EXPLANATORY STATEMENT

APPLICATION A532

RATIO OF LONG CHAIN POLYUNSATURATED FATTY ACIDS IN INFANT FORMULA PRODUCTS

For information on matters relating to this Assessment Report or the assessment process generally, please refer to http://www.foodstandards.gov.au/standardsdevelopment/

EXECUTIVE SUMMARY

Food Standards Australia New Zealand (FSANZ) received a joint Application from the Infant Formula Manufacturers Association of Australia and the New Zealand Infant Formula Marketers' Association (the Applicant) on 27 February 2004. The Application seeks an amendment to Standard 2.9.1 – Infant Formula Products of the *Australia New Zealand Food Standards Code* (the Code) to change the current ratio of omega 6 to omega 3 long chain polyunsaturated fatty acids (LCPUFA) from 2:1 to at least 1:1, when LCPUFA are added to infant formula, including follow-on formula.

The Applicant is seeking to change the omega 6 to omega 3 LCPUFA ratio requirement for infant formula on the basis that recent scientific evidence emerged indicating that the ratio is no longer necessary. Further, there have been recent international developments with regard to the ratio of LCPUFA additions to infant formula, notably the draft revised Codex Alimentarius infant formula standard[1] (now adopted[2]). It is also argued that promoting consistency between domestic and international food standards is important, and that the current ratio may pose a technical barrier to trade for Australian and New Zealand manufacturers and importers.

The Applicant also states that no potential infant formula ingredient provides a natural ratio of 2:1 for arachidonic acid (AA, an omega 6 LCPUFA) and docosahexaenoic acid (DHA, an omega 3 LCPUFA) and therefore a mixture of sources of these individual fatty acids is necessary.

The specific objectives for the assessment of this Application are therefore to:

- protect the public health and safety of formula-fed infants; and
- promote consistency between domestic and international food standards.

The regulatory options available for Application A532 are to either maintain the *status quo* (Option 1), or amend Standard 2.9.1 such that where LCPUFA are added to infant formula they must be present in an omega 6 to omega 3 LCPUFA ratio of at least 1 (Option 2).

To meet the above objectives, FSANZ has undertaken a risk assessment of the relevant scientific issues surrounding the addition of LCPUFA to infant formula. The risk assessment has found that there is no apparent advantage in adding omega 6 and omega 3 to infant formula at a ratio of *approximately 2* over a ratio of *not less than 1*. Also, human milk shows wide variation in omega 6 to omega 3 LCPUFA ratios, and infants appear to tolerate significant variations to this ratio in their milk source.

A cost-benefit analysis has also been undertaken, which shows that Option 1 maintains a unique ratio requirement for Australia and New Zealand, and therefore does not promote consistency between domestic and international food standards.

[1] ALINORM 07/30/26 Appendix II p53 6.
[2] Report of the 30th Session of Codex Alimentarius Commission ALINORM 07/30/REP

In comparison, Option 2 would continue to protect the health and safety of formula-fed infants and would be more consistent with international food standards. A comparison of options therefore indicates Option 2 provides greater net benefits to all affected parties.

Purpose

The Application is seeking to change Standards 2.9.1 sub clause 23(d) from the current requirement for an omega 6 to omega 3 LCPUFA ratio of *approximately 2,* to require an omega 6 to omega 3 LCPUFA ratio that is *a minimum of one*, should LCPUFA be added to infant formula.

Decision

Option 2 is the preferred regulatory approach for Application A532. This approach would result in an amendment to Standard 2.9.1 to require an omega 6 to omega 3 LCPUFA ratio that is *not less than 1*, should LCPUFA be added to infant formula.

Reasons for the Decision

The change to the omega 6 to omega 3 LCPUFA ratio:

- does not pose any health and safety risks to formula-fed infants; and
- is consistent with relevant international regulations currently in place and thus would reduce barriers to trade, increase availability of products and reduce cost for industry and potentially consumers.

Overall, affected parties will receive a net-benefit from Option 2.

FSANZ therefore recommends the proposed draft variation to the Code that is provided in Attachment 1.

Consultation

FSANZ received a total of 12 submissions in response to the Draft Assessment Report during the six week public consultation period of 23 May to 4 July 2007. Seven submissions were received from industry, four from government and one from a health professional organisation.

Generally submitters favoured Option 2, to amend Standard 2.9.1 to include a requirement that the omega 6 to omega 3 LCPUFA ratio should be *not less than 1* in infant and follow-on formula when LCPUFA are added to these products.

Many submitters noted Option 2 is consistent with current scientific opinion and international recommendations including Codex and the European Union (EU), and would continue to protect the health and safety of formula fed infants.

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INTRODUCTION

Food Standards Australia New Zealand (FSANZ) received a joint Application from the Infant Formula Manufacturers Association of Australia and the New Zealand Infant Formula Marketers' Association (the Applicant) on 27 February 2004. The Applicant has requested an amendment to Standard 2.9.1 – Infant Formula Products of the *Australia New Zealand Food Standards Code* (the Code), specifically to subclause 23(d) regarding the voluntary addition of long chain polyunsaturated fatty acids (LCPUFA) to infant formula.

In this report, the notation for ratios is given as single number but should be read as a ratio of that number to one, for example a ratio of 2 equates to 2:1.

This Final Assessment Report discusses issues including those raised in submissions, and recommends variations to the Code (Attachment 1).

1. Nature of the Application

1.1 Basis of the Application

The Applicant initially requested the removal of subclause 23(d) from Standard 2.9.1 of the Code. This subclause requires that if LCPUFA are voluntarily added to infant formula and follow-on formula, then the omega 6 and omega 3 LCPUFA must be present in a ratio of *approximately 2*. Subsequent to the Initial Assessment, the Applicant modified their original Application so that at Draft Assessment an amendment of sub clause 23(d) was sought so if LCPUFA are added to infant formula, the omega 6 to omega 3 LCPUFA must be present in a ratio of a minimum of one.

The Applicant's initial request was based on the view that recent scientific evidence no longer supports the requirement for a specific ratio. The Applicant also contended that sub clause 23(d) could represent a technical barrier to trade because no proposed international legislation or existing overseas legislation requires the ratio currently specified in the Code.

However, the Applicant's position changed in line with scientific opinion and recent international developments with regard to the ratio of LCPUFA additions to infant formula, notably the draft revised Codex Alimentarius infant formula standard[3].

1.2 Scope of Application

This Application pertains solely to infant formula and follow-on formula. Infant formula and follow-on formula are defined in Standard 2.9.1 as follows:

> *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.*

[3] ALINORM 07/30/26 Appendix II p53 6.

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.

This Application does not affect 'infant formula products for special dietary use' (e.g. formulas for premature infants and/or those with specific medical conditions) in Division 3 of Standard 2.9.1. Clauses 25 and 27(1) of Standard 2.9.1 allow manufacturers to specifically formulate these products to meet specific medical requirements. Therefore, the Applicant's request will not impact on the current regulatory requirements for these products.

This Application also excludes 'formulated supplementary foods for young children' (i.e. a formulated supplementary food for children aged one to three years) otherwise known as 'toddler formula'.

For the purpose of this Report, the term 'infant formula' relates to both infant formula and follow-on formula.

2. Background

LCPUFA are unsaturated fatty acids with a chain length greater than or equal to 20 carbon atoms[4], and include fatty acids with omega 6 and omega 3 chemical structures. Arachidonic acid (C20:4 omega 6) (AA) and docosahexaenoic acid (C22:6 omega 3) (DHA) are the predominant LCPUFA added to infant formula. The ratio of omega 6 to omega 3 LCPUFA is 1.5 – 2 in currently available infant formulas. This observed ratio of *approximately 2* falls within the current requirements of the Code.

Humans can only generate omega 6 and omega 3 LCPUFA from fatty acid precursors. AA can be synthesised from linoleic acid (C18:2) (LA), while DHA is synthesised from alpha-linolenic acid (C18:3) (ALA). However, infants appear to have omega 6 and omega 3 LCPUFA requirements that are greater than their LA and ALA conversion processes can provide[5]. It is for this reason that many infant formula manufacturers add LCPUFA to their products. Also, humans cannot interconvert omega 6 and omega 3 fatty acids (including LCPUFA), and so a dietary imbalance in these fatty acids can potentially result in a state of nutritional insufficiency[6].

The combination of the inability to interconvert with the potentially higher LCPUFA requirements for infants has produced significant debate over the correct omega 6 to omega 3 LCPUFA ratio that is required in an infant's diet.

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[4] Across the scientific literature, there is variation in the carbon chain length that is used to define 'long chain polyunsaturated fatty acids'. Consistent with Standard 2.9.1 of the Code, LCPUFA are those fatty acids with a chain length of $\geq$ 20 carbon units.

[5] Simmer, K. (2001) Longchain polyunsaturated fatty acid supplementation in infants born at term. *Cochrane.Database.Syst.Rev.* (4):CD000376.

[6] Mahan, K. and Escott-Stump, S. (2000) Krause's Food, Nutrition and Diet Therapy. 10th ed, Pennsylvania, USA.

2.1 Current Standard

2.1.1 Domestic Regulations

Standard 2.9.1 of the Code regulates the compositional and labelling requirements of infant formula products[7,8]. Subclause 23(d) of Standard 2.9.1 states:

> *The fats in infant formula and follow-on formula must –*
>
> *(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*

In addition, the Table to clause 23 prescribes maximum limits for omega 6 LCPUFA, omega 3 LCPUFA and AA of 2%, 1% and 1% of total fatty acids respectively.

2.1.2 Overseas and International Regulations

The European Union have recently revised their infant formula regulations which include requirements on the voluntary addition of LCPUFA to infant formula and follow-on formula. Clause 5.7 of Annex 1 of the European Commission Infant Formula Directive (2006/141/EC) states that the DHA content of infant formula should not exceed the total content of omega 6 LCPUFA when LCPUFA are voluntarily added.

Since Draft Assessment, Codex Alimentarius has adopted a revised infant formula standard[9]. The standard includes a clause that states 'If docosahexaenoic acid (22:6 n-3) is added to infant formula, arachidonic acid (AHA) (20:4 n-6) contents should reach at least the same concentration as docosahexaenoic acid'. The standard also notes 'National authorities may deviate from the above conditions, as appropriate for the nutritional needs'. Codex Alimentarius has a separate and older standard for 'follow-up formulas' that does not include this requirement.

Aside from European Union and Codex Alimentarius, there are no other overseas or international requirements specific to the LCPUFA contents of infant formula.

2.2 Current Market

2.2.1 Domestic Market

Infant formulas with added LCPUFA are readily available in Australia and New Zealand. Four major brands of infant formula supply the market, and all of these brands are provided as individual products with or without added LCPUFA. Two of these brands are manufactured in New Zealand using locally produced milk powder, and are subsequently sold in both Australia and New Zealand. The remaining two brands are manufactured overseas and imported into Australia and New Zealand.

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[7] Infant formula product (as defined in Standard 2.9.1) 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.

[8] 'Infant formula products' refers to all food regulated by Standard 2.9.1.

[9] Report of the 30th Session of Codex Alimentarius Commission ALINORM 07/30/REP

The word 'gold' is often used in the product title of infant formulas suitable for term infants, (as sold in Australia and New Zealand) to differentiate products that contain added LCPUFA and, in some cases, other optional substances such as nucleotides. The cost of these infant formulas is greater than for formulas that do not contain LCPUFA.

Recent national grocery retail sales information indicates gold products are among the top selling infant formula, with a gold product ranked at number one in Australia[10].

2.2.2 International Market

It is preferable for companies to manufacture one formulation for worldwide distribution, for cost advantage purposes. However, it appears that products made in or imported into Australia and New Zealand are sold only in these two countries. One reason for this manufacturing practice is the ratio requirement for added LCPUFA. In addition, the increased cost of the product, partially related to compliance with the required ratio, may limit the sale of these products outside Australia and New Zealand.

2.3 Historical Background

Prior to the development of the joint Code, there was no regulation on the addition of LCPUFA to infant formula in either of the previous Australian[11] or New Zealand regulations[12]. Any addition of LCPUFA would have occurred via the ability to add fish oil as an ingredient to infant formula.

A Proposal was raised to both harmonise and update the regulation of infant formula within Australia and New Zealand, titled Proposal P93 – Review of Infant Formula. At the Preliminary Inquiry Stage of Proposal P93, the requirements for the addition of LCPUFA were aligned with the maximum level requirements of the European Commission and the United Kingdom (these were the only infant formula regulations at that time with requirements specific to LCPUFA). An omega 6 to omega 3 ratio was not included as part of these overseas regulations.

The decision to include a ratio was based primarily on the findings by the United States Life Sciences Research Office (LSRO) (Raiten *et al*., 1998b), which suggested that different omega 6 and omega 3 LCPUFA intakes interfere with the infant metabolism of these fatty acids to varying extents. A specific concern was that the addition of DHA alone to infant formula had been identified with a decrease in the serum levels of AA. Based on the results of studies in preterm infants and animals, the LSRO considered that the addition of LCPUFA at inappropriate levels could pose a safety risk for clinical outcomes, particularly in relation to growth. Therefore, the LSRO recommended against DHA and AA additions to infant formulas at that time (1998), but agreed to reassess the decision within five years.

To accommodate perceived safety issues with the omega 6 and omega 3 LCPUFA that were already permitted through addition of fish oil ingredients, the Proposal P93 Preliminary Inquiry Report proposed an additional measure of setting the omega 6 to omega 3 LCPUFA content at a ratio of exactly two.

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[10] Ranking Report for Grocery Retail, National AZTEC Information Systems, August 2006

[11] *Australian Food Standards Code*, up to Amendment 53. These regulations are no longer in force.

[12] *New Zealand Food Regulations 1984*, up to Amendment 10. These regulations are no longer in force.

This ratio was based on the level identified from human milk analyses[13]. It was recognised at the time that this additional measure was inconsistent with other overseas and international regulations, but was considered necessary to manage a potential risk in a vulnerable population.

During public consultation, comments were received stating that the ratio of omega 6 to omega 3 LCPUFA in human milk is not always exactly two. Consequently, the requirement for a ratio was retained, although the ratio was changed to *approximately 2*.

3. The Issue / Problem

Standard 2.9.1 prescribes that where LCPUFA (C ≥20) are voluntarily added to infant formula, they must be present in a ratio of omega 6 to omega 3 LCPUFA of *approximately two*. The Applicant states that no potential infant formula ingredient provides a natural ratio of 2:1 for AA and DHA.

The Applicant is seeking to change the omega 6 to omega 3 LCPUFA ratio requirement for infant formula on the basis that more recent and relevant scientific evidence has emerged. It is also argued that promoting consistency between domestic and international food standards is important, and that the current requirement for an omega 6 to omega 3 LCPUFA ratio of *approximately 2*, may pose a technical barrier to trade for Australian and New Zealand manufacturers and importers.

4. Objectives

In developing or varying a food standard, FSANZ is required by its legislation to meet three primary objectives that are set out in section 18 of the FSANZ Act. These are:

- the protection of public health and safety;
- the provision of adequate information relating to food to enable consumers to make informed choices; and
- the prevention of misleading or deceptive conduct.

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

- the need for standards to be based on risk analysis using the best available scientific evidence;
- the promotion of consistency between domestic and international food standards;
- the desirability of an efficient and internationally competitive food industry;
- the promotion of fair trading in food; and
- any written policy guidelines formulated by the Ministerial Council.

[13] Forsyth, J.S. (1998) Lipids in Infant Formulas. *Nutr Res Revs* 11:255-278

The specific objectives for the assessment of this Application are to:

- protect the public health and safety of formula-fed infants; and
- promote consistency between domestic and international food standards.

5. Key Assessment Questions

The key assessment questions considered at Draft Assessment were:

- What is the range of LCPUFA ratios naturally occurring in human milk, and how do these ratios compare to the omega 6 to omega 3 LCPUFA ratio prescribed in Standard 2.9.1?
- Are there any differences in the growth and development of infants fed formulas with varying ratios of omega 6 to omega 3 LCPUFA?
- What are the risks associated with feeding infants formula containing the singular addition of DHA or AA?

RISK ASSESSMENT

A risk assessment has been conducted by FSANZ to determine the risks arising from a change from the current omega 6 to omega 3 LCPUFA ratio of approximately 2, and in doing so to provide a response to the key assessment questions listed above in Section 5. Particular attention has been given to the influence of formulas with different ratios of omega 6 and omega 3 LCPUFA on infant growth and development. The fatty acid profile of human milk and the impact on serum fatty acid levels has also been assessed.

In undertaking this risk assessment, an extensive review of available literature on the addition of LCPUFA to infant formula has been conducted. Also, the risk assessment has been peer-reviewed by Professor William McLean of Ohio State University and Dr Clare Wall of Massey University to ensure that the available evidence was considered in an objective manner.

The following section summarises the risk assessment's literature review and subsequent analysis and conclusions. The full details of the risk assessment can be found at Attachment 2.

6. Risk Assessment Summary

FSANZ identified 17 randomised controlled trials examining the feeding of LCPUFA enriched infant formula to term infants, at omega 6 to omega 3 LCPUFA ratios of 0.3 to 4.3 (excluding those that added only omega 3 LCPUFA to infant formula). These studies were used to determine the role that dietary omega 6 and omega 3 LCPUFA have in the growth and development of infants.

For the most part, the data obtained from the 17 identified studies show little difference in growth or cognitive outcomes when infants are fed formulas with varying levels of added omega 6 and omega 3 LCPUFA. In particular, the anthropometric data shows that LCPUFA addition to infant formulas has no effect compared to standard formulation. However, the addition of LCPUFAs to infant formula does appear to have some positive, albeit minor influence on the development of visual acuity in infants compared to standard formulations.

Additionally, the fatty acid profile of human milk, from a wide geographical range, shows great variation in omega 6 to omega 3 LCPUFA ratios (ranging from <0.5 to approximately 4), and would appear to suggest that infants can tolerate significant variations to this ratio in their milk source.

Overall, there was a consistent lack of influence on infant growth, and visual and neurological development from relative variations in the omega 6 and omega 3 LCPUFA contents of infant formulas. In respect to the singular addition of DHA versus the addition of both DHA and AA to infant formula, the evidence base is currently too small to make a definitive analysis.

There is no apparent advantage in adding omega 6 and omega 3 LCPUFA to infant formula at a ratio of *approximately 2* over a ratio *not less than 1* as proposed.

RISK MANAGEMENT

FSANZ has considered the management of any risks identified through the risk assessment and submissions received during the public consultation period.

7. Safety and Appropriate Ratio

FSANZ's risk assessment indicates that the relative quantities of added omega 6 and omega 3 LCPUFA are unlikely to impact on the growth and development of infants. From the available evidence, it would appear that infants can tolerate significant variations in the omega 6 to omega 3 LCPUFA ratio present in infant formula.

The studies reviewed for the risk assessment undertaken by FSANZ, used formulas with omega 6 to omega 3 LCPUFA ratios ranging from 0.3 to 4.3. Also, the risk assessment does not identify any safety issues for formula-fed infants if the required omega 6 to omega 3 LCPUFA ratio is changed from *approximately 2.*

At Draft Assessment almost all submitters supported a change to the current requirement in the Code of a ratio of omega 6 to omega 3 of *approximately 2,* to require an omega 6 to omega 3 ratio that is *not less than 1*, should LCPUFA be added to infant formula. Several submitters noted the proposed amendment is in agreement with international recommendations and scientific evidence, and will continue to protect the health and safety of formula fed infants.

One submitter supported the *status quo*, contending that studies with a ratio of *1.5-2.5* AA:DHA more frequently reported significant differences in a measured outcome than did studies with ratios of *0.5-1.5* or greater than *2.5*. The submitter also cited two studies not considered at Draft Assessment; one met the inclusion criteria and has now been considered and described.

However at Final Assessment FSANZ maintains that the totality of the evidence considered does not indicate a clear advantage in adding any particular omega 6 and omega 3 ratio. Therefore FSANZ considers the ratio of omega 6:omega 3 that is *not less than 1* as proposed in this Application is safe and appropriate should LCPUFA be added to infant formula.

In addition, the inclusion of an upper limit for DHA and AA also maintains a level of safety with LCPUFA additions to infant formula. The Code currently sets maximum levels for various LCPUFA if these are added to infant formula (Standard 2.9.1 Table to Clause 23).

8. Consistency with International Regulations

Since Draft Assessment, a revised Codex standard for infant formula has been adopted. This standard recommends that if DHA is added to infant formula, then AA contents should reach at least the same concentration as DHA.

The European Union revised ruling, Commission Directive 2006/141/EU on infant formulae and follow-on formulae, includes a requirement that the DHA content shall not exceed the content of omega 6 LCPUFA.

Many submitters have noted the current ratio requirement of omega 6 to omega 3 LCPUFA of approximately 2 is inconsistent with international standards. Some industry submitters have noted the unique ratio requirement for Australia and New Zealand creates trade barriers and adds costs for manufacturers and consumers. Almost all submitters at Draft Assessment noted the proposed amendment was more consistent with international standards.

Therefore, amending the omega 6 to omega 3 LCPUFA ratio requirement from *approximately 2* to a ratio of *not less than 1*, in the context of the current maximum levels set in Standard 2.9.1, would align with international recommendations and standards and assist to facilitate trade.

9. Options

As a result of the Applicant's revised position after Initial Assessment, FSANZ proposed two options at Draft Assessment for this Application. As no additional issues have been identified at Draft Assessment the two options are again proposed at Final Assessment:

9.1 Option 1 – Maintain *status quo*

Maintain the *status quo* by not amending the Code, and thus retaining the requirement for omega 6 to omega 3 LCPUFA to be present in a ratio of *approximately 2*, when added to infant formula and follow-on formula.

9.2 Option 2 – Amend Standard 2.9.1

Amend Standard 2.9.1 to include a requirement that the omega 6 to omega 3 LCPUFA ratio should be *not less than 1* in infant and follow-on formula when LCPUFA are added to these products, in place of the current ratio requirement of *approximately 2*.

10. Impact Analysis

10.1 Affected Parties

The parties affected by this Application are: **consumers** being formula-fed infants consuming infant formula with added LCPUFA and their carers; **industry** being Australian and New Zealand manufacturers and importers of infant formula; and the **Government enforcement agencies** of Australia and New Zealand.

10.2 Cost-Benefit Analysis

This analysis assesses the immediate and tangible impacts of the current food standard under Option 1 and the proposed amendment under Option 2.

10.2.1 Option 1 – Maintain Status quo

10.2.1.1 Consumers

Maintaining the *status quo* is likely to have minimal impact on consumers as infant formula with added LCPUFA will continue to be available. Thus carers of formula-fed infants would continue to have the choice to use these products to gain any potential benefits from LCPUFA.

However, the cost of these products for consumers is likely to remain higher than for infant formula without added LCPUFA, due to the increased costs to manufacture to the omega 6 to omega 3 LCPUFA ratio required specifically for Australia and New Zealand. Industry has noted that if higher costs make a product unacceptable to consumers, products may be withdrawn from the market, reducing competition.

In addition the *status quo* may limit the range of products available for formula fed infants due to barriers to importation of products that do not meet the Code, and therefore limit consumer choice.

10.2.1.2 Industry

Maintaining the *status quo* would continue to impact on industry as it is inconsistent with international recommendations and regulations.

As the requirement to meet an omega 6 to omega 3 LCPUFA ratio of *approximately 2* is unique to Australia and New Zealand, the increased costs for industry to produce infant formula with added LCPUFA for this market would remain, with these costs passed onto the consumer. Industry considers prescriptive ratios to be a cost burden. As there are no natural ingredients with the required ratio of approximately 2, manufacturers incur an additional expense to manufacture for the domestic market with this ratio. Exportation of this product would be more expensive, compared to other less prescriptive formulations. Alternatively, companies could choose to have an additional production line to manufacture products for export with a less prescriptive ratio, thus incurring further costs.

In addition, industry has noted that if a product is not accepted by consumers because of the greater cost, then competition in the marketplace could reduce as these products may be withdrawn from the market.

Maintaining the *status quo* could be a potential technical barrier to trade due to the inconsistency with overseas and international regulations. Some infant formulas are manufactured for worldwide distribution, and Australia and New Zealand is considered a minor market within this global trade. Therefore the industry experiences difficulties from having to manufacture products with added LCPUFA that are suitable for both local and export markets.

The current lack of harmonisation with international regulations and manufacturing requirements can also lead to difficulties for importers when seeking to import products that must comply with the Code. Consequently, the variety of infant formula with added LCPUFA available in Australia and New Zealand may be reduced.

10.2.1.3 Government

The impact of maintaining the *status quo* on the Australian and New Zealand governments is likely to be minimal, with respect to monitoring and enforcing the omega 6 to omega 3 LCPUFA ratio for infant formula.

10.2.2 Option 2 – Amend Standard 2.9.1

10.2.2.1 Consumers

It is likely that requiring an omega 6 to omega 3 ratio of *not less than 1*, in place of *approximately 2*, would have no impact on the safety of consumers of infant formula. Evidence indicates that any impact on growth and development is unlikely to be dependent on the relative quantities of added omega 6 and omega 3 LCPUFA. Infant formula with added LCPUFA would continue to be available, consumer choice would remain, and thus enable formula-fed infants to continue to gain any potential benefits from consuming these fatty acids.

As an omega 6 to omega 3 LCPUFA ratio of *not less than 1* would better align with international regulations and could widen trade opportunities, there is potential for an increased range of products to be available for consumers.

In addition, there may be a cost advantage for manufacturers of infant formula if only one formulation is manufactured for worldwide distribution. This could potentially result in a cost reduction being passed onto consumers.

10.2.2.2 Industry

For industry, replacing the current omega 6 to omega 3 LCPUFA ratio of *approximately 2* with a ratio requirement of *not less than 1* would provide greater harmonisation with the recently adopted Codex recommendations and the European Union Directive.

The manufacture of one formulation for worldwide distribution provides a cost advantage for infant formula manufacturers. The increased costs associated with production of infant formula to meet the current requirements of the Code are likely to reduce as production would not be exclusively for Australia and NZ.

Australian and New Zealand importers may experience less difficulty when seeking to import products that must comply with the Code into Australia and New Zealand. This could result in the importation of a wider range of products.

In addition, infant formula produced locally would be suitable for both local and export markets which will reduce barriers to trade and could potentially increase the sale of these products to countries outside Australia and New Zealand.

There are no significant costs associated with this option as expressed by the Business Cost Calculator Report (Attachment 3), therefore this does not need to be notified to the Office of Best Practice Regulation.

10.2.2.3 Government

There is likely to be no impact on the Australian and New Zealand governments as a result of replacing the current omega 6 to omega 3 LCPUFA ratio of *approximately 2* with a ratio of *not less than 1*.

11. Comparison of Options

A comparison of the Options presented at Final Assessment indicates that Option 1 would continue to protect the health and safety of formula-fed infants as evidence indicates that an omega 6 to omega 3 LCPUFA ratio of *approximately 2* remains an acceptable ratio. However, as studies show that LCPUFA ratios in breast milk vary and that infants can tolerate significant variations of the omega 6 to omega 3 LCPUFA ratio in their source of milk, there would appear to be no additional benefit in prescribing this specific ratio.

In addition Option 1 is a unique ratio requirement for Australia and New Zealand which does not promote consistency between domestic and international food standards. The omega 6 to omega 3 LCPUFA ratio of *approximately 2* results in trade barriers, increased manufacturing and purchase costs and potentially limits the range of products available to consumers. Overall the costs of maintaining a ratio of *approximately 2* appear to outweigh any benefits.

In comparison, Option 2 would also continue to protect the health and safety of formula-fed infants as evidence indicates an omega 6 to omega 3 LCPUFA ratio of at least 1 is recognised as safe and suitable for infants. Evidence also indicates that any impact on growth and development from LCPUFA is unlikely to be dependent on the relative quantities of omega 6 and omega 3 LCPUFA.

Also, a ratio of at least 1 would be more consistent with international food standards, and thus would provide manufacturing, trade and cost benefits to the food industry that would potentially be passed onto consumers.

At Final Assessment, a comparison of options indicates Option 2 provides greater net benefits than Option 1.

COMMUNICATION AND CONSULTATION STRATEGY

12. Communication

FSANZ has reviewed the nature of the feedback received from submitters at Initial and Draft Assessment and does not intend to undertake specific communication and consultation work in addition to the two statutory public consultation periods.

13. Consultation

13.1 Initial Assessment

The Initial Assessment Report was available for public submissions during the six week public consultation period of 31 May to 12 July 2006. A total of 41 submissions[14] were received including eight public health and academic submissions, 12 from industry, three from government, plus one consumer submission.

Submitters' views were mixed in relation to the regulatory options put forward at the Initial Assessment. However, the majority supported a change to the current ratio requirement. Of those supporting the retention of a ratio, most favoured a 1:1 ratio.

13.2 Draft Assessment

FSANZ received a total of 12 submissions in response to the Draft Assessment Report during the six week public consultation period of 23 May to 4 July 2007. Seven submissions were received from the food industry, four from Government and one from a health professional organisation.

Almost all (11) submitters favoured Option 2, to amend Standard 2.9.1 to include a requirement that the omega 6 to omega 3 LCPUFA ratio should be *not less than 1* in infant and follow-on formula when LCPUFA are added to these products.

Many submitters noted Option 2 is in agreement with current scientific opinion and international recommendations including Codex and EU, and would continue to protect the health and safety of formula fed infants.

A full summary of submissions received at Draft Assessment is at Attachment 4.

13.3 World Trade Organization (WTO)

As members of the World Trade Organization (WTO), Australia and New Zealand are obligated to notify WTO member nations where proposed mandatory regulatory measures are inconsistent with any existing or imminent international standards and the proposed measure may have a significant effect on trade.

[14] Seventeen submissions were received from university students, most identified as students of Food Science at the University of Auckland, New Zealand. The submissions generally favoured Option 2 supporting the removal of the current clause requiring a ratio of approximately 2.

Currently some relevant international Standards are in place. Modifying Standard 2.9.1 of the Code by reducing the omega 6 to omega 3 LCPUFA ratio from *approximately 2* to at least 1 will make Australian and New Zealand food standards consistent with EU infant formula legislation and the recently adopted revised Codex infant formula standard**.**

It is expected that the proposed changes will harmonise Australian and New Zealand regulations with current and future international practices, and therefore will not result in a potential barrier to trade. Consequently, WTO member nations were not been notified of the proposed amendment to Standard 2.9.1 under either the Technical Barriers to Trade or Sanitary and Phytosanitary Agreements.

CONCLUSION

14. Conclusion and Decision

Decision

Option 2 is the preferred regulatory approach for Application A532. This approach would result in an amendment to Standard 2.9.1 to require an omega 6 to omega 3 LCPUFA ratio that is *not less than 1*, should LCPUFA be added to infant formula.

The considerations made in reaching this preferred approach are as follows:

The change to the omega 6 to omega 3 LCPUFA ratio:

- does not pose any health and safety risks to formula-fed infants; and
- is consistent with relevant international regulations currently in place; and thus would reduce barriers to trade, increase availability of products and reduce cost for industry and potentially consumers.

Overall, affected parties will receive a net-benefit from Option 2.

FSANZ therefore recommends the proposed draft variation to the Code that is provided in Attachment 1.

15. Implementation and Review

Approval of the Application will result in the proposed variation to Standard 2.91 commencing on gazettal.

Attachments

1. Draft variation to the *Australia New Zealand Food Standards Code*.
2. A Review of the Long Chain Polyunsaturated Fatty Acid Content of Infant Formula and its Effects on the Growth and Development of Infants
3. Business Cost Calculator Report
4. Summary of Submissions from the Draft Assessment Report

Attachment 1

Draft variation to the *Australia New Zealand Food Standards Code*

To commence: On Gazettal

[1] ***Standard 2.9.1*** *of the Australia New Zealand Food Standards Code is varied by omitting from sub clause 23(d)* of approximately 2 *substituting –*

that is not less than 1

Attachment 2

A Review of the Long Chain Polyunsaturated Fatty Acid Content of Infant Formula and its Effects on the Growth and Development of Infants

Executive Summary

Food Standards Australia New Zealand (FSANZ) identified 17 randomised controlled trials examining the feeding of Long Chain Polyunsaturated Fatty Acid (LCPUFA) enriched infant formula to term infants at omega 6 to omega 3 LCPUFA ratios of 0.3 to 4.3 (excluding those that added only omega 3 LCPUFA to infant formula). These studies were used to determine the role that dietary omega 6 and omega 3 LCPUFA have in the growth and development of infants.

For the most part, the data obtained from the 17 identified studies show little difference in growth or cognitive outcomes when infants are fed formulas with varying levels of added omega 6 and omega 3 LCPUFA. In particular, the anthropometric data show that LCPUFA addition to infant formulas has no effect compared to standard formulation. However, the addition of LCPUFA to infant formula does appear to have some positive, albeit minor influence on the visual development of infants compared to standard formulations.

Additionally, the fatty acid profile of human milk (from a wide geographical range) shows great variation in omega 6 to omega 3 LCPUFA ratios, and would appear to suggest that infants can tolerate significant variations to this ratio in their milk source.

In all measures of assessment, there is a consistent lack of influence on infant growth and development from relative variations in the omega 6 and omega 3 LCPUFA contents of infant formulas. In respect to the singular addition of omega 3 LCPUFA, in the form of docosahexaenoic acid, versus the addition of both omega 3 and omega 6 LCPUFA to infant formula, the evidence base is currently too small to make a definitive analysis.

Therefore, there is no apparent advantage in adding omega 6 and omega 3 LCPUFA to infant formula at a ratio of *approximately 2* over a ratio *not less than 1*

1. Introduction

FSANZ received a joint Application from the Infant Formula Manufacturers Association of Australia and the New Zealand Infant Formula Marketers' Association on 27 February 2004. The Application has requested an amendment to Standard 2.9.1 – Infant Formula Products of the *Australia New Zealand Food Standards Code* (the Code); which is intended to modify the current omega 6 to omega 3 long chain polyunsaturated fatty acid (LCPUFA)[15] ratio of *approximately 2* in infant formula (which contain added LCPUFA).

To progress this Application, FSANZ has undertaken a review of the available literature on the addition of LCPUFA to term infant formula. This review will determine the influence on the growth and development of infants from formula with different ratios of omega 6 and omega 3 LCPUFA contents.

In undertaking this assessment, literature has been sourced from the following locations:

- PubMed electronic databases, using the search terms 'infant formula AND long chain AND growth' and 'infant formula AND long chain AND development'; and

- Primary research material from review articles by Makrides *et al.* (2000a), Makrides *et al*. (2005), and Fleith and Clandinin (2005).

- Primary research cited in submissions to the DAR, specifically Bouwstra *et al* (2003 and 2005) and Brenna *et al* (2007).

From this evidence base, FSANZ has excluded studies conducted on pre-term infants, studies that did not commence formula intervention within two weeks of birth, and those studies that did not include an assessment of either anthropometric, visual acuity or behavioural parameters. These exclusions ensure that the evidence base specifically addresses the health outcomes from the addition of LCPUFAs to formulas for term infants.

Twenty-four published articles were obtained using the above search strategies, and these articles discuss the findings of 17 studies (several articles report different aspects of the same study). These studies had the following characteristics:

- all of the trials compare LCPUFA enriched formula to a control of standard infant formula. The standard formulas were commercially available products that would have met the requirements of the Code at the time of the study;

- allocation to different formula types was random and double-blinded in all trials; and

- for those studies assessing visual acuity and/or neurological development, the parental educational level/socioeconomic status was homogenous across all groups (these data were not collected by studies that assessed anthropometric endpoints only).

Full details of the 17 studies can be found in Tables A1-A5 at the end of this document.

[15] Consistent with Standard 2.9.1 of the Code, this report classifies LCPUFA as polyunsaturated fatty acids with a chain length of $\geq$ 20 carbon units.

The following sections discuss the results of these studies and the implications of this research for the addition of LCPUFA to infant formula.

2. Findings of studies on the addition of LCPUFA to infant formula

Of the 17 studies reviewed, most involved comparisons (over time) between different types of infant formula with either docosahexaenoic acid (DHA) added alone, or DHA added with arachidonic acid (AA) in AA to DHA ratios of 0.3:1 to 4.3:1[16].

Eleven of these studies also included a non-randomised group of infants who were breast-fed over the same time period as the formula groups. Because these groups are non-randomised, there are maternal variables associated with the decision to breastfeed that could have potentially contributed to differences between formula-fed and breast-fed groups. These variables include maternal intelligence quotient (IQ), education level, and socioeconomic status; maternal-infant interaction; and the act of breast-feeding itself. However, breast-fed infants are considered to be an important reference group for use in infant feeding studies (Birch *et al*., 2007), and so the human milk results have been discussed below even though it is not the intent of this report to assess the overall performance of infant formula versus human milk.

2.1 The impact on infant growth

Fourteen of the 17 studies reported assessments of infant growth parameters, e.g. weight, length, or head circumference. Nearly all of these studies show that the addition of LCPUFA to infant formula has no effect on growth (either positive or negative) compared to standard formula, regardless of whether this addition consists of DHA alone, or both DHA and AA (at varying ratios).

Three articles (Agostoni *et al*., 1994; Lapillonne *et al*., 2000; Morris *et al*., 2000) did report a significant difference in either weight or head circumferences. In two of these articles (Agostoni *et al*., 1994; Morris *et al*., 2000), the significant differences between study groups occurred only at birth and not at later ages (4 and 12 months); thus there was no demonstrable effect of diet. These differences at birth could reflect a problem with the studies' randomisation processes, although it is more likely that the results reflect the small sample sizes used in both studies (n=15-23 for Agostoni *et al*., and n≈55 for Morris *et al*.).

Lapillonne *et al*. (2000) reported a significant difference ($p<0.05$) of 1.4 cm in the mean head circumference between study groups at 4 months. However, the difference was due to an increased head circumference in the control (standard) formula group compared to the test (DHA modified) formula groups, rather than the reverse. The article also reported that the head circumference results of the test formula group were equivalent to the results for a cohort of breast-fed infants used in the study. The authors of this paper do not give any explanation for the unusual control group results.

[16] AA and DHA are the predominant omega 6 and omega 3 LCPUFA added to infant formula respectively. Permitted preparations of these do contain other fatty acids as well as non-lipid constituents as detailed in Standard 1.3.4 – Identity and Purity – of the Code. Other omega 6 and omega 3 LCPUFA can be added, however their addition is not considered commercially viable.

2.2 The impact on development of visual acuity

Eight of the 17 studies (reported in 9 articles) have investigated the impact from LCPUFA enriched infant formula on the development of visual acuity in infants (Makrides *et al*., 1995a; Carlson *et al*., 1996; Auestad *et al*., 1997; Birch *et al*., 1998; Jorgensen *et al*., 1998; Hoffman *et al*., 2000; Makrides *et al*., 2000b; Auestad *et al*., 2001; Birch *et al*., 2005). These eight studies measured visual acuity using either behavioural, visual evoked potential (VEP) or stereoacuity tests[17].

The majority of the eight visual acuity studies did not demonstrate a significant effect of LCPUFA supplementation over standard formula using either behavioural or VEP assessment techniques (Carlson *et al.,* 1996; Auestad *et al.,* 1997; Birch *et al.,* 1998; Jorgensen *et al.,* 1998; Hoffman *et al.,* 2000; Makrides *et al.,* 2000b; Auestad *et al.,* 2001). Birch et al. (2007) conducted a follow-up study of the results presented in Birch et al. (1998), and found that LCPUFA supplementation continued to have no significant impact on the visual acuity of the cohort up to 4 years of age. Singhal et al. (2007) followed-up an infant cohort previously assessed on anthropometry and neurological development (Lucas *et al*., 1999), and also found that LCPUFA supplementation had no significant impact on stereoacuity up to 6 years of age.

However, there were three studies (Makrides *et al.,* 1995a; Birch *et al.,* 1998; Hoffman *et al.,* 2000; Birch *et al.,* 2005) that reported a positive effect when using VEP techniques. These three studies showed significantly higher ($p<0.05$) changes in VEP of -0.8 to -0.2, -0.3, and -0.14 LogMAR[18] with the consumption of LCPUFA enriched formula at 4, 6 and 12 months of age respectively. Birch *et al*. (2005) also reported a benefit in stereoacuity (of 0.1 LogSec[19]) at 4 months, but not at any other age.

Overall, improvements in visual acuity from the use of LCPUFA enriched formula were predominantly identified with the use of VEP techniques; behavioural assessments of visual acuity predominantly reported no improvement. This pattern may be the result of the problems inherent in the use of behavioural assessments, which rely on an individual's subjective evaluation of an infant and are thus exposed to a greater level of observer error (Birch *et al.,* 1998). The influence of these errors could have overwhelmed any small differences that occurred during the behavioural assessment studies. Because of their increased sensitivity, the VEP derived results are therefore considered to have greater weight than behaviourally assessed results.

2.3 The impact on neurological development

The infant formula research reviewed has utilised a wide range of techniques for evaluating the neurological performance of infants.

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[17] In considering the results it should be noted that an improvement in visual acuity, as measured by either a behavioural assessment (e.g. forced preferential looking) or VEP assessment, is reflected by lower values. Improvements in stereoacuity results are, however, reflected by higher values.

[18] Logarithm_{10} of the eye's minimum angle of resolution. The minimum angle of resolution (measured in minutes) can be derived from the reciprocal of a Snellen notation; e.g. 20/25 vision = 1.25 minutes = 0.1 LogMAR.

[19] Logarithm_{10} of an arcsecond

The most common of these techniques is the Bayley Scales of Infant Development (Bayley, 1993), which are highly refined and accurate tests on the cognitive, motor, and behavioural development of infants. A similar test designed for Western European languages, the Brunet-Lezine test, was used by Agostoni *et al.* (1994).

The MacArthur Communicative Development Inventories have also been used by Scott *et al.* (1998) to assess language development, while Willatts *et al.* (1998) used a means-end problem solving test to evaluate cognitive behaviour. Bouwstra *et al* (2003) used an evaluation of the quality of general movements; a technique previously found to allow accurate evaluation of brain function in young infants (Hadders-Algra, 2001).

A number of the studies assess neurological endpoints beyond the ages of 0-12 months, as neurological development is more consistent after infancy. At these older ages, the subjects are on a full solid diet, and are no longer consuming the test formulas. However, it is reported that nutrition during infancy can continue to have an effect on neurological performance beyond the immediate time period (Birch *et al.,* 2000), and therefore an assessment of the older age results (12-24 months) has been included in this report.

Of the nine studies assessing cognitive development (Agostoni *et al.,* 1994; Agostoni *et al*., 1997; Scott *et al*., 1998; Willatts *et al*., 1998; Lucas *et al.,* 1999; Birch *et al.,* 2000; Makrides *et al*., 2000c; Auestad *et al.,* 2001), a substantial proportion do not show any difference (at various ages) between infants fed standard formula or formula with added LCPUFA, even with the use of different omega 6 to omega 3 LCPUFA ratios across the studies. Five studies (Agostoni *et al.,* 1994; Scott *et al*., 1998; Willatts *et al*., 1998; Birch *et al.,* 2000, Bouwstra *et al*., 2003) reported differences between the various formula study groups, but only at single age points.

An assessment of neurological development by Birch *et al.* (2000), using the Bayley Mental Development Index (MDI), showed that at 18 months of age, children who were fed formula in infancy with added LCPUFA had significantly better scores ($p<0.05$) than those who had been fed standard formula (normative MDI scores of 105.6 and 98.3 respectively). However the psychomotor and behavioural Bayley tests did not show a similar difference. The authors also noted that their assessments of visual acuity at 4 months (see Section 2.2 above) correlated well with the Bayley assessment results at 18 months, suggesting that LCPUFA could affect cognitive development at a younger age.

Using the Brunet-Lezine test, Agostoni *et al.* (1994) showed that at the age of 4 months, infant formula with added DHA and AA resulted in significantly better ($p<0.05$) neurodevelopment than standard formula (normative scores of 105.3 and 96.5 respectively). However, in a follow-up study at 24-months of age (Agostoni *et al*., 1997), the authors found that there was no longer any significant difference in neurological performance between the different study groups.

Scott *et al* (1998) reported that, at 14 months of age, infants fed formula with added DHA but no added AA obtained lower scores ($p<0.05$) on the vocabulary comprehension and production components of the MacArthur Communicative Development Inventories than infants fed standard formula. Results for infants fed formula with added DHA and AA did not differ from those fed standard formula or breast milk.

Willatts *et al* (1998) took a different approach to assessing neurological development, using a test of problem solving ability rather than focusing on measurements of perception and motor skills. Significant improvements ($p<0.05$) were shown with LCPUFA-enriched formula versus standard formula for the overall test, although this improvement occurred only in one of the three behaviour subsets of the test.

Bouwtra *et al* (2003) reviewed video footage of infants' spontaneous motor behaviour at three months of age to assess the quality of their general movements. Infants fed standard formula had mildly abnormal general movements significantly ($p<0.05$) more often than did infants fed formula with added AA and DHA or breast milk, the result being 31%,19% and 20% respectively. A follow up of the infants at 18 months of age showed no differences between any of the three groups in terms of Bayley scales (Bouwstra *et al*, 2005).

In addition to the above evidence, FSANZ has identified that both Scott *et al* (1998) and Birch *et al.* (2000) continued to follow their infant cohorts into early childhood (Auestad *et al*., 2003; Birch *et al*., 2007).

The follow-up studies assessed the IQ of their cohorts between the ages of 3-4 years using standardised techniques, and found no significant difference ($p>0.05$) between the children who had been fed LCPUFA enriched formula and those fed standard formula during infancy.

3. Findings from studies that compare the singular addition of omega 3 LCPUFA to the addition of both omega 6 and omega 3 LCPUFA

FSANZ has identified four studies (reported in eight articles) that have directly compared formula containing DHA alone with formula containing DHA in combination with AA in term infants (Auestad *et al*., 1997; Birch *et al.,* 1998; Scott *et al.,* 1998; Makrides *et al*., 1999; Birch *et al.,* 2000; Hoffman *et al.,* 2000; Makrides *et al.,* 2000c).

Three of the four studies, with participant numbers ranging from 58 - 200, did not find any difference in growth, visual acuity or cognitive outcomes up to 2 years of age between infants fed formula with added DHA only or containing both added DHA and AA. Only one study of 68 infants fed a test diet for 17 weeks (Scott *et al.,* 1998) reported a significant difference between the consumption of formula with the singular addition of DHA versus the addition of DHA and AA together (AA to DHA ratio of 3.6:1).

Scott *et al.* (1998) reported that infants fed formula with the singular addition of DHA had lower vocabulary productions scores (MacArthur Communicative Development Inventories) at 14 months of age than infants fed standard formula; a result that did not occur if AA was added with DHA. However, other skills assessed with the MacArthur Communicative Development Inventories, such as gestural communication and the number of phrases understood by the child (vocabulary comprehension), were not adversely affected by the addition of DHA alone compared to the addition of both DHA and AA. Also, Scott *et al.* (1998) assessed subjects at 12 months of age using the Bayley Scales of Infant Development, and found that the type of formula they consumed since birth had no effect on these tests of cognitive development, regardless of the formula's DHA or AA content.

To explain the reasons for their findings, the authors also analysed the serum DHA levels of their subjects.

It was found that serum DHA levels were negatively correlated with the vocabulary scores across all feeding regimes. The authors were therefore unwilling to dismiss the results as the product of either chance or the absence of AA from test formulas. Further, results from the follow-up of the Scott *et al.* (1998) cohort at three years of age found that there was no significant difference ($p>0.05$) in cognitive performance between the various feeding regimes (Auestad *et al.,* 2003).

4. Analysis of the findings on omega 6 and omega 3 LCPUFA addition to infant formula

The 17 identified studies show little difference in growth or neurological outcomes when infants are fed formulas with varying levels of added omega 6 and omega 3 LCPUFA. In particular, the anthropometric data show no consistent diet-related effect from the addition of LCPUFA to infant formula. However, the addition of LCPUFA to infant formula has been reported in some studies to have a positive influence on the visual development of infants compared to standard formulations. Other studies have not found positive effects on visual acuity.

However, there are exceptions to the visual and neurological development trends that warrant further discussion.

A study of note is that conducted by Auestad *et al.* (2001), which showed no improvement in visual acuity from LCPUFA enriched formula compared to standard formula. This particular study is significant in that it has used the greatest number of subjects ($n = 177$) of all of the studies that have assessed visual acuity, and thus has the greatest statistical power of these studies. Further, the authors made efforts to remove a number of common methodological errors associated with other infant formula trials, including an analysis of variance to limit errors from the use of multiple examination centres, and the use of two different LCPUFA ingredient sources to ensure that results were not due to the origin of added LCPUFA. Because of these additional quality controls, the results from Auestad *et al*. (2001) can be considered as highly reliable, even though the study contradicts the positive outcomes from several other studies (Makrides *et al.,* 1995a; Birch *et al.,* 1998; Hoffman *et al.,* 2000; Birch *et al.,* 2005).

An important exception in respect to neurological development is the study by Scott *et al.* (1998). The lower vocabulary production scores of 14 month-old infants fed formula with DHA as its only source of LCPUFA, compared to 14 month-old infants fed formula containing both DHA and AA, is in contrast to all other studies assessing neurological development and/or comparing these two formula variations. A possible explanation identified by Birch *et al.* (2000) is that the quantity of DHA added to the DHA-only formula (0.23% by weight) was too low; all other studies comparing DHA-only formula to formula with both DHA and AA have used a minimum DHA content of 0.35% by weight in the DHA-only formula. Birch *et al.* (2000) also mentions that another possible reason is that Scott *et al*. (1998) used multiple examiners to conduct the cognitive tests, which could have increased the statistical variability within the study's results. However, it may be that the use of an additional methodology by Scott *et al*. (1998) has identified an effect on a seldom researched aspect of cognition, and therefore is not comparable to other studies on neurological development.

Overall, the quality of research within the evidence base on addition of omega 6 and omega 3 LCPUFA to infant formula is high. The main deficiencies encountered can be summarised as:

- The small sample sizes. Most studies had fewer than 20 subjects allocated to each of their feeding regime groups, and only three studies have examined a total subject population of more than 150 subjects (Carlson *et al*., 1999; Lucas *et al*., 1999; Auestad *et al.,* 2001). The reduced statistical power of the evidence base means that there is a greater level of uncertainty associated with the findings from this literature.

- Inconsistencies in the amount of linoleic acid and alpha-linolenic acid within test formulas (variations of 8.37-34.2% wt and 0.7-5.0% wt respectively). As precursors of DHA and AA, variations in these fatty acids could potentially result in different outcomes when DHA and/or AA are added to test formulas.

- Inconsistencies in the ages for testing, and in the methodologies used to assess study endpoints.

- The lack of correction for baseline anthropometric data.

Even with these deficiencies, the totality of evidence suggests that the addition of LCPUFA to infant formula has a minimal impact on the growth and development of infants. The only potential benefit from LCPUFA addition would appear to be an improvement in the development of visual acuity, although currently available data remains conflicting on this health outcome. Further, in all measures of assessment, there is a consistent lack of influence on infant growth and development from relative variations in the omega 6 and omega 3 LCPUFA contents of infant formulas.

In respect to the singular addition of DHA versus the addition of both DHA and AA to infant formula, the evidence base is currently too small to make a definitive analysis. The little available data does not indicate an advantage to adding DHA in the absence of AA..

5. Other relevant issues

5.1 Systematic reviews of LCPUFA addition to term infant formula

FSANZ has identified several systematic reviews of the literature on the addition of LCPUFA to term infant formula (SanGiovanni *et al*., 2000; Simmer, 2001; Makrides *et al*., 2005; Fleith and Clandinin, 2005). These meta-analyses have been conducted using different selections of studies and focus on different aspects of infant growth and development; however they conclude that LCPUFA-enriched formula has no effect on infant growth, and that there is too much uncertainty in the data to demonstrate a positive effect on infant visual and neurological development.

5.2 Human milk omega 6 and omega 3 LCPUFA content

The Australia New Zealand Food Standards Code prescribes an omega 6 to omega 3 LCPUFA ratio of *approximately 2* if LCPUFA are added to infant formula. This ratio was based on an assumption made by the Life Sciences Research Office (Raiten *et al*., 1998) that the ratio of omega 6 to omega 3 LCPUFA in human milk remains relatively constant. However, more recent published data does not support that assumption.

Data from 20 separate papers reporting analyses of human milk from different geographical regions (and thus different maternal dietary patterns) shows that AA content varies to a small extent, while DHA content varies to a much greater degree (see Figures A1-A3 at the end of this attachment). The results show omega 6 to omega 3 LCPUFA ratio that fluctuates widely depending on the diet of the mother and the stage of lactation. A recent meta-analysis of studies reporting breast milk fatty acid composition supports this summary (Brenna *et al*, 2007).

Given the geographical diversity in these data, including representation from both developing and developed nations, it would appear that infants can tolerate significant variations to the omega 6 to omega 3 LCPUFA ratio of their milk source.

5.3 Impact on infant biochemistry

It has been reported that if DHA is used as the only source of added LCPUFA in infant formula, then the feeding of this formula to infants will produce a significantly reduced red blood cell AA level compared to infants fed standard infant formula (Auestad *et al.,* 1997; Makrides *et al*., 2005). However, the singular addition of DHA ensures that an infant's red blood cell DHA levels remain at a similar or even higher level than those of breast-fed infants.

The results of many studies show that if AA is added with DHA, then the red blood cell AA can be retained at a level commensurate with breast-fed infants (Fleith and Clandinin 2005).

It is therefore clear that the absence of either omega 6 or omega 3 LCPUFA from infant formulas will be reflected in the DHA and AA status of infants fed such formulas. However, it is not clear whether variations in the DHA and AA status of infants fed formulas with varying AA to DHA ratios will affect the growth and development of these infants. The only study that has shown an impact on growth and development from differing ratios (Auestad *et al.,* 1997) reported a decrease in the AA status of its DHA alone group versus its DHA and AA group, however the serum AA data were not cross-referenced with the study's growth and development outcomes.

6. Conclusion

The studies identified by FSANZ show that the addition of LCPUFA to infant formula has no effect on the growth of infants, and at most, a minimal and variable effect on the visual and neurological development of infants. Further, this evidence indicates that any impact on growth and development is unlikely to be dependent on the relative quantities of added omega 6 and omega 3 LCPUFA (within the ranges studied). It is uncertain what effect, if any, the consumption of formula containing either DHA or AA alone has on infants versus the consumption of formula containing both.

The currently available evidence suggests that infants do not experience any adverse health effects from the singular addition of DHA to infant formula. There is no evidence base on which to assess the impact of only adding AA to infant formula.

There is no apparent advantage in adding omega 6 and omega 3 LCPUFA at ratio of *approximately 2* over a ratio *not less than 1.*

Table A1: Methodology and design of studies on the LCPUFA content of infant formulas (0-12 months of age)

Study	Methods	Study Duration	Study Endpoints	Subject Groupings		Infant Dietary Regime Details*				
				Infant Dietary Regime	n	Omega 6 LCPUFA (% wt)	Omega 3 LCPUFA (% wt)	Omega 6: Omega 3 Ratio	Linoleic Acid (% wt)	Alpha-linolenic Acid (% wt)
Agostoni *et al.* (1994; 1995; 1997).	Randomisation into control and LCPUFA formula groups. Breast-fed infants were used as a matched negative control. Randomisation, intervention and assessment were blinded.	0-4 months (Agostoni *et al.,* 1994; Agostoni *et al*., 1995); 4-24 months (Agostoni *et al.,* 1997)	• Assessment of weight, height and head circumference at 4 months. • Assessment of Brunet-Lezine test at 4 and 24 months.	Human Milk	15	n/a	n/a	n/a	n/a	n/a
				Standard formula	21	0	0		11.1	0.70
				Std + DHA + AA	23	0.44	0.35	1.3:1	10.8	0.73
Auestad *et al.* (1997); Scott *et al*. (1998)	Randomisation into control and LCPUFA formula groups. Randomisation, intervention and assessment were blinded.	0-12 months	• Assessment of weight, height and head circumference at 4 and 12 months (Auestad *et al.,* 1997). • Assessment of visual acuity at 4, 6 and 12 months (Auestad *et al.,* 1997). • Assessment of Bayley Scales of Infant Development at 12 months (Scott *et al.,* 1998).	Human Milk	63	1.2	0.9	1.3:1	17.2	1.8
				Standard formula	45	0	0		21.9	2.2
				Standard + DHA	43	0	0.23		20.7	1.9
				Std + DHA + AA	46	0.43	0.12	3.6:1	21.7	1.9

Study	Methods	Study Duration	Study Endpoints	Subject Groupings		Infant Dietary Regime Details*				
				Infant Dietary Regime	n	Omega 6 LCPUFA (% wt)	Omega 3 LCPUFA (% wt)	Omega 6: Omega 3 Ratio	Linoleic Acid (% wt)	Alpha-linolenic Acid (% wt)
Auestad *et al.* (2001)	Randomisation into control and LCPUFA formula groups. Randomisation, intervention and assessment were blinded.	0-12 months	• Assessment of weight, height and head circumference at 4, 6 and 12 months. • Assessment of visual acuity at 2, 4, 6 and 12 months. • Assessment of Bayley Scales of Infant Development at 6 and 12 months.	Human Milk	165	0.51	0.12	4.3:1	16.6	1.3
				Standard formula	77	0	0		22.2	2.6
				Std + DHA + AA (fish/fungal)	80	0.46	0.16	2.9:1	21.0	2.4
				Std + DHA + AA (egg)	82	0.45	0.14	3.2:1	22.4	2.5
Birch *et al.* (1998; 2000); Hoffman *et al.* (2000)	Randomisation into control and LCPUFA formula groups. Intervention and assessment were blinded.	0-12 months; 12-18 months (Birch *et al.,* 2000)	• Assessment of weight, height and head circumference at 4, 6 and 12 months. • Assessment of visual acuity at 4, 6 and 12 months. • Assessment of Bayley Scales at 18 months.	Human Milk	29	0.56	0.29	1.9:1	12.7	0.80
				Standard formula	23	0	0		14.6	1.49
				Standard + DHA	22	0	0.35		15.1	1.54
				Std + DHA + AA	23	0.72	0.36	2:1	14.9	1.53
Birch *et al*. (2005)	Randomisation into control and LCPUFA formula groups. Randomisation, intervention and assessment were blinded.	12 months	• Assessment of visual acuity at 4 and 12 months. • Assessment of stereoacuity at 4, 10 and 12 months.	Standard formula	44	0	0		8.48	0.86
				Std + DHA + AA	42	0.43	0.21	2:1	8.37	0.86

Study	Methods	Study Duration	Study Endpoints	Subject Groupings		Infant Dietary Regime Details*				
				Infant Dietary Regime	n	Omega 6 LCPUFA (% wt)	Omega 3 LCPUFA (% wt)	Omega 6: Omega 3 Ratio	Linoleic Acid (% wt)	Alpha-linolenic Acid (% wt)
Bouwstra *et al* (2003 & 2005)	Randomisation into control and LCPUFA. Randomisation, intervention and assessment were blinded for the initial study, but this is not evident for the follow up.	0-3 months 18 months at follow up	• Assessment of general motion at 3 months	Human Milk	147	n/a	n/a		n/a	n/a
				Standard formula	131	0	0		n/a	n/a
				Std + DHA + AA	119	0.45	0.3	1:0.67	n/a	n/a
Carlson *et al.* (1996)	Randomisation into control and LCPUFA formula groups. Randomisation, intervention and assessment were blinded.	0-12 months	• Assessment of weight, height and head circumference at 4 and 12 months. • Assessment of visual acuity at 4 and 12 months.	Human Milk	19	n/a	n/a		n/a	n/a
				Standard formula	20	0	0		21.9	2.2
				Std + DHA + AA	19	0.43	0.1	4.3:1	21.8	2.0
Carlson *et al.* (1999)	Randomisation into control and LCPUFA formula groups. Randomisation, intervention and assessment were blinded.	0-12 months	• Assessment of weight, height and head circumference at 4 and 12 months. • Visual acuity and the Bayley Scales of Infant Development were assessed, however the data was not reported.	Standard formula	104	0	0		n/a	n/a
				Std + DHA + AA	212	0.6	0.3	2:1	n/a	n/a
Decsi and Koletzko (1995)	Randomisation into control and LCPUFA formula groups. Randomisation and intervention were blinded.	0-4 months	• Assessment of weight, height and head circumference at 4 months.	Standard formula	7	0	0		11.1	0.7
				Std + DHA + AA	9	0.4	0.33	1.2:1	13.8	1.0

Study	Methods	Study Duration	Study Endpoints	Subject Groupings		Infant Dietary Regime Details*				
				Infant Dietary Regime	n	Omega 6 LCPUFA (% wt)	Omega 3 LCPUFA (% wt)	Omega 6: Omega 3 Ratio	Linoleic Acid (% wt)	Alpha-linolenic Acid (% wt)
Innis *et al.* (1996)	Randomisation into control and LCPUFA formula groups. Randomisation, intervention and assessment were blinded.	0-4 months	• Assessment of weight, height and head circumference at 4 months.	Human Milk	26	n/a	n/a		n/a	n/a
				Standard formula	37	0	0		20.5-34.2	2.1-4.8
				Standard + DHA	68	0	0.12-0.24		20.0-32.2	2.1-5.0
Jorgensen *et al*. (1998)	Randomisation into control and LCPUFA formula groups. Randomisation, intervention and assessment were blinded.	0-4 months	• Assessment of visual acuity at 4 months.	Human Milk	42	0.65	0.69	0.9:1	11.1	1.3
				Standard formula	11	0.12	0		12.3	1.2
				Standard + DHA	26	0.22	0.77	0.3:1	12.0	1.2
Lapillonne *et al.* (2000)	Randomisation into control and LCPUFA formula groups. Randomisation, intervention and assessment were blinded.	0-4 months	• Assessment of weight, height and head circumference at 4 months.	Human Milk	13	n/a	n/a		n/a	n/a
				Standard formula	12	0	0		17.4	1.6
				Standard + DHA	12	0	0.39		17.6	1.1
Lucas *et al.* (1999)	Randomisation into control and LCPUFA formula groups. Randomisation, intervention and assessment were blinded.	0-18 months	• Assessment of weight, height and head circumference at 4, 6 and 9 months. • Assessment of Bayley Scales of Infant Development at 18 months.	Standard formula	155	0	0		12.4	1.1
				Std + DHA + AA	158	0.3	0.33	0.9:1	15.9	1.4

Study	Methods	Study Duration	Study Endpoints	Subject Groupings		Infant Dietary Regime Details*				
				Infant Dietary Regime	n	Omega 6 LCPUFA (% wt)	Omega 3 LCPUFA (% wt)	Omega 6: Omega 3 Ratio	Linoleic Acid (% wt)	Alpha-linolenic Acid (% wt)
Makrides *et al.* (1995a)	Randomisation into control and LCPUFA formula groups. Randomisation, intervention and assessment were blinded.	0-12 months	• Assessment of weight, height and head circumference at 4 and 12 months. • Assessment of visual acuity at 4 and 12 months.	Human Milk	23	0.5	0.44	1.1:1	13.9	0.9
				Standard formula	19	0	0		16.8	1.6
				Standard + DHA	13	0	1.0		17.4	1.5
Makrides *et al.* (1999); Makrides *et al*. (2000c)	Randomisation into control and LCPUFA formula groups. Randomisation, intervention and assessment were blinded.	0-12 months (Makrides *et al.,* 1999); 12-24 months (Makrides *et al.,* 2000c)	• Assessment of weight, height and head circumference at 4, 8 and 12 months (Makrides *et al.,* 1999). • Assessment of visual acuity at 4 and 8 months (Makrides *et al.,* 2000c). • Assessment of Bayley Scales of Infant Development at 12 and 24 months (Makrides *et al.,* 2000c).	Human Milk	33	0.39	0.29	1.3:1	13.4	1.0
				Standard formula	21	0	0		16.8	1.5
				Standard + DHA	23	0	0.45		16.8	1.2
				Std + DHA + AA	24	0.34	0.34	1:1	16.6	1.0
Morris *et al.* (2000)	Randomisation into control and LCPUFA formula groups. Randomisation, intervention and assessment were blinded.	0-12 months	• Assessment of weight, height and head circumference at 6 and 12 months.	Standard formula	55	0	0		11.8	2.4
				Std + DHA + AA	54	0.4	0.2	2:1	11.6	2.3

Study	Methods	Study Duration	Study Endpoints	Subject Groupings		Infant Dietary Regime Details*				
				Infant Dietary Regime	n	Omega 6 LCPUFA (% wt)	Omega 3 LCPUFA (% wt)	Omega 6: Omega 3 Ratio	Linoleic Acid (% wt)	Alpha-linolenic Acid (% wt)
Willatts *et al.* (1998)	Randomisation into control and LCPUFA formula groups. Randomisation and assessment were blinded.	0-10 months	• Assessment of cognitive performance using a means-end problem solving test.	Standard formula	23	0	0		12.8	0.7
				Std + DHA + AA	21	0.35	0.2	1.75:1	11.4	0.7

n/a = data not available

* = several studies that included a Human Milk group did not collect breast milk samples for analysis of fatty acid contents (data expressed as 'n/a'). Instead, the researchers relied on previously collected human milk composition data that was relevant to their particular population group.

Table A2: Anthropometric results from studies on the LCPUFA content of infant formulas (0-12 months of age)

Study	Subject groups		Anthropometric Results (mean + sd)[1]																													
			Weight (kg)										Length (cm)										Head Circumference (cm)									
	Type Formula	n	Birth	sd	4 mths	sd	6 mths	sd	8 mths	sd	12 mths	sd	Birth	sd	4 mths	sd	6 mths	sd	8 mths	sd	12 mths	sd	Birth	sd	4 mths	sd	6 mths	sd	8 mths	sd	12 mths	sd
Agostoni *et al.*(1994)	Human Milk	15	3.37	0.49	6.45	0.79							50.4	1.7	63.1	2.6							34.3	1.5	41.8	0.9						
	Standard formula	21	**3.3**[a]	0.46	6.58	0.85							50.2	2.7	63	3.2							34.1	1.1	41.5	1.6						
	Std + DHA + AA	23	**3.22**[b]	0.44	6.36	0.47							50	1.9	62	1.7							34.1	1.4	41.1	1.2						
Auestad *et al.* (1997)	Human Milk	63	3.6	0.46	6.85	0.80					9.95	1.21	50.8	3.1	62.8	2.3					75.3	2.8	34.8	1.5	41.8	1.1					46.6	1.2
	Standard formula	45	3.6	0.47	6.97	0.66					10.23	1.18	50.9	2.9	62.9	2.2					75.4	3	34.8	1.5	41.9	1.1					46.7	1.3
	Standard + DHA	43	3.57	0.46	6.76	0.88					10.16	1.22	51	2.3	62.8	2.2					75.3	2.6	34.9	1.7	41.6	1.1					46.5	1.2
	Std + DHA + AA	46	3.5	0.46	6.79	0.82					10.06	1.26	50.6	2.7	62.9	2.4					75.5	2.6	34.5	1.5	41.8	1.1					46.7	1.2
Auestad *et al.* (2001)	Standard formula	77	3.45	0.44	6.54	0.64					9.78	1	50.8	2.5	63	2.2					75.4	2.7	39.4	1.2	41.8	1.1					46.5	1.2
	Std + DHA + AA	162	3.4	0.47	6.59	0.67					9.67	0.99	50.6	2.6	62.9	1.9					75.2	2.3	39	1.3	41.8	1.2					46.5	1.3
Birch *et al.* (1998)	Standard formula	23			6.89	0.7					9.66	0.52			63.9	2.3					75.5	2.8			42.3	1.1					47	1.3
	Standard + DHA	22			7.1	0.56					10.11	0.92			62.9	2.4					74.7	2.2			42	0.9					46.8	1.2
	Std + DHA + AA	23			7.1	0.58					10.07	1.2			63.4	1.5					74.7	2.5			42.1	1.2					46.6	1.7
Carlson *et al.* (1996)	Standard formula	20	3.33	0.33	6.4	0.72					9.48	1			61.3	2.1					72.5	2.3			41.5	0.8					46.3	1.4
	Std + DHA + AA	19	3.29	0.45	6.32	0.71					10	0.83			61.3	1.1					73.5	1.9			41.3	0.8					46.6	1.1
Carlson *et al.* (1999)	Standard formula	104			6.63	0.74					9.77	1.19			63	2.6					75.4	3			41.7	1.2					46.8	1.4
	Std + DHA + AA	212			6.78	0.75					9.99	1.2			62.9	2.5					75.6	3.1			41.9	1.2					46.7	1.4
Bouwstra *et al* (2003)[*]	Human Milk	147	3.59	0.42	6.27[*]	0.75									63.0	2.5																
	Standard formula	131	3.51	0.43	6.33[*]	0.71									63.0	2.2																
	Std + DHA + AA	119	3.53	0.50	6.41[*]	0.71									63.0	2.6																

Study	Subject groups		Anthropometric Results (mean + sd)[1]																											
			Weight (kg)										Length (cm)										Head Circumference (cm)									
	Type Formula	n	Birth	sd	4 mths	sd	6 mths	sd	8 mths	sd	12 mths	sd	Birth	sd	4 mths	sd	6 mths	sd	8 mths	sd	12 mths	sd	Birth	sd	4 mths	sd	6 mths	sd	8 mths	sd	12 mths	sd
Decsi and Koletzko (1995)	Standard formula	7	3.4	0.41	6.41	0.64							54.5	3.7	64.1	2.7							32.2	3.7	40.2	1.1						
	Std + DHA + AA	9	3.55	0.52	6.62	0.48							52.1	4.9	64.9	1.5							35.3	2.3	41.7	1						
Innis *et al.* (1996)	Standard formula	37			6.62	0.94									63.3	2.9									41.4	1.4						
	Standard + DHA	68			6.68	0.82									62.8	2.8									41.5	1.2						
Lapillonne *et al.* (2000)	Human Milk	13	3.47	0.41	6.6	0.64							50.3	1.4	62.9	1.7							34.8	1.1	41.2	1.1						
	Standard formula	12	3.31	0.45	7.01	0.87							50	2.4	63.3	2.4							35.1	1.4	**42.6[a]**	1.8						
	Standard + DHA	12	3.38	0.43	6.73	0.8							50.7	1.7	64.4	2.4							34.8	1	**41.2[b]**	1.2						
Lucas *et al.* (1999)	Standard formula	125	3.65	0.46			8.00	0.8	9.1	0.9			50.9	1.9			67.3	2.4	72.2	2.4			35.4	1.2			43.8	1.2	45.9	1.4		
	Std + DHA + AA	125	3.54	0.41			7.90	0.9	9.1	1.1			50.5	1.8			67.4	2.5	71.9	2.7			35.3	1.2			43.8	1.1	48.3	1.5		
Makrides *et al.* (1995a)	Standard formula	19	36.5	0.42	6.7	0.79					9.98	1.09	51.2	2.1	62.7	1.5					75.8	2.2	35.2	1.2	42.2	0.9					46.9	1.1
	Standard + DHA	13	32.9	0.53	6.5	0.72					9.94	1.35	50.2	2.8	62.2	2.5					75.8	2.6	34.4	2.2	41.7	1.6					46.3	1.4
Makrides *et al.* (1999)	Standard formula	22	3.55	0.5	6.5	0.53			8.78	0.9	10.62	1.13	51.5	2.6	62.6	2.5			71	2.4	77	2.4	35.3	1.6	41.5	1.1			44.9	1.2	46.9	1.2
	Standard + DHA	25	3.38	0.43	6.53	0.65			8.62	0.99	9.96	1.11	50.8	2	62.2	1.6			70.3	2	75.5	2.3	35.1	1.4	41.8	0.9			44.9	1.2	46.8	1.1
	Std + DHA + AA	24	3.55	0.52	6.65	0.73			8.99	0.99	10.55	1.11	51.3	2.4	62.6	2.5			71	2.4	77	2.4	35.2	1.7	42	1.5			45.6	1.4	47.6	1.5
Morris *et al.* (2000)	Standard formula	55	3.35	0.46			8.13	1.10			10.24	1.31	49.0	2.2			67.8	2.4			75.9	2.7	**34.9[a]**	1.7			43.9	1.6			47.0	1.8
	Std + DHA + AA	54	3.31	0.48			7.94	0.94			9.91	1.13	49.3	2.5			67.9	2.5			75.7	3.1	**34.3[b]**	1.4			43.6	1.3			46.5	1.4

1. Bolded values with different lettered superscripts are significantly different from each other ($p \leq 0.05$), and normal font values without superscripts are not significantly different ($p > 0.05$). Statistical significance is only applied to comparisons between infants fed different study formulas, and not to comparisons with infants fed human milk.

* Weight and length was measured at three months not four.

Table A3: Visual acuity results from studies on the LCPUFA content of infant formulas (4-12 months of age)

Study	Subject groups		Visual Acuity Results (mean + sd)[1]																			
			Behavioural Assessment (LogMAR)[2]						Visual Evoked Potential Assessment (LogMAR)[2]								Stereoacuity Assessment (LogSec)[3]					
	Type Formula	n	4 mths	sd	6 mths	sd	12 mths	sd	4 mths	sd	6 mths	sd	8 mths	sd	12 mths	sd	4 mths	sd	10 mths	sd	12 mths	sd
Auestad *et al.* (1997)	Human Milk	38	0.88	0.13	0.57	0.09	0.52	0.11	0.66	0.13	0.47	0.15			0.34	0.18						
	Standard formula	45	0.90	0.17	0.64	0.09	0.51	0.09	0.64	0.12	0.39	0.15			0.32	0.16						
	Standard + DHA	43	0.92	0.13	0.68	0.09	0.55	0.13	0.69	0.14	0.44	0.16			0.37	0.13						
	Std + DHA + AA	46	0.90	0.16	0.56	0.09	0.51	0.15	0.68	0.09	0.40	0.17			0.32	0.16						
Auestad *et al.* (2001)	Human Milk	165	0.88	0.13	0.57	0.09	0.53	0.13														
	Standard formula	54	0.85	0.13	0.67	0.07	0.51	0.06														
	Std + DHA + AA	123	0.84	0.13	0.57	0.09	0.49	0.03														
Birch *et al.* (1998); Hoffman *et al.* (2000)	Human Milk	29	0.81	0.16	0.74	0.11	0.63	0.14	0.48	0.12	0.32	0.05			0.18	0.08						
	Standard formula	23	0.81	0.17	0.74	0.10	0.63	0.12	**0.54**[a]	0.13	0.38	0.05			**0.33**[a]	0.1						
	Standard + DHA	22	0.88	0.15	0.79	0.12	0.69	0.19	**0.46**[b]	0.08	0.33	0.11			**0.19**[b]	0.12						
	Std + DHA + AA	23	0.88	0.15	0.79	0.17	0.67	0.18	**0.48**[b]	0.1	0.37	0.05			**0.2**[b]	0.11						
Birch *et al*. (2005)	Standard formula	44							**0.56**[a]	0.01					**0.3**[a]	0.01	**2.62**[a]	0.06	2.18	0.05	2.03	0.05
	Std + DHA + AA	42							**0.48**[b]	0.02					**0.15**[b]	0.03	**2.72**[b]	0.05	2.10	0.03	1.87	0.02
Carlson *et al.* (1996)	Human Milk	19	0.69	0.03	0.54	0.02	0.51	0.02														
	Standard formula	20	0.69	0.03	0.60	0.03	0.54	0.02														
	Std + DHA + AA	19	0.75	0.04	0.59	0.03	0.53	0.02														
Jorgensen *et al*. (1998)	Human Milk	17							0.37	0.07												
	Standard formula	11							0.44	0.07												
	Standard + DHA	26							0.4	0.07												

Study	Subject groups		Visual Acuity Results (mean + sd)[1]																			
			Behavioural Assessment (LogMAR)[2]						Visual Evoked Potential Assessment (LogMAR)[2]								Stereoacuity Assessment (LogSec)[3]					
	Type Formula	n	4 mths	sd	6 mths	sd	12 mths	sd	4 mths	sd	6 mths	sd	8 mths	sd	12 mths	sd	4 mths	sd	10 mths	sd	12 mths	sd
Makrides *et al.* (1995a)	Human Milk	23							0.51	0.21	0.1	0.31										
	Standard formula	19							**0.76**[a]	0.1	**0.45**[a]	0.2										
	Standard + DHA	13							**0.56**[b]	0.14	**0.15**[b]	0.35										
Makrides *et al* (2000b)	Human Milk	33							0.73	0.11			0.33	0.20								
	Standard formula	15							0.73	0.11			0.39	0.19								
	Standard + DHA	19							0.77	0.10			0.47	0.18								
	Std + DHA + AA	15							0.74	0.09			0.39	0.17								

1. Bolded values with different lettered superscripts are significantly different from each other ($p \leq 0.05$). Statistical significance is only applied to comparisons between infants fed different study formulas, and not to comparisons with infants fed human milk.
2. Logarithm_{10} of the eye's minimum angle of resolution. Lower values reflect an increased ability to distinguish between two points at a greater distance.
   Logarithm_{10} of an arcsecond.

Table A4: Cognitive development results from studies on the LCPUFA content of infant formulas (4-24 months of age)

Study	Subject groups		Cognitive Development Results (mean + sd)[1]																	
			Bayley Mental Development Index (% normal score)								Bayley Psychomotor Development Index (% normal score)								Bayley Behaviour Rating Scale (% normal score)	
	Type Formula	n	6 months	sd	12 months	sd	18 months	sd	24 months	sd	6 months	sd	12 months	sd	18 months	sd	24 months	sd	18 months	sd
Auestad *et al.* (2001)	Human Milk	165	100.8	5.4	100.0	8.7					100.2	10.4	96.6	12.2						
	Standard formula	77	100.4	5	97.8	8.3					99.1	12.3	94.6	12.5						
	Std + DHA + AA	162	99.6	6.1	96.8	9.2					97.8	11.3	94	13.2						
Birch *et al.* (2000);	Standard formula	23					**98.3[a]**	1.94							98.6	1.34			107.3	23.7
	Standard + DHA	22					**102.4[a,b]**	1.81							99.6	0.97			106.4	20.9
	Std + DHA + AA	23					**105.6[b]**	2.7							101.7	0.69			108.1	24.6
Bouwstra *et al* (2005)	Human Milk	159					107.5	16.0							103.2	14.5				
	Standard formula	169					105.4	15.0							100.9	13.6				
	Std + DHA + AA	146					102.7	15.4							99.4	13.4				
Lucas *et al.* (1999)	Standard formula	155					94.2	12.8							94.7	13.4				
	Std + DHA + AA	158					95.8	10.1							96.4	9.1				
Makrides *et al*. (2000c)	Human Milk	33			116	10			120	18			97	18			98	11		
	Standard formula	22			110	12			104	13			102	17			97	15		
	Standard + DHA	25			114	12			108	16			106	18			104	17		
	Std + DHA + AA	24			108	16			102	23			103	22			96	21		
Scott *et al*. (1998)	Standard formula	45			105	14							105	15						
	Standard + DHA	43			104	15							101	14						
	Std + DHA + AA	46			105	12							98	14						

1. Bolded values with different lettered superscripts are significantly different from each other ($p \leq 0.05$), and normal font values without superscripts are not significantly different ($p > 0.05$). Statistical significance is only applied to comparisons between infants fed different study formulas, and not to comparisons with infants fed human milk.

Table A5: Cognitive development results from studies on the LCPUFA content of infant formulas (4-14 months of age)

Study	Subject groups		Cognitive Development Results[1]																	
			Brunet and Lezine Development Quotient (% normal score + sd)				MacArthur Communicative Development Inventories (% normal score + sd)										Means-end Problem Solving[2] (median values)			
							Phrases Understood		Vocabulary Comprehension		Vocabulary Production		Early Gestures		Late Gestures		Entire Test	Barrier component	Cloth component	Cover component
	Type Formula	N	4 months	sd	24 months	sd	14 months	sd	14 months	sd	14 months	sd	14 months	sd	14 months	sd	10 months	10 months	10 months	10 months
Agostoni *et al.* (1994; 1997)	Human Milk	15	102.2	11.5	99.7	7.0														
	Standard formula	21	**96.5**[a]	10.9	99.1	7.1														
	Std + DHA + AA	23	**105.3**[b]	9.4	100.1	10.3														
Scott *et al.* (1998)	Human Milk	60					104	17	101	13	97	17	105	12	102	13				
	Standard formula	42					100	16	**100**[a]	17	**101**[a]	13	105	18	101	15				
	Standard + DHA	38					96	16	**92**[b]	14	**91**[b]	17	102	19	97	16				
	Std + DHA + AA	33					99	12	**98**[a]	15	**99**[a,b]	18	105	14	100	14				
Willatts *et al.* (1998)	Standard formula	23															**11.5**[a]	4.8	4.5	**2.5**[a]
	Std + DHA + AA	21															**14.0**[b]	5.5	5.0	**4.3**[b]

1. Bolded values with different lettered superscripts are significantly different from each other ($p \leq 0.05$), and normal font values without superscripts are not significantly different ($p > 0.05$). Statistical significance is only applied to comparisons between infants fed different study formulas, and not to comparisons with infants fed human milk.
2. This test consisted of relative scores (0, 1, or 2) for different degrees of cognitive awareness exhibited during each component of the test. The three components each have three behaviour subsets that are assessed, resulting in a maximum possible score of 6 for each component and 18 for the entire test.

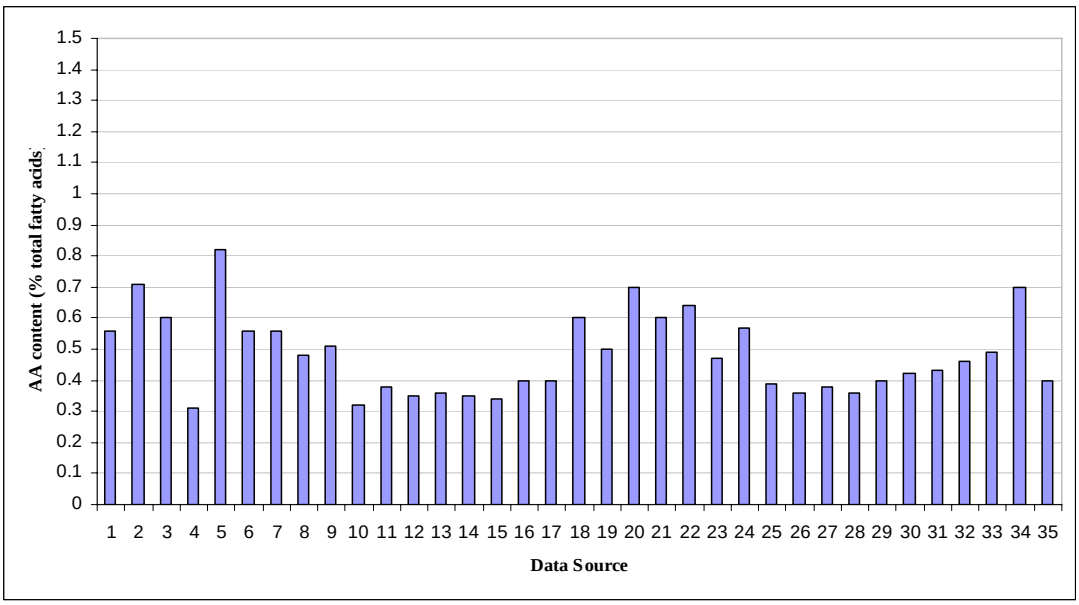

Figure A1: Arachidonic acid content of human milk

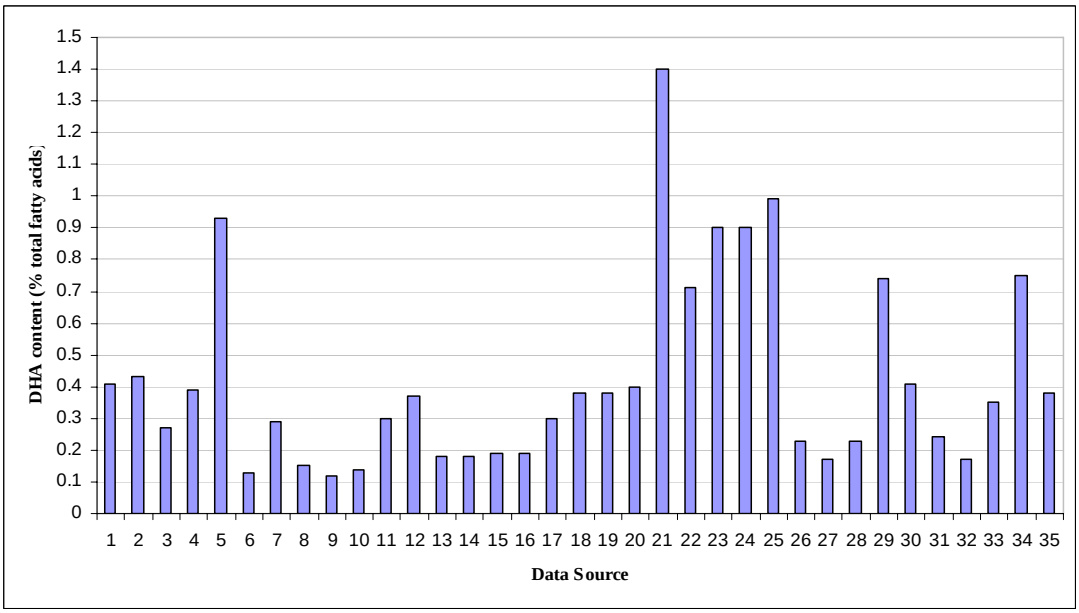

Figure A2: Docosahexaenoic acid content of human milk

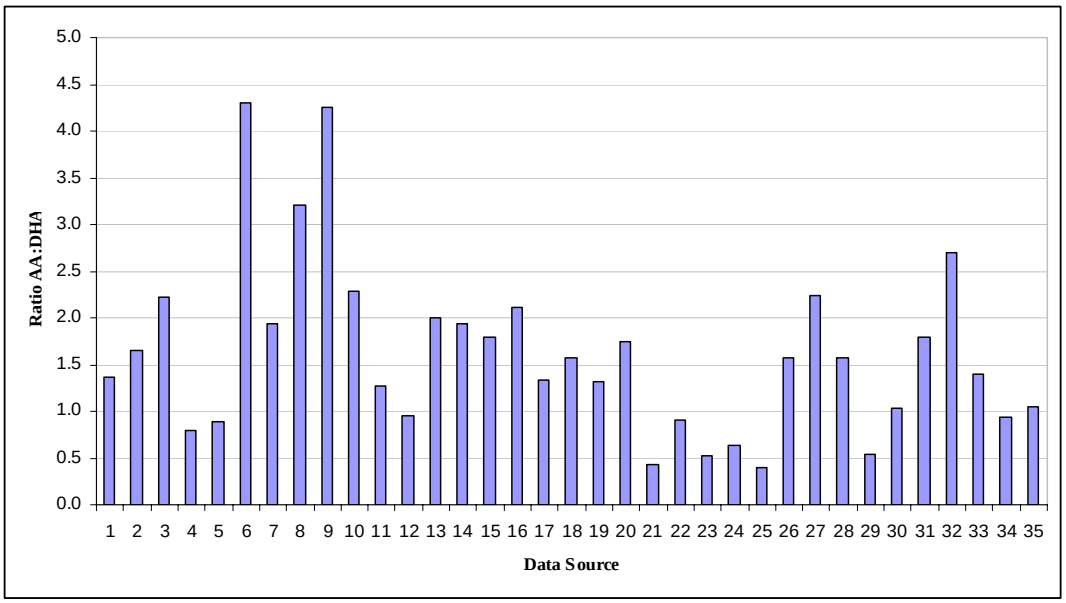

Figure A3: Ratio of arachidonic acid to docosahexaenoic acid in human milk

Data Sources:
1-3: Surinam, Curaçao, Tanzania - Muskiet *et al*. (1987)
4: Gambia – Prentice *et al*. (1989)
5: Nigeria – Koletzko *et al*. (1992)
6-9: United States of America – Jackson *et al.* (1994), Birch *et al.* (1998), Auestad *et al.* (1997), Auestad *et al.* (2001) respectively
10-12: United Kingdom (vegan, vegetarian and omnivore) – Sanders and Reddy (1992)
13: Finland - Luukkainen *et al.* (1994)
14. Germany – Koletzko *et al.* (1988)
15: Netherlands – Huisman *et al.* (1996)
16: Australia – Makrides *et al.* (1995b)
17: Sweden – Jansson *et al.* (1981)
18: Israel – Budowski *et al.* (1994)
19: France – Guesnet *et al.* (1993)
20-21: Canada (Vancouver, Inuit) – Innis and Kuhnlein (1988)
22-23: Malaysia (Chinese, Malay and Indian) – Kneebone *et al.* (1985)
24-32: Japan, United Kingdom, Canada, Australia, Philippines, Chile, Mexico, United States of America, China (respectively) – Yuhas *et al.* (2006)
33: Tanzania – Kuipers *et al.* (2005)
34: Denmark – Jorgensen *et al.* (1998)

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Attachment 3

BUSINESS COST CALCULATOR REPORT

Application A - 532 Ratio of Long Chain Polyunsaturated Fatty Acids in Infant Formula Products

Problem:	The applicant is seeking to change the omega 6 to omega 3 LCPUFA ratio requirement for infant formula on the basis that more recent and relevant scientific evidence has emerged. It is argued that promoting consistency between domestic and international standards is important, and that the current requirement for an omega 6 to omega 3 LCPUFA ratio of approximately 2, may pose a technical barrier to trade for Australian and New Zealand manufacturers and importers.
Objective:	To protect the public health and safety of formula-fed infants and promote consistency between domestic and international standards.

Policy Options

Option Name	**Quickscan Result**
Status Quo	FALSE
Amend Standard 2.9.1	FALSE

Compliance Cost Summary

Option Name: Status Quo
Businesses Affected: 4

Type	**Cost per Business**	**Total Cost of Regulation**
N/A	N/A	N/A

Option Name: Amend Standard 2.9.1
Businesses Affected: 4

Type	**Cost per Business**	**Total Cost of Regulation**
N/A	N/A	N/A

Caution should be used comparing options and interpreting results over time. The Business Cost Calculator does not estimate the future values of ongoing costs. Refer to the User Guidelines for further information.

This report contains summaries of compliance costs only. An assessment on the compliance cost in itself does not provide an answer to which policy option is the most effective and efficient one. Rather, it provides information which needs to be considered alongside other relevant factors and issues when deciding between alternative policy options.

Attachment 4

SUMMARY OF SUBMISSIONS FROM THE DRAFT ASSESSMENT REPORT

Executive Summary of submissions

Background

In July 2006 FSANZ received 12 submissions in response to the Draft Assessment Report of Application A532 – Consideration of an amendment to Standard 2.9.1 of the Code to amend subclause 23(d). This sub clause requires long chain polyunsaturated fatty acids (LCPUFAs) if voluntarily added to infant formula and follow-on formula to be present in a ratio of omega 6 to omega 3 LCPUFAs of *approximately 2*.

There were two options proposed at Draft Assessment namely:

9.1 Option 1 – Maintain *status quo*

Maintain the *status quo* by not amending the Code, and thus retaining the requirement for omega 6 to omega 3 LCPUFAs to be present in a ratio of *approximately 2*, when added to infant formula.

9.2 Option 2 – Amend Standard 2.9.1

Amend Standard 2.9.1 to include a requirement that the omega 6 to omega 3 LCPUFA ratio should be *not less than 1* in infant and follow-on formula when LCPUFAs are added to these products, in place of the current ratio requirement of *approximately 2*.

A total of 12 submissions were received during the six week public consultation period of 23 May to 4 July 2007. Seven submissions were submitted from the food industry, four from Government and one from a health professional organisation.

Almost all (11) submitters favoured Option 2, to amend Standard 2.9.1 to include a requirement that the omega 6 to omega 3 LCPUFA ratio should be *not less than 1* in infant and follow-on formula when LCPUFAs are added to these products.

Many submitters noted Option 2 is in agreement with current scientific opinion and international recommendations including Codex and EU, and would continue to protect the health and safety of formula fed infants

One industry submitter preferred the Status Quo considering most evidence for the benefits of adding LCPUFA to infant formula derives from trials using AA: DHA ratios within the 1.5 – 2.5 range.

KEY ISSUES IDENTIFIED FROM SUBMISSIONS

1. Regulatory options

Reasons for and against each of the regulatory options included:

1.1 Maintaining the status quo

Support:

- the most frequent AA:DHA ratio found in breast milk is 1.8; and
- many of the benefits of LCPUFA found in RCT used AA: DHA ratios within the range 1.5-2.5.

Against:

- is not consistent with current scientific evidence and international practice; and
- infants can tolerate wide variations to this ratio.

1.2 Amending Standard 2.9.1 to include a requirement that the omega 6 to omega 3 LCPUFA ratio should be *not less than 1* in infant and follow-on formula when LCPUFAs are added to these products, in place of the current ratio requirement of *approximately 2*.

Support:

- will continue to protect the health and safety of formula fed infants;
- is in line with current scientific evidence and international practice;
- no safety concerns with the addition of omega 6 and omega 3;
- infants can tolerate wide variations to this ratio;
- is more consistent with international food standards e.g. Codex and EU; and
- will improve trade opportunities.

Against:

- considers majority of benefits with LCPUFA enriched formula were observed in trials using formula with AA: DHA ratios within the 1.5-2.5 range.

Submitter	Comment
Infant Formula Manufacturers Association of Australia & NZ Infant Formula Marketers Association *Janet Carey*	**Supports Option 2** Notes their original submission of 9 August 2006 still stands.
International Formula Council *Mardi Mountford*	**Support Option 2** IFC is an association of manufacturers and marketers of formulated nutrition products, based in North America. Notes Option 2 is consistent with Codex.

Submitter	Comment
Food Technology Association Australia *David Gill*	**Supports Option 2** No comments
Australian Food Grocery Council *Kim Leighton*	**Supports Option 2** Considers that there are no safety concerns with the addition of omega 6 and omega 3, and that infants can tolerate wide variations to this ratio. Considers Option 2 would bring the Code into line with Codex and EU, remove technical barriers, improve trade opportunities and reduce risk of a WTO challenge regarding deviation from Codex recommendations. However advises caution in the conclusion about the role of LCPUFA in the development of greater visual acuity compared with standard formulation, particularly given the current Applications A594 and A597.
Wyeth *Jeanette Fielding*	**Supports Option 2** Considers Option 2 is in agreement with current scientific opinion, international recommendations and also meets FSANZ's objectives.
Nestle *Stephanie Rajczyk*	**Supports Option 2** Draws attention to a paper by Brenna et al 2007 confirming the wide range of DHA: AA ratios in human milk. Has found no further evidence to add to data reviewed by FSANZ.
DSM Food Specialties *B Schulze*	**Supports Option 1 – *status quo*** Considers health concerns should be the main consideration. Considers the role of omega 6 and omega 3 in visual and neural development is well established. Considers the following two points to be the main rationale determining the ratio in IF: ➢ the most frequent AA:DHA ratio found in breast milk is 1.8; and ➢ benefits are most frequently reported in RCT of infant formula containing AA: DHA ratios within the range 1.5-2.5. Considers a ratio of 1.2 to 2 is the market standard worldwide and a ratio of 2 is the market standard in US and most Asian and Pacific countries. Believes the current ratio requirement of approximately 2 aligns better with current international market standards and is not likely to limit sales outside Australia and NZ. Cites 2 double blind RCTs comparing AA and DHA enriched formula to standard formula not included in the DAR (Birch *et* al, 2002, Hoffman *et al*, 2005, Bouwstra *et al*, 2003 and 2005). Notes results indicate infants fed a LCPUFA containing formula had better visual acuity and stereoacuity at specific ages than those receiving formula without LCPUFA.

Submitter	Comment
	Also the frequency of mildly abnormal general movements was higher in infants in the control group than in the LCPUFA group at 3 months. However this did not persist until 18 months. Considers findings indicate AA plays an important role in neurological development, and that dietary AA should always be added to formula in balanced proportions with DHA. Considers it uncertain whether the consumer will benefit from the proposed ratio as industry will be able to produce an inferior quality product to reduce manufacturing costs, but this may not be passed onto the consumer.
Dietitians Association of Australia *Kate Poyner*	**Supports Option 2** Notes Option 2 is in line with international practice and current scientific evidence
NZ Food Safety Authority *Carole Inkster*	**Supports Option 2** Satisfied with the FSANZ risk assessment and independent peer review. Recognises new research and a ratio of 2 may no longer be appropriate. Supports the consistency with CODEX and EU.
NSW Food Authority *Jo Dellow*	**Supports Option 2** Considers Option 2 will continue to protect health and safety of formula fed infants and is more consistent with international food standards.
Queensland Health *Gary Bielby*	**Supports Option 2** Considers Option 2 will continue to protect health and safety, and is more consistent with international food standards.
Department of Human services Victoria *Victor De Paola*	**Supports Option 2** Satisfied concerns at IAR have been addressed regarding safety and levels. Considers Option 2 is consistent with international directive. Has no further concern.