necropsy included examination of the external surface of the body, all orifices, the cranial cavity, external surfaces of the brain and spinal cord, nasal cavity, and thoracic, abdominal and pelvic cavities and viscera. Uteri with no visible implantations were excised and stained for detection of implantations and confirmation of pregnancy status. Selected maternal tissues were collected and held for possible histological examination.

Results

Antemortem observations and survival: All animals survived to gestation day 20 and no animals had any significant clinical signs or symptoms that were test material related.

Body weights and food consumption: There were no effects on mean body weights, body weight changes, gravid uterine weights, and food consumption. The mean food consumption by the low-dose DHASCO group was higher than the control group during the first 6 days of gestation, but was not statistically significant thereafter. These animals had not received any test material during this interval so the difference in food consumption was not related to the treatment.

Postmortem observations: There were no test material-related necropsy findings in the females. No significant differences were evident in mean pre-implantation loss, post-implantation loss, percent live foetuses (male, female and total), resorptions (early, late and total) or sex ratio for any test material-treated groups.

Foetal observations: There were no significant differences in covariate-adjusted mean foetal body weights. A number of foetal external, soft tissue and skeletal abnormalities were present but they occurred in both control and treated groups in a non dose-related pattern and thus do not appear to be treatment related. These included a cleft palate and lip in one control foetus, ablepharia in one Group 2 foetus, and an absent tail and anal atresia in one group 5 foetus.

Several soft tissue variations in development were also observed. The incidence of under-developed renal papilla was increased in several of the treatment groups and was significantly higher in the low DHASCO group (Group 4) compared to the control group (Group 1). This incidence of this effect was not however dose-related as the high DHASCO and ARASCO groups had fewer incidences than the low dose groups. Several foetal and litter incidences, mostly in the DHASCO groups, were outside the laboratories historical control ranges for this effect, but all values fell within regional historical control ranges. The foetal and litter incidence of dilated renal pelvis was also significantly higher in the low ARASCO and a low DHASCO groups compared to the control but were not dose related. These renal effects tended to be clustered within specific litters and the differences in frequencies in the low dose groups could be largely attributed to two litters in each group where 60 – 100% of the examined foetuses were affected. Both dilated renal pelvis and under-developed renal papilla represent variations in development, usually caused by slight delays, and because they have no persistent effects, they are not considered to be toxicologically significant (Arterburn *et al* 2000). Foetal skeletal abnormalities were present in both control and treated groups and their incidence was not dose-dependent.

Conclusion

Administration of ARASCO and DHASCO to pregnant rats during organogenesis at dose levels up to 2500 mg ARASCO/k bw/day and 1250 mg DHASCO/kg bw/day did not produce any adverse developmental effects that could be related to the treatment.

4.7 Genotoxicity

The following studies were conducted:

(i) Mutagenicity test on RBD-ARASCO in the Salmonella/mammalian-microsome reverse mutation assay (Ames test). Lawlor, T.E. (1994) Hazleton Washington, Inc, Virginia, USA. Study 16015-0-401. 23 February 1994.

(ii) Mutagenicity test on RBD-DHASCO in the Salmonella/mammalian-microsome reverse mutation assay (Ames test). Lawlor, T.E. (1994) Hazleton Washington, Inc., Virginia, USA. Study 16016-0-401. 23 February 1994.

(iii) Mutagenicity test on RBD-ARASCO in the L5178Y TK+/- mouse lymphoma forward mutation assay. Cifone, M.A. (1994) Hazleton Washington Inc., Virginia, USA. Study 16140-0-431. 17 June 1994.

(iv) Mutagenicity test on RBD-DHASCO in the L5178Y TK+/- mouse lymphoma forward mutation assay. Cifone, M.A. (1994) Hazleton Washington Inc., Virginia, USA. Study 16141-0-431. 17 June 1994.

(v) Mutagenicity test on RBD-ARASCO measuring chromosomal aberrations in Chinese hamster ovary (CHO) cells. Murli, H. (1994) Hazleton Washington Inc., Virginia, USA. Study 16140-0-437. 23 May 1994.

(vi) Mutagenicity test on RBD-DHASCO measuring chromosomal aberrations in Chinese hamster ovary (CHO) cells. Murli, H. (1994) Hazleton Washington Inc., Virginia, USA. Study 16141-0-437. 15 June 1994.

The studies were all well prepared, performed and presented. All of the studies described were conducted in compliance with the Good Laboratory Practice regulations as set forth in the US Code of Federal Regulations (21 CFR 58, 40 CFR 792, and 40 CFR 160), and the OECD's Principles of Good laboratory Practice C (81) 30 (Final) Annex 2, issued 1979 – 1980. Studies were designed with appropriate positive and negative control test substances and appropriate criteria were defined for positive and negative outcomes. Appropriate preliminary studies were done to determine the solubility of the test material and to assess the dose range for the mutagenicity tests. The preparation of S9 mix for metabolic activation is described, and the procedures were appropriate. There were no deviations from the defined protocols for any of the studies. The main features and findings of each study are summarised in the table below.

Test	Test material	Concentration	Test object	Result
AMES	ARASCO oil	100 – 5000µg/plate (+/- S9)	*S. typhimurium* TA98, TA100, TA1535, TA1537, TA1538	-ve
AMES	DHASCO oil	100 – 5000µg/plate (+/- S9 activation)	*S. typhimurium* TA98, TA100, TA1535, TA1537, TA1538	-ve
Forward mutation assay	ARASCO oil	125 - 4990µg/ml (+/- S9 activation)	Mouse lymphoma L5178Y cell line TK+/-	-ve

Forward mutation assay	DHASCO oil	125 - 5000µg/ml (+/- S9 activation)	Mouse lymphoma L5178Y cell line TK+/-	-ve
Chromosomal aberrations	ARASCO oil	501 - 5010µg/ml (+/- S9 activation)	Chinese hamster ovary (CHO) cells	-ve
Chromosomal aberrations	DHASCO oil	500 - 5000µg/ml (+/- S9 activation)	Chinese hamster ovary (CHO) cells	-ve

Conclusion

DHASCO and ARASCO were found to be negative in a battery of genotoxicity test systems at doses *in vitro* up to 5000 µg/ml, both with and without metabolic activation. This suggests that DHASCO and ARASCO are both non-genotoxic.

4.8 Other studies

4.8.1 Analysis of dinoflagellate extract and spray-dried biomass for the presence of brevetoxins. Anon (1995). Chiral Corporation, Florida, USA. Study No. GTR-26219. June 1995.

A series of studies were done on *Crypthecodinium cohnii* extract (DHASCO oil and spray-dried biomass) for the presence of dinoflagellate toxins. The main features of each study is summarised in the table below.

Test	Test specificity	Sensitivity
Intraperitoneal mouse bioassay	Non-specific for lethal substances	1-4µg/mouse for saxitoxin, 20µg/mouse for brevetoxin. Not sufficiently precise for ciguatoxin or okadaic acid.
Radioimmunoassay (RIA)	Brevetoxin and Ciguatoxin	2.0ng/ml (2 ppb)
Synaptosome binding assay	Site 5 toxins, including brevetoxin and ciguatoxin structures	1.0 ng/ml (1 ppb)
9-anthryldiazomethane (ADAM) esterification fluorescence HPLC (F-HPLC)	Okadaic acid and dinophysistoxin 1	140ng/g sample (140 ppb)
Microtitre plate protein phosphatase inhibition assay	Okadaic acid and dinophysistoxin 1	2µg/g sample (2 ppm)
HPLC	Saxitoxin and derivatives	1 – 10pg/100mg sample (1 – 10 ppb)
ELISA	Saxitoxin	0.03ng/g sample
Capillary electrophoresis	Saxitoxin and derivatives	1µg/g sample (1 ppm)

Study conduct and results

Intraperitoneal mouse bioassay: Extracts were made of 2.0 g of DHASCO or spray-dried biomass using methanol and petroleum ether and the dried methanol phase was resuspended in ethanol for analysis. Samples were suspended in phosphate buffered saline (pH 7.4) and were injected i.p. into Swiss white mice (16 – 20 g each). Animals were dosed with 0, 500, 1000 and 2000 mg equivalents of either DHASCO or spray-dried biomass.

No animal exhibited any visible signs of toxicity. The LD_{50} of this material was calculated to be > 100 g/kg bw.

Synaptosome binding assay: Extracts were made of DHASCO and spray-dried biomass using methanol and petroleum ether and the dried methanol phase was resuspended in ethanol for analysis. Volumes of 10 and 1 µl were used for the synaptosome binding assay. Prepared samples were analysed in triplicate for their ability to displace [^{3}H]-PbTx-3 from its binding site.

There was no displacement with either the 10 µl or 1 µl sample of the oil, and for the spray-dried biomass extract there was displacement equivalent to 1.17 nM for both the 10 µl and 1 µl samples.

The performing laboratory commented that a displacement value of 1.17 nM is very close to the detection limit. Also, for the 1 µl of extract the displacement at individual points was 5063, 5394 and 2411. If the 2411 point is discarded, there is no displacement. The laboratory regarded this as a negative (at the limits of sensitivity).

ADAM esterification fluorescence HPLC (F-HPLC): A 0.9811 g sample of DHASCO was extracted using methanol and petroleum ether and the methanol phase was then dried and weighed out using acetone, yielding 13.308 mg. This material was then tested for okadaic acid (OA) and dinophysistoxin 1 (DTX-1) using ADAM F-HPLC. For analysis of the spray-dried biomass, a 0.5021 g sample was homogenised in methanol and then extracted with petroleum ether. The methanol phase was dried and then weighed using acetone, yielding 0.602 mg. This material was then tested for OA and DTX-1.

Both samples were negative therefore the levels of OA and DTX-1 were below 140 ng/g sample.

p-nitrophenyl phosphate (PNPP)/protein phosphatase 1 (PP1) inhibition assay: The DHASCO and the spray-dried biomass were prepared in the same way as for the ADAM F-HPLC analysis. The PNPP/PP1 inhibition assay is a receptor-based assay for polyether toxins and at the time the test was conducted was still considered to be experimental.

Both samples were found to be negative with no inhibition occuring therefore the levels of OA and DTX-1 can be said to be below 2 µg/g sample

HPLC: The HPLC was conducted according to published procedures for the HPLC analysis of shellfish toxins (Sullivan 1990). A 1 g sample of DHASCO was prepared for analysis by extracting in acetic acid. The aqueous phase was removed and dried and resuspended in acetic acid to a final volume of 1ml.

A 1 g sample of the spray-dried biomass was similarly extracted in acetic acid, with the aqueous phase being removed, cleaned up on a column, dried and resuspended in acetic acid to a final volume of 3ml, which was then filtered
(0.45 μm pore) prior to analysis.

The DHASCO sample exhibited no peaks in the HPLC analysis. The biomass sample exhibited two large peaks early in the chromatogram and a few broad peaks during the later half of the gradient. On further analysis these peaks were found to be artefacts due to fluorescent material in the biomass sample, rather from the presence of saxitoxin or its analogues.

ELISA for saxitoxin: The analysis was done using a commercial saxitoxin testing kit (R-Biopharm GmbH, Germany). Extracts of DHASCO and the spray-dried biomass were prepared as described for the HPLC testing. Samples and standards were analysed in duplicate and two dilutions of each sample were analysed – a 200 and a 2000 times dilution. The samples were analysed according to the test kit instructions and appropriate controls were included.

The level of saxitoxin in both samples was below the detection limit (0.03 ng/g sample)

Capillary electrophoresis: An extract of the spray-dried biomass was prepared as described for the HPLC testing. DHASCO was not analysed because definitive negative results for saxitoxin were obtained from both HPLC and ELISA. Detection was by on-column UV absorbance at 200 nm.

The capillary electrophoresis results confirmed the absence of saxitoxin and its derivatives in the biomass sample; therefore there is no indication of any saxitoxin or its derivatives in either sample.

Conclusion

All tests were negative (at the limit of detection) and therefore DHASCO can be considered non-toxic at the levels tested.

4.8.2 Acute oral toxicity study of fungal biomass in rats. Glaza, S.M. (1997). Covance Laboratories Inc, Wisconsin, USA. Study No.70403367. July 1997.

Study conduct

Test material:	*Mortierella alpina* biomass (Lot No. 6700000019), a tan powder.
Test species:	Young adult albino rats, Crl:CD® (SD)BR (Charles River Laboratories, Inc., Portage MI).
Dose:	5 g/kg body weight administered orally by gavage to 5/sex.
GLP:	US Code of Federal Regulations for Non-clinical Laboratory Studies, 21 CFR 58.

The test material was mixed with distilled water to a concentration of 0.25 g/ml and administered as a single oral dose of 5 g/kg body weight by gavage to five female and five male rats. Food and water were available *ad libitum* throughout the study, except for approximately 17 to 20 hours before test material administration when food, but not water, was withheld. Clinical observations were conducted at 1, 2.5 and 4 hours after test material administration and daily thereafter for 14 days. Mortality checks were conducted twice a day for 13 days after dosing.

Body weights were determined at Day 0, Day 7 and at termination of the study. At the termination of the study all animals were subjected to an abbreviated gross necropsy examination and any abnormalities were recorded. No tissues were saved.

Results

No deaths were recorded during the study and all animals exhibited body weight gain throughout the study with the exception of two females, which exhibited insignificant weight loss of 4 – 9 g during the second week of the study. All animals appeared normal throughout the study with the exception of one female and four males, which exhibited soft stools on the day of treatment. Three of the males also exhibited dark stained urogenital areas. All animals returned to normal appearance by Day 2 after treatment. No gross lesions were observed at necropsy. The estimated LD_{50} for males and females was determined to be greater than 5 g/kg body weight.

5. CLINICAL STUDIES

A large number of clinical studies with pre-term and term infants have been undertaken with infant formula supplemented with DHASCO and ARASCO. These were primarily undertaken for the purposes of establishing efficacy, however many also examined how well the supplemented formulae were tolerated and whether its use was correlated with any adverse effects, especially on growth. These studies all indicate that formula supplemented with DHASCO and ARASCO is well tolerated and is not associated with any apparent adverse effects on growth or development of the infants. The salient features of these studies are summarised in the Table 3 below.

TABLE 3. Clinical studies with DHASCO and ARASCO in pre-term and term infants

Author Location (Sponsor)	**Dose**	**Duration**	**Outcome**
Pre-term infants:			
Carnielli *et al* 1994 Europe (Numico)	SF with 0.75% ARA from ARASCO + 0.6% DHA from DHASCO	Not stated	Plasma PL of SF group similar to HM group; no significant difference between groups in growth.
Clandinin *et al* 1997 Children's Health Centre, Canada (Wyeth)	SF with (i) 0.32% ARA from ARASCO + 0.24% DHA from DHASCO, (ii) 0.49% ARA from ARASCO + 0.35% DHA from DHASCO, (iii) SF with 1.1% ARA from ARASCO + 0.76% DHA from DHASCO.	4 – 6 weeks	No difference in growth or clinical parameters between formula groups. Plasma PL of low and medium dose groups similar to that of HM group. The plasma PL of the high dose group was higher than in the HM group.
Foreman-van Drongelen *et al* 1996 The Netherlands (Numico)	SF with 0.6% ARA from ARASCO + 0.4% DHA from DHASCO	From full GI feeds to 40 weeks postconceptual age	No difference between groups in growth or clinical events. Plasma PL and RBC of SF group higher than CF group.

Gross *et al* 1997 Vanderhoof *et al* 1999 Multi-centre trial – USA & Canada (Wyeth)	SF with 0.6% ARA from ARASCO + 0.4% DHA from DHASCO	From full GI feeds to 40 weeks postconceptual age	No difference in growth, serum chemistries or GI symptoms between formula groups. Plasma PL of SF group similar to HM group.
Hansen *et al* 1997, Diersen-Schade *et al* 1999 Multi-centre trial _ North America (Mead Johnson)	DHA SF with 0.34% DHA from DHASCO, DHA/ARA SF with 0.6% ARA from ARASCO + 0.33% DHA from DHASCO	Approximately 28 days	No adverse events observed. Growth in the DHA/ARA SF group was better than the CF group; no difference in visual acuity between groups.

Full term infants:			
Birch *et al* 1998 Retina Foundation of the Southwest, Dallas, USA (Mead Johnson)	SF with 0.35% DHA from DHASCO, SF with 0.35% DHA from DHASCO + 0.72% ARA from ARASCO	4 months	All groups had similar growth rates and tolerated all diets well.
Carlson *et al* 1999 Multi-centre trial – USA & Canada (Mead Johnson)	SF with 0.3% DHA from fish oil + 0.6% ARA from ARASCO, SF with 0.3% DHA from DHASCO + 0.6% ARA from ARASCO	Not stated	The SF had no adverse effects on growth or development. Infants fed the DHA/ARA SF gained weight more rapidly and weighed more than the CF group through to 12 months of age.
Gibson *et al* 1997 Flinders Medical Centre, Australia (Wyeth Nutritionals)	SF with (i) 0.2% ARA/0.2% DHA, (ii) 0.32% ARA/0.2% DHA, (iii) 0.4% ARA/0.25% DHA	6 weeks	The mid and high dose groups had plasma ARA and DHA levels similar to those in the HM group while supporting normal growth during the first 6 weeks of life.

Abbreviations: CF, control formula; SF, supplemented formula; HM, human milk; PL, phospholipid; RBC, red blood cell

Appendix 1

DISCUSSION OF RECURRENT FINDINGS

A number of recurrent findings (e.g., increased liver weights) were observed in both the short term (4- and 9-week) and sub-chronic studies evaluated above. These findings are also reported to occur in a number of other short term and sub-chronic studies undertaken with DHASCO and ARASCO: these studies have not been specifically assessed for this evaluation.

The performing laboratories who have undertaken the studies have not considered any of the recurrent findings to be of toxicological significance, however because their occurrence might be considered an important finding an Expert Panel was convened by Martek Biosciences (the manufacturer of DHASCO and ARASCO) to undertake a simultaneous evaluation of all the short term and sub-chronic studies conducted to date on ARASCO and DHASCO (thirteen in total) in an attempt to gain a better understanding of the relevance and consistency of these findings. The outcome of the Expert Panel review is summarised below[1].

Liver and spleen weights

One of the most common recurring findings in both the short term and sub-chronic studies evaluated above (and also in the other studies not specifically assessed for this evaluation) is a statistically significant increase in relative liver weights at the highest doses of ARASCO or DHASCO, or ARASCO/DHASCO blends. This finding however is reported to not be consistently observed across all studies, although it was consistently observed in all the short term and sub-chronic studies assessed for this evaluation. Importantly, however, the increases in liver weights observed were generally not accompanied by changes in liver histopathology or abnormally high levels of liver enzymes in the serum.

A simultaneous evaluation by the Expert Panel of the liver-related clinical chemistries in all studies did not reveal any consistent dose-dependent effects. All the studies contained both low fat and high fat controls, although the choice of control fat source varied (corn oil, soybean oil, canola oil, and high oleic sunflower oil). The high fat control was necessary to distinguish physiological responses to a high fat diet from specific test material-related phenomena. The total fat load in these studies were generally two to three times the normal level found in standard rat chow. In addition, synthetic diets were used in some studies, while others used standard rat chow, some groups mixed the oils directly into the diet and others provided the oils by gavage at a specific dose based on animal weight. As a result the trials represented a broad spectrum of designs.

Although some of the studies reported a statistically significant increase in liver weights, relative to body weights compared to the high fat controls, none of the mean relative liver weights were found to be outside the historical control range.

[1] As reported in the submission (formerly Application A437) by the Infant Formula Manufacturers Association of Australia, the New Zealand Infant Formulas Marketers' Association and Martek Biosciences Corporation to P93: Infant Formula.

A slight to moderate accumulation of lipid was also noted in some, but not all, of the high dose treatment groups but the incidence of this finding was not different than the high fat control group and was attributed to the high fat diet or the use of synthetic diets with high fat and carbohydrate, as has been previously reported in the literature (Clapp *et al* 1982, Shah *et al* 1986, Hoek *et al* 1988, Mars *et al* 1988). No other histopathological changes (e.g. necrosis) were observed consistently in any of the groups and there were no consistent changes in clinical chemistry that would suggest toxicity. Some studies reported a decrease in albumin levels and/or total protein levels but this finding was not consistent across studies nor did the changes parallel increases in liver weights within or across studies.

The Expert Panel undertook a comprehensive survey of the published literature which revealed that significant increases in relative liver weights from high doses of LCPUFAs is well established in rats, mice, guinea pigs, and rabbits. Most of these studies used various fish oils. Regardless of the source of the LCPUFA, a recurrent finding of the studies was a consistent 20 – 40% increase in relative liver weights in response to the feeding of test fish oils at levels of 3 – 5% of the diet as LCPUFA.

When the Expert Panel compared studies done with ARASCO and DHASCO to the studies with fish oil referred to above in most cases the doses of ARASCO and DHASCO used were lower than those for the fish oil and there were no significant increases in relative liver weights at these low levels. When the doses of ARASCO and DHASCO were similar to those reported for fish oils, the liver responses to the diets were also similar. Thus, the Expert Panel concluded that the increased liver weights seen in some studies where very high levels of DHASCO and ARASCO were used is consistent with a well-established effect of the LCPUFAs themselves and is not due to some unknown component unique to the oils.

There are several hypotheses in the literature to explain the effect of high doses of LCPUFAs, regardless of source, on liver weights. Polyunsaturated fatty acids are well known to down-regulate lipogenesis (fat biosynthesis) thereby slightly decreasing the total body weight without affecting lean body mass. This is apparently often difficult to detect in the growing animal and in fact significant changes in growth were not seen in any of the studies with DHASCO and ARASCO. If there was a reduction in total body fat as a result of LCPUFAs in the diet then other organs should also show an increase relative to body weight. Organ to organ weight ratios are therefore generally accepted to be a better measure of specific changes in an organ under these circumstances.

When the liver to brain ratios is examined in the studies there is no longer an observable effect of dose on liver weights in twelve out of the thirteen studies conducted to date. The hypothesis that the change in relative liver weights is due to a reduced lipogenesis and body fat content would be consistent with the lack of histological or clinical chemical evidence for any liver toxicity. Literature reports also note that LCPUFAs are generally metabolised in the liver and the increased liver size in response to high doses of LCPUFAs simply represents a natural hypertrophy of this organ to handle the increased metabolic load imposed upon it by the high doses of LCPUFAs.

The other major recurrent finding was with the spleen. Like the liver, relative spleen weights were increased in only some of the studies and the increased spleen weights were found only in the high dose groups. The spleen weight changes were all within the historical normal values and there were no consistent dose-related responses. Furthermore there were no significant changes in any of the studies when comparing spleen/brain weight ratios.

Because there is no associated histopathology or alterations in clinical chemistry the Expert Panel concluded that these findings are not adverse effects. In many of the studies with fish oil the authors also reported an increase in relative spleen weights in addition to increases in relative liver weights.

The Expert Panel reported that clinical studies further demonstrate that the modest increases in liver and spleen weight are of no toxicological significance. A large multi-centre study using ARASCO and DHASCO in pre-term infant formula showed no effects on growth or any serological marker of liver or spleen function (Vanderhoof *et al* 1999). These clinical studies showed no differences between formula-fed groups (with and without DHASCO and ARASCO) for liver function markers such as serum protein, albumin, ALT (alanine aminotransferase), AST (aspartate aminotransferase), ALK P (alkaline phosphatase), bilirubin, BUN (blood urea nitrogen) or other routine analysis. Nor did these studies show any differences in markers for spleen function such as haemoglobin, mean cell volume, haematocrit, basophils, eosinophils, white blood cells, lymphocytes, monocytes, neutrophils, platelets or red blood cells.

The Expert Panel thus concluded that the administration of high doses of ARASCO, DHASCO or fish oil (more than 2 g/kg/day) to rats in a sub-chronic fashion can modestly increase liver and spleen weights relative to body weight. This effect largely takes place within a few weeks of administration of the high levels of LCPUFAs. Regardless of the source of LCPUFAs the magnitude of the response is similar when using similar levels of LCPUFAs and consistent with other reports in the literature for a wide variety of different fish oils and animal models. Thus, the relative liver and spleen weight changes appear to be a generalised LCPUFA effect and are not specific to either DHASCO or ARASCO.

Blood chemistry

As with liver and spleen weights, some of the studies also noted statistically significant changes in certain blood parameters measured. A review of these data by the Expert Panel revealed that although there are a few reported statistically significant effects, these effects are not dose-related, they are not seen consistently across comparable studies and the observations are not consistently observed in both sexes. Due to these and other factors, the Expert Panel concluded that these observations were not of toxicological significance.

The only blood chemistry markers in the thirteen rat studies that reached statistical significance were cholesterol and triglycerides. Significant reductions in cholesterol levels have been seen in two studies and a reduction of serum triglycerides was noted in the highest dose groups of three studies. This observation of cholesterol lowering is not unexpected because cholesterol lowering by fish oil is a well-observed phenomenon (Harris 1989). A reduction in serum triglycerides is also consistent with literature reports on the effect of high dose LCPUFA supplementation (especially fish oil) and is attributed to the LCPUFA not the test materials DHASCO or ARASCO.

REFERENCES

Arterburn, L.M., Boswell, K.D., Henwood, S.M. and Kyle, D.J. (2000). A development safety study in rats using DHA- and ARA-rich single-cell oils. *Food and Chemical Toxicology* **38:** 763 – 771.

Auestad, N., Halter, R., Hall, R.T., Blatter, M., Bogle, M.L., Burks, W., Erickson, J.R., Fitzgerald, K.M., Dobson, V., Innis, S.M., Singer, L.T., Montalto, M.B., Jacobs, J.R., Qiu, W. and Bornstein, M.H. (2001). Growth and development in term infants fed long-chain polyunsaturated fatty acids: a double-masked, randomised, parallel, prospective, multivariate study. *Pediatrics* **108:** 372 – 381.

Birch, E.E., Dennis, R., Hoffman, R., Uauy, R., Birch, D.G. and Prestidge, C. (1998). Visual acuity and the essentiality of docosahexaenoic acid and arachidonic acid in the diet of term infants. *Pediatr. Res*. **44:** 201 – 209.

Boswell, K., Koskelo, E.K., Carl, L., Glaza, S., Hensen, D.J., Williams, K.D. and Kyle, D.J. (1996). Preclinical evaluation of single-cell oils that are highly enriched with arachidonic acid and docosahexaenoic acid. *Food and Chemical Toxocology* **34:** 585 – 593.

Bottino, N.R., Vandenburg, G.A. and Raiser, R. (1967). Resistance of certain long-chain polyunsaturated fatty acids of marine oils to pancreatic lipase hydrolysis. *Lipids* **2:** 489 – 493.

Burns, R.A., Wibert, G.J., Diersen-Schade, D.A. and Kelly, C.M. (1999). Evaluation of single cell sources of docosahexanoic acid and arachidonic acid: 3-month rat oral safety study with an *in utero* phase. *Food and Chemical Toxicology* **37:** 23 – 36.

Breckenridge, W.C. (1969). Triglyceride structure of human milk fat. *Can. J. Biochem*. **47:** 761 – 769.

British Nutrition Foundation (1992). Unsaturated fatty acids and early development. In: *Unsaturated fatty acids: Nutritional and physiological significance*. London: Chapman & Hall, pp 63 – 67.

Carlson, S.E., Rhodes, P.G. and Ferguson, M.G. (1986). Docosahexanoic acid status of preterm infants at birth and following feeding with human milk or formula. *Am. J. Clin. Nutr.* **44:** 798 – 804.

Carlson, S.E., Cooke, R.J., Werkman, S.H. and Tolley, E.A. (1992). First year growth of preterm infants fed standard compared to marine oil n-3 supplemented formula. *Lipids* **27:** 901 – 907.

Carlson, S.E., Werkman, S.H., Peeples, J.M. and Wilson, W.M. (1994). Long-chain fatty acids and early visual and cognitive development of preterm infants. *Eur. J. Clin. Nutr.* **48 (Suppl. 2):** S27 – S30.

Carlson, S.E., Mehra, S., Kagey, W.J., Merkel, K.L., Diersen-Schade, D.A., Harris, C.L. and Hansen, J.W. (1999). Growth and development of term infants fed formulas with docosahexaenoic acid (DHA) from algal oil or fish oil and arachidonic acid (ARA) from fungal oil. *Pediatr. Res*. **45:** 278A.

Carnielli, V.P., Pederzini, F., Luijenkijk, I.H.T., Bomars, W.E.M., Boerlage, A., Degenhart, H.J., Pedrotti, D. and Sauer, P.J.J. (1994). Long chain polyunsaturated fatty acid (LCP) in low birth weight formula at levels found in human colostrum. *Pediatric Research* **35:** 309A.

Carnielli, V.P., Verlato, G., Pederzini, F., Luijendijk, I., Boerlage, A., Pedrotti, D. and Sauer, P.J.J. (1998). Intestinal absorption of long-chain polyunsaturated fatty acids in preterm infants fed breast milk and formula. *Am. J. Clin. Nutr*. **67:** 97 – 103.

Clandinin, M.T., Chappell, J.E., Leong, S., Heim, T., Swyer, P.R. and Chance, G.W. (1980). Intrauterine fatty acid accretion rates in human brain: implications for fatty acid requirements. *Early Hum. Dev*. **4:** 121 – 129.

Clandinin, M.T., Parrott, A., Van Aerde, J.E., Hervada, A.R. and Lien, E. (1992). Feeding preterm infants a formula containing C_{20} and C_{22} fatty acids stimulates plasma phospholipid fatty acid composition of infants fed human milk. *Early Human Dev*. **31**: 41 – 51.

Clandinin, M.T., Van Aerde, J.E., Parrott, A., Field, C.J., Euler, A.R. and Lien, E.L. (1997). Assessment of the efficacious dose of arachidonic and docosahexaenoic acids in preterm infant formulas: fatty acid composition of erythrocyte membrane lipids. *Pediatr. Res*. **42:** 819.

Clapp, M.J.L., Wade, J.D. and Samuels, D.M. (1982). Control of nephrocalcinosis by manipulating the calcium phosphorus ratio in commercial rodent diets. *Laboratory animals* **16:** 130.

Davis, B.D., Dulbecco, R., Eisen, H.N. and Ginsberg, H.S. (1980). Microbiology, third edition. Harper & Row Publishers, Inc., U.S.A. 1355 pp.

Diersen-Schade, D.A., Hansen, J.W., Harris, C.L., Merket, K.L., Wisont, K.D. and Boettcher, J.A. (1999). Docosahexaenoic acid plus arachidonic acid enhance preterm infant growth. In: *Essential Fatty Acids and Eicosanoids*, R.A. Riemersma, R. Armstrong, R.W. Kelly, and R. Wilson (eds), AOCS Press, Champaign, USA, pp 123 – 127.

Duthie, T.F., Barlow, S.M., Ashby, R., Tesh, J.M., Whitney, J.C., Saunders, A., Chapman, E., Norum, K.R., Svaar, H. and Opsrvedt, J. (1988). Feeding of partially hydrogenated fish oils to rats in comparison with partially hydrogenated soybean oils and refined rapeseed oil. *Acta Medica Scandinavica* **726 (Suppl.):** 1 – 89.

Eckert, R. and Randall, D. (1983). *Animal Physiology. Mechanisms and Adaptations*. W.H. Freeman and Company, U.S.A. 830 pp.

FAO (1994) *Fats and oils in human nutrition*. Report of a joint WHO/FAO expert consultation held in Rome, 19-26 October 1993. Food and Nutrition Paper No. 57, Food and Agriculture Organisation, Rome.

Farquharson, J., Cockburn, F., Patrick, W.A., Jamieson, E.C. and Logan, R.W. (1992). Infant cerebral cortex phospholipid fatty acid composition and diet. *Lancet* **340:** 810 – 813.

Foreman-van Drongelen, M.M.H.P., van Houwelingen, A.C., Kester, A.D.M., Blanco, C.E., Hasaart, T.H.M. and Hornstra, G. (1996). Influence of feeding artificial formulas containing docosahexaenoic and arachidonic acids on the postnatal long-chain polyunsaturated fatty acid status of health preterm infants. *Br. J. Nutr*. **76:** 649 – 667.

Gibson, R., Makrides, M., Neumann, M., Hawkes, J., Pramuk, K., Lien, E. and Euler, A. (1997). A dose response study of arachidonic acid in formulas containing docosahezaenoic acid in term infants. *Prostaglandins Leukotrienes and Essential Fatty Acids* **57:** 198.

Gross, S., Vanderhoof, J., Hegyi, T., Clandinin, T., Porcelli, P., DeCristofaro, J., Rhodes, T., Tsang, R., Shattuck, K., Cowett, R., Adamkin, K., McCarton, C., Heird, W., Hook, B., Pereira, G., Pramuk, K. and Euler, A. (1997). A new arachidonic acid (ARA) and docosahexaenoic acid (DHA) supplemented preterm formula: effect on plasma and erythrocyte phospholipid fatty acids. *Pediat. Res.* **41:** 232A.

Hansen, J., Schade, D., Harris, C., Merkel, K., Adamkin, D., Hall, R., Lim, M., Moya, F., Stevens, D. and Twist, P. (1997). Docosahexaenoic acid plus arachidonic acid enhance pretern infant growth. *Prostaglandins Leukotrienes and Essential Fatty Acids* **57:** 196.

Harris, W.S. (1989). Fish oils and plasma lipid and lipoprotein metabolism in humans: a critical review. *J. Lipid Res*. **30:** 785.

Heird, W.C. (2001). Biological effects and safety issues related to long-chain polyunsaturated fatty acids in infants. *Lipids* **34:** 207 – 214.

Hempenius, R.A., Lina, B.A.R. and Haggitt, R.C. (2000). Evaluation of a subchronic (13-week) oral toxicity study, preceded by an *in utero* exposure phase, with arachidonic acid oil derived from *Mortierella alpina* in rats. *Food and Chemical Toxicology* **38:** 127 – 139.

Hoek, A.C., Lemmens, A.G., Mulink, J.W.M.A. and Beynen, C.C. (1988). Influence of dietary calcium;phosphorus ratio on mineral excretion and nephrocalcinosis in female rats. *J. Nutr.* **118:** 1210.

Innis, S.M. (1991). Essential fatty acids in growth and development. *Prog. Lipid Res*. **30:** 39 – 103.

Innis, S.M. (1992). Human milk and formula fatty acids. *J. Pediatr*. **120:** S56 – S61.

Jay, J.M. (1992). Modern Food Microbiology. Van Nostrand Reinhold, New York.

Jensen, R.G. (1989). Lipids in human milk – composition and fat-soluble vitamins. In: *Textbook of gastroenterology and nutrition in infancy*, 2nd edition, E. Lebenthal (ed). Raven Press, New York, pp 157 – 208.

Koletzko, B., Schmidt, E., Berner, H.J., Haug, M. and Harzer, G. (1989). Effects of dietary long chain polyunsaturated fatty acids on the essential fatty acid status of premature infants. *Eur. J. Ped*. **148:** 669 – 675.

Kyle, D.J. (1996). Production and use of a single cell oil which is highly enriched in docosahexanoic acid. *Lipid Technology* **2:** 107 – 110.

Kyle, D.J. (1997). Production and use of a single cell oil highly enriched in arachidonic acid. *Lipid Tech*. **9:** 116 – 121.

Lehninger, A.L. (1982). *Principles of Biochemistry*. S. Anderson and J. Fox (eds), Worth Publishers, Inc., New York, 1011 pp.

Leyton, J., Drury, P.J. and Crawford, M.A. (1987). Differential oxidation of saturated and unsaturated fatty acids in vivo in the rat. *Br. J. Nutr*. **57:** 383 – 393.

Luthria, D.L., Mohammed, B.S. and Sprecher, H. (1996). Regulation of the biosynthesis of 4,7,10,13,16,19-docosahexaenoic acid. *J. Biol. Chem*. **271:** 16020.

Makrides, M., Neumann, M.A., Byard, R.W., Simmer, K. and Gibson, R.A. (1994). Fatty acid composition of brain, retina and erythrocytes in breast- and formula-fed infants. *Am. J. Clin. Nutr*. **60:** 189 – 194.

Mars, Y.W.H.M., Lemmens, A.G. and Beynen, A.C. (1988). Dietary phosphorus and nephrocalcinosis in female rats. *Nutr. Reports Intl*. **38:** 249.

Martin, J.C., Bougnoux, P., Antoine, J.M., Lanson, M. and Couet, C. (1993). Triacylglycerol structure of human colostrum and mature milk. *Lipids* **28:** 637 – 643.

Martinez, M. (1992). Tissue levels of polyunsaturated fatty acids during early human development. *J. Paediatr*. **120** (suppl): 129 – 138.

Montalto, M.B., Mimouni, F.B., Sentipal-Waterius, J., Bender, C.V. and Groh-Wargo, S. (1996). Reduced growth in hospital discharged low birth weight (LBW) infants fed formulas with added marine oil (MO). *Pediatr. Res*. **39:** 316A.

Myher, J.J., Kuksis, A., Geher, K. et al (1996). Stereospecific analysis of triacylglycerols rich in long-chain polyunsaturated fatty acids. *Lipids* **31:** 207 – 215.

Nes, W.D. and Le, P.H. (1990). *Biochim. Biophys. Acta* **1042:** 119 – 125.

Norman, A., Strandrik, B. and Ojamae, O. (1972). Bile acids and pancreatic enzymes during absorption in the newborn. *Acta Paediatr. Scand*. **61:** 571 – 577.

O'Connor, D.L., Hall, R., Adamkin, D., Auestad, N., Castillo, M., Connor, W.E., Connor, S.L., Fitzgerald, K., Groh-Wargo, S., Hartmann, E.E., Jacobs, J., Janowsky, J., Lucas, A., Margeson, D., Mena, P., Neuringer, M., Nesin, M., Singer, L., Stephenson, T., Szabo, J. and Zemon, V. (2001). Growth and development in preterm infants fed long-chain polyunsaturated fatty acids: a prospective, randomised controlled trial. *Pediatrics* **108:** 359 – 371.

Patterson, G.W. (1991). Sterols of algae. In: *Physiology and Biochemistry of Sterols*, G.W. Patterson and W.D. Ness (eds), American Oil Chemists' Society, U.S.A. pp 118.

Pita, M.L., Fernández, M.R., De-Lucchi, C., Medina, A., Martinez-Valverde, A., Uauy, R. and Gil, A. (1988). Changes in the fatty acids pattern of red blood cell phospholipids induced by type of milk, dietary nucleotide supplementation, and postnatal age in preterm infants. *J. Ped. Gastroent. Nut*. **7:** 740 – 747.

Shimizu, S., Kawashima, H., Wada, M. and Yamada, H. (1992). Occurrence of a novel sterol, 24,25-methylenecholest-5-en-3β-ol, in *Mortierella alpina* 1S-4. *Lipids* **27:** 481 – 483.

Sinclair, A.J. (1975). Incorporation of radioactive polyunsaturated fatty acids into liver and brain in developing rat. *Lipids* **10:** 175 – 184.

Steidinger, K.A. and Baden, D.G. (1984). Toxic marine dinoflagellates. In: *Dinoflagellates*, D.L. Spector (ed), Academic Press, Orlando, pp 210.

Sullivan, J.J. (1990). High-performance liquid chromatographic method applied to paralytic shellfish poisoning research. In: *Marine Toxins: Origin, Structure, and Molecular Pharmacology*, American Chemical Society, Washington DC, pp 66 – 77.

Tso, P. (1985). Gastrointestinal digestion and absorption of lipid. *Adv. Lipid Res*. **21:** 143-186.

Van der Hoek, C., Mann, D.G. and Jahns, H.M. (1995). *Algae: an introduction to modern phycology*. Cambridge University Press, Cambridge, 244 pp.

Vanderhoof, J., Gross, S., Hegyi, T., Clandinin, T., Porcelli, P., DeCristofaro, J., Rhodes, T., Tsang, R., Shattuck, K., Cowett, R., Adamkin, K., McCarton, C., Heird, W., Hook-Morris, B., Pereira, G., Chan, G., VanAerde, J., Boyle, F., Pramuk, K., Euler, A. and Lien, E. (1999). Evaluation of a long-chain polyunsaturated fatty acid supplemented formula on growth, tolerance, and plasma lipids in preterm infants up to 48 weeks postconceptual age. *J. Paediatr. Gastroenterol. Nutr*. **29:** 318 – 326.

VanPelt, C.K., Huang, M.-C., Tschanz, C.L. and Brenna, T. (1999). An octane fatty acid, 4,7,10,13,16,19,22,25-octacosaoctaenoic acid (28:8n-3), found in marine oils. *J. Lipid Res*. **40:** 1501.

Watkins, J.B. (1975). Mechanism of fat absorption and the development of gastrointestinal function. *Pediatr. Clin. North Am*. **22:** 721.

Watkins, J.B. (1985). Lipid digestion and absorption. *Pediatrics* **75 (suppl):** 151 – 156.

Widdowson, E.M. (1965). Absorption and excretion of fat, nitrogen, and minerals from "filled" milks by babies one week old. *Lancet* **2:** 1099 – 1105.

ATTACHMENT 3

REGULATION IMPACT STATEMENT

PROPOSAL P93 – REVIEW OF INFANT FORMULA

1. INTRODUCTION

The development of food standards by the Australia New Zealand Food Authority (ANZFA) is carried out in accordance with the principles and guidelines adopted by the Council of Australian Governments (COAG)[1] and the draft Code of Good Regulatory Practice (New Zealand).

The review of infant formula (Proposal P93) has been in progress since 1993. Public submissions were received in the preparation of the proposal in 1993, at Full Assessment in 1995 and at the Preliminary Inquiry in 1999. ANZFA completed an Inquiry into the proposed draft standard in November 1999. However, the Inquiry Report and proposed draft standard were not presented to the Australia New Zealand Food Standards Council, due to stakeholder concerns.

Following considerable further consultation with stakeholders since 1999, ANZFA believes it has suitably addressed the concerns of stakeholders. In recognition of the significant time delay and changes that have been made to the draft standard as proposed at Inquiry, the previous regulation impact statement as assessed at Preliminary Inquiry (May 1999) is now revised and updated as part of this Supplementary Final Assessment (Inquiry – s.24). The Office of Regulation Review has assessed this revised regulation impact statement as adequate.

2. BACKGROUND

2.1 History of Proposal P93

Proposal P93 has been in progress since 1993 when the then National Food Authority initiated a review of the existing infant formula standard (R7) of the *Food Standards Code* (Volume 1). Public submissions were received in the preparation of the proposal in 1993 and at Full Assessment in 1995.

On 1 July 1996, an Agreement between Australia and New Zealand (The Treaty) came into force that established a joint Australian New Zealand Food Standards System, which served to underpin the development of the joint *Australia New Zealand Food Standards Code* (Volume 2). Under The Treaty agreement, during the transition period to the joint system, products sold in New Zealand and Australia could comply with either the *New Zealand Food Regulations 1984* (NZFR), (if manufactured or imported into New Zealand) or Volume 1 (existing Australian *Food Standards Code*) until such time as Volume 2 had been developed and became the sole set of regulations for the two countries.

[1] COAG (1997) Principles and Guidelines for National Standard Setting and Regulatory Action by Ministerial Councils and Standard Setting Bodies.

Volume 2 came into effect in Australia and New Zealand in December 2000. It is expected that most of the existing Australian and New Zealand food regulations (other than Volume 2) will be repealed at the end of 2002.

In 1998, Proposal P93 was included as part of the Review of Food Standards and the development of Volume 2. A round of public consultation in 1999 (Preliminary Inquiry) was included, additional to the usual process, to provide an opportunity for consultation in New Zealand. A draft regulatory impact statement was included in the Preliminary Inquiry Report.

ANZFA completed an Inquiry into the review of infant formula in November 1999. However prior to the date of effect of Volume 2, ANZFA was unable to resolve a number of issues related to the draft standard with industry stakeholders. Consequently, ANZFA proposed a transitional arrangement for infant formula (Proposal P226) that withdrew the draft standard from Volume 2 and maintained the status quo for infant formula, namely Standard R7. This arrangement was to allow ANZFA further time to resolve outstanding issues with stakeholders.

2.2 Regulatory Framework

Under the current transitional arrangements of Volume 2, Standard R7 regulates the composition and labelling of infant formula in Australia. In New Zealand manufacturers currently can choose to comply with either Standard R7 or Regulation 242 of the NZFR. Both Standard R7 and Regulation 242 do not specifically specific provisions for pre-term infant formula or modified formula. The proposed draft standard accommodates all types of infant formula products.

Internationally, Codex standards exist for both for Infant Formula (CODEX STAN 72-1981) and follow-on formula (CODEX STAN 156-1987). The Codex standard for infant formula is currently under review. Completion of this review is not expected within the next two years.

2.3 Current Infant Formula Market

There is strong scientific evidence to show that exclusive breastfeeding to the age of about six months provides the best nutritional start for infants[2]. When compared internationally, initiation rates for breastfeeding in Australia and New Zealand are relatively high (82%[3] and 94%[4] respectively). However the rate of breastfeeding declines significantly with time after birth. In Australia it is estimated that fewer than 20% of infants are achieving the goal of being exclusively breast fed to six months of age[3]. These figures indicate that a substantial number of Australian and New Zealand infants are reliant on the availability of safe alternatives to breast milk for nourishment.

[2] World Health Organisation. The optimal duration of exclusive breastfeeding. Geneva: WHO, 2 April 2001. Note for Press No 7.
[3] National Health and Medical Research Council (2001) Draft Dietary Guidelines for Children and Adolescent, pg 10
[4] Essex C, et al. 1995. Breastfeeding rates in New Zealand in the first six months and the reasons for stopping. NZ Med J 108: 355-7

There is significant international trade in infant formula with 60% of infant formula products being imported from overseas. Five multi-national companies supply the market: two companies manufacture locally (one in Australia and one in New Zealand) whereas three companies import directly into the domestic market. The market for infant formula is static (corresponding to a relatively static birth rate) and is estimated at $118 million in Australia and $18 –20 million in New Zealand.

Products that are imported into Australia and New Zealand are currently formulated and labelled to comply with local food standards. The estimated cost in reformulation or labelling depends on the complexity of changes required. The cost associated with minor re-formulation is estimated at $10 000 per formulation, whereas re-labelling cost for one product line is between $4 300 and $18 000.

Product innovation is strongly linked to advances in scientific research. The existing regulations are outdated and are ambiguous as to whether they permit recent scientific developments to be incorporated into infant formula products. Therefore, currently an inequitable situation exists where product innovation is dependent on manufacturers' interpretation of existing regulations, which may be differ from one manufacturer to another.

2.4 WHO International Code of Marketing of Breast Milk Substitutes

The World Health Organization International Code of Marketing of Breast-milk Substitutes (WHO Code) was adopted at the 34th Session of the World Health Assembly, 20 May 1981. The Code aims, through appropriate marketing and distribution, to contribute to the safe and adequate nutrition of infants by ensuring the proper use of breast milk substitutes. Many countries, including Australia and New Zealand, are signatories to this agreement and have taken action to effect the principles and aims of the WHO Code.

2.5 Implementation of the WHO Code in Australia and New Zealand

The Australian and New Zealand governments have each taken a number of different steps in support of their international commitments to the WHO, either by incorporating the relevant articles of the WHO Code into food standards, or the establishment of voluntary Codes of Practice. The aspects of the WHO Code related to composition and labelling of infant formulas are incorporated into food standards.

The marketing aspects of the WHO Code are implemented in Australia through an authorised agreement under the Trade Practices Act 1974 (the Marketing in Australia of Infant Formulas: Manufacturers and Importers Agreement (1992) (MAIF Agreement). The MAIF Agreement has been adopted by the Infant Formula Manufacturers as their Code of Conduct. The MAIF Agreement is monitored by the Advisory Panel for the Marketing in Australia of Infant Formula (APMAIF).

In Zealand, the marketing aspects of the WHO Code are implemented through an industry Code of Practice (1997) which is monitored by the New Zealand Infant Formula Marketers' Association (NZIFMA).

In both countries the Codes of Practice place certain restrictions on the advertising and promotion of infant formulas. There is general agreement that these Codes of Practice are effective in limiting the advertising of infant formula products to the general public and therefore these restrictions continue, rather than be included in food regulation.

3. PROBLEM

Infants are a very vulnerable group in the community and are at a stage in life where adequate nutrition is essential for their growth and development. Infants that rely either fully or partially on infant formula for their sustenance are at risk if these products do not provide a proper balance of nutrients or contains impurities. Infant formula products are complex and could not be independently verified by consumers; hence it is essential to the health and development of infants that the composition of formula products be assessed as safe under a food standard.

The existing infant formula standards for Australia and New Zealand are out-dated and do not reflect contemporary scientific research. There is confusion for both the infant formula industry and government in the interpretation of the standards, and different judgments are being made on the legality of incorporating scientific developments into the products. There is a need to improve the clarity of the food standards and facilitate the application of recent scientific research to these products.

4. OBJECTIVES

The development and variation of a standard for infant formula must have regard to the following objectives (Section 10, *ANZFA Act* (1991)), which are (in descending priority order):

(a) the protection of public health and safety;

(b) the provision of adequate information relating to food to enable consumers to make informed choices and to prevent fraud and deception;

(c) the promotion of fair trading in food;

(d) the promotion of trade and commerce in the food industry; and

(e) the promotion of consistency between domestic and international food standards where these are at variance.

The specific objectives of Proposal P93 are to:

1. protect the health and safety of formula fed infants;
2. provide carers with enough information about infant formula to enable them to make appropriate choices in feeding their infant and in the safe use of products;
3. develop unambiguous food regulations that reflect contemporary scientific knowledge; and
4. harmonise the food regulations applying to infant formula in Australia and New Zealand.

5. OPTIONS FOR REGULATION

There are two options to this proposal.

Option 1 – Maintain the status quo

This option maintains Standard R7 as regulating infant formula in Australia and allows manufacturers/importers in New Zealand to comply with either Standard R7 or Regulation 242.

Option 2 – Regulation by inclusion of the proposed revised standard in Volume 2.

This option harmonises the regulation of infant formula products in Australia and New Zealand by inclusion of draft Standard 2.9.1 in Volume 2. Draft Standard 2.9.1 prescribes in greater detail the compositional requirements, incorporating recent scientific developments, as well as additional labelling requirements for infant formula products. The standard provides for infant formula products intended for infants with special dietary needs.

5.1. Affected Parties

The parties affected by this proposal are: **consumers** and the general community, particularly formula fed infants and their carers; the **governments** of New Zealand, the States and Territories and the Commonwealth of Australia; and the **infant formula industry** supplying either through the manufacture or importation of products to the Australian and New Zealand markets.

6. IMPACT OF REGULATORY OPTIONS

Option 1 – Maintain the status quo

Benefits

Consumers/Community

- Continued access to the current range of products that are essential to the health and wellbeing of formula fed infants.
- There is sufficient information available to consumers from current product labelling to enable their choices to effectively reflect their preferences.

Government

- The existing standard is effective in ensuring that infant formula products are safe for infants with no negative health impacts.

Industry

- The standard being effective in ensuring product safety, supports the sustainability of the current market and maintains consumer confidence in these products.

Costs

Consumers/Community

- In principle, the current lack of clarity in the regulations can impede product innovation, which in turn has the potential to reduce the future range of products available to consumers. In practise, the market currently provides for considerable diversity.

Government

- Costs of enforcement by government agencies, which are presumed to be small.

Industry

- Increased cost to industry by restriction on ingredients or levels of ingredients that differ from formulas sold overseas or lack of permission for new nutritive substances; necessitating reformulation for the local Australian and New Zealand market.
- Some labelling provisions are different from those required by other countries, which necessitates the relabelling of some formulas.
- Cost to those manufacturers which interpret the current regulations conservatively, and do not supply the market with innovative products.

Option 2 – Regulation by proposed Standard 2.9.1

Benefits

Consumers/Community

- The proposed standard accommodates recent scientific research and product development, allowing formula fed infants to consume products formulated to provide a better nutritional outcome. It allows scope for superior products to be supplied to Australia and New Zealand.
- Greater clarity of the regulation for both composition and labelling of infant formula products provides better information to carers and improves their choices.
- Potential increase in the range of products available

Government

- The greater clarity of regulation, which incorporates the more recent scientific advances in infant formula composition, has the potential to provide for a better nutritional outcome for infants, and reduced enforcement costs.

Industry

- Greater clarity in the regulations leads to less confusion and thereby lowers costs for industry in ensuring compliance with the standard.

- Harmonised Australian and New Zealand regulations with scope for industry innovation, consistent with the latest scientific research and product development that also facilitate international trade.

Costs

Consumers/Community

- There may be products that do not meet the requirements of the new standard and will not be available in the future. This is not expected to be a significant number and it is known that Industry will be making application for assessment of these products during the proposed transition period.

Government

- There are no expected material impacts on the cost of enforcement from this option, and to a certain extent the greater clarity of the regulations may make enforcement easier.

Industry

- Costs to industry associated with any necessary analysis, re-formulation or labelling changes required to comply with the new standard. Industry has indicated that the current costs associated with minor re-formulation is approximately $10 000 per formulation, whereas re-labelling cost for one product line is between $4 300 and $18 000. Two companies have indicated that they will need to re-formulate up to 11 and 8 products, respectively. On this basis, the initial re-formulation costs for one of these companies has been estimated at $1.2 million with on-going costs predicted to be approximately $300 000.

7. CONSULTATION

7.1 Public and Stakeholder Consultation

Three rounds of public consultation have occurred as part of the review of infant formula since 1993. A summary of public submissions from the last consultation is contained at Attachment 7 to the Supplementary Final Assessment Report (Feb 2002).

Additionally, targeted consultations with representatives of industry, health professionals and consumer groups have been conducted. This consultation took place through the establishment of a panel of experts in infant health, an external stakeholder advisory group and the consideration of material provided in submissions.

Following the completion of the Inquiry in November 1999, the infant formula industry requested further consultation on the draft standard claiming some provisions in the standard would affect the affordability and availability of products on the local market. A large number of issues were raised at the time with the key themes being:

- composition particularly where the proposed requirements differed significantly from regulations overseas;

- labelling; and
- special purpose infant formula products.

These issues were considered at a Stakeholders Forum in May 2000, and by the members of the External Advisory Group at a meeting in June 2000. Subsequent meetings between ANZFA staff and industry representatives were also held in August 2000 and in October 2001 to discuss outstanding issues. ANZFA has actively worked with industry stakeholders to resolve all outstanding issues following Inquiry (Nov 1999). ANZFA believes that it has now effectively addressed these issues and has made further recommendations to accommodate the concerns of Industry. Industry has indicated support for these recommendations and the revised draft standard as proposed at Supplementary Final Assessment (Feb 2002). Further details on the assessment of issues and recommendations can be found in Attachment 1 to the Supplementary Final Assessment Report (Feb 2002).

8. RECOMMENDATION

Option 1 satisfies some important objectives of this proposal, namely the basic protection of health and safety of formula fed infants; and provision of information to carers to make appropriate choices in feeding their infant. However, it does not satisfy the other objectives being: development of unambiguous regulations that reflect contemporary scientific knowledge and the harmonisation of regulations in Australia and New Zealand. In contrast, Option 2 satisfies all objectives, and provides for greater clarity of regulation that incorporates the recent scientific advances in infant formula composition, thereby having greater potential to provide for a better nutritional outcome for infants.

Option 2 appears to provide greater net benefits than Option 1. While the transitional costs of Option 2 may be more than minor, ongoing costs of re-formulation and re-labelling are expected to be generally similar. In addition, Option 2 has lower costs in not penalising those manufacturers that interpret the current regulations conservatively and do not market their innovative products. This is an advantage, for Option 2, of greater clarity of the regulations. Option 2 also benefits consumers in allowing scope for superior products to be supplied to the Australia and New Zealand market.

9. IMPLEMENTATION AND REVIEW

9.1 ANZFA Process

It is anticipated that provisions for a 2 year transition period, from the commencement of Standard 2.9.1, will be established involving concurrent operation of the existing regulations (R7) and Standard 2.9.1 to allow manufacturers time to comply with the new regulations.

Monitoring and review of the impact of this regulatory change is likely to occur, in due course, as part of the general evaluation program that ANZFA has in place to evaluate the effectiveness of new standards.

It is also anticipated that ANZFA will closely monitor developments internationally in respect to other agencies' (eg. Codex) review of their respective food standards for infant formula and scientific advances. Any new developments are expected to be considered either through the review of the infant formula standard or by receipt of applications from Industry.

Industry has already indicated that they will be submitting applications to amend the new standard for infant formula products to further update it with the latest scientific developments.

9.2 International and World Trade Organization obligations

Australia and New Zealand are members of the World Trade Organization (WTO) and are bound as parties to WTO agreements. In Australia, an agreement developed by the Council of Australian Governments (COAG) requires States and Territories to be bound as parties to those WTO agreements to which the Commonwealth is a signatory. Under the Treaty between the Governments of Australia and New Zealand on joint Food Standards, ANZFA is required to ensure that food standards are consistent with the obligations of both countries as members of the WTO.

In certain circumstances Australia and New Zealand have an obligation to notify the WTO of changes to food standards to enable other member countries of the WTO to make comment. Notification is required in the case of any new or changed standards which may have a significant trade effect and which depart from the relevant international standard (or where no international standard exists).

Following Preliminary Inquiry (May 1999), this matter was notified to the WTO as a technical barrier to trade matter as the proposed revisions to the existing infant formula standards are more prescriptive than other standards internationally. One submission from the United States of America was received on this matter.

ATTACHMENT 4

DRAFT VARIATIONS TO VOLUME 1 AND VOLUME 2 OF THE *FOOD STANDARDS CODE*

To commence: on gazettal

The Food Standards Code *is varied by –*

[1] ***Standard A11*** *of Volume 1 is varied by –*

[1.1] *inserting in the Schedule to A11 into Column 1 and Column 2 respectively, after the entry for* Divinylbenzene copolymer –

Docosahexaenoic acid (DHA) – rich oil derived from the algae *Crypthecodinium cohnii*	Addendum 17

[1.2] *inserting in the Schedule to A11 into Column 1 and Column 2 respectively, after the entry for* Anthocyanins –

Arachidonic acid (ARA) – rich oil derived from the fungus *Mortierella alpina*	Addendum 18

[1.3] *inserting following* ADDENDUM 16 –

ADDENDUM 17

SPECIFICATION FOR DOCOSAHEXAENOIC ACID (DHA) - RICH OIL DERIVED FROM THE ALGAE *CRYPTHECODINIUM COHNII*

Full chemical name for DHA	4,7,10,13,16,19-docosahexaenoic acid (22:6n-3)
Appearance	Free flowing oil
Colour	Yellow to orange
Odour	Characteristic
DHA (%)	min. 40 max. 45
Dodecanoic acid 12:0 (%)	min. 0 max. 6
Tetradecanoic acid 14:0 (%)	min. 10 max. 20
Hexadecanoic acid 16:0 (%)	min. 10 max. 20
Octadecenoic acid 18:1 (%)	min. 10 max. 30
Peroxide value (meq/kg)	max. 5
Moisture and volatiles (%)	max. 0.01
Non-saponifiables (%)	max. 3.5
Trans fatty acids (%)	max. 1.0
Free fatty acid (%)	max. 0.4
Lead (ppm)	max. 0.2
Arsenic (ppm)	max. 0.5
Copper (ppm)	max. 0.1

Iron (ppm)	max. 0.5
Mercury (ppm)	max. 0.2
Hexane (ppm)	max. 0.3

ADDENDUM 18

SPECIFICATIONS FOR ARACHIDONIC ACID (ARA) – RICH OIL DERIVED FROM THE FUNGUS *MORTIERELLA ALPINA*

Full chemical name for ARA	5,8,11,14-eicosatetraenoic acid (20:4n-6)	
Appearance	Free flowing oil	
Colour	Yellow	
Odour	Characteristic	
ARA (%)	min. 38	max. 44
Hexadecanoic acid 16:0 (%)	min. 3	max. 15
Octadecanoic acid 18:0 (%)	min. 5	max. 20
Octadecenoic acid 18:1 (%)	min. 5	max. 38
Octadecadienoic acid 18:2 (%)	min. 4	max. 15
Peroxide value (meq/kg)	max. 5	
Moisture and volatiles (%)	max. 0.05	
Non-saponifiables (%)	max. 3.5	
Trans fatty acids (%)	max. 1.0	
Free fatty acid (%)	max. 0.4	
Lead (ppm)	max. 0.2	
Arsenic (ppm)	max. 0.5	
Copper (ppm)	max. 0.1	
Iron (ppm)	max. 0.5	
Mercury (ppm)	max. 0.2	
Hexane (ppm)	max. 0.3	

[2] ***Standard 1.1.1*** *of Volume 2 is varied by omitting from* clause 2, *in the definition for* warning statement *subclause* (d) –

substituting

(d) subclauses 14(1), 14(3) and 26(1) of Standard 2.9.1; and

[3] ***Standard 1.3.4*** *of Volume 2 is varied by inserting in the Schedule immediately after the* Specification for tall oil phytosterols derived from tall oils *the following* -

Specification for docosahexaenoic acid (DHA) – rich oil derived from the algae *Crypthecodinium cohnii*

Full chemical name for DHA	4,7,10,13,16,19-docosahexaenoic acid (22:6n-3)	
Appearance	Free flowing oil	
Colour	Yellow to orange	
Odour	Characteristic	
DHA (%)	min. 40	max. 45
Dodecanoic acid 12:0 (%)	min. 0	max. 6
Tetradecanoic acid 14:0 (%)	min. 10	max. 20
Hexadecanoic acid 16:0 (%)	min. 10	max. 20

Octadecenoic acid 18:1 (%)	min. 10 max. 30
Peroxide value (meq/kg)	max. 5
Moisture and volatiles (%)	max. 0.01
Non-saponifiables (%)	max. 3.5
Trans fatty acids (%)	max. 1.0
Free fatty acid (%)	max. 0.4
Lead (ppm)	max. 0.2
Arsenic (ppm)	max. 0.5
Copper (ppm)	max. 0.1
Iron (ppm)	max. 0.5
Mercury (ppm)	max. 0.2
Hexane (ppm)	max. 0.3

Specification for arachidonic acid (ARA) – rich oil derived from the fungus *Mortierella alpina*

Full chemical name for ARA	5,8,11,14-eicosatetraenoic acid (20:4n-6)
Appearance	Free flowing oil
Colour	Yellow
Odour	Characteristic
ARA (%)	min. 38 max. 44
Hexadecanoic acid 16:0 (%)	min. 3 max. 15
Octadecanoic acid 18:0 (%)	min. 5 max. 20
Octadecenoic acid 18:1 (%)	min. 5 max. 38
Octadecadienoic acid 18:2 (%)	min. 4 max. 15
Peroxide value (meq/kg)	max. 5
Moisture and volatiles (%)	max. 0.05
Non-saponifiables (%)	max. 3.5
Trans fatty acids (%)	max. 1.0
Free fatty acid (%)	max. 0.4
Lead (ppm)	max. 0.2
Arsenic (ppm)	max. 0.5
Copper (ppm)	max. 0.1
Iron (ppm)	max. 0.5
Mercury (ppm)	max. 0.2
Hexane (ppm)	max. 0.3

[4] ***Standard 2.9.1*** *of Volume 2 is varied by* -

[4.1] *omitting* Standard 2.9.1 *and substituting* -

STANDARD 2.9.1

INFANT FORMULA PRODUCTS

Purpose

This Standard provides for the compositional, and labelling requirements for foods intended or represented for use as a substitute for breast milk, herein referred to as 'infant formula products'. This Standard applies to all infant formula products whether in powder, liquid concentrate or 'ready to drink' forms.

This Standard also provides for infant formula products intended for infants with special nutritional requirements.

Additionally, recommended guidelines regarding vitamins and minerals are contained at the end of this Standard. Standard 1.3.1 contains provisions relating to the food additives permitted in infant formula products. Standard 1.6.1 contains the microbiological limits in relation to infant formula products. Standard 1.3.4 contains specifications for permitted nucleotides and added nutrients. Standard 1.1.1 defines nutritive substances for the purposes of this Code.

Table of Provisions

Clauses

Division 1

Subdivision 1 – Interpretation

1 Definitions

(1) The definitions in clauses 1 and 2 of Standard 1.2.8 apply to this Standard.

(2) In this Code –

follow-on formula means an infant formula product represented as either a breast-milk substitute or replacement for infant formula and which constitutes the principal liquid source of nourishment in a progressively diversified diet for infants aged from six months.

infant means a person under the age of 12 months.

infant formula means an infant formula product represented as a breast milk substitute for infants and which satisfies the nutritional requirements of infants aged up to four to six months.

Editorial note:

A reference to infant formula product may include a reference to infant formula but the converse does not apply.

infant formula product means a product based on milk or other edible food constituents of animal or plant origin which is nutritionally adequate to serve as the principal liquid source of nourishment for infants.

Editorial note:

The intent of this definition is to limit the addition of ingredients to infant formula product to ingredients that would be considered to be foods. The addition of an ingredient that is not considered to be a food is prohibited unless specifically permitted elsewhere in this Standard.

Standard 1.5.1 contains prohibitions and restrictions relating to novel foods and novel food ingredients. Nothing contained in this Standard permits infant formula products to contain novel foods or novel food ingredients that are not permitted in Standard 1.5.1.

lactose free formula and **low lactose formula** means infant formula products which satisfy the needs of lactose intolerant infants.

medium chain triglycerides means triacylglycerols which contain predominantly the saturated fatty acids designated by 8:0 and 10:0.

pre-term formula means an infant formula product specifically formulated to satisfy particular needs of infants born prematurely or of low birthweight.

protein substitute means L-amino acids and/or the hydrolysate of one or more of the proteins on which infant formula product is normally based.

soy-based formula means an infant formula product in which soy protein isolate is the sole source of protein.

2 Interpretation

A reference to any infant formula product in the compositional provisions of this Standard is a reference to –

(a) a powdered or concentrated form of infant formula product which has been reconstituted with water according to directions; or
(b) an infant formula product in 'ready to drink' form.

Subdivision 2 – Calculations

3 Calculation of energy

The energy content of infant formula product, expressed in kilojoules (kJ), must be calculated using –

(a) only the energy value contributions of the fat, protein and carbohydrate ingredients of the infant formula product; and
(b) the relevant energy factors set out in Standard 1.2.8.

4 Calculation of protein

The prescribed formula for the calculation of the protein content of infant formula product for the purposes of this Standard is -

Formula

For milk proteins and their partial protein hydrolysates -

Protein content = nitrogen content x 6.38; or

In any other case -

Protein content = nitrogen content x 6.25.

5 Calculation of potential renal solute load

The prescribed formula for the calculation of the potential renal solute load for the purposes of this Standard is -

Formula

Potential renal solute load in mOsm/100 kJ = [Na (mg/100 kJ) /23] + [Cl (mg/100 kJ) /35] + [K (mg/100 kJ) /39] + [P_{avail} (mg/100 kJ)/ 31] + [N (mg/100 kJ) /28)].

In this formula

P_{avail} = P of milk-based formula + 2/3 of P of soy-based formulas.

Subdivision 3 - General compositional requirements

6 Restrictions and prohibitions

(1) A vitamin, mineral, food additive or nutritive substance must not be added to infant formula product unless -

(a) expressly permitted by this Code; or
(b) it is naturally present in an ingredient of the infant formula product.

(2) Infant formula product must contain no detectable gluten.

7 Permitted nutritive substances

(1) Any nutritive substance listed in column 1 of the Table to this clause may be added to infant formula product provided that -

(a) the nutritive substance is in one or more of the forms specified in column 2 of the Table in relation to that substance; and

(b) the total amount of the nutritive substance in the infant formula product is no more than the amount specified in column 4 of the Table.

(2) The label on a package of infant formula product must not include any words indicating, or any other indication, that the product contains a nutritive substance specified in column 1 or in column 2 of the Table to this clause unless the total amount of the nutritive substance in the food is no less than the amount specified in column 3 of the Table.

Editorial note:

The intent of subclause 7(1) is that the maximum permitted amounts only apply when the substance is added, and in that case, it then applies to the sum of the naturally occurring and added nutritive substances.

This Standard contains guidelines on the use and format of nutrient information tables.

Table to clause 7

Column 1	Column 2	Column 3	Column 4
Nutritive substance	**Permitted forms**	**Minimum amount for claim per 100 kJ**	**Maximum amount per 100 kJ**
Choline	Choline chloride Choline bitartrate	1.7 mg	7.1 mg
Inositol	Inositol	1.0 mg	9.5 mg
Taurine	Taurine	0.8 mg	3 mg
L-carnitine	L-carnitine	0.21 mg	0.8 mg
Cytidine 5’-monophosphate	Cytidine 5’-monophosphate Cytidine 5’-monophosphate sodium salt	0.22 mg	0.6 mg
Uridine 5’-monophosphate	Uridine 5’-monophosphate Uridine 5’-monophosphate sodium salt	0.13 mg	0.42 mg
Adenosine 5’-monophosphate	Adenosine 5’-monophosphate Adenosine 5’-monophosphate sodium salt	0.14 mg	0.38 mg
Guanosine 5’-monophosphate	Guanosine 5’-monophosphate Guanosine 5’-monophosphate sodium salt	0.04 mg	0.12 mg
Inosine 5’-monophosphate	Inosine 5’-monophosphate Inosine 5’-monophosphate sodium salt	0.08 mg	0.24 mg

8 Limit on nucleotide 5’-monophosphates

Infant formula product must contain no more than 3.8 mg/100 kJ of nucleotide 5'-monophosphates.

Editorial note:

Standard 1.3.4 contains specifications for nucleotides.

9 Lactic acid cultures

L(+) producing lactic acid cultures may be added to infant formula product.

10 Limit on aluminium

(1) Infant formula product, other than a pre-term formula or soy-based formula product, must contain no more than 0.05 mg of aluminium per 100 mL.

(2) Pre-term formula must contain no more than 0.02 mg of aluminium per 100 mL.

(3) Soy-based formula must contain no more than 0.1 mg of aluminium per 100 mL.

Editorial note:

Standard 1.4.1 contains the maximum level (ML) of lead contaminant in infant formula products.

Subdivision 4 - General labelling and packaging requirements

11 Representations of food as infant formula product

A food must not be represented as an infant formula product unless it complies with this Standard.

12 Prescribed names

'Infant Formula' and 'Follow-on Formula' are prescribed names.

13 Requirement for a measuring scoop

(1) A package of infant formula product in a powdered form must contain a scoop to enable the use of the infant formula product in accordance with the directions contained in the label on the package.

(2) Subclause (1) does not apply to single serve sachets, or packages containing single serve sachets of an infant formula product in a powdered form.

14 Required warnings, directions and statements

(1) The label on a package of infant formula product must include the following warning statement -

(a) in the case of infant formula product in powdered form -

'Warning – follow instructions exactly. Prepare bottles and teats as directed. Do not change proportions of powder except on medical advice. Incorrect preparation can make your baby very ill'; and

(b) in the case of concentrated infant formula product -

'Warning – follow instructions exactly. Prepare bottles and teats as directed. Do not change proportions of concentrate except on medical advice. Incorrect preparation can make your baby very ill'; and

(c) in the case of 'ready to drink' infant formula product -

'Warning – follow instructions exactly. Prepare bottles and teats as directed. Do not dilute or add anything to this 'ready to drink' formula except on medical advice. Incorrect preparation can make your baby very ill'.

(2) The label on a package of infant formula product must include directions for the preparation and use of the infant formula product which include words and pictures instructing -

(a) that each bottle should be prepared individually; and
(b) that if a bottle of made up formula is to be stored prior to use, it must be refrigerated and used within 24 hours; and
(c) that potable, previously boiled water should be used; and
(d) where a package contains a measuring scoop, that only the enclosed scoop should be used; and
(e) that formula left in the bottle after a feed must be discarded.

(3) Subject to subclause (4), the label on a package of infant formula product must contain the following warning statement -

'Breast milk is best for babies. Before you decide to use this product, consult your doctor or health worker for advice.';

under a heading that states –

'Important Notice' or any word or words having the same or similar effect.

(4) Subclause (3) does not apply to infant formula products for metabolic, immunological, renal, hepatic or malabsorptive conditions.

(5) The label on a package of an infant formula product must contain statements indicating that -

(a) the infant formula product may be used from birth, in the case of infant formula; and

(b) the infant formula product should not be used for infants aged under 6 months in the case of follow-on formula; and
(c) except in the case of packages of pre-term formula, it is recommended that infants over the age of 6 months should be offered foods in addition to the infant formula product.

15 Print and package size

(1) Where an infant formula product is in a package having a net weight of more than 500g, the statements required by subclauses 14(1), (3) and 26(1) must be in size of type of no less than 3 mm.

(2) Where an infant formula product is in a package having a net weight of 500 g or less the statements required by subclauses 14(1), (3) and 26(1) must be in size of type of no less than 1.5 mm.

16 Declaration of nutrition information

(1) The label on a 'ready to drink' infant formula product must include a statement, which may be in the form of a table, that contains the following information –

(a) the average energy content expressed in kJ per 100 mL; and
(b) the average amount of protein, fat and carbohydrate expressed in g per 100 mL; and
(c) the average amount of each vitamin, mineral and any other nutritive substance permitted by this Standard expressed in weight per 100 mL.

(2) The label on a powdered or concentrated form of infant formula product must include a statement, which may be in the form of a table that contains the following information -

(a) the average energy content expressed in kJ per 100 mL of infant formula product that has been reconstituted according to directions; and
(b) the average amount of protein, fat and carbohydrate expressed in g per 100 mL of infant formula product that has been reconstituted according to directions; and
(c) the average amount of each vitamin, mineral and any other nutritive substance permitted by this Standard expressed in weight per 100 mL of infant formula product that has been reconstituted according to directions; and
(d) a declaration –

(i) of the weight of one scoop in the case of powdered infant formula; and
(ii) of the proportion of powder or concentrate required to reconstitute the formula according to directions.

17 Date marking and storage instructions

(1) Paragraphs 2(1)(c) and (d) of Standard 1.2.5 do not apply to this Standard.

(2) A label on a package of infant formula product must contain storage instructions covering the period after it is opened.

Editorial note:

The appropriate storage instructions should be valid for the full range of climatic conditions that exist in Australia and New Zealand.

18 Statement of protein source

The label on a package of infant formula product must contain a statement of the specific source, or sources, of protein in the infant formula product immediately adjacent to the name of the infant formula product.

Editorial note:

Standard 1.2.2 requires that all food be labelled with its name. The requirement in clause 18 of this Standard applies only to the name on the label on the product in accordance with the requirement in Standard 1.2.2.

19 Statement on dental fluorosis

(1) An infant formula product must comply with subclause (2) where it contains -

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

(2) The label on a package of infant formula product referred to in subclause (1) must contain statements -

(a) indicating that consumption of the formula has the potential to cause dental fluorosis; and
(b) recommending that the risk of dental fluorosis should be discussed with a medical practitioner or other health professional.

20 Prohibited representations

The label on a package of infant formula product must not contain -

(a) a picture of an infant; or
(b) a picture that idealises the use of infant formula product; or
(c) the word 'humanised' or 'maternalised' or any word or words having the same or similar effect; or
(d) words claiming that the formula is suitable for all infants; or
(e) information relating to the nutritional content of human milk; or
(f) subject to clause 28, a reference to the presence of any nutrient or nutritive substance, except for a reference to a nutrient or nutritive substance in -

(i) the name of a lactose free formula or a low lactose formula; or
(ii) a statement of ingredients; or
(iii) a nutrition information statement; or

(g) subject to Division 3, a representation that the food is suitable for a particular condition, disease or disorder.

Editorial Note:

Division 3 relates to Infant Formula Products for Special Dietary Use. Clause 28 permits labelling which varies from this clause.

Division 2 – Infant Formula and Follow-on Formula

21 Composition

(1) Infant formula and follow-on formula must -

(a) have an energy content of no less than 2500 kJ/L and no more than 3150 kJ/L in the case of infant formula, and no less than 2500 kJ/L and no more than 3550 kJ/L in the case of follow-on formula; and
(b) contain an amount of each nutrient specified in column 1 of the Table to this clause which is no less than the amount specified in column 2 of the Table and no more than the amount specified in column 3 of the Table.

Table to clause 21

Column 1	Column 2	Column 3
Nutrient	**Minimum amount per 100 kJ**	**Maximum amount per 100 kJ**
Protein	0.45 g	0.7 g for infant formula 1.3 g for follow-on formula
Fat	1.05 g	1.5 g

(2) Follow-on formula must have a potential renal solute load value of no more than 8 mOsm/100 kJ.

22 Protein

(1) The L-amino acids listed in column 1 of the Table to this clause must be present in infant formula and follow-on formula at the minimum level specified in column 2 of the Table, subject to subclause 2 and 3.

Table to clause 22

Column 1	Column 2
L-Amino Acid	**Minimum amount per 100 kJ**
Histidine	12 mg
Isoleucine	21 mg
Leucine	42 mg

Lysine	30 mg
Cysteine & Methionine	19 mg
Phenylalanine & Tyrosine	32 mg
Threonine	19 mg
Tryptophan	7 mg
Valine	25 mg

(2) Infant formula or follow-on formula must provide no less than -

(a) 6 mg cysteine per 100 kJ; and
(b) 17 mg phenylalanine per 100 kJ.

(3) L-amino acids listed in the Table to this clause must be added to infant formula or follow-on formula only in an amount necessary to improve protein quality.

23 Fat

The fats in infant formula and follow-on formula must -

(a) not contain medium chain triglycerides except where a medium chain triglyceride is present in a particular infant formula or follow-on formula as the result of being a natural constituent of a milk-based ingredient of that particular infant formula or follow-on formula; and
(b) have a ratio of linoleic acid to α–linolenic acid of no less than 5 to 1 and no more than 15 to 1; and
(c) if specified in column 1 of the Table to this clause, comply with the limits, if any, specified in columns 2 and 3 of the Table; and
(d) have a ratio of total long chain omega 6 series fatty acids (C>= 20) to total long chain omega 3 series fatty acids (C>= 20) of approximately 2 in an infant formula or follow-on formula which contains those fatty acids; and
(e) where long chain polyunsaturated fatty acids are present in an infant formula or follow-on formula, an eicosapentaenoic acid (20:5 n-3) content of no more than the docosahexaenoic acid (22:6 n-3) content.

Table to clause 23

Column 1	**Column 2**	**Column 3**
Fatty acids	**Minimum % total fatty acids**	**Maximum % total fatty acids**
Essential fatty acids		
Linoleic acid (18:2)	9	26
α-Linolenic acid (18:3)	1.1	4
Long chain polyunsaturated fatty acids		
Long chain omega 6 series fatty acids (C>= 20)		2
Arachidonic acid (20:4)		1
Long chain omega 3 series fatty acids (C>= 20)		1
Total *trans* fatty acids		4
Erucic acid (22:1)		1

Editorial note:

Standard 1.3.4 contains specifications for Docosahexaenoic acid (DHA) rich oil derived from the algae *Crypthecodinium cohnii* and Arachidonic acid (ARA) rich oil derived from the fungus *Mortierella alpina*.

24 Vitamins and minerals

(1) Infant formula and follow-on formula must contain the vitamins and minerals specified in column 1 of the Table to this subclause provided that, in relation to each vitamin or mineral -

(a) the added vitamin or mineral is in a permitted form as listed in Schedule 1; and

(b) the infant formula or follow-on formula contains no less than the amount specified in column 2 of the Table; and

(c) the infant formula or follow-on formula contains no more than the amount specified in column 3 of the Table, if any.

Table to clause 24(1)

Column 1	Column 2	Column 3
Nutrient	**Minimum amount per 100 kJ**	**Maximum amount per 100 kJ**
Vitamins		
Vitamin A	14 µg	43 µg
Vitamin D	0.25 µg	0.63 µg
Vitamin C	1.7 mg	
Thiamin	10 µg	
Riboflavin	14 µg	
Preformed Niacin	130 µg	
Vitamin B_6	9 µg	36 µg
Folate	2.0 µg	
Pantothenic acid	70 µg	
Vitamin B_{12}	0.025 µg	
Biotin	0.36 µg	
Vitamin E	0.11 mg	1.1 mg
Vitamin K	1.0 µg	
Minerals		
Sodium	5 mg	15 mg
Potassium	20 mg	50 mg
Chloride	12 mg	35 mg
Calcium	12 mg	
Phosphorus	6 mg	25 mg
Magnesium	1.2 mg	4.0 mg
Iron	0.2 mg	0.5 mg
Iodine	1.2 µg	10 µg
Copper	14 µg	43 µg
Zinc	0.12 mg	0.43 mg
Manganese	0.24 µg	24.0 µg
Selenium	0.25 µg	1.19 µg

(2) Infant formula and follow-on formula must contain no less than 0.5 mg of Vitamin E per g of polyunsaturated fatty acids.

(3) The ratio of calcium to phosphorus in infant formula and follow-on formula must be no less than 1.2 to 1 and no more than 2 to 1.

(4) The ratio of zinc to copper -

(a) in infant formula must be no more than 15 to 1; and
(b) in follow-on formula must be no more than 20 to 1.

Editorial note:

This Standard contains guidelines setting out the recommended levels of vitamins and minerals that as a matter of good practice should not be exceeded.

Division 3 - Infant Formula Products for Special Dietary Use

Subdivision 1 – Infant formula products formulated for premature or low birthweight infants

25 Composition and labelling

Infant formula products may be specifically formulated for premature or low birthweight infants provided that in all other respects they comply with this Standard.

26 Additional labelling

(1) The label on a package of pre-term formula must include the warning statement -

'Suitable only for pre-term infants under specialist medical supervision'.

(2) The words 'pre-term' must appear as part of the name of a food standardised in this subdivision.

Subdivision 2 - Infant formula products for metabolic, immunological, renal, hepatic and malabsorptive conditions

27 Composition

(1) Subject to subclause (2), infant formula products may be specifically formulated to satisfy particular metabolic, immunological, renal, hepatic or malabsorptive conditions.

(2) The permission in subclause (1) only applies where the infant formula products comply with –

(a) this Division; and
(b) all the other requirements of this Standard that are not inconsistent with this Division.

(3) Other than for the operation of clause 28, subclause (2) takes effect 5 years after the commencement of this Standard.

28 Claims

Where a label contains a claim that the infant formula product is suitable for infants with metabolic, immunological, renal, hepatic or malabsorptive conditions, then the label on the package of infant formula product must include a statement indicating -

(a) that the product is not suitable for general use and should be used under medical supervision; and
(b) the condition, disease or disorder for which the food has been specially formulated; and
(c) the nutritional modifications, if any, which have been made to the infant formula product.

29 Composition of lactose free and low lactose formulas

(1) A lactose free formula or low lactose formula must, except for the lactose content, comply with the compositional and labelling requirements which apply to the infant formula product of which they are a variety.

(2) Lactose free formula must contain no detectable lactose.

(3) Low lactose formula must contain no more than 0.3 g lactose per 100 mL of infant formula product.

30 Claims relating to lactose free and low lactose formulas

Where a label contains a claim that the infant formula product is lactose free, low lactose or words of similar import, the label on a package of lactose free or a low lactose formula product must include -

(a) the words ‘lactose free' as part of the name of lactose free formula; and
(b) the words ‘low lactose' as part of the name of low lactose formula; and
(c) the following statements -

(i) the amount of lactose expressed in g per 100 mL; and
(ii) the amount of galactose expressed in g per 100 mL.

Subdivision 3 - Infant formula products for specific dietary use based upon protein substitutes

31 Composition

An infant formula product for specific dietary use based upon protein substitutes must -

(a) have an energy content of no less than 2500 kJ/L and no more than 3150 kJ/L in the case of infant formula, and no less than 2500 kJ/L and no more than 3550 kJ/L in the case of follow-on formula; and
(b) have a potential renal solute load of no more than 8 mOsm per 100 kJ; and

(c) contain an amount of each nutrient specified in column 1 of the Table to this clause which is no less than the amount specified in column 2 of the Table and no more than the amount specified in column 3 of the Table.

Table to clause 31

Column 1	Column 2	Column 3
Nutrient	**Minimum amount per 100 kJ**	**Maximum amount per 100 kJ**
Protein	0.45 g	1.4 g
Fat	0.93 g	1.5 g

32 Protein

(1) The protein content of an infant formula product for specific dietary use based upon protein substitutes may be in the form of protein substitute.

(2) The L-amino acids listed in column 1 of the Table to this clause must be present in infant formula product for special dietary use at the minimum level specified in column 2 of the Table, subject to subclause 3 and 4.

Table to clause 32

Column 1	Column 2
L-Amino Acid	**Min amount per 100 kJ**
Histidine	12 mg
Isoleucine	21 mg
Leucine	42 mg
Lysine	30 mg
Cysteine & Methionine	19 mg
Phenylalanine & Tyrosine	32 mg
Threonine	19 mg
Tryptophan	7 mg
Valine	25 mg

(3) Infant formula product for specific dietary use based upon protein substitutes must provide no less than -

(a) 6 mg cysteine per 100 kJ; and
(b) 17 mg phenylalanine per 100 kJ.

(4) L-amino acids listed in the Table to this clause must be added to infant formula product for specific dietary use base upon protein substitutes only in an amount necessary to improve protein quality.

33 Vitamins and minerals

An infant formula product for specific dietary use based upon protein substitutes must contain -

(a) chromium in an amount of no less than 0.35 µg per 100 kJ and no more than 2.0 µg per 100 kJ; and

(b) molybdenum in an amount of no less than 0.36 μg per 100 kJ and no more than 3.0 μg per 100 kJ.

Editorial note:

The provisions of clause 24 of this Standard also apply in respect of the vitamins and minerals permitted in an infant formula product for specific dietary use based upon protein substitutes.

34 Additional permitted triglycerides

An infant formula product for specific dietary use based upon protein substitutes may contain added medium chain triglycerides.

SCHEDULE 1

PERMITTED FORMS OF VITAMINS AND MINERALS IN INFANT FORMULA PRODUCTS

Column 1 Vitamins or minerals	Column 2 Permitted Forms
Vitamin A	Retinol Forms vitamin A (retinol) vitamin A acetate (retinyl acetate) vitamin A palmitate (retinyl palmitate) retinyl propionate Carotenoid Forms beta-carotene
Vitamin C	L-ascorbic acid L-ascorbyl palmitate calcium ascorbate potassium ascorbate sodium ascorbate
Vitamin D	vitamin D_2 (ergocalciferol) vitamin D_3 (cholecalciferol) vitamin D (cholecalciferol-cholesterol)
Thiamin	thiamin hydrochloride thiamin mononitrate
Riboflavin	riboflavin riboflavin-5'-phosphate, sodium
Niacin	niacinamide (nicotinamide)
Vitamin B_6	pyridoxine hydrochloride pyridoxine-5'-phosphate
Folate	folic acid
Pantothenic acid	calcium pantothenate Dexpanthenol
Vitamin B_{12}	Cyanocobalamin Hydroxocobalamin
Biotin	d-Biotin
Vitamin E	dl-α-tocopherol d-α-tocopherol concentrate tocopherols concentrate, mixed

	d-α-tocopheryl acetate dl-α-tocopheryl acetate d-α-tocopheryl acid succinate dl-α-tocopheryl succinate
Vitamin K	vitamin K_1, as phylloquinone (phytonadione) phytylmenoquinone
Calcium	calcium carbonate calcium chloride calcium citrate calcium gluconate calcium glycerophosphate calcium hydroxide calcium lactate calcium oxide calcium phosphate, dibasic calcium phosphate, monobasic calcium phosphate, tribasic calcium sulphate
Chloride	calcium chloride magnesium chloride potassium chloride sodium chloride
Chromium	chromium sulphate
Copper	copper gluconate cupric sulphate cupric citrate
Iodine	potassium iodate potassium iodide sodium iodide
Iron	ferric ammonium citrate ferric pyrophosphate ferrous citrate ferrous fumarate ferrous gluconate ferrous lactate ferrous succinate ferrous sulphate
Magnesium	magnesium carbonate magnesium chloride magnesium gluconate magnesium oxide magnesium phosphate, dibasic magnesium phosphate, tribasic magnesium sulphate
Manganese	manganese chloride manganese gluconate manganese sulphate manganese carbonate manganese citrate
Molybdenum	sodium molybdate VI dehydrate
Phosphorus	calcium glycerophosphate calcium phosphate, dibasic calcium phosphate, monobasic calcium phosphate, tribasic magnesium phosphate, dibasic potassium phosphate, dibasic potassium phosphate, monobasic potassium phosphate, tribasic

Potassium	sodium phosphate, dibasic sodium phosphate, monobasic sodium phosphate, tribasic potassium bicarbonate potassium carbonate potassium chloride potassium citrate potassium glycerophosphate potassium gluconate potassium hydroxide potassium phosphate, dibasic potassium phosphate, monobasic potassium phosphate, tribasic
Selenium	sodium selenite seleno methionine
Sodium	sodium bicarbonate sodium carbonate sodium chloride sodium chloride iodised sodium citrate sodium gluconate sodium hydroxide sodium iodide sodium lactate sodium phosphate, dibasic sodium phosphate, monobasic sodium phosphate, tribasic sodium sulphate sodium tartrate
Zinc	zinc acetate zinc chloride zinc gluconate zinc oxide zinc sulphate

GUIDELINES FOR INFANT FORMULA PRODUCTS
(These guidelines are not part of the legally binding Standard)

Guideline for maximum amount of vitamins and minerals in infant formula products

It is recommended that the quantities specified in the table below be observed as the maximum levels of vitamins and minerals in infant formula product.

Nutrient	Recommended maximum amount per 100 kJ
Vitamins	
Vitamin C	5.4 mg
Thiamin	48 µg
Riboflavin	86 µg
Preformed Niacin	480 µg
Folate	8.0 µg
Pantothenic acid	360 µg
Vitamin B_{12}	0.17 µg
Vitamin K	5.0 µg
Biotin	2.7 µg
Minerals	
Calcium	33 mg
Phosphorus	22 mg
Manganese	7.2 µg for infant formula products regulated by Division 3, Subdivision 2 only
Chromium	2.0 µg
Molybdenum	3 µg

Guideline on advice regarding additional vitamin and mineral supplementation

Manufacturers are recommended to provide an advice in the label on a package of infant formula product to the effect that consumption of vitamin or mineral preparations are not necessary.

Nutrition information table

The nutrition information contained in the label on a package of infant formula product is recommended in the following format -

NUTRITION INFORMATION

	Average amount per 100 mL made up formula *1	**Average amount per 100 g of powder (or per 100 mL for liquid concentrate)** *2
Energy	kJ	kJ
Protein	g	g
Fat	g	g
Carbohydrate	g	g

Vitamin A	µg	µg
Vitamin B_6	µg	µg
Vitamin B_{12}	µg	µg
Vitamin C	mg	mg
Vitamin D	µg	µg
Vitamin E	µg	µg
Vitamin K	µg	µg
Biotin	µg	µg
Niacin	mg	mg
Folate	µg	µg
Pantothenic acid	µg	µg
Riboflavin	µg	µg
Thiamin	µg	µg
Calcium	mg	mg
Copper	µg	µg
Iodine	µg	µg
Iron	mg	mg
Magnesium	mg	mg
Manganese	µg	µg
Phosphorus	mg	mg
Selenium	µg	µg
Zinc	mg	mg
Chloride	mg	mg
Potassium	mg	mg
Sodium	mg	mg
(insert any other nutritive substance to be declared)	g, mg, µg	g, mg, µg

***1** – Delete the words 'made up formula' in the case of formulas sold in 'ready to drink' form.
***2** – Delete this column in the case of formulas sold in 'ready to drink' form.

Note: The information in column 2 is not mandatory.

[5] *omitting from the* Table of Contents *of Volume 2 the following –*

Standard 2.9.1 Reserved (Infant Formula Products)

substituting –

Standard 2.9.1 Infant Formula Products

13 March 2002
08/02

PROPOSAL P93 - REVIEW OF INFANT FORMULA

SUPPLEMENTARY FINAL ASSESSMENT (INQUIRY – s.24)

STATEMENT OF REASONS

AND

DRAFT VARIATIONS TO VOLUME 1 AND VOLUME 2 OF THE *FOOD STANDARDS CODE*

PROPOSAL P93 – FOR RECOMMENDING A STANDARD FOR INFANT FORMULA PRODUCTS

The Australia New Zealand Food Authority (ANZFA) has before it Proposal P93 to develop a draft standard for infant formula products for inclusion in Volume 2 of the *Food Standards Code* and a draft variation to Standard A11 in Volume 1 and Standard 1.3.4 in Volume 2 of the *Food Standards Code*.

STATEMENT OF REASONS

ANZFA recommends the adoption of the draft Standard and draft variations, as amended, for the following reasons:

1. to protect the health and safety of formula-fed infants, who are the most vulnerable group in the Australian and New Zealand population and who may consume infant formula products as the sole or principal source of nourishment;

2. to ensure carers have adequate information about infant formula products to enable them to make appropriate choices in feeding their infant and in the safe use of products;

3. to ensure that food regulations reflect contemporary scientific knowledge about breast milk substitutes and infant nutritional requirements to protect the health of infant consumers;

4. to ensure that innovation in the infant formula industry that would benefit infant health is not hindered; and

5. to harmonise the food regulations applying to infant formula products in Australia and New Zealand.

Following consideration of public comments and an assessment against the objectives of the *Australia New Zealand Food Authority Act 1991 (ANZFA Act)*, a draft standard for Infant Formula Products has now been prepared, for Volume 2, with draft variations recommended for Standard A11 (Volume 1) and Standard 1.3.4 (Volume 2) of the *Food Standards Code*.

The proposed standard includes provisions for different categories of infant formula products to cater for different ages and special purpose formula intended for infants with specific diseases or disorders that contraindicate breastfeeding or the use of formula for healthy infants.

The proposed provisions are generally aligned internationally except where necessary to protect the health of infants in Australia and New Zealand. The following elements have been incorporated into the proposed standard -

- The quality and quantity of the protein content of infant formula products are regulated but it was considered not necessary to regulate the protein source. However, information about the source of protein will be declared on the label to assist carers make suitable product selection.

- The total energy, total fat, and essential and long chain polyunsaturated fatty acid contents are regulated to ensure infants who are formula fed receive sufficient but not excess energy and fatty acid intakes. Fatty acids that are considered harmful to infants are restricted where necessary to protect infants from adverse health consequences.

- The carbohydrate content of infant formula is indirectly controlled by the regulations on protein, fat and energy content.

- Unlimited vitamin and mineral contents for infant formula products represented as human milk substitutes are not recommended as in the best interests of infants, and maximum levels of these nutrients have been imposed. To eliminate unnecessary cost for industry, mandatory maximum levels are prescribed only for those vitamins and minerals which are considered to pose a significant risk to infants if consumed in excess, whilst advisory maximum levels are recommended for other nutrients whose risk characterisation is provisionally assessed as 'not of significance on the basis of current scientific knowledge'. Guidelines are included to provide manufacturers with guidance as to these recommended maximum levels and the implementation of these guidelines is expected to occur by Good Manufacturing Practice.

- The potential renal solute load of follow-on formula and infant formula for metabolic, immunological renal, hepatic or malabsorptive conditions is regulated to minimise the risk of dehydration illness from formula with high protein and electrolyte contents.

- Permission is given to voluntarily add carnitine, taurine, choline, inositol and specific nucleotides to infant formula. The maximum permitted content of these substances in infant formula is regulated, as is the minimum claimable level.

- Novel ingredients, nutrients, nutritive substances or novel sources of these are required to be assessed as safe and suitable for infants (under Standard 1.5.1 – Novel Foods) prior to approval being given for their use in infant formula products.

- Limits for lead and aluminium contents are imposed to protect infants. The limit for lead is controlled within Standard 1.4.1 – Contaminants and Natural Toxicants. An advisory labelling statement to alert carers to seek specific health advice is proposed for formula with unnecessarily high fluoride contents as sold.

- The risk to infants in Australia and New Zealand from potential gluten content of infant formula is such that gluten is directly prohibited in infant formula products.

- ANZFA supports the use of soy-based infant formula by infants for whom human milk or a modified cow's milk formula is contraindicated. Soy-based infant formula products will be regulated as special purpose infant formula products if a nutrient claim or a claim for special medical purpose is made for the product; other wise they will be regulated as general purpose infant formula products.

- Microbiological criteria and the use of specific food additives are recommended to ensure safety of infant formula. The microbiological criteria are contained within the Standard 1.6.1 - Microbiological Limits for Foods and Standard 1.3.1 - Food Additives provides specific permissions on food additives in infant formula.

- Specific labelling is required to inform carers to seek health advice to determine whether formula is the most appropriate method of feeding and if so, whether the specific formula is most appropriate for the individual infant. Labelling is also required to ensure carers have advice as to the nutritional content of the formula and the safe preparation, storage, and use of the formula. The relevant labelling provisions of the *WHO International Code of Marketing Breast-milk Substitutes* are also reflected within the Standard. These include a reference to breast milk as the optimum source of nourishment for infants so that potential purchasers of infant formula products can be informed of the full range of feeding options.

The specific provisions in the drafting prepared after Full Assessment (1995), Preliminary Inquiry (May 1999), Inquiry (November 1999) and Supplementary Final Assessment (Inquiry - s24) (Feb 2002) have been amended for the following reasons:

Purpose

- The word 'microbiological' has been deleted from this part of the standard to reflect the change to Clause 27 detailed below.

- Reference to Standards that contain requirements pertaining to Standard 2.9.1 have been included.

- The term 'added nutrients' has been included in reference to Standard 1.3.4 containing specifications for certain oils used as sources of long chain polyunsaturated fatty acids.

Clause 1 - Definitions

- Inclusion of definitions from clauses 1 and 2 of Standard 1.2.8 as this standard does not apply to infant formula products unless specified.

- The definitions for infant formula product, infant formula, follow-on formula, lactose-free and low lactose, and pre-term formula have been altered as follows:

  - Concerns were raised in submissions about the proposed definition of infant formula products stating that these are suitable as the principal source of nourishment for infants, when those over 6 months of age are being introduced to weaning foods. The definition for infant formula product has therefore been revised to:

    a product based on milk or other edible food constituents of animal or plant origin and which is nutritionally adequate to serve as, the principal liquid source of nourishment for infants.

  - The definition of infant formula has been changed to be consistent with the then intent of the draft Codex standard. The new definition is:

    an infant formula product represented as a breast milk substitute for infants and which satisfies the nutritional requirements of infants aged up to four to six months.

- The definition of follow-on formula has been changed to be consistent with the direction of the Codex standard for follow-up formula to acknowledge that it can either replace breast milk or infant formula and to identify the place of follow-on formula in the diet of infants who are being introduced to new foods. The new definition is:

  an infant formula product represented as either a breast milk substitute or replacement for infant formula and which constitutes the principal liquid source of nourishment in a progressively diversified diet for infants aged from six months.

- The definition of lactose free and low lactose formula has been changed to be consistent with other definitions in the standard. The new definition is:

  infant formula products which satisfy the needs of lactose intolerant infants.

- The definition of pre-term formula has been changed to accommodate concerns that pre-term formulae can be used for infants who are both born early or who are of low birth weight. The new definition is:

  an infant formula product represented as being suitable as the principal source of food for infants born prematurely or of low birth weight.

- The definition for protein equivalent has been removed, as there is no reference made to this definition in the standard.

Clause 4 – Calculation of protein

- This clause has been re-formatted for general consistency with Volume 2 of the *Food Standards Code*.

Clause 5 – Calculation of Potential Renal Solute Load (PRSL)

- The calculation of PRSL has been modified to exclude the unavailable phosphorus content of formula from the estimation of PRSL. The calculation has also been modified to calculate PRSL using nitrogen rather than protein. Comment was received that manufacturers measure nitrogen, not protein, and therefore the protein value for inclusion in the calculation of PRSL would need to be derived from the nitrogen value.

- This clause has been re-formatted for general consistency with Volume 2 of the *Food Standards Code*.

Clause 6 – Calculation of amino acid score

- This clause has been removed and the table to Clause 6 transferred to Clauses 22 and 32 as calculation of amino acid score is no longer required.

The removal of Clause 6 has reduced the clause numbering by one from that proposed at Preliminary Inquiry (May 99) and the tables to Clauses have been re-numbered accordingly.

Clause 8 – Permitted nutritive substances (Now Clause 7)

- The title of this clause has been changed from 'permitted optional nutritional substances' to 'permitted nutritive substances' to be generally consistent with Volume 2 of the *Food Standards Code*.

- The values in the table to Clause 8 for carnitine, choline and inositol have been modified to correct an error at Preliminary Inquiry. The new maximum values are 0.8 mg/100 kJ for carnitine, 7.1 mg/100 kJ for choline and 9.5 mg/100 kJ for inositol.

- An editorial note has also been added to note that it is the intent of the standard to regulate the maximum level of nutritive substances of formula only when the substance is added to the formula. In this case the maximum level refers to both the naturally occurring level and that which is added as an ingredient. This has arisen over some concerns about the setting of a maximum level for <u>added</u> carnitine, which some groups claimed was lower than the level of carnitine naturally present in milk.

Clause 9 – Limit on nucleotide 5'-monophosphates (Now Clause 8)

- The figures proposed at Preliminary Inquiry for nucleotides were based upon the EC directive, which appears to have underestimated the levels of nucleotides in breast milk. The drafting has been amended to allow for a maximum permitted total 5'-monophosphate nucleotide content of 3.8 mg/100 kJ as recommended in the Life Sciences Research Office (LSRO) report.

Clause 11 – Food additives (Transferred to Standard 1.3.1)

- The drafting for the permission to add carrageenan has been amended slightly to more expressly permit its addition. The wording proposed at Preliminary Inquiry was interpreted as implying that carrageenan was not permitted to be added.
- The appropriate food additives numbers have been added to the mono- and di-glycerides entry to clarify which food additives are permitted.
- This clause has been moved to the Standard 1.3.1 – Food Additives.

The transfer of Clauses 11 and 12 to Standard 1.3.1 – Food Additives has reduced the clause numbering by another two from that proposed at Preliminary Inquiry (May 99) and the tables to Clauses have been re-numbered accordingly.

Clause 10 – Lactic acid cultures (Now Clause 9)

- The drafting of the this clause has been has been slightly amended by the removal of "*subject to Standard 1.6.1*" as Standard 1.6.1 has general application and reference to lactic acid cultures should automatically required compliance with Standard 1.6.1.

Clause 11 – Limit on Aluminium (Now Clause 10)

- Clause 14 (previously Limit on lead) as been removed and replaced with an editorial note referring to Standard 1.4.1 - Contaminants and Natural Toxicants that now contains the limits on lead. This editorial note to Clause 11 has been changed to '*The maximum level*

(ML) of lead in infant formula products is specified in Standard 1.4.1" to better reflect terminology used in Standard 1.4.1.

Clause 14 – Requirement for a measuring scoop (Now Clause 13)

- The drafting of this clause has been amended to exempt both single serve sachets, or a package containing single serve sachets from being required to contain a scoop to facilitate the use of infant formula products in accordance with the directions contained in the label on the package.

Clause 15 – Composition of lactose-free and low-lactose formulas (Now Clause 29)

- This clause has been moved to Part 3, Division 2 – Infant formula products formulated for metabolic, immunological, renal and malabsorptive conditions as it is more appropriately situated in this part of the Standard.
- The clause has been amended to specify that low lactose formula must contain no more than 0.3 g lactose per 100 mL of infant formula product to be consistent with the new limit imposed for general purpose foods.

Clause 15 – Required statements (Now Clause 14)

- It was proposed at Preliminary Inquiry that manufacturers place a statement on the label that contained information about the superiority of breast milk over infant formula and that formula should only be used on the advice of a medical practitioner or health worker. The actual wording of the statement was left to manufacturers to develop. There was considerable concern expressed about this in submissions. The drafting of this clause has therefore been amended to require the following statement on labels:

  Breast milk is best for babies. Before you decide to use this product, consult your doctor or health worker for advice.

  Clause 14 (3) has been added to exclude products for metabolic, immunological, renal, hepatic or malabsorptive conditions from requiring this statement as it is considered not appropriate for these products.

- It was proposed in subclause (1) to require the statement 'Inappropriate use or preparation can make your baby very ill'. This statement has been amended to 'Incorrect preparation can make your baby very ill' on the advice of stakeholders.

- the wording to subclause (3)(e) has also been amended to clarify the intent.

Clause 16 – Print and package size (Now Clause 15)

- The drafting of this clause has been amended to classify a small package as 500g or less. This means that the wording of the warning statements and other required statements will be 1.5mm on these packages, and 3mm on larger packages. This change was made as a result of concerns with the proposal at Preliminary Inquiry that a small package was defined as 1 kg, as the majority of packages of infant formula products are less than 1 kg.

Clause 17 – Declaration of nutrition information (Now Clause 16)

- This clause has been amended to require nutrient declaration only per 100 mL as consumed and to require the declaration of the weight of product per scoop and proportion of solution on a weight/volume basis for the product to reduce the amount of label space required to provide nutrient information.
- This clause has been re-formatted to improve clarity.

Clause 18 – Date marking and storage instructions (Now Clause 17)

- This title of this clause has been amended to be consistent with Standard 1.2.5 - Date Marking of Packaged Foods.
- A subclause has been included to ensure compliance with Standard 1.2.5
- The editorial note to Clause 18 has been simplified to "*The appropriate storage instructions should be valid for the full range of climatic conditions that exist in Australia and New Zealand*"

Clause 19 – Statement of protein source (Now Clause 18)

- This clause has been amended to clarify that the declaration of source, or sources, of protein should be specific rather than as class names.

Clauses 23 and 33 – Protein (Now Clause 22 and 32)

- This clause has been amended to reflect the change in expression of protein quality to mg/100 kJ as at Clause 6. Due to this change the requirement for an amino acid score of 0.8 has been deleted. The Table to clause 6 has been transferred into clauses 23 and 33 and provides the minimum essential amino acid values /100 kJ.

- The table to Clauses 22 and 32 has been modified to permit the summation of cysteine and methionine; and phenylalanine and tyrosine as originally proposed at Full Assessment (Schedule 1). The units of expression have been modified from amino acid per protein content (g/100 g) to a per energy value (mg/100 kJ). The amino acid values from Schedule 1 (FAO/WHO 1991) have been converted to mg/100 kJ.

- Human milk is cysteine-rich and methionine-poor but infant formula products are made from cow's milk proteins that are poor in cysteine but rich in methionine, therefore summation assists to overcome this difficulty. To ensure that some cysteine is present in infant formulas for very young infants, an absolute minimum cysteine content (6 mg/100 kJ) has been prescribed. Additionally for a similar reason a minimum value for phenylalanine (17 mg/100 kJ) has also been included.

- A subclause has been included to allow addition of amino acids for the sole purpose of improving protein quality.

Clause 24 – Minimum percentage alpha linolenic acid (Now Clause 23)

- The table to this clause has been amended to reduce the minimum percentage alpha linolenic acid (1.1%) consistent with recent research that shows this level is safe.

Clause 27 – Microbiological standards (Transferred to Standard 1.6.1)

- The microbiological standards for infant formula products are regulated in Standard 1.6.1 – Microbiological Limits for Foods. This clause has therefore been deleted.

Clause 30 – Fat (Now Clause 23)

- The drafting of clause 30(d) has been amended to provide for the ratio of total long chain omega 6 series fatty acids (C>= 20) to total long chain omega 3 series fatty acids (C>= 20) of approximately 2 in an infant formula or follow-on formula which contains those fatty acids. This change was made in recognition of the difficulty in ensuring that the ratio is exactly 2.

- An Editorial Note has been included to provide reference of specifications for certain oils as sources of long chain polyunsaturated fatty acids in Standard 1.3.4 – Identity and Purity. These oils were assessed as safe for use in infant formula during the review of infant formula, and the safety assessment is included in the Supplementary Final Assessment (Inquiry) Report.

Clause 31 – Vitamins and minerals (Now Clause 24)

- The selenium values proposed at Preliminary Inquiry (0.36-0.9 mcg/100 kJ) have been modified to 0.25-1.19 mcg/100 kJ. The maximum level is consistent with the maximum level of selenium recommended by LSRO based upon the upper limits of selenium in breast milk. The minimum level is consistent with the minimum level recommended in the standard for Foods for Special Medical Purposes (infants) recently adopted by the European Commission.

- The table to Clause 31 has been amended to permit the following forms of vitamins and minerals to be added:

    - Retinyl propionate as a source of vitamin A
    - Cholecalciferol-cholesterol as a source of vitamin D
    - Dl – alpha- tocopherol succinate as a source of vitamin E
    - Phytylmenoquinone as a source of vitamin K
    - Sodium chloride iodised as a source of sodium
    - Cupric citrate as a source of copper
    - Manganese carbonate and manganese citrate as sources of manganese
    - Sodium selenate as a source of selenium
    - Pyridoxine-5'-phosphate.

- The maximum zinc: copper ratio has been raised to 15:1 for formulas for infants less than 6 months of age and 20:1 for formulas intended for infants over 6 months of age to meet the manufacturing concerns of industry.

Clauses 32-35 – Pre-term formula (Now Clause 25)

- There was considerable concern expressed by submitters about the levels of vitamins, minerals and fats proposed at Preliminary Inquiry for pre-term formula, particularly in

the absence of any international precedents. Clauses 32-35 have therefore been deleted and replaced with the following clause: "*Infant formula product may be specifically formulated to satisfy the particular needs of premature infants or infants born low in birth weight and must comply with all the other requirements of this Standard that are not inconsistent with Division"*.

- ANZFA will raise a separate proposal to develop specific provisions for pre-term formula within 5 years of this Standard 2.9.1 coming into effect.

Part 3 Division 2 – Infant formula products formulated for metabolic and immunological conditions

- The title of this Division has been amended to: Division 2 - Infant formula products formulated for metabolic, immunological, renal, hepatic and malabsorptive conditions. This amendment has been made to more specifically accommodate formulas for these conditions and has the effect of excluding anti-reflux formulas from being described as such.

An exemption from the compositional requirements for these products is provided for a period of 5 years to guarantee supply of specialised products. A Proposal to develop a standard for Foods for Special Medical Purposes (P242) is under development and these products may be covered by this new standard. These products are also exempted from the requirement to label *' Breast milk is best for babies. Before you decide to use this product, consult your doctor or health worker for advice'* as breast milk may not be appropriate for these babies and the advice of a doctor will already be being sought.

Clause 38 – Additional labelling (Now Clause 28)

- The wording of this clause has been amended slightly to require the additional labelling on the broader range of products now covered under this part of the Standard (i.e. products for metabolic, immunological, renal, hepatic and malabsorptive conditions).

Clause 42 – Other permitted additions (Now Clause 34)

- The following changes have been made to the table to Clause 42:
  - the appropriate food additives numbers have been added to the mono- and di-glycerides entry to clarify which food additives are permitted;
  - citric esters of mono- and di-glycerides of fatty acids are permitted for formulas based upon protein substitutes; and
  - the value for DATEM was changed to correct a typographical error of a factor of 10 in the Table at Preliminary Inquiry.
- The table to this clause has been moved to the Standard 1.3.1 – Food Additives and therefore the title of the clause has be amended to "Additional permitted triglycerides"

Specifications

- As noted at Preliminary Inquiry, the specifications for nucleotides are moved to Standard 1.3.4 – Identity and Purity.

- Specifications for certain oils as sources of long chain polyunsaturated fatty acids have been included in Standard 1.3.4 – Identity and Purity.

- The provisions for bacteriological profile under part 9 of this section have been deleted as they are covered by Standard 1.6.1 – Microbiological Limits for Foods.

REGULATION IMPACT

In meeting the objectives of this proposal, ANZFA has assessed the relative costs and benefits of regulatory options and their respective impacts on identified affected parties. As part of Preliminary Inquiry (May 1999), ANZFA undertook a regulation impact analysis. However, in recognition of the significant time delay and changes that have been made to the draft standard as proposed at Inquiry (Nov 1999), the previous draft regulation impact statement as assessed at Preliminary Inquiry has been revised and updated.

The revised regulation impact statement has recommended that the review of regulations for infant formula is of potential benefit to infant health. The Office of Regulation Review has assessed this revised regulation impact statement as adequate.

WORLD TRADE ORGANIZATION (WTO) NOTIFICATION

Australia and New Zealand are members of the World Trade Organization (WTO) and are bound as parties to WTO agreements. In Australia, an agreement developed by the Council of Australian Governments (COAG) requires States and Territories to be bound as parties to those WTO agreements to which the Commonwealth is a signatory. Under the Treaty between the Governments of Australia and New Zealand on joint Food Standards, ANZFA is required to ensure that food standards are consistent with the obligations of both countries as members of the WTO.

In certain circumstances Australia and New Zealand have an obligation to notify the WTO of changes to food standards to enable other member countries of the WTO to make comment. Notification is required in the case of any new or changed standards which may have a significant trade effect and which depart from the relevant international standard (or where no international standard exists).

Following Preliminary Inquiry (May 1999), this matter was notified to the WTO as a technical barrier to trade matter as the proposed revisions to the existing infant formula standards are more prescriptive than other standards internationally. One submission from the United States of America was received on this matter.

FOOD STANDARDS SETTING IN AUSTRALIA AND NEW ZEALAND

The Governments of Australia and New Zealand entered an Agreement in December 1995 establishing a system for the development of joint food standards. On 24 November 2000, Health Ministers in the Australia New Zealand Food Standards Council (ANZFSC) agreed to adopt the new *Australian New Zealand Food Standards Code*. The new Code was gazetted on 20 December 2000 in both Australia and New Zealand as an alternate to existing food regulations until December 2002 when it will become the sole food code for both countries.

It aims to reduce the prescription of existing food regulations in both countries and lead to greater industry innovation, competition and trade.

Until the joint *Australia New Zealand Food Standards Code* is finalised the following arrangements for the two countries apply:

- **Food imported into New Zealand other than from Australia** must comply with either Volume 1 (known as Australian *Food Standards Code)* or Volume 2 (known as the joint *Australia New Zealand Food Standards Code)* of the Australian *Food Standards Code*, as gazetted in New Zealand, or the New Zealand *Food Regulations 1984*, but not a combination thereof. However, in all cases maximum residue limits for agricultural and veterinary chemicals must comply solely with those limits specified in the New Zealand *(Maximum Residue Limits of Agricultural Compounds) Mandatory Food Standard 1999.*

- **Food imported into Australia other than from New Zealand** must comply solely with Volume 1 (known as Australian *Food Standards Code)* or Volume 2 (known as the joint *Australia New Zealand Food Standards Code)* of the Australian *Food Standards Code*, but not a combination of the two.

- **Food imported into New Zealand from Australia** must comply with either Volume 1 (known as Australian *Food Standards Code)* or Volume 2 (known as *Australia New Zealand Food Standards Code)* of the Australian *Food Standards Code* as gazetted in New Zealand, but not a combination thereof. Certain foods listed in Standard T1 in Volume 1 may be manufactured in Australia to equivalent provisions in the New Zealand *Food Regulations 1984.*

- **Food imported into Australia from New Zealand** must comply with Volume 1 (known as Australian *Food Standards Code)* or Volume 2 (known as *Australia New Zealand Food Standards Code)* of the Australian *Food Standards Code*, but not a combination of the two. However, under the provisions of the Trans-Tasman Mutual Recognition Arrangement, food may **also** be imported into Australia from New Zealand provided it complies with the New Zealand *Food Regulations 1984.*

- **Food manufactured in Australia and sold in Australia** must comply with Volume 1 (known as Australian *Food Standards Code)* or Volume 2 (known as *Australia New Zealand Food Standards Code)* of the Australian *Food Standards Code* but not a combination of the two. Certain foods listed in Standard T1 in Volume 1 may be manufactured in Australia to equivalent provisions in the New Zealand *Food Regulations 1984.*

In addition to the above, all food sold in New Zealand must comply with the New Zealand *Fair Trading Act 1986* and all food sold in Australia must comply with the Australian *Trade Practices Act 1974*, and the respective Australian State and Territory *Fair Trading Acts.*

Any person or organisation may apply to ANZFA to have the *Food Standards Code* amended. In addition, ANZFA may develop proposals to amend the Australian *Food Standards Code* or to develop joint Australia New Zealand food standards. ANZFA can provide advice on the requirements for applications to amend the *Food Standards Code*.

FURTHER INFORMATION

Submissions

No submissions on this matter are sought as the Authority has completed its assessment and the matter is now with the Australia New Zealand Food Standards Council for consideration.

Further Information

Further information on this and other matters should be addressed to the Standards Liaison Officer at the Australia New Zealand Food Authority at one of the following addresses:

Australia New Zealand Food Authority
PO Box 7186
Canberra BC ACT 2610
AUSTRALIA
Tel (02) 6271 2258
email: slo@anzfa.gov.au

Australia New Zealand Food Authority
PO Box 10559
The Terrace WELLINGTON 6036
NEW ZEALAND
Tel (04) 473 9942
email: anzfa.nz@anzfa.gov.au

Assessment reports are available for viewing and downloading from the ANZFA website www.anzfa.gov.au or alternatively paper copies of reports can be requested from the Authorities Information Officer at info@anzfa.gov.au.

DRAFT VARIATIONS TO VOLUME 1 AND VOLUME 2 OF THE *FOOD STANDARDS CODE*

To commence: on gazettal

The Food Standards Code *is varied by –*

[1] ***Standard A11*** *of Volume 1 is varied by –*

[1.1] *inserting in the* Schedule *to A11 into* Column 1 *and* Column 2 *respectively, after the entry for* Divinylbenzene copolymer –

Docosahexaenoic acid (DHA) – rich oil derived from the algae *Crypthecodinium cohnii*	Addendum 17

[1.2] *inserting in the* Schedule *to A11 into* Column 1 *and* Column 2 *respectively, after the entry for* Anthocyanins –

Arachidonic acid (ARA) – rich oil derived from the fungus *Mortierella alpina*	Addendum 18

[1.3] *inserting following* ADDENDUM 16 –

ADDENDUM 17

SPECIFICATION FOR DOCOSAHEXAENOIC ACID (DHA) - RICH OIL DERIVED FROM THE ALGAE *CRYPTHECODINIUM COHNII*

Full chemical name for DHA	4,7,10,13,16,19-docosahexaenoic acid (22:6n-3)
Appearance	Free flowing oil
Colour	Yellow to orange
Odour	Characteristic
DHA (%)	min. 40 max. 45
Dodecanoic acid 12:0 (%)	min. 0 max. 6
Tetradecanoic acid 14:0 (%)	min. 10 max. 20
Hexadecanoic acid 16:0 (%)	min. 10 max. 20
Octadecenoic acid 18:1 (%)	min. 10 max. 30
Peroxide value (meq/kg)	max. 5
Moisture and volatiles (%)	max. 0.01
Non-saponifiables (%)	max. 3.5
Trans fatty acids (%)	max. 1.0
Free fatty acid (%)	max. 0.4
Lead (ppm)	max. 0.2
Arsenic (ppm)	max. 0.5
Copper (ppm)	max. 0.1
Iron (ppm)	max. 0.5
Mercury (ppm)	max. 0.2
Hexane (ppm)	max. 0.3

ADDENDUM 18

SPECIFICATIONS FOR ARACHIDONIC ACID (ARA) – RICH OIL DERIVED FROM THE FUNGUS *MORTIERELLA ALPINA*

Full chemical name for ARA	5,8,11,14-eicosatetraenoic acid (20:4n-6)	
Appearance	Free flowing oil	
Colour	Yellow	
Odour	Characteristic	
ARA (%)	min. 38	max. 44
Hexadecanoic acid 16:0 (%)	min. 3	max. 15
Octadecanoic acid 18:0 (%)	min. 5	max. 20
Octadecenoic acid 18:1 (%)	min. 5	max. 38
Octadecadienoic acid 18:2 (%)	min. 4	max. 15
Peroxide value (meq/kg)	max. 5	
Moisture and volatiles (%)	max. 0.05	
Non-saponifiables (%)	max. 3.5	
Trans fatty acids (%)	max. 1.0	
Free fatty acid (%)	max. 0.4	
Lead (ppm)	max. 0.2	
Arsenic (ppm)	max. 0.5	
Copper (ppm)	max. 0.1	
Iron (ppm)	max. 0.5	
Mercury (ppm)	max. 0.2	
Hexane (ppm)	max. 0.3	

[2] ***Standard 1.1.1*** *of Volume 2 is varied by omitting from clause 2, in the definition for* warning statement *subclause* (d) –

substituting

(d) subclauses 14(1), 14(3) and 26(1) of Standard 2.9.1; and

[3] ***Standard 1.3.4*** *of Volume 2 is varied by inserting in the* Schedule *immediately after the* Specification for tall oil phytosterols derived from tall oils *the following* -

Specification for docosahexaenoic acid (DHA) – rich oil derived from the algae *Crypthecodinium cohnii*

Full chemical name for DHA	4,7,10,13,16,19-docosahexaenoic acid (22:6n-3)	
Appearance	Free flowing oil	
Colour	Yellow to orange	
Odour	Characteristic	
DHA (%)	min. 40	max. 45
Dodecanoic acid 12:0 (%)	min. 0	max. 6
Tetradecanoic acid 14:0 (%)	min. 10	max. 20
Hexadecanoic acid 16:0 (%)	min. 10	max. 20
Octadecenoic acid 18:1 (%)	min. 10	max. 30
Peroxide value (meq/kg)	max. 5	
Moisture and volatiles (%)	max. 0.01	

Non-saponifiables (%)	max. 3.5
Trans fatty acids (%)	max. 1.0
Free fatty acid (%)	max. 0.4
Lead (ppm)	max. 0.2
Arsenic (ppm)	max. 0.5
Copper (ppm)	max. 0.1
Iron (ppm)	max. 0.5
Mercury (ppm)	max. 0.2
Hexane (ppm)	max. 0.3

Specification for arachidonic acid (ARA) – rich oil derived from the fungus *Mortierella alpina*

Full chemical name for ARA	5,8,11,14-eicosatetraenoic acid (20:4n-6)
Appearance	Free flowing oil
Colour	Yellow
Odour	Characteristic
ARA (%)	min. 38 max. 44
Hexadecanoic acid 16:0 (%)	min. 3 max. 15
Octadecanoic acid 18:0 (%)	min. 5 max. 20
Octadecenoic acid 18:1 (%)	min. 5 max. 38
Octadecadienoic acid 18:2 (%)	min. 4 max. 15
Peroxide value (meq/kg)	max. 5
Moisture and volatiles (%)	max. 0.05
Non-saponifiables (%)	max. 3.5
Trans fatty acids (%)	max. 1.0
Free fatty acid (%)	max. 0.4
Lead (ppm)	max. 0.2
Arsenic (ppm)	max. 0.5
Copper (ppm)	max. 0.1
Iron (ppm)	max. 0.5
Mercury (ppm)	max. 0.2
Hexane (ppm)	max. 0.3

[4] ***Standard 2.9.1*** *of Volume 2 is varied by* -

[4.1] *omitting* Standard 2.9.1 *and substituting* -

STANDARD 2.9.1

INFANT FORMULA PRODUCTS

Purpose

This Standard provides for the compositional, and labelling requirements for foods intended or represented for use as a substitute for breast milk, herein referred to as 'infant formula products'. This Standard applies to all infant formula products whether in powder, liquid concentrate or 'ready to drink' forms.

This Standard also provides for infant formula products intended for infants with special nutritional requirements.

Additionally, recommended guidelines regarding vitamins and minerals are contained at the end of this Standard. Standard 1.3.1 contains provisions relating to the food additives permitted in infant formula products. Standard 1.6.1 contains the microbiological limits in relation to infant formula products. Standard 1.3.4 contains specifications for permitted nucleotides and added nutrients. Standard 1.1.1 defines nutritive substances for the purposes of this Code.

Table of Provisions

Division 1

Subdivision 1 – Interpretation

1 Definitions

(1) The definitions in clauses 1 and 2 of Standard 1.2.8 apply to this Standard.

(2) In this Code –

follow-on formula means an infant formula product represented as either a breast-milk substitute or replacement for infant formula and which constitutes the principal liquid source of nourishment in a progressively diversified diet for infants aged from six months.

infant means a person under the age of 12 months.

infant formula means an infant formula product represented as a breast milk substitute for infants and which satisfies the nutritional requirements of infants aged up to four to six months.

Editorial note:

A reference to infant formula product may include a reference to infant formula but the converse does not apply.

infant formula product means a product based on milk or other edible food constituents of animal or plant origin which is nutritionally adequate to serve as the principal liquid source of nourishment for infants.

Editorial note:

The intent of this definition is to limit the addition of ingredients to infant formula product to ingredients that would be considered to be foods. The addition of an ingredient that is not considered to be a food is prohibited unless specifically permitted elsewhere in this Standard.

Standard 1.5.1 contains prohibitions and restrictions relating to novel foods and novel food ingredients. Nothing contained in this Standard permits infant formula products to contain novel foods or novel food ingredients that are not permitted in Standard 1.5.1.

lactose free formula and **low lactose formula** means infant formula products which satisfy the needs of lactose intolerant infants.

medium chain triglycerides means triacylglycerols which contain predominantly the saturated fatty acids designated by 8:0 and 10:0.

pre-term formula means an infant formula product specifically formulated to satisfy particular needs of infants born prematurely or of low birthweight.

protein substitute means L-amino acids and/or the hydrolysate of one or more of the proteins on which infant formula product is normally based.

soy-based formula means an infant formula product in which soy protein isolate is the sole source of protein.

2 Interpretation

A reference to any infant formula product in the compositional provisions of this Standard is a reference to –

(a) a powdered or concentrated form of infant formula product which has been reconstituted with water according to directions; or
(b) an infant formula product in 'ready to drink' form.

Subdivision 2 – Calculations

3 Calculation of energy

The energy content of infant formula product, expressed in kilojoules (kJ), must be calculated using –

(a) only the energy value contributions of the fat, protein and carbohydrate ingredients of the infant formula product; and
(b) the relevant energy factors set out in Standard 1.2.8.

4 Calculation of protein

The prescribed formula for the calculation of the protein content of infant formula product for the purposes of this Standard is -

Formula
For milk proteins and their partial protein hydrolysates -
Protein content = nitrogen content x 6.38; or
In any other case -
Protein content = nitrogen content x 6.25.

5 Calculation of potential renal solute load

The prescribed formula for the calculation of the potential renal solute load for the purposes of this Standard is -

Formula
Potential renal solute load in mOsm/100 kJ = [Na (mg/100 kJ) /23] + [Cl (mg/100 kJ) /35] + [K (mg/100 kJ) /39] + [P_{avail} (mg/100 kJ)/ 31] + [N (mg/100kJ) /28)].
In this formula
P_{avail} = P of milk-based formula + 2/3 of P of soy-based formulas.

Subdivision 3 - General compositional requirements

6 Restrictions and prohibitions

(1) A vitamin, mineral, food additive or nutritive substance must not be added to infant formula product unless -

(a) expressly permitted by this Code; or
(b) it is naturally present in an ingredient of the infant formula product.

(2) Infant formula product must contain no detectable gluten.

7 Permitted nutritive substances

(1) Any nutritive substance listed in column 1 of the Table to this clause may be added to infant formula product provided that -

(a) the nutritive substance is in one or more of the forms specified in column 2 of the Table in relation to that substance; and

(b) the total amount of the nutritive substance in the infant formula product is no more than the amount specified in column 4 of the Table.

(2) The label on a package of infant formula product must not include any words indicating, or any other indication, that the product contains a nutritive substance specified in column 1 or in column 2 of the Table to this clause unless the total amount of the nutritive substance in the food is no less than the amount specified in column 3 of the Table.

Editorial note:

The intent of subclause 7(1) is that the maximum permitted amounts only apply when the substance is added, and in that case, it then applies to the sum of the naturally occurring and added nutritive substances.

This Standard contains guidelines on the use and format of nutrient information tables.

Table to clause 7

Column 1	Column 2	Column 3	Column 4
Nutrititive substance	**Permitted forms**	**Minimum amount for claim per 100 kJ**	**Maximum amount per 100 kJ**
Choline	Choline chloride Choline bitartrate	1.7 mg	7.1 mg
Inositol	Inositol	1.0 mg	9.5 mg
Taurine	Taurine	0.8 mg	3 mg
L-carnitine	L-carnitine	0.21 mg	0.8 mg
Cytidine 5’-monophosphate	Cytidine 5’-monophosphate Cytidine 5’-monophosphate sodium salt	0.22 mg	0.6 mg
Uridine 5’-monophosphate	Uridine 5’-monophosphate Uridine 5’-monophosphate sodium salt	0.13 mg	0.42 mg
Adenosine 5’-monophosphate	Adenosine 5’-monophosphate Adenosine 5’-monophosphate sodium salt	0.14 mg	0.38 mg
Guanosine 5’-monophosphate	Guanosine 5’-monophosphate Guanosine 5’-monophosphate sodium salt	0.04 mg	0.12 mg
Inosine 5’-monophosphate	Inosine 5’-monophosphate Inosine 5’-monophosphate sodium salt	0.08 mg	0.24 mg

8 Limit on nucleotide 5’-monophosphates

Infant formula product must contain no more than 3.8 mg/100 kJ of nucleotide 5’-monophosphates.

Editorial note:

Standard 1.3.4 contains specifications for nucleotides.

9 Lactic acid cultures

L(+) producing lactic acid cultures may be added to infant formula product.

10 Limit on aluminium

(1) Infant formula product, other than a pre-term formula or soy-based formula product, must contain no more than 0.05 mg of aluminium per 100 mL.

(2) Pre-term formula must contain no more than 0.02 mg of aluminium per 100 mL.

(3) Soy-based formula must contain no more than 0.1 mg of aluminium per 100 mL.

Editorial note:

Standard 1.4.1 contains the maximum level (ML) of lead contaminant in infant formula products.

Subdivision 4 - General labelling and packaging requirements

11 Representations of food as infant formula product

A food must not be represented as an infant formula product unless it complies with this Standard.

12 Prescribed names

'Infant Formula' and 'Follow-on Formula' are prescribed names.

13 Requirement for a measuring scoop

(1) A package of infant formula product in a powdered form must contain a scoop to enable the use of the infant formula product in accordance with the directions contained in the label on the package.

(2) Subclause (1) does not apply to single serve sachets, or packages containing single serve sachets of an infant formula product in a powdered form.

14 Required warnings, directions and statements

(1) The label on a package of infant formula product must include the following warning statement -

(a) in the case of infant formula product in powdered form -

'Warning – follow instructions exactly. Prepare bottles and teats as directed. Do not change proportions of powder except on medical advice. Incorrect preparation can make your baby very ill'; and

(b) in the case of concentrated infant formula product -

'Warning – follow instructions exactly. Prepare bottles and teats as directed. Do not change proportions of concentrate except on medical advice. Incorrect preparation can make your baby very ill'; and

(c) in the case of 'ready to drink' infant formula product -

'Warning – follow instructions exactly. Prepare bottles and teats as directed. Do not dilute or add anything to this 'ready to drink' formula except on medical advice. Incorrect preparation can make your baby very ill'.

(2) The label on a package of infant formula product must include directions for the preparation and use of the infant formula product which include words and pictures instructing -

(a) that each bottle should be prepared individually; and
(b) that if a bottle of made up formula is to be stored prior to use, it must be refrigerated and used within 24 hours; and
(c) that potable, previously boiled water should be used; and
(d) where a package contains a measuring scoop, that only the enclosed scoop should be used; and
(e) that formula left in the bottle after a feed must be discarded.

(3) Subject to subclause (4), the label on a package of infant formula product must contain the following warning statement -

'Breast milk is best for babies. Before you decide to use this product, consult your doctor or health worker for advice.';

under a heading that states –

'Important Notice' or any word or words having the same or similar effect.

(4) Subclause (3) does not apply to infant formula products for metabolic, immunological, renal, hepatic or malabsorptive conditions.

(5) The label on a package of an infant formula product must contain statements indicating that -

(a) the infant formula product may be used from birth, in the case of infant formula; and
(b) the infant formula product should not be used for infants aged under 6 months in the case of follow-on formula; and
(c) except in the case of packages of pre-term formula, it is recommended that infants over the age of 6 months should be offered foods in addition to the infant formula product.

15 Print and package size

(1) Where an infant formula product is in a package having a net weight of more than 500g, the statements required by subclauses 14(1), (3) and 26(1) must be in size of type of no less than 3 mm.

(2) Where an infant formula product is in a package having a net weight of 500g or less the statements required by subclauses 14(1), (3) and 26(1) must be in size of type of no less than 1.5 mm.

16 Declaration of nutrition information

(1) The label on a 'ready to drink' infant formula product must include a statement, which may be in the form of a table, that contains the following information –

(a) the average energy content expressed in kJ per 100 mL; and
(b) the average amount of protein, fat and carbohydrate expressed in g per 100 mL; and
(c) the average amount of each vitamin, mineral and any other nutritive substance permitted by this Standard expressed in weight per 100 mL.

(2) The label on a powdered or concentrated form of infant formula product must include a statement, which may be in the form of a table that contains the following information -

(a) the average energy content expressed in kJ per 100 mL of infant formula product that has been reconstituted according to directions; and
(b) the average amount of protein, fat and carbohydrate expressed in g per 100 mL of infant formula product that has been reconstituted according to directions; and
(c) the average amount of each vitamin, mineral and any other nutritive substance permitted by this Standard expressed in weight per 100 mL of infant formula product that has been reconstituted according to directions; and
(d) a declaration –

(i) of the weight of one scoop in the case of powdered infant formula; and
(ii) of the proportion of powder or concentrate required to reconstitute the formula according to directions.

17 Date marking and storage instructions

(1) Paragraphs 2(1)(c) and (d) of Standard 1.2.5 do not apply to this Standard.

(2) A label on a package of infant formula product must contain storage instructions covering the period after it is opened.

Editorial note:

The appropriate storage instructions should be valid for the full range of climatic conditions that exist in Australia and New Zealand.

18 Statement of protein source

The label on a package of infant formula product must contain a statement of the specific source, or sources, of protein in the infant formula product immediately adjacent to the name of the infant formula product.

Editorial note:

Standard 1.2.2 requires that all food be labelled with its name. The requirement in clause 18 of this Standard applies only to the name on the label on the product in accordance with the requirement in Standard 1.2.2.

19 Statement on dental fluorosis

(1) An infant formula product must comply with subclause (2) where it contains -

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

(2) The label on a package of infant formula product referred to in subclause (1) must contain statements -

(a) indicating that consumption of the formula has the potential to cause dental fluorosis; and
(b) recommending that the risk of dental fluorosis should be discussed with a medical practitioner or other health professional.

20 Prohibited representations

The label on a package of infant formula product must not contain -

(a) a picture of an infant; or
(b) a picture that idealises the use of infant formula product; or
(c) the word 'humanised' or 'maternalised' or any word or words having the same or similar effect; or
(d) words claiming that the formula is suitable for all infants; or
(e) information relating to the nutritional content of human milk; or
(f) subject to clause 28, a reference to the presence of any nutrient or nutritive substance, except for a reference to a nutrient or nutritive substance in -

(i) the name of a lactose free formula or a low lactose formula; or
(ii) a statement of ingredients; or
(iii) a nutrition information statement; or

(g) subject to Division 3, a representation that the food is suitable for a particular condition, disease or disorder.

Editorial Note:

Division 3 relates to Infant Formula Products for Special Dietary Use. Clause 28 permits labelling which varies from this clause.

Division 2 – Infant Formula and Follow-on Formula

21 Composition

(1) Infant formula and follow-on formula must -

(a) have an energy content of no less than 2500 kJ/L and no more than 3150 kJ/L in the case of infant formula, and no less than 2500 kJ/L and no more than 3550 kJ/L in the case of follow-on formula; and

(b) contain an amount of each nutrient specified in column 1 of the Table to this clause which is no less than the amount specified in column 2 of the Table and no more than the amount specified in column 3 of the Table.

Table to clause 21

Column 1	Column 2	Column 3
Nutrient	**Minimum amount per 100 kJ**	**Maximum amount per 100 kJ**
Protein	0.45 g	0.7 g for infant formula 1.3 g for follow-on formula
Fat	1.05 g	1.5 g

(2) Follow-on formula must have a potential renal solute load value of no more than 8 mOsm/100 kJ.

22 Protein

(1) The L-amino acids listed in column 1 of the Table to this clause must be present in infant formula and follow-on formula at the minimum level specified in column 2 of the Table, subject to subclause 2 and 3.

Table to clause 22

Column 1	Column 2
L-Amino Acid	**Minimum amount per 100 kJ**
Histidine	12 mg
Isoleucine	21 mg
Leucine	42 mg
Lysine	30 mg
Cysteine & Methionine	19 mg
Phenylalanine & Tyrosine	32 mg

Threonine	19 mg
Tryptophan	7 mg
Valine	25 mg

(2) Infant formula or follow-on formula must provide no less than -

(a) 6 mg cysteine per 100 kJ; and
(b) 17 mg phenylalanine per 100 kJ.

(3) L-amino acids listed in the Table to this clause must be added to infant formula or follow-on formula only in an amount necessary to improve protein quality.

23 Fat

The fats in infant formula and follow-on formula must -

(a) not contain medium chain triglycerides except where a medium chain triglyceride is present in a particular infant formula or follow-on formula as the result of being a natural constituent of a milk-based ingredient of that particular infant formula or follow-on formula; and
(b) have a ratio of linoleic acid to α–linolenic acid of no less than 5 to 1 and no more than 15 to 1; and
(c) if specified in column 1 of the Table to this clause, comply with the limits, if any, specified in columns 2 and 3 of the Table; and
(d) have a ratio of total long chain omega 6 series fatty acids (C>= 20) to total long chain omega 3 series fatty acids (C>= 20) of approximately 2 in an infant formula or follow-on formula which contains those fatty acids; and
(e) where long chain polyunsaturated fatty acids are present in an infant formula or follow-on formula, an eicosapentaenoic acid (20:5 n-3) content of no more than the docosahexaenoic acid (22:6 n-3) content.

Table to clause 23

Column 1	**Column 2**	**Column 3**
Fatty acids	**Minimum % total fatty acids**	**Maximum % total fatty acids**
Essential fatty acids		
Linoleic acid (18:2)	9	26
α-Linolenic acid (18:3)	1.1	4
Long chain polyunsaturated fatty acids		
Long chain omega 6 series fatty acids (C>= 20)		2
Arachidonic acid (20:4)		1
Long chain omega 3 series fatty acids (C>= 20)		1
Total *trans* fatty acids		4
Erucic acid (22:1)		1

Editorial note:

Standard 1.3.4 contains specifications for Docosahexaenoic acid (DHA) rich oil derived from the algae *Crypthecodinium cohnii* and Arachidonic acid (ARA) rich oil derived from the fungus *Mortierella alpina*.

24 Vitamins and minerals

(1) Infant formula and follow-on formula must contain the vitamins and minerals specified in column 1 of the Table to this subclause provided that, in relation to each vitamin or mineral -

(a) the added vitamin or mineral is in a permitted form as listed in Schedule 1; and

(b) the infant formula or follow-on formula contains no less than the amount specified in column 2 of the Table; and

(c) the infant formula or follow-on formula contains no more than the amount specified in column 3 of the Table, if any.

Table to clause 24(1)

Column 1	Column 2	Column 3
Nutrient	**Minimum amount per 100 kJ**	**Maximum amount per 100 kJ**
Vitamins		
Vitamin A	14 µg	43 µg
Vitamin D	0.25 µg	0.63 µg
Vitamin C	1.7 mg	
Thiamin	10 µg	
Riboflavin	14 µg	
Preformed Niacin	130 µg	
Vitamin B_6	9 µg	36 µg
Folate	2.0 µg	
Pantothenic acid	70 µg	
Vitamin B_{12}	0.025 µg	
Biotin	0.36 µg	
Vitamin E	0.11 mg	1.1 mg
Vitamin K	1.0 µg	
Minerals		
Sodium	5 mg	15 mg
Potassium	20 mg	50 mg
Chloride	12 mg	35 mg
Calcium	12 mg	
Phosphorus	6 mg	25 mg
Magnesium	1.2 mg	4.0 mg
Iron	0.2 mg	0.5 mg
Iodine	1.2 µg	10 µg
Copper	14 µg	43 µg
Zinc	0.12 mg	0.43 mg
Manganese	0.24 µg	24.0 µg
Selenium	0.25 µg	1.19 µg

(2) Infant formula and follow-on formula must contain no less than 0.5 mg of Vitamin E per g of polyunsaturated fatty acids.

(3) The ratio of calcium to phosphorus in infant formula and follow-on formula must be no less than 1.2 to 1 and no more than 2 to 1.

(4) The ratio of zinc to copper -

(a) in infant formula must be no more than 15 to 1; and
(b) in follow-on formula must be no more than 20 to 1.

Editorial note:

This Standard contains guidelines setting out the recommended levels of vitamins and minerals that as a matter of good practice should not be exceeded.

Division 3 - Infant Formula Products for Special Dietary Use

Subdivision 1 – Infant formula products formulated for premature or low birthweight infants

25 Composition and labelling

Infant formula products may be specifically formulated for premature or low birthweight infants provided that in all other respects they comply with this Standard.

26 Additional labelling

(1) The label on a package of pre-term formula must include the warning statement -

'Suitable only for pre-term infants under specialist medical supervision'.

(2) The words 'pre-term' must appear as part of the name of a food standardised in this subdivision.

Subdivision 2 - Infant formula products for metabolic, immunological, renal, hepatic and malabsorptive conditions

27 Composition

(1) Subject to subclause (2), infant formula products may be specifically formulated to satisfy particular metabolic, immunological, renal, hepatic or malabsorptive conditions.

(2) The permission in subclause (1) only applies where the infant formula products comply with –

(a) this Division; and

(b) all the other requirements of this Standard that are not inconsistent with this Division.

(3) Subclause (2) takes effect 5 years after the commencement of this Standard.

28 Claims

Where a label contains a claim that the infant formula product is suitable for infants with metabolic, immunological, renal, hepatic or malabsorptive conditions, then the label on a package of infant formula product must include a statement indicating -

(a) that the product is not suitable for general use and should be used under medical supervision; and
(b) the condition, disease or disorder for which the food has been specially formulated; and
(c) the nutritional modifications, if any, which have been made to the infant formula product.

29 Composition of lactose free and low lactose formulas

(1) A lactose free formula or low lactose formula must, except for the lactose content, comply with the compositional and labelling requirements which apply to the infant formula product of which they are a variety.

(2) Lactose free formula must contain no detectable lactose.

(3) Low lactose formula must contain no more than 0.3 g lactose per 100 mL of infant formula product.

30 Claims relating to lactose free and low lactose formulas

Where a label contains a claim that the infant formula product is lactose free, low lactose or words of similar import, the label on a package of lactose free or a low lactose formula product must include -

(a) the words ‘lactose free' as part of the name of lactose free formula; and
(b) the words ‘low lactose' as part of the name of low lactose formula; and
(c) the following statements -

(i) the amount of lactose expressed in g per 100 mL; and
(ii) the amount of galactose expressed in g per 100 mL.

Subdivision 3 - Infant formula products for specific dietary use based upon protein substitutes

31 Composition

An infant formula product for specific dietary use based upon protein substitutes must -

(a) have an energy content of no less than 2500 kJ/L and no more than 3150 kJ/L in the case of infant formula, and no less than 2500 kJ/L and no more than 3550 kJ/L in the case of follow-on formula; and

(b) have a potential renal solute load of no more than 8 mOsm per 100 kJ; and

(c) contain an amount of each nutrient specified in column 1 of the Table to this clause which is no less than the amount specified in column 2 of the Table and no more than the amount specified in column 3 of the Table.

Table to clause 31

Column 1	Column 2	Column 3
Nutrient	**Minimum amount per 100 kJ**	**Maximum amount per 100 kJ**
Protein	0.45 g	1.4 g
Fat	0.93 g	1.5 g

32 Protein

(1) The protein content of an infant formula product for specific dietary use based upon protein substitutes may be in the form of protein substitute.

(2) The L-amino acids listed in column 1 of the Table to this clause must be present in infant formula product for special dietary use at the minimum level specified in column 2 of the Table, subject to subclause 3 and 4.

Table to clause 32

Column 1	Column 2
L-Amino Acid	**Min amount per 100 kJ**
Histidine	12 mg
Isoleucine	21 mg
Leucine	42 mg
Lysine	30 mg
Cysteine & Methionine	19 mg
Phenylalanine & Tyrosine	32 mg
Threonine	19 mg
Tryptophan	7 mg
Valine	25 mg

(3) Infant formula product for specific dietary use based upon protein substitutes must provide no less than -

(a) 6 mg cysteine per 100 kJ; and

(b) 17 mg phenylalanine per 100 kJ.

(4) L-amino acids listed in the Table to this clause must be added to infant formula product for specific dietary use base upon protein substitutes only in an amount necessary to improve protein quality.

33 Vitamins and minerals

An infant formula product for specific dietary use based upon protein substitutes must contain -

(a) chromium in an amount of no less than 0.35 μg per 100 kJ and no more than 2.0 μg per 100 kJ; and

(b) molybdenum in an amount of no less than 0.36 μg per 100 kJ and no more than 3.0 μg per 100 kJ.

Editorial note:

The provisions of clause 24 of this Standard also apply in respect of the vitamins and minerals permitted in an infant formula product for specific dietary use based upon protein substitutes.

34 Additional permitted triglycerides

An infant formula product for specific dietary use based upon protein substitutes may contain added medium chain triglycerides.

SCHEDULE 1

PERMITTED FORMS OF VITAMINS AND MINERALS IN INFANT FORMULA PRODUCTS

Column 1 **Vitamins or minerals**	**Column 2** **Permitted Forms**
Vitamin A	Retinol Forms vitamin A (retinol) vitamin A acetate (retinyl acetate) vitamin A palmitate (retinyl palmitate) retinyl propionate Carotenoid Forms beta-carotene
Vitamin C	L-ascorbic acid L-ascorbyl palmitate calcium ascorbate potassium ascorbate sodium ascorbate
Vitamin D	vitamin D_2 (ergocalciferol) vitamin D_3 (cholecalciferol) vitamin D (cholecalciferol-cholesterol)
Thiamin	thiamin hydrochloride thiamin mononitrate
Riboflavin	riboflavin riboflavin-5'-phosphate, sodium
Niacin	niacinamide (nicotinamide)
Vitamin B_6	pyridoxine hydrochloride pyridoxine-5'-phosphate
Folate	folic acid
Pantothenic acid	calcium pantothenate Dexpanthenol

Vitamin B_{12}	Cyanocobalamin Hydroxocobalamin
Biotin	d-Biotin
Vitamin E	dl-α-tocopherol d-α-tocopherol concentrate tocopherols concentrate, mixed d-α-tocopheryl acetate dl-α-tocopheryl acetate d-α-tocopheryl acid succinate dl-α-tocopheryl succinate
Vitamin K	vitamin K_1, as phylloquinone (phytonadione) phytylmenoquinone
Calcium	calcium carbonate calcium chloride calcium citrate calcium gluconate calcium glycerophosphate calcium hydroxide calcium lactate calcium oxide calcium phosphate, dibasic calcium phosphate, monobasic calcium phosphate, tribasic calcium sulphate
Chloride	calcium chloride magnesium chloride potassium chloride sodium chloride
Chromium	chromium sulphate
Copper	copper gluconate cupric sulphate cupric citrate
Iodine	potassium iodate potassium iodide sodium iodide
Iron	ferric ammonium citrate ferric pyrophosphate ferrous citrate ferrous fumarate ferrous gluconate ferrous lactate ferrous succinate ferrous sulphate
Magnesium	magnesium carbonate magnesium chloride magnesium gluconate magnesium oxide magnesium phosphate, dibasic magnesium phosphate, tribasic magnesium sulphate
Manganese	manganese chloride manganese gluconate manganese sulphate manganese carbonate manganese citrate
Molybdenum	sodium molybdateVI dehydrate

Phosphorus	calcium glycerophosphate calcium phosphate, dibasic calcium phosphate, monobasic calcium phosphate, tribasic magnesium phosphate, dibasic potassium phosphate, dibasic potassium phosphate, monobasic potassium phosphate, tribasic sodium phosphate, dibasic sodium phosphate, monobasic sodium phosphate, tribasic
Potassium	potassium bicarbonate potassium carbonate potassium chloride potassium citrate potassium glycerophosphate potassium gluconate potassium hydroxide potassium phosphate, dibasic potassium phosphate, monobasic potassium phosphate, tribasic
Selenium	sodium selenite seleno methionine
Sodium	sodium bicarbonate sodium carbonate sodium chloride sodium chloride iodised sodium citrate sodium gluconate sodium hydroxide sodium iodide sodium lactate sodium phosphate, dibasic sodium phosphate, monobasic sodium phosphate, tribasic sodium sulphate sodium tartrate
Zinc	zinc acetate zinc chloride zinc gluconate zinc oxide zinc sulphate

GUIDELINES FOR INFANT FORMULA PRODUCTS

(These guidelines are not part of the legally binding Standard)

Guideline for maximum amount of vitamins and minerals in infant formula products

It is recommended that the quantities specified in the table below be observed as the maximum levels of vitamins and minerals in infant formula product.

Nutrient	Recommended maximum amount per 100 kJ
Vitamins	
Vitamin C	5.4 mg
Thiamin	48 µg
Riboflavin	86 µg
Preformed Niacin	480 µg
Folate	8.0 µg
Pantothenic acid	360 µg
Vitamin B_{12}	0.17 µg
Vitamin K	5.0 µg
Biotin	2.7 µg
Minerals	
Calcium	33 mg
Phosphorus	22 mg
Manganese	7.2 µg for infant formula products regulated by Division 3, Subdivision 2 only
Chromium	2.0 µg
Molybdenum	3 µg

Guideline on advice regarding additional vitamin and mineral supplementation

Manufacturers are recommended to provide an advice in the label on a package of infant formula product to the effect that consumption of vitamin or mineral preparations are not necessary.

Nutrition information table

The nutrition information contained in the label on a package of infant formula product is recommended in the following format -

NUTRITION INFORMATION

	Average amount per 100 mL made up formula *1	**Average amount per 100 g of powder (or per 100 mL for liquid concentrate)** *2
Energy	kJ	kJ
Protein	g	g
Fat	g	g
Carbohydrate	g	g
Vitamin A	µg	µg
Vitamin B_6	µg	µg
Vitamin B_{12}	µg	µg
Vitamin C	mg	mg
Vitamin D	µg	µg
Vitamin E	µg	µg

Vitamin K	µg	µg
Biotin	µg	µg
Niacin	mg	mg
Folate	µg	µg
Pantothenic acid	µg	µg
Riboflavin	µg	µg
Thiamin	µg	µg
Calcium	mg	mg
Copper	µg	µg
Iodine	µg	µg
Iron	mg	mg
Magnesium	mg	mg
Manganese	µg	µg
Phosphorus	mg	mg
Selenium	µg	µg
Zinc	mg	mg
Chloride	mg	mg
Potassium	mg	mg
Sodium	mg	mg
(insert any other nutritive substance to be declared)	g, mg, µg	g, mg, µg

***1** – Delete the words 'made up formula' in the case of formulas sold in 'ready to drink' form.
***2** – Delete this column in the case of formulas sold in 'ready to drink' form.

Note: The information in column 2 is not mandatory.

[5] *omitting from the* Table of Contents *of Volume 2 the following –*

Standard 2.9.1 Reserved (Infant Formula Products)

substituting –

Standard 2.9.1 Infant Formula Products

ATTACHMENT 6

PROPOSAL P93 – REVIEW OF INFANT FORMULA

SUMMARY OF ISSUES RAISED IN A SUBMISSION FROM THE INFANT FORMULA MANUFACTURERS' ASSOCIATION OF AUSTRALIA (IFMAA) AND THE NEW ZEALAND INFANT FORMULA MARKETERS' ASSOCIATION (NZIFMA) FOLLOWING INQUIRY (NOV 1999).

Issue	Details
The definition of follow-on formula	Industry disagreed with the use of the term "breast milk substitute" within the definition for a follow-on formula. It was believed that this term misrepresented the intended purpose of follow-on formula, and that such products should be considered as a significant part of an infant's diet but not as a "substitute".
The units of measure for expressing amino acid composition	Industry requested that the proposed units of g/100g of protein be reverted to mg/100kJ as previously contained in Standard R7 of Volume 1. This position was taken on the basis that the majority of infant formula products would fail to comply with amino acid units expressed as g/100g of protein, and that the resulting levels were more restrictive than international requirements (draft Codex and European Union infant formula standards).
The proposed minimum level of cysteine (2.45g/100g protein)	Industry disagreed with the level of cysteine proposed for the draft standard. Industry's position was that protein levels in infant formula were higher than human milk, and this ensured the adequate provision of cysteine. Adding cysteine to infant formula as a means of meeting the proposed level was not considered feasible by Industry, who indicated that this would increase the sulphur content of the product, would significantly increase the cost of infant formula, and make the products foul tasting. When Industry raised this issue with ANZFA, it was requested that no distinct value for cysteine be provided in Standard 2.9.1 (see the issue of separate cysteine values). It should however be noted that Industry also requested the entire amino acid profile for infant formula be changed to the profile specified by the European Commission (EC) Directive (91/321/EEC) on infant formula (see below). This would therefore require a minimum cysteine content of 1.3g/100g of protein, a value that ANZFA referred to when minimum cysteine levels were discussed with Industry.
Provision of separate minimum values for cysteine and methionine	Industry disputed the requirement for an independent value of cysteine based on the position that a significant level of cysteine is only necessary for premature infants. It was proposed that amino acid requirements for non-premature infant formula have cysteine values summed with those for methionine.

Issue	Details
The minimum values of amino acids	Industry disagreed with the proposed amino acid profile specified in the Table to Clause 6. Industry raised particular concerns over the requirements for cysteine (see above), histidine, phenylalanine, tryptophan and tyrosine. Industry stated that the products on the market would not comply with these minimum levels, and that infant formula already had a history of promoting normal infant growth and development. They proposed that the amino acid requirements specified in the European Commission Directive for infant formula (91/321/EEC) be used in Standard 2.9.1.
The maximum level for locust bean gum permitted for addition to infant formula	Industry requested that locust bean gum be allowed in levels up to 1.0g/100mL of infant formula as opposed to the maximum level of 0.1g/100mL as stated in the draft standard. This increase was to accommodate the use in thickened infant formula (promoted as anti-reflux formula). The supporting argument cited the European Union Scientific Committee on Food's recommendation for a maximum level of 1.0g/100mL as a justification for the increase from 0.1g/100mL.
Required warning on infant formula labels	Industry disagreed with the mandatory warning *'…Inappropriate use or preparation [of infant formula] can make your baby very ill'*. Industry requested that "inappropriate" be replaced with "incorrect" and that the term "very ill" should be removed as it was an ambiguous and alarmist statement.
Required statement on infant formula labels	Industry requested that the required labelling statement indicating infants over the age of 6 months should receive foods in addition to the infant formula product is unnecessary as it reiterates common knowledge and crowds available space on labels.
Print and package size	The November 1999 draft of Standard 2.9.1 required that infant formula products with a net weight greater than 450g were to print statements on their labels in a minimum type of 3mm. Industry argued that this should be increased to 1kg as this type size was deemed too large for the common 900g and 454g cans that were available on the market.
Declaration of nutrition information - values per 100g	Industry requested that the requirement for a "per 100g" column of the nutrition information panel be removed. This request was made on the basis that such information crowded a label, would confuse general consumers, and was only necessary for health professional use, which is met by other means.
Permission for an "added iron" claim.	Industry requested that the permission of an "added iron" claim be allowed on the label of infant formula as a public health measure (addressing infant iron deficiency).

Issue	Details
Prohibited representations; Anti-reflux formula	Industry requested that the prohibition on claims relating to particular conditions, diseases or disorders should be restricted to a prohibition on disease states only. The supporting argument stated that consumers would benefit from knowing the health condition for which an infant formula product was promoted. This request was made in relation to thickened formula providing a benefit to reflux conditions.
Fat Content - Alpha Linolenic Acid (ALA) requirements	Industry proposed to reduce the required level of ALA from 1.75% of total fat to 12mg/100kJ (using proposed units of expression – see below). Industry's supporting argument was that reduction to 12mg/100kJ of ALA was safe as supported by the Lucas[1] study and Makrides[2] report.
Fat Content – ratio of n-3 to n-6 long chain fatty acids	Industry requested that the ratio specified for n-3 to n-6 long chain polyunsaturated fatty acids (LCPUFA) be removed from the standard. The supporting argument was that research had indicated that infants required docosahexanoic acid (DHA), a n-3 LCPUFA, for effective growth and development, but it was Industry's view that the same could not be said for arachidonic acid (ARA), a n-6 LCPUFA. No other international infant formula standards specified such a ratio, and therefore Industry did not consider that its inclusion was justified.
Fat Content - units of expression	Industry proposed to have ALA expressed as mg/100kJ instead of being expressed as a proportion of total fat. The basis for this argument was that the draft Codex Alimentarius Standard contained values expressed in this format.
Maximum phosphorus composition requirements	Industry requested that the maximum permitted phosphorus content be increased from 25mg/100kJ to 40mg/100kJ. This increase was requested due to the increase in protein limits of 0.43g/100kJ to 1.3g/100kJ for follow-on formula. Industry indicated that the typical phosphorus content of cow's milk was 28mg/100g protein, and therefore any follow-on formula based on cow's milk with a protein level above 0.9g/100kJ would fail to comply with a 25mg/100kJ restriction.
Minimum iron composition requirements	Industry requested that the minimum requirements for iron content be lowered from 0.2mg/100kJ to 0.12mg/100kJ. The supporting argument for this position was that the draft Codex Alimentarius Standard on Infant Formula had proposed a minimum iron content of 0.12mg/100kJ.

[1] Lucas A, Stafford M, Morley R et al. *Efficacy and safety of long chain polyunsaturated fatty acids supplementation of infant formula milk: a randomised trial.* The Lancet 1999; 345: p1948-54.
[2] Makrides M, Bryan D, Paine B, Gibson R (2000) *Review of amino acid profiles, zinc to copper ration and essential fatty acid composition of infant formulas.* A Report to the Infant Formula Manufacturers' Association of Australia.

Issue	Details
Zinc to copper ratio	Industry proposed that the upper limit on the ratio of zinc to copper for infant formula be raised from 12:1 to 20:1. Industry stated that studies have indicated a ratio up to 25:1 as being safe; Codex Alimentarius, European and United States infant formula standards do not specify a zinc to copper ratio; the 12:1 ratio was based on an extreme dietary modelling process; and that significant reformulation of infant formula would need to occur to meet a ratio of 12:1.
Special Purpose Infant Formula	Industry indicated that the majority of infant formula for pre-term and rare medical conditions did not comply with the proposed regulation of these products. A request was therefore made to ANZFA to consider an exemption of such products from composition, labelling and health claim requirements due to their specialised use and method of purchase.
Chromium and molybdenum provisions	Industry noted that chromium and molybdenum were permitted for addition to special purpose infant formula, but not for standard formula. It was therefore requested that Standard 2.9.1 provide a provision for standard infant formula that permitted the voluntary addition of these minerals as listed for special purpose formula (up to 0.35 g/100kJ for chromium and up to 0.36 g/100kJ for molybdenum).
General Microbiological Requirements	Industry indicated that the proposed Standard Plate Count (SPC) for *Bacillus Cereus* was more restrictive than that stated in Standard R7 of Volume 1. Therefore Industry proposed that the requirements stated in the draft Standard should revert back to such levels.
Innovation Clause	Industry tabled a request for a new clause to be added to the standard to the effect that nutritive substances may be added to infant formula to the levels found in human milk. Industry claim the usual ANZFA application process to vary a standard is unacceptable because this would then be assessed in the public domain and this removes any exclusivity rights to the company that has made a significant resource investment.

ATTACHMENT 7

PROPOSAL P93 – REVIEW OF INFANT FORMULA

SUMMARY OF SUBMISSIONS TO PRELIMINARY INQUIRY (MAY 1999)

List of Submitters

Fifty-eight Submissions were received in response to the Preliminary Inquiry Report of P93, including consumer, public health and food industry representations. The names of submitters are listed below.

Abbott Australasia Pty Ltd
Abbott Laboratories (NZ) Ltd
Advisory Panel on the Marketing in Australia of Infant Formula (APMAIF)
Attwood, Elaine
Australian College of Midwives Inc (Victoria) and Baby Friendly Hospital Initiative (Victoria)
Bowman, Diane
Bristol-Myers Squibb Australia Pty Ltd
Compston, Fiona
Consulchem Pty Ltd
Consumer Food Network of the Consumers Federation of Australia
Dairy Goat Co-operative (NZ) Ltd
Daniels, Dr Lynne, Flinders Medical Centre, Centre for Perinatal Medicine
Department of Nutrition and Dietetics and the James Fairfax Institute of Paediatric Clinical Nutrition
Dunstone, Mark and Smith, Julie
Embassy of the United States of America, Office of the Agricultural Counselor
Food Technology Association of Western Australia Inc.
Food Technology Association of Victoria Inc
Freyer, A G
Gastric Reflux Association for Support of Parents/Babies
Gibson, Robert A, Director, Child Nutrition Research Centre and Makrides, Maria, Research Dietitian and NHMRC Fellow
Glare, Barbara
Guy, Camille
Home Economics Institute of Australia Inc
InforMed Systems Ltd
Institute of Environmental Science and Research Ltd, New Zealand
International Baby Food Action Network (IBFAN)
International Formula Council (IFC)
James, R F
James, Valerie
Kamerman, Marg
Killalea, Dr Sheila and Mc Neil, Dr John, Department of Epidemiology and Preventive Medicine, Monash University
Kingett Mitchell and Associates Ltd
La Leche League NZ for Breastfeeding Supports and Information
La Roche, Patricia
Ministry of Agriculture, Fisheries and Food (MAFF), UK
Marsh, Raeura

McIntyre, Gail
McVeagh, Patricia, Consultant Paediatrician
Minchin, Maureen, IBCLC
National Council of Women of New Zealand
Nestlé Australia Ltd
New Zealand Dairy Board
New Zealand Ministry of Health
Nursing Mothers' Association of Australia
NZ Dairy Marketing and Customer Services
NZ Infant Formula Marketers' Association
Royal Australasian College of Physicians - Division of Paediatrics
Royal New Zealand Plunket Society Inc
Safetywize Consultants
Simmer, Karen, Neonatologist and Associate Professor
Soy Information Network
Toth, Peter
Toth, Susan
Tudehope, Dr David, Director Division of Neonatology, Mater Hospital
Parnell, W, University of Otago, Human Nutrition Department
Victorian Food Safety Council Food Standards Sub-Committee
Western Australian Food Advisory Committee
Wyeth Australia Pty Ltd

General Comments

Submitter	Comments
NZ Infant Formula Marketers' Association	- recognises that breast-feeding during the first four to six months of life is the best way to ensure good health and development of babies - where the mother does not breast-feed, or when breast-milk alone is insufficient to meet all the baby's nutritional needs, access to safe alternative foods is essential - health authorities and infant food manufacturers have responsibility to provide balanced, factual and objective information about benefits of breast-feeding and proper use of infant formula and appropriate weaning foods when needed - states infant formula cannot replicate all the qualities of breast-milk - states it is important to note that many substitutes for breast milk are totally unsuitable and often dangerous (e.g. raw milk, gruels made from rice, cassava etc.) - committed to the development and implementation of appropriate infant nutrition policies based on the principles and aims of the WHO Code of Marketing of Breast-Milk Substitutes - proposal lacks balance: there is no commentary on the contra-indications of breast-feeding, after an infant reaches 6 months of age, and the benefits of complementary feeding ignored - findings concentrate on well-meaning desire for breast-feeding to be maintained during the first 12 months; totally silent on needs of 40% mothers who are not breastfeeding after 6 months - concerned about the negative impact the proposed standard may have on some members of the NZ health sector, which would impact on the NZ Ministry of Health's ability to effectively monitor the NZ Interpretation of the WHO Code
Marg Kamerman	- believes the dangers of feeding babies with artificial milk are not publicised enough - parents are not given enough information to make an informed choice regarding whether to breast-feed or not - suggests infant formula be available via prescription only - suggests WHO Code on the Marketing of Breast Milk Substitutes written into standard on infant formula - suggests women who choose not to breast-feed tend to have less education, and do not seek relevant information before making a choice - believes multi-national companies selling infant formula have huge influence and "can apply pressure and bend the rules"
Karen Simmer, Neonatologist and Associate Professor	- overall, thinks report is sound - issues a plea for ANZFA not to weaken standards further in response to pressure from industry
InforMed Systems Ltd	- concerned that standard is extremely prescriptive, significantly more so than current Codex draft revision - serious danger that standard will become outdated and require amendment
International Formula Council	- pleased to note several proposed changes to earlier drafts, which were overly restrictive and not supported by the scientific literature, were not adopted

Dairy Goat Co-Operative (NZ) Ltd	- goat milk follow-on formula will need to be significantly reformulated to comply -accept the rationale for the majority of the formulation modifications - seek a lead-in time of two years instead of the proposed 12 months to allow for product reformulation, trial production(s), and stability trials.
Consumer Food Network of the Consumers Federation of Australia	- standard needs to be considered in the light of overwhelming evidence that formula feeding of infants poses a serious risk to the health of both the infants and their mothers - infants who are formula fed are at significantly greater risk that infants who are breast fed of suffering many health conditions including infectious diseases, hypernatremic dehydration, neonatal hypocalcaemic tetany and cardiopulmonary disturbances in the neonatal period, sudden infant death syndrome, allergies and chronic diseases in later life. - estimated in USA for every 1000 babies, 4 die because they are fed artificial formula (references provided) - it is likely that similar death rates from the use formula occur in Australia, which means that hundreds of babies could be dying each year as a result of formula feeding - mothers who artificially feed rather than breast-feed their infants are at increased risk of contracting pre-menopausal breast cancer, osteoporosis, cervical cancer and ovarian cancer - proposal gives approval to a number of potentially unsafe ingredients in infant formula - proposal weakens current labelling provisions - would continue to allow unethical promotion of infant formula - does not provide sufficient warning to mothers of the deleterious effects of formula feeding on the health of both infants and mothers - concerned to read in proposal that ingredients have been added to infant formula "without rigorous, objective safety assessments, which are required for other food ingredients" - urges that no untested ingredients be permitted in infant formula - where uncertainty, or varying views, on safety of an ingredient, that it not be allowed to be included in infant formula - rigorous requirements for assessing the purity of ingredients be included in the standard
Elaine Attwood	- supports Consumer Food Network submission
Victorian Food Safety Council Food Standards Sub-Committee	- supports option 2. - there are no specific provision for MRLs for pesticide residues in infant formula - only source of assurance is from Total Dietary Surveys which are limited in the range of samples analysed - the potential for endocrine disruption from pesticide residues should be assessed before a decision about pesticide MRLs in infant formula is finalised

Nestlé Australia Ltd	- has always stated that breast-feeding is the best form of nutrition for babies, however it also believes (like the WHO) that there is a place for infant formula as the best alternative for those babies who cannot be breast-fed - supports AFGC submission - supports review, particularly where it accounts for updating the standard with respect to harmonising internationally and current scientific knowledge - extremely concerned that some current infant formula products could become illegal products under the proposed standard - states ANZFA has chosen not to harmonise with international regulations in some areas and have not properly justified this against the objectives in section 10 of the ANZFA Act - this will have a major cost impact on Nestlé due to the necessity for monitoring the raw materials in use, more extensive testing of products, increased inventory to allow for the appropriate testing regime, and also the cost of clinical trials - main areas of concern: * any formula that is manufactured to comply with an international regulation would be illegal within Australia or New Zealand * products that are manufactured as speciality products in an overseas manufacturing facility for global distribution would not comply with this draft standard * specific regulation of pre-term formula will create difficulties for current products. * some proposed labelling statements are not consistent with other legislation
Patricia McVeagh, Consultant Paediatrician	- as there is no medical indication for goat's milk, safe limits should not be adapted to accommodate goat milk based infant formula
Barbara Glare	- concerned that draft standard represents a weakening of the standards, and it is vital that they be strengthened
Food Technology Association of Western Australia Inc	- prefers option 2: to regulate using the proposed revised standard and codes of practice
Australian College of Midwives Inc (Victoria) and Baby Friendly Hospital Initiative (Victoria)	- widely accepted infant feeding practices have, over several generations, resulted in a common perception that artificial formula is standard or normal - strongly recommend that any statement of standards for infant formula made by ANZFA be consistent with the current standards which are recognised both in Australia and globally (WHO CoP, the Maternal and Infant Care Services Standard)
Fiona Compston	- opposes draft standard, as it appears to be a weakening of the old standard, which reflects industry objections to earlier proposals - breast milk is known to help reduce the risk of a range of cancers in both child and mother, it helps reduce gastro and ear infections in children, it helps foster a more self confident child, it is more environmentally friendly - breast milk can ultimately save the community millions of dollars in health costs each year - there are no requirements presently to warn consumers of the adverse health consequences of feeding babies formula - provided figures from the US illustrating the costs associated with formula feeding
Food Technology Association of Victoria Inc	- agree with regulatory option 2

International Baby Food Action Network (IBFAN)	- it is premature to finalise a standard on infant formula at this time because Codex is currently revising their standard on infant formula, and Codex is also drafting Working Principles of Risk Analysis
Embassy of the United States of America, Office of the Agricultural Counselor	- requests that the proposal be held in draft form for another round of comment, which would allow for more detailed and constructive comment - have not reviewed the risk assessment or other relevant data and information underpinning this proposal - the proposed standard has various inconsistencies with standards in other counties, that would likely result in unnecessary trade difficulties
Home Economics Institute of Australia Inc.	- expressed concern at the proposed inclusion of a very broad range of unfamiliar ingredients - urge that a precautionary approach be adopted and that substances that have no confirmed benefit not be permitted until further more specific information is provided by industry
Abbott Australasia Pty Ltd	- appreciates the amendments made to the standard to bring the document in line with international standards, namely Codex and European TSMP regulations - however, still many areas in which the proposed standard remains too restrictive - proposed standard would not enable Abbott to introduce any of its current infant formulas which are available overseas - it would remove from the market those current Abbott products which are imported fully finished into Aust and sold in very small volumes
National Council of Women New Zealand	- believes in using prescriptive regulations. However, advise that care must be taken not to hinder any future development of infant formulas.
Bristol Myers Squibb Australia Pty Ltd	-strongly disagree with many points arising from the draft. -products would need to be removed from the market and reformulation would be required if the standard were adopted. -the draft is more prescriptive and lengthy- some of the requirements are not required elsewhere in the world. -implies that the present standard does not result in products that provide adequate nutrition for growth and development of the infant. - a food standard should include prescriptive conditions only where these are shown to be necessary, such as to ensure appropriate nutrient levels. - the inclusion of sections for pre-term formula, infant formula for metabolic and immunological conditions, aluminium, fluoride and infant formula based upon protein substitutes do not reflect the Codex or EC standards for infant formula. - to require reformulation of a product - evidence must be supported e.g. that infants are actually suffering harm at present or are in a position of real harm. - the standard for infant formula is not the appropriate place to include specifications for any particular ingredient. It purity specifications are required, they should be included in the food additives standards and be cross referenced.

Nursing Mothers' Association of Australia	- the safety, or otherwise, of formula ingredients, both proposed and current, needs to be established. - regulatory impact analysis needs to consider the effect of increased breastfeeding rates. - if regulatory standards cannot provide sufficient protection then changes to the regulatory system should be made in order that they do so. - international standards should not be used as justification for any practices in the composition, products, distribution or sale of formula that can adversely affect the health and safety of Australian infants. - submission contains conference papers from the Nursing Mothers' Association Australia's Conference (October 23-25 1997).
Mark Dunstone and Julie Smith	- the objectives set out in the issues paper for the proposed standard are not the same as those required by the legislation. The statutory objectives relating to promotion of trade and commerce do NOT provide any latitude to ANZFA to pursue the objective of "not unnecessarily hindering innovation in the infant formula industry". - promotion trade and commerce do not, even by implication, include innovation. As infants consume a fixed quantity of milk, innovation will not increase trade or commerce, and therefore innovation would not promote trade or commerce. - innovation amounts to uncontrolled experimentation on infants without informed consent. It may risk infant health. The proposed Standard is contrary to legislation because the proposed standard's requirements on "novel ingredients", "innovation" and "soy" milk place a higher priority on industry interests than on minimising adverse public health and safety risks. - the statement on page 4 - "The Preliminary Inquiry concludes that a food standard for infant formulas which protects the health and safety of infants who are routinely fed substitutes for human milk is necessary"- does not aim to discourage the routine (or even ad-hoc) feeding of infants with artificial formula. - there is evidence that infants fed artificial formula or animal milk suffer increased risks of mortality and morbidity, including in developed countries such as Australia. These adverse outcomes are from improper use of formula (i.e. mixing, using unclean water) but also when formula is used as directed.
Royal New Zealand Plunket Society Inc	- supports a revision to ensure health and safety of formula fed infants and to overcome barriers to trade. -are concerned with the prescriptive approach proposed. State that the proposed approach would hinder the addition, revision or deletion of individual ingredients necessary to reflect current scientific knowledge. - suggest an approach where manufacturers must conform with a NZ Standard which is consistent with Codex requirements e.g. in terms of permitted quantities, ingredients, safety, special needs etc. -believe self-regulation by industry is important. -compliance with the standard should be mandatory because of the importance of infant formula as a principal source of nourishment.

Parnell, W, Department of Human Nutrition, University of Otago	-it is never possible to harmonise with several international standards which are themselves inconsistent. Suggests that ANZFA follow Codex (or USA or European standards). - does not believe that the prescriptive standards will reduce costs to government. --questioned whether any infant formula manufacturers, in a highly competitive environment, are marketing an unsatisfactory product, i.e. a product with an inappropriate nutrient profile or a product not microbiologically safe or with undesirable contaminant levels?
Maureen Minchin. IBCLC	-expressed a number of serious concerns in relation to the consultation process undertaken by ANZFA (see submission). - this Proposal is to protect infant health. Therefore it needs to be far more stringent scientifically. -the current proposal cannot ensure the health and safety is protected and that carers have adequate information about infant formula to enable them to make informed choices in feeding their infant. - believe that infants that are not breastfed are at greater risk from a wider range of diseases and disorders, in infancy and adulthood. -states that ANZFA has produced a standard that; * creates a basic assumption of "safe until proven unsafe" as the basis for ingredients. The more conservative approach would be to require proof of safety, and so ensure that industry funds dedicated long-term studies that limit the risk of harm, from whole populations worldwide to study participants; * creates no additional costs for greater quality control or as saving to protect infant health(not even $1300 to reduce aluminium risks) for an industry which spends billions on advertising a product with an enormous profit margin; * allows every formula currently on the market to be left there until it is re-formulated at industry's convenience. * allows any formula made anywhere in the world by the major companies to be imported into Australia under threat of WHO sanctions, by "accommodating all known market levels". * allows industry to keep publishing misleading information on labels rather than including the detailed information that would assist in educating about infant formula risk, and put s responsibility for such education on to health professionals despite the evidence that almost all health workers are never adequately educated about such risks; * sets in place no provision for regular assays of product or other monitoring of industry's compliance with the new standard. - suggests a number of changes to strengthen the standard (see suggested changes under separate issues in summary of submissions).
Wyeth Australia Pty Ltd	- do not believe that ANZFA's objectives have been adhered to in the development of the standard because: * stipulating nutritional composition is overly prescriptive; * a risk based assessment is not used to determine the prescribed composition of infant formula; * many levels of nutrients are not harmonised with international standards' * information is confusing and not easily disseminated to carers. - any change to the standard needs to be risk based. - suggest urgent discussions with industry are required. - the current draft of the standard may contravene the WTO requirements to allow products that are safe.

La Leche League NZ for Breastfeeding Supports and Information	- urges including the strongest possible protection for breastfeeding when considering a standard for infant formula
MAFF UK	- EU Directive sets a maximum limit of 0.01 mg/kg for individual pesticides in infant formula and follow-on formula, and prohibits the use of more toxic pesticides in the agricultural products intended for their manufacture

Issue: Composition of Infant Formulae

Submitter	Comments
New Zealand Dairy Board	- believe that probiotics (oligosaccharides) are significant components of human milk and have a number of benefits, so their inclusion in infant formula could be beneficial
Nursing Mothers' Association of Australia	- any foods produced using gene technology should be labelled as such to allow mothers to make an informed choice for infant feeding - the safety of the ingredients needs to be established - if safety is not established product information should carry an easily visible and easily understood message warning that the ingredient is experimental and side effects have not yet been determined

Issue: Use of Novel Ingredients In Infant Formula

Submitter	Comments
Nestle Australia Ltd	- does not agree with proposal - suggests ANZFA also needs to accept a history of use overseas - if Aust/NZ is retained, then ANZFA needs to ensure that there is a minimal approval time for a novel ingredient, which should be a maximum of 3 months; expect ANZFA to accept data sourced from overseas as part of an application
Australian College of Midwives Inc (Victoria) and Baby Friendly Hospital Initiative (Victoria) and Fiona Compston	- proposed acceptance of untested 'novel' ingredients, including LCPUFAs, is too lax - any artificial formula sold with 'novel ingredients' should carry large warning messages that the ingredient is experimental, and the appropriate consent arrangements be put in place for its use, consistent with other medical clinical trials in humans
Mark Dunstone and Julie Smith	- experimentation and innovation should not be allowed by the Standard - unlike older children and adults, babies are not normally exposed to other foods - allowing the inclusion of "novel ingredients" on the basis of a history of safe consumption of similar food by adults or older children is unsatisfactory - such experiments should be conducted under appropriate, designed, approved and supervised clinical trials with the informed consent of the parties involved
Bristol Myers Squibb Australia Pty Ltd	- if a substance is classed as a food then it is suitable for use in a food. If this food is widely used elsewhere in the world, in the same or similar applications, there needs to be a strong argument put forward why it cannot be used in Australia - as we are signatories to world trade agreements and trade in a global marketplace, Australia cannot arbitrarily impose isolationist restrictions.

Wyeth Australia Pty Ltd	- novel nutrients are often identified initially as components of breast milk and then investigated for clinical benefit through clinical appraisal for addition to infant formula. The safety of such nutrients should not be unfairly constrained by the safety standards that apply for novel food additives - novel nutrients are added for nutritional benefit, therefore, a 100 or even 10 fold no-observed effect level (NOEL) cannot be applied to nutrients in assessing novel safety - safety assessments of novel nutrients must be made at human milk levels (with average for manufacturing)
Winsome Parnell, Department of Human Nutrition, University of Otago	- would not discount retaining a variation of Option 1 i.e. retaining a general recommendation such as Regulation 242 in the New Zealand Food Regulations 1984, with any necessary generic prohibitions such as on novel ingredients, not safety tested.

Issue: Lactic Acid Cultures

Submitter	Comments
Nestlé Australia Ltd	- supports permission to add L(+) producing lactic acid cultures to infant formula; in line with Codex

Issue: Addition of Nucleotides to Infant Formula

Submitter	Comments
Maureen Minchin IBCLC	- synthetic analogues of 5 of the 13 nucleotides in breast milk are already in infant formula in Australia, despite the fact that this breaches existing law - parents are mislead into believing "marine oils" come from healthy fish, not algae. considerable consumer resistance could be expected to a product manufactured by these organisms. - proof of benefit to infants, and absence of longer term harm in childhood, must be demonstrated before widespread use of novel products in infant formula - it is a decade since Bristol Myers warned that nucleotides might hyper-stimulate the immune system and lead to greater rates of allergic disease. Not a single study has evaluated this possibility - misleading advertising campaigns e.g. in the UK which implied that now "immune factors" were added to formula and had "bridged the gap" with breast milk must be prevented. This must be prevented to ensure breastfeeding rates are not affected. ANZFA needs to provide for national penalties and corrective advertising
New Zealand Dairy Board	- agree that it is appropriate that specifications are included in the joint standard - nucleotides are found in human milk and there are many suggested benefits - recommends levels as per breast milk

Abbott Australasia Pty Ltd	- proposes following changes to nucleotide levels (in mg/100 kJ): cytidine 5'-monophosphate 1.56 uridine 5'-monophosphate 0.89 adenosine 5'-monophosphate 0.72 guanosine 5'-monophosphate 0.84 inosine 5-monophosphate 0.24 - proposed levels are based on Abbott research (included in submission) and are in alignment with current literature (additional information included on nucleotide production and toxicological data on nucleotides, plus relevant published information on nucleotides)
Wyeth Australia Pty Ltd	- provided specifications for 5 nucleotides for the preliminary inquiry. - recognise that the moisture specification and bacteriological profile may be redundant, as they are included in the finished product specifications - Division 5 - General Microbiological Requirements.
Bristol Myers Squibb Australia Pty Ltd	- the standard for infant formula is not the appropriate place to include specifications for any particular ingredient. This applies to nucleotides as much as any other ingredient. If purity specifications are required, they should be included in the food additives standard and be cross-referenced.
Nursing Mothers' Association of Australia	- the safety of specific nucleotides and other ingredients needs to be established. If not, the product should carry an easily visible and easily understood message warning that the ingredient is experimental and the side effects have not yet been determined.
Abbot Laboratories (NZ) Ltd	- believes the nucleotide levels in Standard R7 are too low and proposes to increase the maximum permitted nucleotide levels (see submission for levels). - the proposed levels are based on Abbott research and are in alignment with current literature (attaches a report from LSRO). States that science has evolved considerably with respect to the analysis of nucleotides and that past analytical techniques have greatly underestimated nucleotide levels in human milk. - products containing the proposed higher nucleotide levels are available elsewhere in the world (excluding the EU, Singapore, Malaysia and New Zealand). - currently international trade in infant formulas is limited to New Zealand and Australia by the maximum nucleotide limits. Applaud the inclusion of the current EC limits for the compounds but recommend flexibility to allow alignment with international limits. Without such flexibility the international trade in infant formulas will remain restricted.

Issue: Cadmium and Lead

Submitter	Comments
Maureen Minchin, IBCLC	- questioned whether the 1989 studies of Canadian and Belgian infant formula revealed levels of cadmium that were of concern. Pointed out that the fact that raw materials are low in cadmium does not mean there is no risk of high cadmium levels in a heavily processed product - welcomes the restriction on lead. It is strange that cadmium, which is also widespread in the modern environment, is cumulative in bodies and has long-term irreversible effects is not also restricted

Issue: Lactose Free

Submitter	Comments
Abbott Australasia Pty Ltd	- current testing methodologies do not possess a detection limit of zero for lactose, therefore the requirement for any formula deemed to be 'lactose free' to not contain any detectable lactose is queried

Issue: Protein

Submitter	Comments
Nestlé Australia Ltd	- protein level set at 0.45 mg/100 kJ. Codex level is 0.43 mg/100 kJ - Codex level should be adopted to ensure a harmonised approach - declaration of source of protein appears to be overly prescriptive, particularly when manufacturers include the ingredients in the ingredient statement (discusses in detail, cow's milk vs. other sources, Fair Trading laws, Proposal P156 Naming of Foods, etc.) - objects to placing maximum levels for some nutrients even where the nutrient is not added (natural components of milk-based products contain choline and carnitine) - seasonal variation would render some Nestlé products illegal at certain times each year (graphs included to support claim), including products containing whey powder - it is impossible to formulate within these levels (detail on process included)
Infant Formula Council	- concerned that caline content in the reference amino acid composition of human milk is much higher than the reference cited by the EU (4.5g/100 g of protein) - suggest that 4.5g/100 g protein is more accurate
Dairy Goat Co-operative (NZ) Ltd	- goats milk infant formula and follow-on formula will be required to be supplemented with at least two amino acids (tryptophan and cystine) - levels stated are not consistent with EU directive in that the concentrations of methionine and cystine can not be added together in the proposal. Adoption of EC directive protein quality requirements would mean there would be no requirement to add cystine to these products - strongly opposed to amino acid fortification of goat milk infant formula and follow-on products - no evidence to suggest that protein quality of these products is inadequate - concerned about additional risks that can be associated with amino acid fortification (enclosed information on L-tryptophan) - suggests that protein quality requirements be included in the final standard, but that products that use unmodified cow or goat milk protein be excluded from meeting these requirements - if amino acid fortification is required, a minimum lead-in time of two years is sought (three being preferable), as sources need to be found, suitable modes of addition developed, impact on product flavour and stability investigated (in this context, shelf-life of these products is currently three years)

Maureen Minchin IBCLC	- Questioned whether ANZFA was aware of the research that indicates that the standard but excessive protein content of infant formula and its unphysiological amino acid patterns is linked with brain deficits. - indicated that there is evidence that autism is related to casein intolerance. - expressed concern about parents giving their infants (under 6 months of age) follow on formula (which is often cheaper), particularly when the protein level is almost double that meant for this age group. Questions whether anyone will monitor RSLs of infant formula independently or whether industry will do this. - ANZFA needs an intensive education campaign addressing the changes to the infant formula standard and particularly pre-term formula. - believes that ANZFA has legal duty of care to state on the can: "This product contains a level of protein that can be dangerous to infant bowel, kidney and brain. Medical monitoring of infants using this product is essential".

Issue: Levels of Total Fat in Infant Formula

Submitter	Comments
International Formula Council	- endorse proposed expanded fat range of 1.05 - 1.5 g/100 kJ
Abbott Australasia Pty Ltd	- question the rationale for the very narrow fat range (1.05 – 1.5 g/100 kJ) allowed for infant formula - there is extensive, on-going research, as well as controversy regarding fats in infant formulas - unnecessary restrictions on fat levels and sources of fat for infant formulas could prevent significant progress in infant nutrition - would like to propose a minimum level of 0.8 g/100 kJ which is the level stated by Codex and the EC for follow-on formula
Dairy Goat Co-Operative (NZ) Ltd	- to meet the ALA requirements, fat blend will need to be reformulated

Issue: Addition of Long Chain Polyunsaturated Fatty Acids to Infant Formula

Submitter	Comments
Western Australian Food Advisory Committee	- it is recommended that the proposed standard be adopted, with the amendment that the Codes of Practice be adopted by reference (i.e. become mandatory)

InforMed Systems Ltd	- it is true evidence for benefit for LCPUFAs is not yet conclusive, but more recent studies are increasingly persuasive - arachidonic acid produced by fermentation technology from single-cell sources has been approved in major overseas jurisdictions and levels resemble those in human milk. Can see no justification for further restrictions on their use - while there may be evidence that ARA:DHA ratio in human milk is roughly 2:1; it would be extremely improbable on biological grounds that such a ratio would be so precisely fixed - requiring such a precise ratio is technologically infeasible. If a definition is required, it should include 'roughly' or 'approximately' - it seems unlikely that a manufacturer would deliberately use a ratio markedly divergent from this value because of the use of human milk patterns as a model - table values are puzzling; the predominant VLC omega-6 acid is arachidonic acid, so setting a value of 2% but only 1% for ARA seems illogical - recommends entry for ARA be deleted - although reports (Koletzko in Germany) reported values of ARA and DHA well under 1%, in more primitive circumstances values for ARA over 1% have been recorded - recommends option 2 be adopted with the deletion of the line on ARA
Nestlé Australia Ltd	- no good scientific data showing benefits of addition of LCPUFAs to follow-on formula and the scientific data is still being evaluated with respect to starter formulas - EU directive does not permit addition of LCPUFAs to follow-on formula and this permission should be deleted for follow on formula - acknowledged that there is a provision for these to be added into infant formula within the EU Directive - option 3 (ratio requirement 2:1 for total long chain n-6 to total long chain n-3 for C≥20) is extremely prescriptive requirement; variation in the natural sources of LCPUFAs and the errors involved with analysis will make this requirement extremely difficult to attain (data supplied) - this provision would constitute a barrier to trade
Patricia McVeagh, Consultant Paediatrician	- option 3 is preferable - should recall there are a number of PUFA in human milk and that they share the same desaturase enzyme - we have learnt the hazards of adding only one PUFA
New Zealand Dairy Board	- agree that the preferred option is option 3 - agree that there needs to be some suitable purity specifications for LCPUFAs, which assure the safety of the LCPUFAs
Food Technology Association of Vic Inc	- agree with option 3 on general policy issues – LCPUFAs
Wyeth Australia Pty Ltd	- agree with option 3 to amend express permission proposed at full assessment "to align with the EC and UK but require a series 6 to series 3 ration of 2 as in human milk' - believe LCPUFAs in infant formula have demonstrated beneficial effects on early infant development
Nursing Mothers' Association of Australia	- concerned about unpurified constituents in infant formulas - particularly for the addition of LCPUFAs and nucleotides - the long term safety of all optional ingredients needs to be established by well designed trials before allowing them to be added to formula

Bristol-Myers Squibb Australia Pty Ltd	- acknowledge the addition of VLCPUFAs is contentious. BM indicate that it is the actual levels of two fatty acids, docosahexaenoic acid (DHA, 22:6 n-3) and arachidonic acid (AA 20:4 n-6) and the ratios of one to another - research indicates that dietary and geographical factors influence the levels and ratios of DHA to AA in human milk. Codex has not set a ratio level. It would be premature to set a fixed ratio on present evidence as they can be difficult to change at a later date - recommends that ANZFA include levels and ratios but that these are not prescribed in the standard.
Robert Gibson Director , Child Research Centre Maria Makrides Research Dietitian & NHMRC Fellow	- indicated there is no scientific basis for having one aspect of option 3 as the preferred option - indicated that the ratio of n-6:n-3 LCPUFAs in the breast milk of Australian and American mothers is currently about 2:1 but this is entirely a phenomenon of the current diet in these two countries. Examples given of how the ratio varies in different countries according to the diet of the mothers. - recommend that the Authority have the maximum levels of LCPUFA in formulas as shown in Option 3 (n-6 LCPUFA - max 2%; 20: 4n-6 - max 1%; n-3 LCPUFA - max 1%) but NO ratio IMPLIED for n-6:n-3 - oils containing n-3 LCPUFA should have a ratio of DHA to eicosapentaenoic acid (EPA) of at least 2 so that high EPA oils such as Maxepa are not used in infant formula - If the committee had reservations about this it could add the expression: "If n-3 LCPUFA are added to infant formula, n-6 PUFA should be added in such a way as to prevent a decline in the arachidonic acid (AA) status of the infant (as measured by plasma total fatty acid) below that of infant fed unsupplemented formula". In that way, manufacturers have the option of adding either AA itself or a precursor of AA in order to maintain plasma AA levels in the infant. - table to clause 30 is accepted without qualification - the suggestion that fats in formula for pre-term infants must comply with the fats in formula for term infants is not based on scientific evidence. There is little known about the fat requirement for term infants. EG the accretion rate of DHA of an infant in utero is such that the fats in the formula should contain at least 1% DHA and not the 0.25% in current pre-term formula. Therefore, it is incongruous to be basing the fat composition of formula for pre-term infants on the fats that are in breast milk of mothers who gave birth to term infants. It is clear that this model was totally inadequate for dietary protein, calcium, iron and many other nutrients for pre-term infants, and there just isn't the data available to be making these recommendations for the fats for pre-term infant.
Maureen Minchin IBCLC	- option 3 is the only option consistent with ANZFA's primary duty for care of infant health - ANZFA needs to work with APMAIF to restrict industry claims being made to suggest that LCPUFAs alone account for better cognitive development. There is no evidence to date of better cognitive development in term bottle-fed infants.

Issue: Use of Medium Chain Triglycerides in Infant Formula

Submitter	Comments
Karen Simmer, Neonatologist and Associate Professor	- to ban the addition of MCT to pre-term formula is not based on evidence
InforMed Systems	- if there is evidence that these substances are dangerous for pre-term infants they should be prohibited, otherwise the presence or absence should be left to the judgement of those using these special products - Codex does not having any restrictions on MCTs
NZ Dairy Marketing and Customer Services	- endorses recommendations of ANZFA's expert panel that MCT be present to a maximum of 10% total fatty acids in infant formula. However, do not agree that MCT from vegetable oils should not be permitted. An imposition of a maximum MCT content of 10% fatty acids would provide a practicable way of controlling the level of MCT in infant formula products without targeting the vegetable oil industry. The current MCT levels in vegetable oil blends used in infant formula range from less than 1% up to 8%. MCT is present in coconut oil which is used in many of the vegetable oil blends currently used in infant formula. It is also present, to a lesser extent, in other vegetable oils. - represents a barrier to trade
International Formula Council	- endorse decision to permit addition of MCT to specific dietary use formulas - remain concerned regarding the prohibition regarding the addition of MCTs to other formulas
Victorian Food Safety Council Food Standards Sub-Committee	- agrees that there have been no adequate long term studies on MCTs and these should be prohibited - it is not clear how this provision will provide for current formulas that contain added MCTs - since provision only provides for levels of MCTs naturally present the interim measure is supported
New Zealand Ministry of Health	- supports approach, particularly that evidence must be presented to ANZFA to show MCTs at currently used levels are safe and efficacious
Nestlé Australia Ltd	- disagree with prohibition on use of MCTs in formulas for healthy infants and for pre-term infants. This would make pre-term formula manufactured by Nestlé illegal - provided details of MCT content of their formulas and units sold in Australia and New Zealand - literature review on favourable effect of MCTs
Wyeth Australia Pty Ltd	- on the basis of risk assessment, there is no evidence that the health and safety of low birth weight babies has been compromised by inclusion of MCT to their formula. - provided details of MCT content of their formulas and units sold in Australia and New Zealand - provided details of specific studies that had shown beneficial effects of MCTs (see submission). - the current draft Standard provides for an MCT content that is the natural constituent of the milk based ingredient of formulas. The Vegetable fat blends used in most infant formulas contain MCT as natural components, therefore the draft standard should provide for a MCT content that is the natural constituent of the plant or milk-based ingredients. - provided some background on MCT and their metabolism (see submission).

Robert A Gibson Director, Child Nutrition Research Centre Maria Makrides Research Dietitian and NHMRC Fellow	- recommended that MCTs be permitted to be added to all formulas - up to 20%. Could see no scientific reason for preventing their use. commented that there are about 15% MCT in breast milk fats (albeit of more complex structure than coconut oil). - acknowledged initial concerns that if MCTs were too high then infants may become EFA deficient, that evidence about the absorption of MCT was poor and that high levels of MCT meant that the fat composition deviated too much from breast milk.
Maureen Minchin IBCLC	-sees no reason to permit high levels of MCT if there is any health risk and because companies are making and selling these products. -if there were to be any danger of restricted supply of formula the requirement could have a lead in time of 3 years for industry to reformulate. - all novel food ingredients - those not natural constituents of the milk-based ingredients of formula should be proven to be safe and efficacious prior to addition. - permitting nucleotides while prohibiting MCTs would be discriminatory.
Bristol Myers Squibb Australia Pty Ltd	- do not agree that the use of MCFA should be prohibited. BM is not aware of any manufacturers lowering the content of MCT in their infant formulae and have no plans to do this themselves. The proposal to change existing products of longstanding is highly questionable. - prohibition of MCFA in infant formula is totally inappropriate as they are found in human milk (4-12%) depending on which fatty acid groups are included, animal and vegetable fats. The fatty acid profile of human milk will vary - however the aim of infant formula manufacturers is always to match a "typical" profile of human milk fat as closely as possible. The amount of MCFA added will only be added to match the typical profile. MCFA are expensive therefore their addition in formula is self limiting. - the fact that MCFA are not normally present in large quantities in human milk is essentially irrelevant as an argument. Bovine albumin and B-lactoglobulin are not present in human milk - the nitrogen is present in the form of human milk proteins and significant quantities of non-protein nitrogen. - up until now cows milk protein has been accepted as a relatively safe, inexpensive and convenient form of protein to use in an infant formula. MCTs can be viewed in a similar light when regarding the special needs of infants where there are concerns with fat malabsorption. MCTs have been used for 30 years in several Mead Johnson formulations. Several studies confirm the efficacy and safety of the use of MCTs in the standard. - provided details of MCT content of their formulas and units sold in Australia and New Zealand
Nursing Mothers' Association of Australia	- health and safety of infants needs to be the primary consideration at all times. The argument that pre-term infants may be disadvantaged by disallowing MCTs needs to be clarified to ensure that it is infant health which is the main consideration here, and not the industry market share.
Abbott Australasia Pty Ltd	- proposed prohibition of MCT is inappropriate, particularly for pre-term formulas - improvement of lipid absorption with MCTs in the pre-term infant has been documented in the scientific literature - provided details of MCT content of their formulas and units sold in Australia and New Zealand

Issue: Trans Fatty Acids

Submitter	Comments
NZ Dairy and Marketing services	- 4% would require modification of some oil blend currently in use. It is recommended that a max level of 8% TFA be imposed for an intervening period of 2 years to enable any required modifications to oil blend compositions to be introduced with sufficient time to enable clinical trials and evaluations of stability to be completed.
Nestlé Australia Ltd	- limitation of a maximum of 4% trans fatty acids in infant formula may exclude use of significant amounts of milk fat - natural levels of trans fatty acids in milk fat can be as high as 6-7% of total fatty acids - trans fatty acids can also occur at these same levels in human milk

Issue: Fatty Acids: Alpha-linolenic Acid

Submitter	Comments
International Formula Council	- endorse decision to reduce proposed minimum to 1.75% of total fatty acids
Nestlé Australia Ltd	- EU Directive and draft Codex standard specifies the minimum alpha-linolenic acid at 12 mg/100 kJ which is approximately 1% of the total fatty acids - consideration needs to be given to harmonising with these standards to ensure that the obligations under WTO are met

Issue: Linoleic Acid to Alpha-linolenic Fatty Acid Ratio

Submitter	Comments
International Formula Council	- endorse proposed ratio of not less than 5:1 and no greater than 15:1

Issue: Valine

Submitter	Comments
Abbott Australasia Pty Ltd	- valine content of 5.5 g/100 kJ of protein is much higher than the reference cited by the EU (4.5 g/100 kJ of protein) - believe 4.5 g/100 kJ of protein is a more accurate value

Issue: General Comments

Submitter	Comments
Department of Nutrition and Dietetics and the James Fairfax Institute of Paediatric Clinical Nutrition	- monitoring required to ensure that good manufacturing practice occurs - see no problem in having the same level of vitamins and minerals in special formula as in formulas for healthy infants - special need cases would be monitored on an individual basis
Karen Simmer, Neonatologist and Associate Professor	- the removal of maximum levels for many nutrients is not acceptable
NZ Dairy Marketing and Customer Services	- recommended guideline for maximum level of vitamins and minerals in infant formula products is commended

International Formula Council	- commend evaluation of maxima for individual nutrients, and recommending levels for vitamins and minerals on basis of significant risk to infants, while establishing advisory guideline maximum levels for other nutrients
Dairy Goat Co-Operative (NZ) Ltd	- goat milk infant formula will require some minor modifications to levels of some vitamin and mineral additions - this could lead to an increased price to the consumer
Victorian Food Safety Council Food Standards Sub-Committee	- supports approach, however subsequent to the preliminary inquiry report, the EC has adopted a standard for infant formulas for special medical purposes that sets levels for 13 vitamins and 15 minerals - it would be of value to first examine the arguments for setting levels for all vitamins and minerals in the EC directive (1999/21 of 25.03.99)
Nestlé Australia Ltd	- agrees there is a need to impose maximum limits on vitamins and minerals where there is a health and safety issue involved - guideline levels should not become pseudo legislation - where the minimum and maximum levels are different to the EU requirements, then formula that is manufactured in Europe would hardly ever comply to the requirements of the combined Aust NZ standard (uses example of copper) - findings of LSRO report based on some of the maximum levels on the 90th percentile found in infant formula in the USA; there has been no health and safety reason for imposing the maximum limits on some of these vitamins and minerals
Patricia McVeagh, Consultant Paediatrician	- the LSRO report developed for the Center for Food Safety and Applied Nutrition, Food and Drug Administration (reference included) addresses many of the issues raised
Maureen Minchin IBCLC	- if ANZFA goes with average ingredients rather than ranges of expected maxima and minima, it must be clearly stated that these are NOT actual averages calculated by batch assay, but expected averages for this brand when made to the company's specified recipe. - ranges are less misleading and useless for clinical purposes. - nutrition information panels take up space which could be better used to give clear instructions and warning s in many languages. - recommend that nutrition information panels be abandoned. Community health workers on the ANZFA teleconference agreed here - opposed to only having advisory guidelines. - maximum levels should be set for every ingredient where this is currently possible and made mandatory for all infant formula. - as the EC Directive on Dietary Foods for Special Medical Purposes , heavily influenced by industry, specifics a narrower range of vitamin and mineral levels, these minima and maxima are clearly achievable - compliance should be monitored by an independent agency. If advisory maxima are allowed for any ingredient, widespread publication of the mandatory monitoring results should advise consumers about products which breach the advisory maxima

Bristol Myers Squibb Australia Pty Ltd	- agree with the present nutrition information panel requirements, however questions the use of the nutrition information panel for the parent who uses the information. If every formula has relatively narrow compositional guidelines to meet at present, is this panel used for comparison with other brands? The panel appears to be presented to reassure the parent that the nutrients are in the product. - it seems unnecessary to add a column of nutrients per 100g of powder per 100 ml of concentrated liquid. The change would impose an enormous cost upon industry, affecting every single product on the market.
W Parnell, Department of Human Nutrition, University of Otago	- comments that the statement "recommended mandatory maximum levels be set for those vitamins and minerals which are considered...." for the reason of "eliminating unnecessary costs for industry" is wide off the mark of commercial reality - comments that no food industry uses resource unnecessarily
Nursing Mothers' Association of Australia	- the long term safety of vitamins and minerals needs to be established before allowing them to be added to formula.
Wyeth Australia Pty Ltd	- maximum levels should be determined by risk assessment and harmonisation with international standards - inference of unlimited nutrient contents for infant formula without R7 regulation is unrealistic and misleading, as all infant formula manufacturers are committed and legally bound to producing safe products both at common law and under various State and Federal Legislation - it is not appropriate to state that human milk has a self-limiting level for all vitamins and minerals. The composition of human milk varies considerably, dependent on maternal diet, stage of and even during a feed. The setting of maximum levels should therefore, be based on risk assessment. Advisory maximum levels which are recommended for nutrients whose risk is insignificant should not be included in guidelines. Although guidelines do not have force of law, compliance is expected to be monitored. The question arises of who will monitor compliance, monetary constraints within government agencies and even industry make the process seem unlikely and it adds unnecessary complexity and prescription to the Standard. (see references)

Issue: Selenium

Submitter	Comments
Karen Simmer, Neonatologist and Associate Professor	- suggests available data does not support proposed maximum and minimum selenium values - RDI for selenium (Aust) is 10µg/day, equivalent to amount a breastfeed baby receives. Lower levels may meet nutritional needs of infants - cites Adelaide: breast milk selenium 13±4µg/l (mean±SD) and formula selenium varies from 3-10µg/l.

International Formula Council	- recommends a higher max of at least 1.1 mcg/100 kJ, if selenium is added to infant formula - establishing a selenium maximum based on added selenium would enable continued use of manufacturers' existing premix systems, which has been shown by experience to be safe and reliable. It is critical to add selenium in an accurate, safe and reliable way because the range between adequate selenium and potentially selenium toxicity is relatively narrow. The most accurate, safe and reliable way to add selenium to infant formula is via a premix
InforMed Systems	- selenate: studies available on the bioavailability of selenate (reference given); papers suggests selenate may be better absorbed than either selenite or selenomethionine - it may be preferable to set a lower level for selenate on the basis of that study, but not to prohibit its use
NZ Dairy Marketing and Customer Services	fortification of some current formula will be required, which will incur additional monitoring costs
Dr Lynne Daniels, Flinders Medical Centre, Centre for Perinatal Medicine	- submits that infant formula should permit supplementation with either selenate or selenite to the levels proposed [note: detailed submission on selenium, including 30 references]
Nestlé Australia Ltd	- sodium selenate is a permitted form within New Zealand Food Regulations and the EU Directive for infant formula. If sodium selenate is not permitted, formulas manufactured in NZ and Europe would become illegal products - sodium selenate is a more stable salt and is less sensitive to reduction to the inactive selenium by ascorbic acid (references included) - limits proposed for selenium are rather narrow based on the analytical methods available and the varying level of selenium found in raw materials
Abbott Australasia Pty Ltd	- limit to the amount of added selenium in infant formulas is still too low - due to variations of selenium in soil, and therefore raw materials, a higher maximum level is needed - selenium in human milk varies, depending on geographic region and maternal selenium intake - proposed level of 1.19 mcg/100 kJ, which is in line with LSRO recommended maximum of 5.0 mcg/100 kcal - level is consistent with the levels found in human milk from women consuming foods from selenium adequate areas, and their infants have no problems with this level - proposes inclusion of sodium selenate as a permitted form, in line with EU Directive
Abbott Laboratories (NZ) Ltd	- agree that it is appropriate to limit the amount of added selenium in infant formulas. -state the new limit still remains too low given the natural variation in selenium content in soils and therefore the raw materials used in the manufacture of infant formulas. -propose a maximum level for selenium of 1.1 ug/100 KJ because it is consistent with the level found in human milk from women consuming foods from selenium adequate areas. The level is also in line with the LSRO (Life Sciences Research Office) recommended maximum of 1.19 ug/100 KJ. -propose the addition of sodium selenate as an allowed selenium fortifier in accordance with EC Directive 91/321/EEC Annex III.

Issue: Manganese

Submitter	Comments
International Formula Council	- pleased an advisory guideline maximum level is recommended for proximate modified human milk substitutes - concur the required maximum is not warranted - remain concerned that proposed manganese maximum for pre-term formulas is unchanged at 1.8 mcg/100 kJ; recommendation should be rescinded or justification for this recommendation provided
Abbott Australasia Pty Ltd	- pre-term formulas have not been addressed in the proposed standard - do not support proposed maximum levels for pre-term formula

Issue: Aluminium

Submitter	Comments
International Formula Council	- endorse decision to raise proposed aluminium max for non-soy formula to 0.5 mg/L
NZ Dairy Marketing and Customer Services	- additional monitoring costs will be incurred
Maureen Minchin IBCLC	- the lower level should be universal, not the higher - $1300 per annum is not too much to pay for assays that ascertain industry compliance with aluminium and cadmium levels
Nestlé Australia Ltd	- prescription of an aluminium level is consistent with international regulations - if there is no issue with the level of aluminium proposed for soy-based products, then there should be one limit only - in keeping with WTO obligations, it would be more suitable to retain the aluminium levels in a guideline
Bristol Myers Squibb Australia Pty Ltd	- suggest there is no international agreement on limits for aluminium. There has been no demonstrated danger to public health and safety with present levels of aluminium under the present standard - any level imposed, must be regarded as a public health and safety issue and supported with clinical evidence that present levels are actually harmful. If this is the case, then one level of aluminium must be applied to all formulae. To do otherwise is inconsistent. The level set also needs to be achievable. ANZFA needs to consult with industry to set this level.

Issue: Fluoride

Submitter	Comments
International Formula Council	- endorse decision not to set a maximum for fluoride
InforMed Systems Ltd	- function of advisory label on high fluoride seems superfluous - if unnecessarily high fluoride levels might be present, this should be addressed in an entry in the table of permitted levels of vitamins and minerals, giving a max level of 17 µg/100 mL - Codex makes no reference to fluoride
NZ Dairy Marketing and Customer Services	- additional monitoring costs will be incurred

Dr Sheila Killalea, Dr John McNeil, Department of Epidemiology and Preventive Medicine Monash University	- there is increased evidence to suggest that prolonged intake of infant formula may contribute to dental fluorosis, which is increasing in prevalence in Australia and many other countries (references included) - fluoride intake from infant formula reconstituted with low-fluoride or optimally-fluoridated water may exceed the recommended intake in infancy, in some cases, more than two-fold (included information on estimates of intakes in fluoridated and non-fluoridated areas for children up to one year of age) - reduction of dry formula fluoride level to negligible amounts would reduce fluoride intake from this source by up to 30% - acknowledges that many factors may contribute to the increase in dental fluorosis, and that a multifaceted approach to the reduction of inappropriate ingestion of fluoride is needed. Nevertheless, feels there is sufficient evidence to warrant a limitation of the fluoride content of infant formula at this time (references included) - suggests two ways of limiting excessive fluoride intake from infant formula: * regulate the fluoride content of water used at the manufacturing site, which some manufacturers already monitor
Dr Sheila Killalea, Dr John McNeil, Department of Epidemiology and Preventive Medicine Monash University (cont)	* infant formula be reconstituted with low-fluoride water in a natural or artificially fluoridated area; would add to cost of infant formula if distilled or mineral water has to be purchased; likely to result in variable compliance; less effective method of lating rise in prevalence of dental fluorosis in Australian children
New Zealand Ministry of Health	- received expert advice on this issue - the upper limits for fluoride are, although on the high side, acceptable - advisory statement required under clause 24 should refer to “a dentist”; although preference would be to delete reference to a medical practitioner or other health professional, as there is some confusion amongst health professionals on this issue
Nestlé Australia Ltd	- do not agree that there is a need to include advisory statements on products regarding fluoride and dental fluorosis - no international equivalent legislation and would constitute a technical barrier to trade
National Council of Women of New Zealand	- suggest a regulated required maximum level should be determined
Bristol Myers Squibb Australia Pty Ltd	- fluoride is not mentioned in either the Codex or EC standards - if fluoride intake by infants is truly a public health and safety issue, the fluoridation of the water supply around Australia needs to be reviewed - concerns have been expressed previously regarding the safety of fluoridation of water supplies; in this case, a level of intake of 1 mg fluoride per litre of formula from the powder or concentrate was regarded as the proper limit of safety, assuming the water itself contained 1 mg fluoride per litre - this translates to approximately 36 ug fluoride per 100 kJ for a routine formula, compared to the 17 ug/100 kJ in the draft; this level is unnecessarily low

Issue: Tocopherols

Submitter	Comments
International Formula Council	- endorse decision relative to food additives, to allow for carryover from ingredients - concur the antioxidant, mixed tocopherols concentrate, should be allowed up to 1 mg/100 mL

Issue: Zinc to Copper Ratio

Submitter	Comments
International Formula Council	- endorse proposed ratio of 12:1
Nestlé Australia Ltd	- ratio will mean that the majority of Nestlé products will be illegal under this draft standard - ANZFA is obviously not aware of the current situation in Australia - recommends that 20:1 be adopted, as per LSRO report - ratio not included in Codex or EU Directives, therefore be considered a technical barrier to trade with no scientific justification for its inclusion

Issue: Permitted Form of Nutrients

Submitter	Comments
International Formula Council and Abbot Australasia Pty Ltd	- object to a prescriptive list of nutrients, which prohibits the use of any nutrient or source not listed - can disrupt and impair the development and provision of special infant formulas for those vulnerable infants who critically need them - standard should be based on practical and timely criteria which would allow new nutrients based upon science to be used - such a standard would enable use of ingredients when approved by major authorities (e.g. Codex, US FDA, EU)
Nestlé Australia Ltd	- nicotinic acid is currently allowed as a permitted form of niacin in the EU Directive, NZFR, and Codex. Should be a permitted form within draft standard - magnesium citrate and magnesium hydroxide are permitted forms of magnesium and sodium selenate is a permitted form of selenium in both NZFR and EU Directive - cupric citrate, cupric carbonate and copper-lysine complex are allowed forms of copper in NZFR and EU Directive - chromic chloride is a permitted form of chromium in NZFR, have information that form of chromium sulphate is not always readily available
Wyeth Australia Pty Ltd	- permitted forms of nutrients should be harmonised with the EU and Codex standards - includes list of permitted forms in table - see submission

Issue: Iodine

Submitter	Comments
InforMed Systems Ltd	- questioned reducing the maximum iodine level from 11 to 10? - questioned having different values of vitamin and mineral levels for special purpose food for infants. In almost all cases nutritional requirements same as for normal infants except for the constraints of the metabolic disorder

Issue: Chromium and Molybdenum

Submitter	Comments
InforMed Systems Ltd	- it is not clear why chromium and molybdenum must be added in this case but not for similar ordinary formula. Are they not essential for all infants? - assumes permitted, though not prescribed, since they are listed in the recommended guidelines maxima on page 29

Issue: Carnitine and Choline

Submitter	Comments
Dairy Goat Co-Operative (NZ) Ltd	- carnitine composition of goat milk needs to be considered in relation to protein quality requirements included and the recommended maximums set for carnitine
Nestlé Australia Ltd	- the way this clause is written will require infant products where the optional nutritive substances are not added to comply with the maximum levels specified for each of the nutrients - range proposed for carnitine too narrow - this does not take into account the natural variation of these nutrients that can occur with the ingredients of the products - permission should also be included for lecithin: lecithin also naturally contains a proportion of choline - these permissions do not harmonise with any international legislation and would be considered as technical barriers to trade. EU Directive allows addition of choline and choline citrate as well as choline chloride and choline bitartrate - EU Directive allows addition of the hydrochloride of L-carnitine - these forms need to be permitted for choline and carnitine
Abbott Australasia Pty Ltd and Bristol Myers Squibb Australia Pty Ltd	- proposed level for carnitine is still too low - carnitine is naturally present in cows milk, typically at concentrations as high as 1 mg/100 kJ - therefore the restriction to 0.8 mg/100 kJ is unrealistic - propose a level of NMT 1 mg/100 kJ

Issue: Choline

Submitter	Comments
InforMed Systems Ltd	- suggests that as choline is now officially recognised as an essential nutrient (Codex 3.2.1) and has an American RDI - it should be listed under 'vitamins'

Issue: Vitamin B6

Submitter	Comments
Nestlé Australia Ltd	- report stated that the retention of maximum level for vitamin B6 unlikely to cause any trade restriction based on the LSRO conclusion - inclusion of a maximum for vitamin B6 has the potential to provide a technical barrier to trade

Issue: Riboflavin

Submitter	Comments
New Zealand Dairy Board	- maximum level of riboflavin at 86µg is set too low - some products can have naturally occurring levels of riboflavin as high as 86.5µg - recommends that level be increased to 87µg to accommodate the variability of the naturally occurring nutrient

Issue: Follow-on Formula

Submitter	Comments
NZ Infant Formula Marketers' Association	- it is essential for infants from four to six months to be introduced to a progressively diversified diet - main area of contention in definition is 'principle source of food for infants' - follow-on formula should have a separate and stand-alone standard from infant formula - definition should include "an important liquid component of a weaning diet" - proposal in conflict with WHO Code and Codex Standard for follow-on formula - neither European Directive nor the UK refer to follow-on formula as an infant formula product - believes proposed standard represents a major potential trade barrier - follow-on formula has been excluded from the NZ Interpretation of the WHO Code (refer to Ministry of Health Publication: Infant Feeding). ANZFA will "inevitably create unnecessary code interpretation and management problems for NZ, therefore, undermining the ability of the Ministry of Health to effectively monitor the NZ Interpretation of the WHO Code - believes it is totally inappropriate for ANZFA to impose restrictions on advertising. Currently do not advertise infant formula in NZ, in line with WHO Code - believes proposed labelling would breach the Fair Trading Act - understands that only five countries (Bahrain, Botswana, Malaysia, Tanzania, Vietnam) have extended the interpretation of the WHO Code to include follow-on formula - strong scientific evidence available proving that iron-fortified formulas are nutritionally necessary for the continued growth and development of infants, especially those who are no longer breast-feed - supports current wording, which is basically identical to the recommended WHO Code wording - ANZFA must reassess the essential differences between infant formula and follow-on formula, and to correctly define follow-on formula as a weaning or complementary food in a separate stand-alone standard

InforMed Systems Ltd	- in the diet of an infant over 6 months, formula (or breast milk) will remain an important component - it is incorrect after early weaning stage to define it as the principal source of nutrition - prefers Codex definition (a food intended for use as a liquid part of the diet for the infant from the sixth month on)

Issue: Special Purpose Formulas

Submitter	Comments
Department of Nutrition and Dietetics and the James Fairfax Institute of Paediatric Clinical Nutrition	- queries why special purpose formulas are limited to infants with metabolic or immunological diseases or disorders - other medical conditions such as gastrointestinal and renal diseases may necessitate the use of lactose-free or low lactose formulas, as they should not be for general consumption, but on medical advice only - congenital lactose is very rare and secondary lactose intolerance occurs after infancy; transitory post-gastroenteritis lactose intolerance is also not common in Aust and NZ and needs to be managed medically
Nestlé Australia Ltd	- draft standard proposes additional labelling stating that these products are not suitable for general use and that they should be used under medical supervision - formulas that are based on hydrolysed proteins and that are nutritionally complete would also be suitable for general use - current provision allowing infant formula to be formulated for a particular need based on a physical or physiological condition, disease or disorder needs to be retained
Patricia McVeagh, Consultant Paediatrician	- definition refers to metabolic and immunological conditions but needs to be broader to include other infants requiring special purpose formulas such as malabsorptive disorders including pancreatic deficiency, cholestasis, short bowel etc., lymphatic disorders, chronic renal failure, hepatic disorders - appropriate indication for their use would be galactosaemia, proven cow protein allergy or cow milk protein intolerance with tolerance of soya protein, vegetarian parents who elect not to give their children feeds of animal origin - lactose is also a suggested use although there is no need to change the protein source of the infant formula in the condition

Issue: Pre-Term Formula

Submitter	Comments
Nestlé Australia Ltd	- does not agree with the regulation of a pre-term formula, as the area is changing rapidly, especially where micronutrients are concerned - no other country regulates this products - products exclusively used for sick infants under strict medical supervision in hospitals only. Risk of improper use is therefore at a minimum - pre-term formulas are only available in hospitals for babies under specialist medical supervision; therefore unnecessary to include a statement on the label to this effect as it is the only way that the products can be made available to infants - pre-term formulas should be based more on weight than age - scientifically, it is now being recognised that this segment needs to be split into two parts:- one for infants less than 1.5 kg and one for infants greater than 1.5 kg (attachment included on Nestlé publication: Nutrition of the very low birth weight infant) - number of pre-term infants is approx. 3% total births, so from a commercial point of view amount of pre-term formula used is very small and companies generally make one formulation which is used globally
Nestlé Australia Ltd (cont)	- when segment is divided into two, quantities in each segment will be even smaller and companies will not make special pre-term formulas to suit different regulations in each country - therefore these regulations run the risk of these products of not being available to Australia and NZ infants and the regulations will be out-of-date very quickly - Nestlé's pre-term formula contains less vitamin D than specified within draft standard; level in product corresponds to ESPGAN, which recommends a max of 3 µg/100 kcal (0.7 µg/100 kJ) - ESPGAN also recommends a minimum folic acid content of 60 µg/ 100 kcal (14.3 µg/100 kJ) in pre-term formulas; product meets these requirements and contains the minimum amount - pantothenic acid content of product complies with ESPGAN recommendation of 0.45 mg/100 kcal (0.11 mg/kJ) which is lower than the levels specified in the draft. This would mean that the pre-term formula would not comply with the standard
Dr David Tudehope, Director Division of Neonatology, Mater Hospital	- pre-term formulas comprise approximately 3-5% of the total market of infant formulas - because of the relatively small market, there is not a wide range of pre-term infant formulas available - most infant formulas take 7 – 8 years of formula development - it is not reasonable to expect Australia to play a significant role in development of pre-term formulas - pre-term formulas are prescribed by a relatively small number of paediatricians specialising in neonatology - individual hospitals make decisions regarding availability or purchase of pre-term formulas based on scientific evidence - nutritional committees are established to make these difficult decisions - the regulation of pre-term formulas would result in an unnecessary delay in introduction of recently developed formulas - any decision regarding regulation of pre-term infant formula needs a great deal of consideration with extensive input from neonatologists, nutritionists and probably the pharmaceutical industry

Issue: Infant Formula Products for Special Dietary Uses Based on Protein Substitutes

Submitter	Comments
Nestlé Australia Ltd	- clause 41 requires a chromium content of between 0.35 and 2 µg/100 kJ - table on page 118 of preliminary inquiry report states proposed maximum is 15 µg/100 kJ both as a guideline for infant formula and follow-on formula and as a requirement for products based on protein substitutes - EU Directive recently allowed a claim for reduction of risk to allergy to milk proteins for hydrolysed protein formulas where they meet the specific requirements regarding the amount of immunoreactive protein in the product - recommend that this claim also be included in draft standard for this category of product - inclusion would harmonise with EU

Issue: Anti Reflux/Thickened Formula

Submitter	Comments
Department of Nutrition and Dietetics and the James Fairfax Institute of Paediatric Clinical Nutrition	- not allowing a physiological claim for anti reflux formula does not go far enough because these formulas could be named 'anti reflux' - additional labelling is required for these formulas that breastfeeding is the preferred feed for infants with reflux - these formulas should not be available without a prescription
National Council of Women New Zealand	- are unsure what can be gained by eliminating the term "physiological" in this recommendation - understand that thickened formulas marketed as "anti-reflux" may influence carers to cease breastfeeding. They believe that medical advice should always be sought before changing feeding programmes. For those with babies suffering from regurgitation problems who already use infant formulas, these products may well bring relief - adequate labelling needs to be on the package outlining the most appropriate use of the formula
Gastric Reflux Association for Support of Parents/Babies	- supports breastfeeding (enclosed specific pamphlet on breastfeeding and gastric reflux). Acknowledge that some parents choose to bottle feed for a number of reasons - based on over 2000 families in the last two years, there has been no increased evidence of breast feeding parents switching to a milk formula simply because they are thickened - the use of thickeners is a common and well respected treatment for babies with gastric reflux. Thickened formula may be suited to these babies because the specific modifications to the formula suit their specific condition - thickened formula takes less to prepare, is easier than mixing in other glutinous products to unthickened formula, and reduces stress for already stressed parents - for these parents there is a need for thickened formula which: * is in an obvious consumer location e.g. supermarkets * should be priced to make them easily accessible to all socio-economic groupings * should be available without prescription

Maureen Minchin, IBCLC	- formulas such as anti-reflux (currently on the market) are not "special purpose formulas" - their principal reason for existence is clearly commercial, not medical - all special purpose formula as defined by ANZFA should not be widely displayed or readily available at retail outlets, and marketing to health professionals should be approved by ANZFA's proposed TAG in conjunction with APMAIF
Bristol-Myers Squibb Australia Pty. Ltd	- recent introduction of thickened infant formula met a consumer need - the product conforms to the standard and does not pose a risk to infants. - health professionals have the training to interpret data to make considered recommendations - any restriction of use would be unjustified restriction of trade - these formula are not marketed directly to the consumer, (only health professionals) and therefore the decision is based upon recommendation - expressed concern that APMAIF find the use of thickened formula problematic. The purpose of the standard is to ensure safety and efficacy of infant formula, not partake in the agenda of another organisation
Wyeth Australia Pty Ltd	- indicate that there is no evidence at present to show that anti-reflux formulas are detrimental to breast feeding rates or put formula fed infants at any health and safety risk - state that thickened formulas are "sold" and not "marketed" in supermarkets, as marketing would contravene the MAIF agreement. - dispute the statement that "thickened formula are marketed in supermarkets at a similar price to "standard" infant formula. Recent market data indicates that the price for thickened formulas is 10%-20% more than standard infant formula - ANZFA should recognise that unlike retailers, manufacturers/ importers of infant formula have little control over the price to consumers - scientific material is only presented to health professionals who advise consumers about appropriate formulas. If claims in relation to physiological conditions are not allowed, then infant formula thickeners should also be banned. The result will be that carers will use any normal thickener to thicken the infants formula (this advice has been commonly given by health professionals prior to sale of thickened formula)
W Parnell, Dept of Human Nutrition, University of Otago	- many of the formula for special dietary needs are not sold "over the counter" but made available on prescription - legislative prescription for them would seem best to be general and separate from the formula standard

Issue: Drafting

Submitter	Comments
Department of Nutrition and Dietetics and the James Fairfax Institute of Paediatric Clinical Nutrition	page 9 - requirement for measuring scoop:- it would be preferable to have a standard size scoop for measuring infant formula, e.g. 30 mL or 60 mL, to reduce consumer confusion when changing brands page 10 - required statements:- 3 (a) 'breast feeding **for at least six months** is superior to the use of infant formula...' - pleased that mandatory feeding table has been deleted, as it caused anxiety for parents when their infant deviated from the recommendations of the manufacturer page 12 - labelling of lactose free and low lactose formulas:- appears adequate for galactosaemia page 14 - composition:- carbohydrate - type should be controlled; lactose should be the preferred carbohydrate in formula that is not for special purpose. Lack of regulation will allow the pre-thickened formulas, of which the scientific evidence for efficacy is questionable
InforMed Systems Ltd	Table to clause 6:- Codex provides a composition of human milk protein as its definition, which includes arginine, which is not strictly an essential amino acid. Values in Codex differ from proposed standard, and values are listed in Codex as g/100 kJ, whereas proposed standard uses per 100 g protein; queries whether is there is good justification for the deviation

InforMed Systems Ltd (cont)	Clause 7 - gluten:- could be seen as more restrictive than draft Codex standard, even though unlikely anyone would want to add gluten; queries whether this amounts to special pleading on the part of the Coeliac organisations Clause 8 (2):- Codex does not mention label claims for minimum levels of micronutrients, not clear what purpose clause serves; suggests that if to prevent deception, that should be covered by general requirements for labels Clauses 13 - 15:- while these may be justified on safety grounds, Codex draft does not set specific limits **Part 4 Labelling** Codex has no statement on scoops Clause 19:- suggests "could lead to serious illness" Clause 19 (2):- should either be deleted or should state "that each bottle should preferably be prepared individually"; states this is commonly ignored, and has seen no problems if directions followed Clause 20:- more restrictive than Codex in specifying actual print size Clause 20 (1):- should refer to packages "having net weight of not less than 1 kg"; current wording excludes packages of exactly 1 kg Clause 22 (1):- the words "best before" should be in quotes, also "or" "use by" should be added Clause 27 - microbiology:- **Part 2 Composition** Clause 28 (2) - osmolality:- see above; queries why value is in 'per L' when all others are /100 mL, suggests all be 'per L' Clause 30 (b):- has not seen adequate evidence to support a prohibition Clause 30 (e):- the usual ratios are around 4 or 5:1, assumes this is meant to be that the EPA level shall not be greater than the DHA level, which is not what it says. Draft Codex standard makes no reference to these constituents - do we need to be so prescriptive? Table to clause 30 has a max level of both omega-6 (which ones are contemplated apart from ARA?) and of omega 3 (EPA plus DHA) of 1:1, which conflicts with the 2:1 mentioned in 30 (d) Clause 34:- section after clause 30 is cumbersome and redundant; simply say pre-term formula must comply with sections 30 (a) to 30 (e) or whatever is left Clause 35 table:- **Schedule 1** - Codex does not have a list of permitted forms; surely the prohibitions and requirements for formula generally can cover this?

InforMed Systems Ltd (cont)	- specifications for nucleotides: needlessly detailed. Codex has no such requirements. Should require that a constituent be "proved to be suitable for infant feeding" as in Codex draft - the section on thickened formula is needlessly complex; these products should be categorised as special purpose formulas and restricted accordingly; it is not the function of food standards to define what is or is not clinically appropriate; it is not the function of food standard to support breastfeeding - should be left to WHO Code - section 4a - specifications. Borage oil has been widely used as a source of gamma-linoleic acid, should not be confused with whole borage plant; no justification for excluding its use in infant formula - it is not the function of the standard to be active in the implementation of WHO Code provision, except for labelling provisions; adequate mechanisms in place in Aust and NZ to care for such issues; the extensive reference to the Code in the standard should be deleted
NZ Dairy Marketing and Customer Services	Clause 8 - inositol:- analytical variation may create difficulties in determining levels of this nutrient Clause 8 - choline:- small amount of choline (0.3 mg/100 kJ) contributed by lecithin used as a processing/ functionality aid (emulsification) should not be considered as an addition of choline in terms of the need to comply with the max noted in table to clause 8 Clause 8 - carnitine:- natural levels typically found in milk and whey-based infant formula range from 0.6 - 1.0 mg/100 kJ; total carnitine levels three times the required max (0.42 mg/100 kJ) can be found in non-fortified whey-based infant formulas Clause 28 osmolality/potential renal solute load:- Clause 29 (1) - amino acid score:- agrees with the proposed introduction of the amino acid score; additional costs will be incurred with compliance, monitoring, and testing; some products will require reformulation and therefore be subject to additional supplementation and relabelling costs Clause 29 (2) - added amino acid maximum:- wording that "L-amino acids may be added solely for the purpose of achieving the minimum amino acid score specified in subclause (1)" is quite restrictive; would prefer the permission to add L-amino acid up to a max of X (e.g. 1.1) times the level noted from the specific amino acid listed in column 2 of the Table to Clause 6, which conforms with Codex requirements and also places controls on added ingredient levels Clause 31 (3) - calcium to phosphorus ratio:- the current Codex guidelines for follow-on formula is 1.0; consideration should be given to allowing this lower min for follow-on formulas

NZ Dairy Marketing and Customer Services (cont)	**Schedule 1** - potassium iodide is missing from list of potassium containing salts - calcium pantothenate is not included under calcium salts - choline chloride is not included under chloride containing salts - magnesium hydroxide is not included under magnesium containing salts **Standard 1.3.4 - Nucleotides** - specifications need to be carefully checked prior to their inclusion; chemical nomenclature on p26 appear to be incorrect; awaiting further information from suppliers to pass on to ANZFA
Dairy Goat Co-Operative (NZ) Ltd	Table to clause 8 - the innate carnitine level in infant formula and follow-on products using unmodified goat milk protein frequently exceeds the max permitted amount - the innate carnitine level in whey-based cow milk formulations also frequently exceeds this max - recommends max be deleted or set higher
Nestlé Australia Ltd	- the way clause 20 is drafted actually does not allow for a nominal weight of 1 kg. Recommends clause 20(2) be redrafted to state that a package having a net weight of 1 kg of less then the size of type must be not less than 1.5 mm - clause 21(2)(b)(ii) needs to state 'the average amount of' rather than 'the amount of' for consistency - not necessary to include the average amount of product on a per 100g basis; this information is not used and is therefore not necessary - relevant information is per the made up product - proposed nutrition labelling standard and current labelling provisions require products that are to be reconstituted with water to only be labelled as the reconstituted amount, not as the dehydrated or concentrated amount - labelling requirements should be consistent - clause 22 (1) should state that a date mark must be included rather than a best before date - ANZFA should not pre-empt use of a best before date as our requirement for these products is that they should carry a use by date rather than a best before date - differences between best before and use by date will be picked up in the revised date marking standard. Reference to requirement for a best before date here will not allow Nestlé to sell their products with a use by date, without creating confusion. Draft date marking standard will permit products to be sold past its best before date but not past its use by date

Wyeth Australia Pty Ltd	-there is not maximum applied to the level of choline in infant formula either in Codex or the EC. Unless it can be demonstrated that this is PH issue, the maximum should be omitted. -Nutrient addition is self limiting - only those levels that are necessary are added. -Choline can be present as a carryover nutrient from the cows milk ingredient. It is possible that actual levels may be higher than the proposed maximum. -"Food additives" 11 (3) - more appropriate wording would be "Liquid infant formula product may contain not more than 0.03g carrageenan per 100 ml". - Point 12 should read: " Other than by direct addition, a food additive or nutrient may be present ". This takes into account nutrients like choline. -specifying a method for measuring lactose is necessary as varying methods are inconsistent. As with levels of cholesterol and fat under the present code of practice, limits of detection and clinical significance need to be considered. Division 4, clause 18 should read: "A package, other than a single serve sachet or a package containing single serve sachets, containing infant formula product". -disagree with the use of "very" in Division 4, clause 19(a), (b) and (c) as it is emotive and unnecessary. Division 4, clause 22 (i) - the standard needs to be flexible enough to allow for "use by" and "best before" date marks. Division 4, clause 25 (3)(b)- this requirement presumably relates to the needs for infants with galactosaemia. For those infants with problems digesting lactose (lactose deficiency, disaccharide intolerance etc) the level of galactose is irrelevant. -believe it is unnecessary to list the presumed galactose content on the label and will contribute to confusion. Issues relating to galactosaemia are best addressed by specialises in the area of genetic and metabolic disorders. They are not issues that are considered at the retail level, as a consumer buys an infant formula. Division 4, clause 26(f) - this prevents a manufacturer from making any reference to a new formulation as distinct from a previous formulation. This restricts trade and consumer information. Food companies invest time and money supporting research into diet and nutrition and believe it is legitimate to inform consumers in this manner.
Wyeth Australia Pty Ltd (cont)	Division 4, clause 30(e) - The fatty acids are properly spelt "eicosapentaenoic acid" and "docosahexaenoic acid". Division 4, clause 31 - Codex or the EC prescribe maxima for vitamins other than Vitamins A and D. There is no maximum for Manganese or Iodine and no minimum for Selenium. The proposed levels are inconsistent with international standards and should be withdrawn. - Division 2 - Infant formula for metabolic and immunological conditions.

	-these formula are designed for when breast feeding is contra indicated and therefore should be used under medical guidance. -many of these products are listed, with their indications, in the Pharmaceutical Benefits Scheme, as the Federal Government contributes funding for their use. They are significantly more expensive to manufacture and to formulate. There are several points to make: Codex does not have this standard. EU includes this product as "Foods for Special Medical Purposes". It is not appropriate to control these products under a general standard. metabolic disorders are different from immunological conditions. Metabolic disorders will require the omission of a particular nutrient (e.g. PKU). in immunological conditions the form of nitrogen is designed to prevent the immunological or allergic reaction. The notation "not suitable for general use" is not correct". The nutritionally complete products are not designed for general use, however, their suitability is not an issue. recommend that infant formula that are not nutritionally complete and are designed to meet nutritional requirements in special medical cases be included in the standard for Foods for Special Medical Purposes. For nutritionally complete infant formula where, for instance, the protein has been hydrolysed or amino acids used as the source of nitrogen, we recommend that the standard be broad enough in its descriptions and allowances to allow these products to conform without alteration.
Bristol Myers Squibb Australia Pty Ltd	<u>Definitions</u> - recommend a definition of "follow-on formula" to be similar to Codex. definition for "infant formula product" is too prescriptive and should follow Code. Clause 6 - Calculations of amino acid score: the proposed increases of amino acid levels are scientifically unsubstantiated and will result in reformulation of many of BM products. Unjustified because there have been no health risks with these products. -submission contains a table where shows that if the current R7 amino acid values are converted to g per 100g protein, values do not produce the proposed amino acid score of 0.8 in all cases. Also, the current R7 standard and Codex express individual amino acid requirements on a calorie basis. Clause 9 - Limit on Nucleotide 5'-monophosphate maximum total nucleotide level should be set at 1.76 mg/100 kJ (the sum of the maximum nucleotide permitted) and not 1.2 mg/100 kJ. Clause 7 - restrictions and prohibitions. (1) the clause is prescriptive and limiting and restricts innovation. Recommend the relevant Codex Clause 3.2.1. -inappropriate for ANZFA to include a clause for infant formula to contain no undetectable gluten without including a method for analysis or minimum levels of detection (see submission for explanation). The phrase "must not contain any detectable gluten" should be replaced by "must be gluten free" as defined by Section 32.991.19 of the Second Supplement to the AOAC, 15th edition (1990).

Bristol Myers Squibb Australia Pty Ltd (cont)	Suggest actual method of testing for gluten should be stated. ELISA method is not easily performed. Clause 8 - Permitted optional nutritive substances - proposed levels for choline are not achievable e.g. seasonable variability. Support removal of level to align with international standards. -Clause 12 should use consistent terminology e.g. all references to food additive or nutrient should be "food additive, nutrient, vitamin and/or mineral". Clause 15 Composition of lactose free and low lactose formula. -do not agree that a clause should be included without a method for analysis or minimum levels of lactose. Do not think there is a need to detect minuscule levels of lactose which are clinically irrelevant. Lactose free formula should be allowed, based on ingredients being naturally lactose free without further analysis. If potential lactose-containing ingredients are added then 1 ppm or less lactose should qualify for the claim. -Clause 18 - Measuring scoop -should read "A package, other than a single serve sachet or a package containing single serve sachets, must contain a scoop which facilitates the use of the infant formula product in accordance with directions contained in the label of the package" Clause 12 Required Statements 1(a)(b) and (c) - Do not agree with statement "can make baby very ill" suggest "Inappropriate use or preparation may make your baby ill". (c) it is difficult to concentrate ready to drink formula. It is more appropriate to say "Do not dilute this ready to drink formula except on medical advice". (e) it is common practice in Australia to begin feeding additional food at ages 4 to 6 months. Clause 20 Print and package size. -clause should be modified to state "in a package having a net weight of 1 kg or less". Clause 21 Declaration of nutritional information -expression of nutrient levels per 100g does not add value to the NIT and doesn't mean anything to the consumer as all products have different densities. -market research indicates the carer is interested in the volume that the infant has consumed. -this information would contribute to overcrowding the can. Clause 25 - Lactose free and low lactose; if product is lactose free then there is no benefit by including the amount of lactose expressed in g/100 ml.

Bristol Myers Squibb Australia Pty Ltd (cont)	-do not routinely test for galactose when infants with galactosaemia are under medical supervision. Clause 26 Prohibited representations -(a)(b)(c) these clauses are under the MAIF agreement and should be removed from the proposal. -clause (b) is subjective without a "firm picture which idealises the use of infant formula". (f)opposed to this clause - does not allow company to educate the consumer about the presence of new ingredients e.g. nucleotides.- Market research conducted by Wyeth indicates that consumers would be comfortable with these ingredients if they knew what they were and why they were included in infant formula. Clause 27 Microbiological standards Codex Standard is no more than 100,000 micro-organisms per g. Division 4, clause 23 - The statement of protein source is already present on the can, both as a separate statement and in the ingredient list. The requirement to add this statement adjacent to the name of the infant formula product is totally unnecessary
Maureen Minchin IBCLC	L(+) producing lactic acid cultures (Clause 10) - what trials or safety and efficacy have been produced to ANZFA. Carrageenan (Clause 11) - the restriction seems sensible.

Issue: General Definitions

Submitter	Comments
New Zealand Ministry of Health	- believes that definition of infant formula needs to be described not only as being suitable as the *principal* but also the *sole* source of nutrition for infants in the first four to six months of life (except in follow-on formula, where *sole* is not appropriate) - believes definition for follow-on formula should reflect that this formula is the principal liquid element in the diet of infants; however can agree with proposed definition - suggests an editorial note to explain reasoning behind this definition - could be helpful to cross-reference to the advisory statement required in clause 19(3)
Nestlé Australia Ltd	- alternative name for follow-on formula is follow-up formula; this should be included - starter formula is also used to describe the products that are suitable for infants under 6 months of age; this term needs to be considered
Abbott Australasia Pty Ltd	- endorse the term 'Infant Formula Standard' - however, would like to suggest the use of specific terms, such as hydrolysates or amino acids instead of the proposed term "protein substitutes" - believe the definition "fat-modified" is still inappropriate due to the fact that there are other means of modifying the lipid component than through the use of MCTs

Issue: Definition of Pre-Term Formula

Submitter	Comments
Wyeth Australia Pty Ltd	**"Pre term formula"** - recommend that a more appropriate definition be based upon the weight of the infant or at least include the weight of the infant. There can be categorisation of the Extremely Low Birth Weight infant (ELBW) as less than 1,000g and pre-term as 1,00g - 1,750g in weight.
Bristol Myers Squibb Australia Pty Ltd	"pre-term" should take into account infants weight and gestation age as the amount of formula is determined by the weight of the baby.
Nestlé Australia Ltd	- definition for pre-term formulas needs to be modified; infants of less than 37 weeks gestation are generally used on the basis of weight rather than age
Informed Systems Ltd	- the definition of a pre term formula should be for infants less then 38 weeks gestation, since 38 – 42 completed weeks is defined as term infant.
Maureen Minchin, IBCLC	- pre-term formula means infant formula products specially modified / intended for use by infants of less than 36 weeks gestation.

Issue: Definition of an Infant

Submitter	Comments
Maureen Minchin, IBCLC	A definition for infant should be included in the standard. She suggests the following definition. "An infant is a person under 12 months of age."

Issue: Definition for Lactose Free and Low Lactose

Submitter	Comments
Maureen Minchin, IBCLC	A definition for 'lactose-free' or 'low lactose' formula should highlight the temporary nature of the condition and the short-term nature of the formula use. 'Lactose –free' or 'low lactose' formula means infant formula products with reduced lactose content for short-term use by infants with medically diagnosed problems with lactose malabsorption.

Issue: Definition of Soy Protein Formula

Submitter	Comments
Maureen Minchin, IBCLC	- it may limit the definition of soy protein formula if it only mentions soy protein isolate.

Issue: Definition of Special Purpose Formula

Submitter	Comments
Patricia McVeagh, consultant paediatrician	- the definition of special purpose formula refers to metabolic and immunological conditions but needs to be broader to include other infants requiring special purpose formulas such as malabsorptive disorders including pancreatic deficiency, cholestasis, short bowel etc. She states that soy formula should be included in special purpose formulas. Appropriate indication for their use would be galactosaemia, proven cow protein allergy or cow milk protein intolerance.

Issue: Definition of Protein Substitute

Submitter	Comments
Abbott Australasia Pty Ltd	- the use of specific terms such as hydrolysates or amino acids instead of the proposed term protein substitutes.

Issue: Definition of Fat Modified

Submitter	Comments
International Formula Council	- endorses ANZFA's decision to rename the standard Infant Formula Standard and to drop the proximate modified. They had earlier expressed concern about the term "fat modified" and wish to clarify that this term has been dropped.
Abbott Australasia Pty Ltd	- they believe the definition 'fat-modified' is still inappropriate due to the fact the there are other means of modifying the lipid component than through he use of MCTs.

Issue: Warning Statements

Submitter	Comments
Consumer Food Network of the Consumers Federation of Australia	- proposals weaken current labelling provisions by downgrading prescribed statements into advisory statements - believes infant formula should be treated as potentially dangerous products, with mandatory warning statements - recommends that a mandatory warning statement, in 6 mm type, to the effect that artificial formula feeding can be dangerous to the health of the infant
Nestlé Australia Ltd	- provision to require infant formula to carry statements advising carers to seek medical advice where the fluoride content is unnecessarily high imposes restrictions that would be considered a technical barrier to trade

Barbara Glare	- very worried about warning that should appear on the can - there are a growing number of additives to infant formulas, such as LCP formulas, and thickened formulas to supposedly treat reflux - there needs to be clear warnings on the can that these are experimental - these additives are completely unproven, and yet are being accepted as 'normal' - parents should have the right to know that their children are being experimented upon, and to give their informed consent, as they would in any other trial - - believes slogan "breast is best" is totally inadequate
Fiona Compston	- requirement for a statement that "Breast milk is best" and for consumers to "seek advice from health professionals" is inadequate in informing consumers of the health risks of formula - current labelling does not warn consumers that even one formula feed is likely to affect ongoing breastfeeding of the baby, and could produce a reaction in the child - "Breast is best" also suggests artificial formula is standard or normal
Australian College of Midwives Inc (Victoria) and Baby Friendly Hospital Initiative (Victoria)	- requirement for "Breast is best" and for consumers to "seek advice from health professionals" is inadequate in informing consumers of the health risks of formula
Maureen Minchin, IBCLC	- the standard allows industry to keep publishing useless and misleading information on labels. It would be preferable to include detailed information that would assist in educating about infant formula risk and put responsibility for such education on to health professionals despite the evidence that almost all health workers are never adequately educated about such risks. States that appropriate mandatory hazard warnings should be included on the label. Suggests the following statements. 'WARNING Artificial feeding can make your baby ill. It also costs a lot of money and can result in more days off work for the baby's parents. If you are having breast-feeding problems, most can be solved, so seek expert help before using this product. Breast IS best.' 'WARNING Follow the instructions below. Infant formula can harm your baby if you do not. Always read the instructions on every can of formula you use, as they may be different. Never use more or less powder or water or a different measuring scoop and use only shrink proof bottles with reliable markings. DO not overheat infant formula, as you can destroy important ingredients. Do not heat infant formula in a microwave.'
The Dietitians of the New Children's Hospital	- recommend the statement 'breast feeding for at least six months is superior to the use of infant formula'. Supply of breast milk is reduced by the introduction of infant formula. The duration of breast-feeding is the problem in developed countries rather than the initiation rates.

Nursing Mothers Association of Australia	- if there are no reliable studies to establish the safety of the formula it should not be allowed. Alternatively the product should carry an easily visible and easily understood message warning that the ingredient is experimental and side effects have not yet been determined. This will allow the public to make a more informed decision about the infant feeding. It is not enough to say breast-feeding is best. Mothers have the right to know the current state of knowledge or ignorance about the safety of formula.
Mark Dunstone and Julie Smith	- the labelling requirements do not warn consumers of the health risks to the child or mother of using artificial formula. - consumers will not generally seek information from health professions and advice from health professionals may be incorrect. - the required statement that breast milk is best is ambiguous. It may maintain the misconception that feeding infants artificial formula is 'standard' or normal. It does not convey that there are adverse health risks associated with use of the formula. - the labelling requirements do not require information to be on the product that would enable consumers to avoid being deceived about the relative merits of formula and human milk. - the label does not prevent a consumer being deceived by wrong advice provided by a relative or friend etc. - the labelling requirements in the draft Standard are defective in that they fail to inform consumers of the risks from using formula; they fail to prevent deception; and they do not discourage the unnecessary use of formula.

Issue: Soy and Phytoestrogens

Submitter	Comments
Patricia McVeagh, Consultant Paediatrician	- soy formula should be included in special purpose formulas
Department of Nutrition and Dietetics and the James Fairfax Institute of Paediatric Clinical Nutrition	- these formula should be classified as special purpose formula - not recommended as first choice for infants who are not breastfeed - should be used only under medical advice considering the high levels of aluminium and unknown, long term effects of a high phytoestrogen intake
Western Australian Food Advisory Committee	- expressed concern about the metabolic effects of phytoestrogens in soy milk

International Formula Council	- Extremely disappointed regarding overly restrictive position on soy-based infant formulas. Concerns about the safety of soy formulas due to their phytoestrogen content are scientifically unfounded. For over 60 years, these products have been fed to millions of infants and studied in controlled clinical research, no adverse effects related to phytoestrogens in soy protein isolate formulas have been identified. - US FDA determined that soy-based infant formula are safe - refers to Dr Karen Kline report on isoflavones, soy-based infant formulas and relevance to endocrine function. - refers to studies by Luisa Businco and Dr Ken Setchell. - provided information on a study in infants fed a soy-based formula compared to a reference group of infants fed human milk. - IFC and US National Institutes of Health are sponsoring a study "Follow-up study of subjects fed soy-based formulas during infancy", which is currently underway - strongly urges that, as a minimum, ANZFA not implement or encourage the implementation of strategies to deter use of soy-based infant formulas pending the completion of this study, which is anticipated this year - recommend that standard clarify that, in addition to soy protein isolate, other forms of soy protein (e.g. soy flour, soy extract) should be permitted
Victorian Food Safety Council - Food Standards Sub-committee	- until safety of soy-based products is resolved, recommends that use of this formula be appropriately labelled to discourage use save on the advice of a health professional
New Zealand Ministry of Health	- pleased that ANZFA is considering strategies to deter the use of soy-based infant formula - thinks clause 19(3)(b) could be altered to "*Soy infant formula should not be used except on the advice of a health professional*" - queries whether water quality guidelines are sufficient to protect infants fed soy infant formula, given that nitrates are present in soy protein - given the presence of phytates in soy formula, has ANZFA considered if there is a need to increase the levels of certain minerals (e.g. calcium, iron)? - questioned whether there is a need to specify a level or a denaturation process for trypsin inhibitors - questioned whether ANZFA has considered if the level of iodine is high enough in soy formula, given possible phytoestrogen effects - concerned with the 1.0 mg/L limit proposed for aluminium in soy infant formula. The toxicological assessment does not provide a robust argument demonstrating the safety of 1.0 mg/L limit. Some references suggest infants may be at risk of aluminium toxicity at levels above 300 micrograms per litre (reference included)
Peter Toth	- concerned about infant soy formulae (included letter to editor of one parent, stating that there are many more worried parents)
Susan Toth	- information tells her that there is no safe level of soy for infants (or adults) - infants feed on soy formulas receive the estrogenic equivalent of at least five birth control pills a day - provides information on the adverse effects of phytoestrogens - the FDA did not give a GRAS approval for the use of soy protein

Patricia La Roche	- published evidence shows that chemicals found in soy formula may cause infertility in human adults and animals, and cause reproductive tract abnormalities in monkeys at doses similar to those in infant formula - feels that strategies suggested and the recommendations made are completely inadequate to protect children from the potential and possible risks suggested by research to date - at the very least, prominent warnings should be printed on the label - a more appropriate standard would be the elimination of soy products and their potential to cause adverse effects from infant formulas
Raeura Marsh	- cannot understand how the marketers of soy infant formulas can possibly say there is no evidence of health damage from the estrogen in these products, in light of the findings of the FDA (enclosed copy of letter discussing research is this field from Daniel Sheehan) - believes soy should be banned from baby food
Gail McIntyre	- believes it is wrong to have large quantities of chemicals in baby foods which can course thyroid damage and infertility - should be removed from sale before any more damage is done
Diane Bowman	- knows that estrogen can cause ovarian and breast cancers, and probably leukaemia - it seems unacceptably risky to have large quantities of chemicals in baby foods which are known to increase these risks - believe they should be removed; where children's health is a factor, there should never be a risk factor included in the equation - soy protein in soy products is risky
International Baby Food Action Network (IBFAN)	- safety of soy formula has not been established - high levels of phytoestrogens in soy formulas is of great concern to many researchers and health professionals - researchers found a 13000 – 20000 times plasma concentration of these substances in soy fed infants compared with levels found in breast or cow-milk fed infants - these doses are 6-11 times higher than the body weight adjusted intake which has been found to cause important changes in the hormonal regulation of the menstrual cycle in women (reference included) - since research on the short and long term effects of the phytoestrogens in soy formulas is ongoing and the information which has been found to date is very disquieting, it is recommended that a precautionary principle be applied
Valerie James	- since ANZFA has acknowledged the risk that phytoestrogen in some soy based infant formula poses, ANZFA is morally and legally bound to inform the consumer by labelling or by education (attachments supplied) - research shows that infants do metabolise phytoestrogens in exactly the same as adults (reference provided) - the use of soy protein in weaning products is not a traditional use or custom; it was introduced in 1962 (reference provided) -enclosed copies of published documents because of concern with research on perinatal exposure of rats to oestrogens. -references provided.

Abbott Australasia Pty Ltd	- concerns about 'alleged hazards associated with the consumption by infants of soy-based formula' containing phytoestrogens are not well-founded and are contradicted by scientific data - additionally, there is insufficient data to support a warning statement on soy-based formulas. For over 60 years, soy based infant formulas have been fed to millions of infants and studied in controlled clinical research; no adverse effects related to phytoestrogens have been identified - soy-based infant formulas are a safe and important feeding option for many infants - scientific data have demonstrated that infants fed soy-based infant formulas grow normally; US FDA determined that soy-based infant formulas are safe - standard should clarify that other forms of soy protein (e.g. Soy flour and soy extract) also could be utilised in the production of soy-based infant formulas
Maureen Minchin IBCLC	- it is not clear why ANZFA has focussed solely on soy formula, when bovine milk not only contains phyto-oestrogens but can contain higher levels of the more active compounds. - making less hypo-allergenic infant formula available should be a priority , not simply continuing the use of products whose impact on reproductive and physical health are at least questionable - research into the impact of phyto-oestrogens in infancy on later gender differentiation might make any decision to ignore these questions now seem less than responsible in future. The NZ public statement will have little impact on parental behaviour when a desperately unhappy infant improves (as many still do, even if about 40% will also become soy allergenic) when taken off bovine formula and tried on soy - Soy protein isolate - is soy protein isolate the only possible form of soy that might be used in infant formula? It may cause problems to limit the definition this way otherwise.
Mark Dunstone and Julie Smith	- given the absence of clinical trials showing soy-based artificial formula is not harmful, and the evidence that it may be, soy-based artificial formulas should not be allowed.
Nursing Mothers' Association of Australia	- where the safety of the product cannot be established the public have the right to know that this is the situation. This will allow them to make a more informed decision about infant feeding - withholding information about the potential risk from the phytoestrogen content of some soy-based formula prohibits informed choice. It is not enough to say breastfeeding is best - it is important to remember that formula can be the sole form of nutrition for an infant whose digestive system that is designed for breast milk and whose immune system relies on the protective properties of breast milk. An infant fed on soy-based formula is a very different situation from an adult having an occasional meal of soy beans

Wyeth Australia Pty Ltd	- soy based formula have been used as a sole source of nutrition for infants for over forty years - there is no potential risk to normal infants fed soy formula. Soy formula does not cause thyroid dysfunction (or hypothyroidism, which may be classed as a metabolic disorder) - For vegetarian/vegan carers who cannot, or do not wish to breast feed, soy-based formula provides complete nutrition for their infants without health or safety risks. Potential strategies to reduce the level of unnecessary soy-based infant formula consumption should not be included in this Standard
Bristol Myers Squibb Australia Pty Ltd	- the use of soy protein as an alternative source of protein continues to be a safe and a valid alternative to cows milk protein - use of soy protein is a viable, safe alternative. A recent review of data (see reference in submission) on the use of soy protein based infant formula, confirms the normal growth and development of the infant - requirement for a warning statement is unwarranted and reflects activities of "anti-soy" lobby groups, more than true science
Safetywize Consultants	- expressed concern that so many manufacturers are stating that there is no evidence of adverse effects from soy protein in infant formula - enclosed document called "Soy Infant Formula: The Health Concerns - A Food Commission Briefing Paper" which provides evidence to illustrate some adverse hormonal effects of soy products which have been know for many years
Camille Guy	- animal studies show clear evidence of reduced fertility due to phytoestrogen intake. - submission discusses in some detail concerns in Japan over the country's exceedingly low birth rate, low incidence of dizygotic twinning - In the report ANZFA does not recognise that there is a great deal of recent work with a bearing on phytoestrogen risk assessment. Specific evidence is provided on Professor Clifford Irvines presentation on the Role of Soy in Preventing and Treating Chronic Disease (Brussels 1996). Other data on primate post-natal estrogen exposure is presented. - refute the Authority's claim that "there is no evidence that exposure of healthy infants to soy-based infant formula over 30 years of use has been associated with any demonstrated harm" - explained concerns relating to development of soy fed children e.g. menstrual disorders, early puberty, excessive breast development etc which were outlined in her NZ Herald article (26.8.95) Attachments (letters to and from Pat Tuohy to Camille Guy)

Kingett Mitchell and Associates Ltd	- does not agree with ANZFA's conclusion that there is no potential for adverse effects. Believes there is clear evidence of harm - supports some of ANZFA's comments relating to food contaminants (see submission - pleased that ANZFA talks about the precautionary approach but believes that this approach needs to be accompanied with precautionary action. Urges ANZFA to require the removal of phytoestrogens from soy- - main concern is that ANZFA does not address concerns that relate to thyroid, the accuracy of evidence presented and various issues of interpretation - see submission which includes discussion of the Ishizuki study and other relevant studies related to phytoestrogens
Soy Information Network	- challenges submissions stating that "that concern over the health hazards of soy formula raised in New Zealand are not well founded" Provides discussion on scientific literature, arguments presented in submissions and in public presentations. (see detail in submission)
R F James	- isoflavones should be removed from soy protein based infant formulas, pursuant to the precautionary principle of avoidance of unnecessary risk (attached several references to support their removal) - oppose the view that "no evidence of harm" appear in the Preliminary Inquiry Report - provides numerous references to scientific literature and views of other countries (see submission) - soy formulas cause mineral deficiencies due to the high and variable amounts of phytate in them which cannot be exactly balanced by mineral addition , or the widely variable trypsin levels in soy protein isolates - states that at least a precautionary approach should be advocated, particularly when there are a number of compelling retrospective dietary studies which indicate isoflavones should be removed from soy baby foods (including "follow-on" products") - calcium levels are associated with the levels of phytate which decrease the bioavailability of calcium. Has anecdotal evidence about dental deficiencies in male children who have been fed soy formulas several years previously - food standards must be consistent with international trade obligations. SGOGS Committee have not given nitrosamine and nitrate contamination of soy protein GRAS status - perhaps because the industry has concealed the nitrate content of soy protein and soy formula. The water quality issue is a red herring which diverts attention from the issue of soy protein itself. (cites references) -disagrees with certain statements made in the preliminary report and comments on other submissions to the full assessment report (see submission) -references included in submission

Issue: Microbiological Standards

Submitter	Comments
International Formula Council	- concerned that unnecessarily restrictive, particularly for coliforms - US regulations allow 10 microorganisms per gram of dry product

InforMed Systems Ltd	queries why a standard for Listeria has been omitted, recommends that it be left in place
NZ Dairy Marketing and Customer Services	proposed standards for *Bacillus cereus*, Coagulase positive staphylococci, coliforms and *Salmonella* are acceptable for powdered infant formula; proposed standard for standard plate count is too restrictive and will unnecessarily increase costs to the industry; consumer safety should be protected by the specific standards (i.e. other than SPC), current level much more practicable, a modification to M=5000/g would be acceptable recommend n=5, c=2, m=1000, M=10000
Abbott Australasia Pty Ltd	- proposed microbiological standards still remain too restrictive, particularly with respect to coliforms - current US microbiological guidelines for powdered infant formulas allow for a maximum of 10 micro-organisms per gram
Consulchem Pty Ltd	- highlighted errors in the report - the existing New Zealand standard is more rigorous than the others. Believes that there is a strong agreement for the maintenance of the standards.
Abbot Laboratories (NZ) Ltd	- micro standards remain too restrictive particularly with respect to coliforms - notably the current US microbiological guidelines for powdered infant formulas allow for a maximum of 10 micro organisms per gram.

Issue: Renal Solute Load

Submitter	Comments
Department of Nutrition and Dietetics and the James Fairfax Institute of Paediatric Clinical Nutrition	- page 4 - calculation of potential renal solute load:- There is a revised formula for calculating renal solute in Fomon, Zeigler: Renal solute load and potential renal solute load in infancy *Journal of Paediatrics 134 (1): 4-11 1999*
InforMed Systems Ltd	- suggests being more restrictive than Codex would be "most unwise"; unnecessary to be included in standard
NZ Dairy Marketing and Customer Services	- accepts change to PRSL - limit proposed will necessitate reformulation of a few products currently on the Australasian market - the imposition of a max PRSL on follow-on formula due to potential high contribution from other dietary sources appear to be unfairly targeting follow-on formulas
Nestlé Australia Ltd	- renal system of infants over the age of six months is more mature than that of the 0-6 month infant - inclusion of this provision may create difficulties for manufacturers - does not comply with international legislation, therefore some imported foods may become illegal
Bristol Myers Squibb Australia Pty Ltd	- method for Potential Renal Solute Load and the proposed limits for PRSL need to be reassessed - a recent article by Fomon and Ziegler (see reference) raised the issue of available phosphorous - this method also uses total nitrogen rather than protein, thereby excluding differing conversion factors for different protein - the conversion of the nitrogen to yield the nitrogenous solutes also appears to be slightly different to the one given in the draft

Issue: Food additives - General Comments

Submitter	Comments
InforMed Systems Ltd	- Codex does not specify precise forms of additives in their draft standard - queries if the list could be considered more restrictive than Codex

Issue: Food Additives - Carrageenan

Submitter	Comments
International Formula Council	- endorses position not to prohibit use of carrageenan in liquid infant formulas
InforMed Systems Ltd	- Codex permits up to 0.1 g/100 mL in hydrolysed and amino acid based formula - proposed standard is more restrictive
Victorian Food Safety Council - Food Standards Sub-committee	- recommends that carrageenan not be permitted for use in infant formula until the conflicting international results concerning its effect on immunosuppression are resolved
New Zealand Ministry of Health	- some reservations to permit carrageenan to liquid infant formula, particularly as it is the more vulnerable infants (e.g. pre-term) who consume this product - JECFA review stated specifically that its ADI does not apply to infants under 12 weeks old - advised that scientific reports listed on p175 do not give reliable data on the potential toxicity of carrageenan in infant formula - data limited in terms of length of study, whereas intake of infant formula may go on for longer in some situations - appreciate use of liquid formula is usually limited to hospital situations, however there is potential for commercial sale - as additive is still under review internationally, request further consideration be given to its permission for use
Nestlé Australia Ltd	- drafting does not actually give permission for addition of carrageenan into liquid infant formula - 'must not contain more than' should be written as 'may contain not more than'

Issue: Food Additives - Citric Esters of Mono- and Di-Glyceride of Fatty Acids

Submitter	Comments
Nestlé Australia Ltd	- where infant formulas use extensively hydrolysed protein, there is a need to use citric acid esters of mono- and di-glycerides of fatty acids - recently approved in EU (98/72/EC Nov 4 1998)

Issue: WHO Code of Marketing of Breast-Milk Substitutes

Submitter	Comments
Consumer Food Network of the Consumers Federation of Australia	- disagrees that the CoP is effective in limiting the advertising of infant formula products to the general public - common and widespread use of artificial infant foods by hospitals and many health professionals - many hospitals and health professionals are very ready to recommend artificial infant foods when a mother has problems breastfeeding - not convinced that all free or discount supplying of infant formula to hospitals for giving to nursing mothers has ceased - cites several reasons why a CoP will never be effective including: * it is voluntary, only applying to manufacturers who sign up to it * does not apply to retailers, importers and others involved in marketing and promotion of artificial infant formulas * does not apply to all human milk substitutes and solid foods * manufacturers frequently breach provisions with no adverse consequence (see last annual APMAIF report) * no effective enforcement provisions * has not resulted in any consumer information on the risk of artificial feeding being placed on product labels - world wide experience is that regulation through voluntary codes such as APMAIF does not work (reference included) - recommends reliance on the voluntary code cease, with the standard including specific clauses prohibiting all promotion and advertising of infant formulae
Nestlé Australia Ltd	- inclusion of statements from CoP in the FSC is a duplication
Barbara Glare	- the CoP should be written into the ANZFA Act
Marg Kammerman	- the CoP should be written into the standard
Department of Nutrition and Dietetics and the James Fairfax Institute of Paediatric Clinical Nutrition	- is the code of conduct for the marketing of infant formula going to be standardised between Australia and New Zealand?

NZ Infant Formula Marketers' Association	- NZ Ministry of Health regulates the CoP in New Zealand - committed to the development and implementation of appropriate infant nutrition policies based on the principles and aims of the WHO Code of Marketing of Breast-Milk Substitutes - concerned about the negative impact the proposed standard may have on some members of the NZ health sector, which would impact on the NZ Ministry of Health's ability to effectively monitor the NZ Interpretation of the WHO Code - proposal in conflict with WHO Code and Codex Standard for follow-on formula - believes proposed standard represents a major potential trade barrier, and ANZFA may be called on by the WTO to justify the proposed changes on health and safety grounds - follow-on formula has been excluded from the NZ Interpretation of the WHO Code (refer to Ministry of Health Publication: Infant Feeding) - ANZFA will "inevitably create unnecessary code interpretation and management problems for NZ, therefore, undermining the ability of the Ministry of Health to effectively monitor the NZ Interpretation of the WHO Code -NZ Ministry of Health recently acknowledged that many health professionals are far to literal in their interpretations of the WHO Code, communicating only negative information on bottle feeding to infant carers who are unable, or wish not, to breast-feed - currently do not advertise infant formula in NZ, in line with WHO Code - quotes Chen and Palmer, who argued that banning the advertising of infant formula and follow-on formula represents a serious violation of several sections of the NZ Bill of Rights Act 1990 - understands that only five countries (Bahrain, Botswana, Malaysia, Tanzania, Vietnam) have extended the interpretation of the WHO Code to include follow-on formula - believe APMAIF have consistently over-interpreted the intent of the WHO Code
La Leche League NZ for Breastfeeding Supports and Information	- does not consider that the NZ Infant Marketers' Association's CoP for the Marketing of Infant Formula provides the same degree of protection as the WHO Code, either in its intent or in its wording - NZIFMA CoP applies only to a few companies, and only to infant formula - unlike WHO CoP, it excludes bottles, teats, follow-on formula and any other breast milk substitutes - WHO Code states no advertising, whilst NZIFMA CoP states that "general advertising of infant formula by NZIFMA companies through mass media ... or at point of purchase should be avoided" - NZIFMA CoP contravenes Australian and NZ MoH's definition of an infant as a child under twelve months of age