FULL ASSESSMENT REPORT

SUBJECT - PROPOSAL P93: REVISION OF STANDARD R7 - INFANT FORMULA

EXECUTIVE SUMMARY

At NFA 14, as a consequence of one of the recommendations made in the review of special infant formula (P49), the Authority prepared a proposal (P93), to review Standard R7 - Infant Formula. Ms Nancy Palmer, a paediatric nutritionist, was employed by the Authority to progress the revision of Standard R7 towards full assessment and subsequently additional consultants were appointed to advise on compositional aspects.

Standard R7 was originally gazetted in 1988 but needs revision because it is:

- out-of-date with current scientific knowledge and opinion;
- not harmonised with the infant formula standards of overseas organisations such as Codex, the US Food and Drug Administration, the European Community and New Zealand; and
- difficult to interpret, especially the definition of infant formula.

In addition, there are some types of infant formula in the Australian marketplace which are not regulated by Standard R7.

Other aspects of Standard R7 which the Authority has considered include:

- permitted forms of the various nutrients;
- labelling and advertising requirements;
- contaminant levels (aluminium and fluoride);
- possible additional regulatory procedures, such as pre-market clearance; and
- the basis for permitting some substances as "optional" ingredients.

At NFA 26, the Authority agreed to the establishment of an Expert Panel to assist the project team in its decision-making on the issues of "optional" ingredients and fluoride levels. The Panel met in February and March 1995. The Panel's

assessment of these issues and the rationale for their decisions are included in the report at Appendix 2 to the Full Assessment Report.

At NFA 29, the Authority agreed to the appointment of a consultant to advise on the appropriate composition of formula based on modified protein, fat and carbohydrate. Her recommendations formed the basis for a new category, "proximate-modified" human milk substitute, now contained in the draft revised Standard R7. The consultant's report is at Appendix 6 to the Full Assessment Report.

The draft revised Standard R7 - Human Milk Substitutes, prescribes in detail the compositional, microbiological and labelling requirements for infant formula, follow-on formula, and human milk substitutes for special dietary use (including pre-term, lactose free and low lactose and proximate-modified human milk substitutes). Limits on aluminium and fluoride have been introduced and consequential amendments have also been made to regulate claims, provide specifications or references to specifications for substances not previously permitted, list new additives together with their food additive code numbers in the appropriate schedule and ensure that ranges specified for "selenium" in Standard R7 are the only ones applicable to human milk substitutes.

BACKGROUND

The National Food Authority has before it a proposal to revise Standard R7 - Infant Formula. The proposal arose as a consequence of the Authority's review of the regulation, availability and marketing of "special infant formula" in Australia (P49 - Special Infant Formula). A major recommendation of this review was that the current Standard R7 - Infant Formula, should be revised before the Authority further investigated the regulation of "special infant formula".

Reasons underpinning this recommendation included:

- the need to align compositional aspects of products covered by Standard R7 with current knowledge and scientific opinion;
- the need for harmonisation with the infant formula standards of international and overseas organisations such as the Codex Alimentarius, the US Food and Drug Administration and the European Community's Scientific Committee for Food;
- the special relationship now being developed between Australia and New Zealand with regard to food standards and trade;
- the need to develop definitions which would allow categorisation of products covered by Standard R7 and provide some guidance with regard to appropriate use as well as marketing and promotion.

History of the Current Standard R7 and Aspects of Concern

The current Standard R7 was gazetted in July 1988, after consideration by the NHMRC over a period of 11 years. At the time of gazettal, the Standard was already obsolete in some respects. It was a cumbersome document presenting difficulties in interpretation. Because it did not permit certain essential elements, nor internationally recognised forms of some vitamins, minerals and electrolytes there were difficulties for many manufacturers with global markets.

Since the Authority was considering assuming responsibility for the regulation of "special infant formula" (P49), it considered that the revised Standard R7 should serve to differentiate between these two distinct classes of formulae.

World Health Organisation International Code of Marketing of Breast Milk Substitutes

At the 34th Session of the World Health Assembly, held 20 May 1981, Australia voted affirmatively for the resolution adopting an International Code of Marketing of Breast-milk Substitutes (1). One of the aims of this Code, adopted in regulation form, was "by ensuring the proper use of breast-milk substitutes, when these are necessary, on the basis of adequate information and through appropriate marketing and distribution".

The Code places certain restrictions on manufacturers and marketers of infant formulae regarding advertising and related promotional activities directed at both the general public and health workers. Information provided about individual products must be "scientific and factual".

In addition, articles 9 and 10 of this Code are concerned with, respectively, the labelling of products (infant formula) and quality-applicable standards recommended by Codex.

The Australian Government has taken a number of steps in support of its international commitment to the WHO, including the incorporation of relevant articles into Standard R7, and, most recently, through an agreement reached between manufacturers and marketers of infant formulae and the Bureau of Consumer Affairs. This agreement, Marketing in Australia of Infant Formulas - Manufacturers and Importers (May, 1992), places certain restrictions on the advertising and promotion of infant formulae, and also requires that formula marketed in Australia conforms with quality and labelling provisions of both the WHO Code and the Australian Food Standard R7 - Infant Formula.

The agreement was authorised by the Trade Practices Commission (September 1992). It is a voluntary agreement which gives effect in Australia to the principles of the WHO Code. Its provisions are monitored by the Advisory Panel on the Marketing in Australia of Infant Formula (APMAIF), a major function of which is to assure that information supplied by manufacturers and marketers is "scientific and factual". This panel has already determined that much

information provided by the industry is not strictly "scientific and factual". It should be noted that the Federal Trade Commission (USA) in 1992 and 1993 determined that certain claims in promotional materials were misleading and should cease. These same claims in relation to "fatty acids", "sodium" and "closeness to human milk", appear frequently in Australia.

Philosophy of Approach to Review

There is a need for a human milk substitute which will provide all known nutrients to support normal growth and development, but while it may mimic human milk in many aspects, it cannot match many of the unique nutritional or immunological properties of this species-specific food. Formula is, however, acknowledged as a useful substitute.

Two papers (2,3) from the medical department of a multi-national marketer of infant formula, and a leader in research and development of these products, illustrate how the industry applies new information and makes recommendations for product development and/or modification. These contributions to the literature identify a concern for efficacy by some parts of the industry and identify factors which should be taken into account before products are reformulated.

Although infant formula products, and the marketing of them, are subject to careful regulation world-wide, the competitiveness of the market-place means that companies seek to increase their share of sales through intense promotional activities. These are often directed not to parents, but rather to health workers, who in turn influence parents or others who care for infants. In the development of Standard R7 the following have been taken into account:

- breastmilk is of unequalled value as a food source for infants up to six months of age, "encourage and support breastfeeding" being first on the list of Australian "Dietary Guidelines for Children" (1995); and

- promotional activities, based on the incorporation into infant formula of particular ingredients whose benefit has not been scientifically substantiated, should not be allowed.

This review has been undertaken with the underlying philosophy that development of a standard for human milk substitutes should not provide opportunities for further erosion of the principle that breast feeding is the preferred way of providing nutrients and immunological protection for infants.

Determination of the Essential Compositional Aspects of Formula

It is acknowledged that nutrient recommendations for human milk substitutes cannot be safely made by a total reliance on formulating a close analogue of human milk. Human milk is a unique food and a complex substance. Many interactions between constituents have yet to be identified. There is ample evidence that creating an artificial feed by including nutrients found in human

milk, at the same concentrations, does not necessarily ensure that the formula will be adequate for growth and development (4).

The behaviour of formulae prepared with nutrients from new sources, or in which proportions of nutrients are changed, cannot be predicted with certainty. Nutrients present in human milk and added to formulae may also be lost during processing, sterilisation and storage, and must be restored by manufacturers. In addition, the bioavailability of many trace elements (eg zinc, iron, copper, manganese) is higher from breast milk when compared with formula, due to the presence of other constituents which facilitate uptake.

In determining nutrient levels in infant formulae it may not necessarily be appropriate to use tables of nutrients found in human milk. It is more appropriate to refer to estimates of recommended intake, and then take into account all known factors affecting bioavailability, absorption and stability of nutrients in the substitute feed.

APPOINTMENT OF CONSULTANTS

Ms Nancy Palmer, a paediatric nutritionist, was contracted by the Authority to progress the revision of Standard R7 towards full assessment.
At NFA 17 (June 1993), at the request of Ms Palmer, Dr Karen Simmer, neonatologist at the Flinders Medical Centre Paediatric Research Unit and Dr David Tudehope, neonatologist at the Mater Children's Hospital, Brisbane, were appointed as consultants to review nutrient levels for products covered by Standard R7.

OTHER SOURCES OF ADVICE

Expert advice was provided by the Expert Panel on Infant Formula, which the Authority established in February 1995 (for the Panel's Report, including the list of members, see Appendix 2 to the Full Assessment Report).

In addition to public submissions, Ms Nancy Palmer sought technical, regulatory, and nutritional advice from research and development resources of major North American manufacturers and exporters. Specific discussions about fatty acids, nucleotides, iron and selenium in infant formulae were held with the following international researchers:

> Dr George Owen (paediatrician), Medical Director Asia/Australia, Mead Johnson Research Center, Evansville, Indiana.
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> Dr William MacLean (paediatrician), Vice President for Pediatric Research and Development, Ross Products Division, Abbott Laboratories, Colombus, Ohio.

Dr John Benson (nutritionist), Director, Pediatric Nutrition Research, Ross Products Division, Abbott Laboratories, Colombus, Ohio.

Dr Duane Benton (nutritionist), Director, Nutrition Research, Ross Products Division, Abbott Laboratories, Colombus, Ohio.

Dr Ricardo Uauy (paediatrician), Instituto de Nutricion, Universidad Chile, (fatty acids, nucleotides).

Dr Thomas Sanders (nutritionist), Kings College, London (fatty acids).

Dr Michael Woolridge (paediatrician), Bristol University, UK (iron, nucleotides).

Professor John Birkbeck (paediatrician), Professor Emeritus, University of Otago, Dunedin (selenium, iron, fatty acids).

Professor Roger Whitehead, Director, Dunn Nutrition Centre, UK (energy, iron, fatty acids).

ISSUES RAISED IN PUBLIC SUBMISSIONS

Seventeen submissions on Proposal 93 were made by industry, professional and consumer groups, and individuals.

The significant issues identified were:

1. The need for revision

Many submissions agreed that there was a need to revise Standard R7. Specific aspects mentioned were definitions, composition and categories of infant formula.

2. The need for harmonisation with the food regulations of other countries

Submissions identified this issue as being particularly important, as there is significant trade in infant formula between Australia and many overseas countries.

3. Selection of nutrients to be part of the essential composition of infant formula, and determination of appropriate levels of these nutrients

Specific nutrient issues raised were:

- permission to add selenium,
- determination of a suitable range of values for iron, iodine, sodium, trace elements, and vitamin D; and
- the need for revision of the fatty acid profile.

4. Nutrition information panel

Whether Standard R7 needs to be exempt from the nutrition information panel requirements in Standard A1.

5. Labelling and advertising

Whether or not the existing regulations should be changed, and if so what the new ones should be.

6. The need for additional regulatory procedures

Whether or not a procedure should be set in place for the evaluation of new or modified infant formulae, and what measures can be taken to ensure the removal of non-compliant formulae from the marketplace.

7. Energy value for carbohydrate

The value provided in Standard R7 differs from that in Standard R2.

8. Basis for permitting substances as optional ingredients in infant formula

What should be the criteria for determining whether or not permission should be granted?

9. Level of taurine

Whether the current minimum level required is too high.

10. Whey-dominant versus casein-dominant formula

Is it appropriate to classify formulae on this basis?

11. The inclusion of a follow-on formula category

Should there be special provision for this category of formula which is described as "suitable for term infants after 6 months of age"?

12. The inclusion of a pre-term formula category and restrictions on the availability of this type of formula

Should there be special provision for this category of formula which is described as "suitable for infants of less than 37 weeks gestation" and is there a need to restrict its availability?

13. Iron levels and claims about the iron content of formulae

It was submitted that a need exists to determine what range of values should be specified for iron and whether claims about iron content should be allowed.

14. Inclusion of selenium as an essential nutrient

Whether it is appropriate to include selenium in the essential composition, and if so what the specified range should be.

15. Levels of antioxidants

A request was made to permit the addition of antioxidants, to a level of 10 mg per litre, as substances which are permitted sources of vitamins A and E in the draft revised Standard R7.

EVALUATION AND ASSESSMENT OF PUBLIC COMMENT AND EXPERT ADVICE

1. The need for revision

The need for revision was raised in the majority of submissions. Dissatisfaction was expressed with current definitions, some compositional aspects and the lack of more than one category of infant formula in Standard R7.

Queensland Health supported the need for review. Abbott Australasia Pty Ltd (Abbott), the Queensland State Committee of the College of Paediatrics and Mead Johnson Australia (Mead Johnson) sought clarification of definitions. The Flinders Medical Centre (Paediatric Nutrition Research Staff) said that they want formulae with particular indications to be defined, and NSW Health stated that the present definition for infant formula was inappropriate and that they were concerned about additives which could be allowed. Jane Allen said that the definition should suggest that the product contains nutrients to promote normal growth and development.

Abbott, Dorothy Francis, the Council of Australian Food Technology Associations Inc (CAFTA), the Dietitians Association of Australia (DAA), Douglas Pharmaceuticals (New Zealand), Flinders Medical Centre (Paediatric Nutrition Staff), Mead Johnson and Wyeth Australia (Wyeth) all recommended specific changes to compositional aspects of infant formula. The Australian College of Paediatrics (Nutrition Sub-Committee), the Australian Consumers' Association (ACA) and the Queensland State Committee of the Australian College of Paediatrics recommended compositional change in more general terms.

Abbott, DAA and Dorothy Francis supported the idea of having more than one category of product within Standard R7. Jane Allen was more specific, calling for the Standard to cover three categories of product - "pre-term", "term from birth"

and "suitable for term infants after six months of age". Wyeth requested that follow-on formulae continue to be identified as part of Standard R7. ACA made the point that categorisation of products should be consistent with the provisions of the WHO Code.

Evaluation

It is concluded that Standard R7 needs to be revised to include more than one category of product, each one being clearly defined and having compositional requirements which reflect contemporary scientific knowledge and opinion on infant nutrition. It is further concluded that the definition of infant formula in the current Standard should be revised, to ensure clarity.

2. The need for harmonisation with the food regulations of other countries

Abbott, DAA and Mead Johnson supported international harmonisation, with the Codex Alimentarius Commission's standard as the reference. Mead Johnson requested that the USA provisions for infant formula (FDA Infant Formula Act) also be used as a reference, and the DAA and CAFTA specified that the Codex advisory list of vitamins and minerals be used.

Evaluation

It is concluded that in the revision of Standard R7, harmonisation with overseas standards, particularly those of the Codex Alimentarius Commission, should be taken into consideration, especially with respect to required nutrients and their levels, the sources of nutrients, permitted optional ingredients and permitted food additives.

3. Selection of nutrients to be part of the essential composition of infant formulae, and determination of appropriate levels of these nutrients

CAFTA requested that the list of vitamins and minerals permitted should be expanded to that developed by WHO and Codex. Both CAFTA and the Queensland College of Paediatrics stated that infant formula should be required to include all sources of essential nutrients, including selenium and manganese. Douglas Pharmaceuticals (NZ) also requested that selenium be permitted. The DAA stated that levels of vitamins and minerals should be comparable with current Recommended Dietary Intakes (RDIs), that the minimum level of iron should be reconsidered and that there should be a maximum level for sodium and limits set for trace elements. The Australian College of Paediatrics recommended that the ranges of nutrients should be as advised by the American College of Pediatrics. Flinders Medical Centre (Paediatric Nutrition Staff), Dorothy Francis and DAA suggested that the fatty acid profile should be revised.

Abbott and Mead Johnson requested that choline be a mandatory addition to infant formula, as it is in Codex.

Evaluation

The position of the Authority's Expert Panel on Infant Formula on the essentiality of nutrients for infant formula is as follows:

- nutrients for which there is an Australian RDI are to be considered essential;
- essentiality can be assumed if a deficiency disorder has been demonstrated;
- essential nutrients must be present in infant formula; and
- new substances should only be regarded as essential if there has been an unequivocal demonstration of their efficacy through long term, controlled, randomised clinical trials on healthy term infants (demonstration of growth alone will not be deemed sufficient).

The rationale for the Panel's position was:

- infant formulae should provide nutrients in amounts that support normal growth and development and ideally result in formula-fed infants having biochemically equivalent plasma and tissue levels to breast-fed infants.
- the safety and tolerance of all substances added to formulae must have been clearly demonstrated in human clinical studies.

Compositional requirements pertaining to standard and follow-on infant formula and to pre-term human milk substitute were established on the basis of the consultants' recommendations. Copies of Dr Karen Simmer's and Dr David Tudehope's reports will be available at NFA 33.

The rationales for changes made in the levels of essential nutrients, from those which are specified in the current Standard R7, are at Appendix 3. The main considerations in setting nutrient levels were:

- as far as possible, covering formulae already on the market in Australia;
- as far as possible, harmonising with the USFDA, the EU and Codex; and
- research findings reported in the current literature, especially recommendations from a 1988 symposium in Iowa (USA) on "Upper Limits of Nutrients in Infant Formulas" (sponsors included the American Academy of Pediatrics & the USFDA, and it was supported by major formula manufacturers).

It is concluded that:

- all essential nutrients, as defined by the Expert Panel, should appear in the general composition, with specified ranges as recommended by the Authority's consultants;

- the lipid profile should be revised according to the recommendations of the Authority's consultants, who are experts in this field, so that it reflects contemporary scientific opinion on the attributes of the various fatty acids.

(Evaluation and assessment of issues relating to selenium and iron are discussed under those headings.)

4. Nutrition Information Panel

NSW Health stated that "the nutrition information panel differs and is in conflict with the general requirements for nutrition information under A1 (13), from which requirements it should probably be exempted".

Evaluation

In Standard R7, reference is made to a nutrition information **table**, not a nutrition information panel.

It is concluded that there is no reason for the Authority to make the requested exemption.

5. Labelling and advertising

ACA requested that labelling and advertising be consistent with the WHO International Code of Marketing of Breastmilk Substitutes. CAFTA and Wyeth asked that certain labelling restrictions be exempted with respect to advertising material directed at health professionals. Mead Johnson also made a request for this exemption, although stressing support for prohibitions on labels.

Abbott have requested that in special cases, products using USA or UK labelling be allowed to be made available in Australia.

Wanda Oram-Miles requested mixing and preparation instructions be retained as in the existing Standard.

The DAA recommended specific labelling changes with respect to feeding tables, standardisation of scoops and substitution of the term "unsterilised bottles" for the current description of "unboiled bottles". Dorothy Francis recommended standardisation of scoops, via introduction of a rule which requires that there be one scoop of powder to 30 mL of water, as in the UK.

NSW Health saw no reason why the prohibition in clause A1(9)(a), for the addition of vitamins and minerals unless specifically permitted, should be exempted for infant formula, and why the controls exercised over labelling and claims should not apply. They supported clarification of labelling clauses,

commenting that the word "pictogram" was "not known in the English language".

Evaluation

The labelling and advertising requirements in the current Standard R7 which specifically comply with the WHO International Code of Marketing of Breast-milk Substitutes should be retained, as they reflect the underlying philosophy of the approach to this review.

With respect to the requested exemptions on advertising material directed to health professionals, it is considered necessary that prohibitions on labels also apply to advertising material directed to health professionals, because of the considerable influence these health professionals have on parental and carer feeding choices. Since nutrients which have been demonstrated to be essential are required in all formulae within prescribed levels, the main difference between one brand and another could be in the optional ingredients added. The efficacy of optional ingredients has not been scientifically substantiated, therefore it is important that claims for superiority based on the presence of such nutrients not be allowed. Claims that a certain formula is "more like human milk" on the basis of the level of a certain nutrient or nutrients could be quite misleading. It has not been successfully shown that when substances identified as being present in human milk are added to formula they necessarily confer the same benefit to the formula-fed infant as they do to those receiving them in breast milk. The promotion of a formula on the basis of its being closer to human milk than others could also influence a mother to choose this product rather than to breastfeed.

Exemptions from Australian labelling regulations would be justified in instances where a special formula might have to be imported for one or a very small number of infants with a particular inborn metabolic error, however such nutritionally "incomplete" formulae are not regulated by Standard R7.

It is considered that mixing and preparation instructions should be retained, but with some small changes, namely:

- "unboiled" to "unboiled or **unsterilised**" (to cater for those who use sterilising solutions);
- the inclusion of "**teats**" in the sterilising instructions;
- substituting "**may**" for "will" in "using more or less powder or liquid concentrate than indicated **will** either lead to dehydration or..." (the outcome depends on whether or not the infant is consuming other fluids);
- substituting "vitamin and mineral **supplements**" for "vitamin and mineral **preparations**" (supplements being a more widely used term); and

- changing "after 4-6 months your baby **may** need additional nourishment" to "for infants over the age of 6 months **it is advisable** to introduce other foods" (in order not to promote the introduction of solids at an earlier than desirable age, and to provide more definite advice).

Suggestions were made that suitable additional foods for infants over 6 months should be listed, but it was decided that such a requirement was not appropriate for an infant formula label.

The following changes associated with feeding tables were assessed:

- requiring an additional column, with weight ranges, in addition to the "age" column. It was decided that this would be confusing in a situation where an infant of one age group was within the weight range for another age group;

- because the requirements of infants between the ages of 6 and 12 months are so varied, it was decided that it would be beneficial to include both a 6-9 month and a 9-12 month category;

- a change from "previously boiled" to "cooled, boiled" water, so that there is no ambiguity and the preparation instructions are reiterated;

- omitting the "other feeds" column required in the current Standard R7 for follow-on formula. This could be confusing and is not necessary because there is already a requirement for a statement on the advisability of introducing other foods for infants over 6 months;

- the required pre-term feeding table should be set out on a daily rather than a per bottle basis, because pre-term infants are usually fed under medical supervision in a neo-natal unit, and these instructions are more appropriate to a hospital setting, especially since most of the infants are tube fed. If they wish, manufacturers may also provide preparation instructions on a per bottle basis.

While recognising the value of requiring standardised scoops for use with formula powder, there would be problems with the different formula densities, and the Authority regards such a requirement as being outside its mandate.

It is Standard R7, not Standard A1, which regulates permissions and claims for vitamins and minerals in human milk substitutes.

The word "pictogram" should be omitted if its meaning is not clear.

It is concluded that:

- those labelling requirements in clause (6) of the current Standard R7, which are consistent with the requirements of the WHO Code must be retained, as well as other WHO requirements, such as the statement on breast milk, and the preparation instructions (including the warnings). The

prohibition in current R7 on "a reference to the presence of vitamins, minerals, electrolytes or L-amino acids" should be changed to "a reference to **nutrients**..... ", to ensure that references cannot be made to the presence of other substances, such as some optional ingredients. The exemption on references to iron should be removed;

- all nutritionally complete formulae on the market in Australia must conform with the labelling and advertising requirements of Standard R7;
- mixing and preparation instructions should continue to be required on the label of the package of formula, with the suggested changes, which are designed to make the instructions more comprehensive and accurate;
- feeding tables should be retained, with the suggested changes incorporated, to improve clarity and remove ambiguity;
- there should be no regulation in Standard R7 relating to scoop size; and
- the word "pictogram" should be replaced by "words and pictures".

6. The need for additional regulatory procedures

Pre-market clearance is a procedure for evaluating new infant formulae and existing formulae which have been modified. Because new imported products are coming onto the market from time to time, there is concern over the issue of compliance with Standard R7. Some have suggested pre-market clearance as a means of achieving this. The Australian Institute of Environmental Health (AIEH) suggested a system of registration. The notion of pre-market clearance was supported by Abbott, the Australian College of Paediatrics, ACA, Dorothy Francis, the Nursing Mothers' Association of Australia (NMAA) and Queensland Health.

The DAA, CAFTA, NSW Health, Wyeth and Mead Johnson rejected the idea of pre-market clearance. CAFTA expressed the opinion that a more flexible procedure than the current method was needed for approval for the addition of nutrients found in breast milk. Mead Johnson stated that the highly prescriptive nature of Standard R7 makes pre-market clearance unnecessary, for standard infant formula. NSW Health claimed it would be a "bureaucratic nightmare", and DAA rejected the idea, stating that more appropriate avenues could be found for ensuring that regulations are not breached. As an alternative, they suggested that increased efforts should be made to ensure that products which do not comply are brought to the attention of authorities.

Flinders Medical Centre (Paediatric Nutrition Research Staff) suggested the need for an expert paediatric nutrition committee to continually assess the efficacy of infant formulae. Such a committee could not only alert authorities to the existence of non-compliant formulae in the marketplace, but play a role in improving Standard R7 over time. Abbott, DAA and the Australian College of

Paediatrics all advocated the need for an expert committee to provide advice on infant formula.

Evaluation

There is obviously much concern over the non-compliant products in the marketplace. Most industry groups rejected the concept of pre-market clearance, whilst most consumer and professional bodies tended to support it.

Whilst pre-market clearance may be appropriate where a special infant formula which does not conform with the Code is urgently required for limited use, it is concluded that a system of pre-market clearance is not appropriate for standard formulae covered by R7. It is expected that a manufacturer who wishes to make a product that does not conform with Standard R7 will make an application to have the Standard varied, as is normal protocol.

It is further concluded that:

- the attention of State and Territory Health authorities should be drawn to those formulae on sale in Australia which do not conform with the requirements of Standard R7; and
- the Expert Panel on Infant Formula should remain as a committee to be consulted with in the future, should the need arise.

7. Energy value for carbohydrate

Mead Johnson have requested that the energy value for carbohydrate be changed from 16 g/kJ in the current R7 to 17 g/kJ in the revised Standard, to align it with the value provided in Standard R2.

Evaluation

The figure of 16 g/kJ is appropriate for infant formula, where up to 100% of the carbohydrate is in the form of sugar, which has an energy values of close to 16 g/kJ. The figure in Standard R2 is intended to cover dietary carbohydrates in general, and therefore must take into account the energy value of both sugars and starch (17 g/kJ).

It is concluded that there should be no change to the energy values stated in the current R7.

8. Basis for permitting substances as optional ingredients in infant formula

The consensus of experts is that infant formula should include all nutrients whose essentiality has been established and for which recommended intakes have been developed. There is however some debate over the basis on which optional ingredients should be permitted in infant formula. For example, should

the addition of substances which occur naturally in human milk, to the level at which they are present in human milk, be allowed, as long as safety and toxicity are not issues? Would this be sufficient, or should scientific substantiation of the efficacy of the substances in infant formula also be required? This could be done for example, by comparing the results of clinical trials (carried out according to agreed protocols) which assessed the growth and nutritional status of babies fed either standard formula, formula containing the test substance or breast milk.

The Codex Standard for Infant Formula (Worldwide Standard) states in Section 4.2 Optional Ingredients - "the usefulness of these nutrients shall be scientifically shown". Most paediatric nutritionists and research workers in the infant formula industry agree with this principle (Mead Johnson stated that Section 4.2 of the Codex Standard should be taken into account). It has not been successfully shown that when substances identified as being present in human milk are added to formula they necessarily confer the same benefit to the formula-fed infant as they do to those receiving them in breast milk.

Permitting the addition of substances to infant formula simply because they are "safe", and are known to occur in human milk, may have undesirable marketing consequences. Certain advertising material (directed to health professionals and/or occurring in advertorials) has previously promoted products on the basis that they are "more like human milk". This practice could be regarded as contrary to the aims of the agreement on "The Marketing in Australia of Infant Formulas" on the grounds that it is not "scientific and factual". Any promotion of infant formula is regarded as being at the expense of breastfeeding.

Evaluation

In the submissions received from the public there was total support for harmonisation with standards of the EC, the USFDA and Codex. Both the EC and the USFDA have allowed choline, inositol and nucleotides to be added to infant formula on the basis that they are present in human milk and there are no known safety issues, although in the opinion of the Authority's principal consultant, efficacy has not been unequivocally demonstrated.

The Authority's Expert Panel on Infant Formula developed the following criteria for permitting the addition of optional nutrients to infant formula:

- optional nutrients may be added to infant formula; and
- to qualify as optional nutrients substances must be normally present in human milk; lack of toxicity or adverse interactions must have been demonstrated and there must also be some data suggesting that their inclusion in infant formula would benefit infants.

The rationale for the Panel's position is that:

- infant formula should provide nutrients in amounts that support normal growth and development and ideally result in formula-fed infants having

biochemically equivalent plasma and tissue levels to breast fed infants; and

- the safety and tolerance of all substances added to formulae must have been clearly demonstrated in human clinical studies.

With regard to claims for optional nutrients, the Panel expressed the opinion that an entry for such a nutrient in the nutrition information table on the label of a formula should not be permitted unless the total amount of that nutrient in the formula is at least equal to the minimum level of the specified range.

The "optional" ingredients of current concern with respect to Standard R7 are certain nucleotides, choline, inositol, taurine, carnitine, oligosaccharides and medium chain triglycerides (MCT).

Nucleotides

The infant formula manufacturer Wyeth, who holds several patents for infant formula with added nucleotides, made an application to the Authority in February 1993 to add to formula the following nucleotide 5'-monophosphates: cytidine (CMP), adenosine (AMP), guanosine (GMP), inosine (IMP) and uridine (UMP) to a level between the mean and upper ranges of human milk values. The application was subsequently withdrawn on the Authority's advice, and it was agreed that the documentation would be taken into consideration as part of their submission on the review of Standard R7. Wyeth claim that the addition of these nucleotides to infant formula would result in a formula which is compositionally more like human milk, while conferring possible health benefits to infants. The company stated that nucleotides added to their formula "could be expected to be of benefit to the infant taking the supplemented formula".

Nucleotides are the basic building blocks of the nucleic acids RNA and DNA. They are involved in cellular functions such as energy transfer and modulation of enzyme activity.

An extensive review of the literature has confirmed that:

At least 13 acid soluble nucleotides have been identified in human milk. Their characteristics and functions have been reviewed, and while the amounts present are variable, CMP, AMP, GMP, IMP and UMP are present in the greatest amounts. A wide range of values for these exists in human milk.

A recent report on nucleotides (5) has raised doubts as to whether IMP is present in human milk. The authors believe it may be a sample-preparation artefact. If further evidence substantiates this claim, the Authority would review its decision to permit the addition of IMP to infant formula. Public comment is particularly sought on this issue during inquiry.

Biological effects of nucleotides in human milk with potential significance for infant feeding and human health are: -

enhancement of immune functions;
greater iron availability;
modifications in intestinal microflora;
changes in plasma lipoproteins and other lipids and
promotion of gut growth and maturation.

Evaluation

The Authority's Expert Panel on Infant Formula adopted the following position:

The nucleotides CMP, UMP, AMP, GMP, IMP should be permitted in infant formula, within specified ranges which correspond to the levels in human milk ((6), (7)), the maxima being the same as the maximum levels stated in the European Communities Preliminary Draft amending Directive 91/321/EEC.

The rationale of the Panel was as follows:

- nucleotides are normally present in human milk;
- there is no evidence of toxicity or adverse effects and they have been components of some infant formulae for 20 years; and
- there are some clinical trials which suggest they could benefit infants.

It is concluded that the Panel's position should be adopted, namely that the nucleotides specified in the following list should be permitted as optional ingredients in human milk substitutes, up to the maximum level specified. For an entry in the nutrition information table, the level must be at least the minimum level specified.

nucleotide	**mg/100 kJ**
cytidine 5'-monophosphate	0.22 - 0.60
uridine 5'-monophosphate	0.13 - 0.42
adenosine 5'-monophosphate	0.14 - 0.38
guanosine 5'-monophosphate	0.04 - 0.12
inosine 5'-monophosphate	0.08 - 0.24

and with the total concentration of nucleotides not exceeding 1.2 mg/100 kJ.

Inositol

Both Abbott Australasia and Mead Johnson Australia requested that inositol be allowed as an optional ingredient in infant formula, and one of the Authority's consultants recommended that it be required in pre-term formula.

Inositol has been found in human milk, but dietary essentiality in humans has not been demonstrated with certainty.

Inositol (muscle sugar) is an alcohol. Its exact role is not known, but it is suggested that it is essential for growth of cells in tissue culture. Enough inositol can be synthesised from glucose to meet the metabolic needs of humans.

Inositol is permitted as an optional ingredient by some overseas agencies. In the USA it is only mandatory in formulae which are not milk-based. The USFDA made a decision to permit inositol as an optional ingredient so that products already on the market and containing inositol would not be in contravention of the US Infant Formula Act when it was introduced in 1980.

Evaluation:

The position adopted by the Expert Panel was:

Most formula-fed infants would be receiving some inositol from the cow's milk and/or added lecithin in formula. The effects of inositol-deficient diets on infants are not known.

Although there is no evidence from clinical studies that addition of inositol to formula confers any benefit to normal formula-fed infants, and researchers in the field are not advocating the addition of inositol to formula, it was agreed that:

- the addition of inositol to infant formula should be permitted in the range 3 - 15 mg /100 mL (1.0 - 5.4 mg/100 kJ).

The minimum value represents the level of inositol in cow's milk, and the maximum is at the lower end of the range in human milk, 14 - 45 mg/100mL.

The rationale of the Panel was as follows:

- inositol is normally present in human milk;
- there is no evidence of toxicity or adverse effects in humans;
- there is strong evidence that dietary inositol is beneficial under certain circumstances, especially for premature infants with respiratory problems;

- the relatively high levels of serum inositol in neonates and in colostrum suggest that this substance is of importance, particularly in the first week of life; and

- its addition to infant formula is permitted by several significant overseas food regulatory agencies, and required by the US in non-milk based formulae, albeit to only 2.7 mg/100 mL, (0.96 mg/ 100kJ), approximately the level in cow's milk.

It is concluded that the addition of inositol to human milk substitutes should be permitted to a maximum of 5.4 mg/100 kJ. For an entry in the nutrition information table, the level must be at least 1.0 mg/100 kJ.

Choline

Abbott Australasia requested that choline be required, as it is in the Codex Infant Formula Standard. Mead Johnson stated that necessary nutritional factors (e.g. choline) should be added to the Standard and to the Schedule of forms of nutrients.

Choline plays a role in fat metabolism and prevents the accumulation of fat in the liver. It can be synthesised endogenously, and no deficiency has been identified in humans. Consultants to the Authority have noted that phosphatidyl choline (which occurs in breast milk) is often present as an emulsifier in infant formulae, and that endogenous synthesis of choline is adequate in well nourished infants. In their opinion it is not firmly established that the neonate needs a dietary supply of choline, though they believe this could be the case.

The addition of choline to formula is mandatory in the Codex standard and, for non milk-based formulae, in the US. It is permitted as an optional ingredient in the US (for milk-based formulae), New Zealand, the United Kingdom and the European Union (EU). In supporting their decision to allow supplementation, the EU states "neonates utilise a great deal of choline in membrane synthesis ... and several biochemical pathways, in which choline is a precursor, are crucial for them. Therefore the possibility cannot be excluded that feeding formulae with choline content much lower than human milk may have long term consequences." Choline is present (albeit illegally) in some formulae on the Australian market.

Evaluation

The position adopted by the Expert Panel was:

- the addition of choline to infant formula should be permitted in the range 50 -150 mg/L (1.7 - 5.4 mg/100kJ); and

- the minimum and maximum levels should relate to total choline, i.e. added choline plus any which may come from other ingredients, such as the phosphatidyl choline in lecithin (permitted as an emulsifying agent).

The minimum level for choline corresponds to the lower end of the range in human milk, and the maximum level to the amount of choline which would be supplied by 5 g/L of lecithin (the maximum permitted level for lecithin in infant formula). Based on a value of 23% for the level of phosphatidyl choline in commercial lecithin, and 13% for the choline content of phosphatidyl choline, 5 g/L of lecithin is the equivalent of 150 mg/L of choline.

The rationale for the Panel's position was as follows:

- choline is normally present in breast milk;
- toxicity/adverse reactions have not been reported, and there are no known safety issues;
- there are some data to suggest that inclusion of choline in infant formula would benefit infants;
- choline is permitted by the EC and New Zealand, and **required** in non-milk based formulae by the US and Codex (1.7 mg/100 kJ) (47 mg/ L) and Canada 2.9 mg/100kJ (80 mg/L); and
- it is important to have a maximum level, because of concern over interactions of choline with methionine and folate.

It is concluded that the addition of choline to human milk substitutes should be permitted to a maximum of 5.4 mg/100kJ. For an entry in the nutrition information table, the level must be at least 1.7 mg/100 kJ. The minimum and maximum levels specified apply to total choline.

9. Level of taurine

CAFTA have requested that the required minimum level of 1.5 mg/100kJ be halved to align it more closely with the levels in human milk.

Evaluation

Reported values for the taurine concentration of human milk vary widely, from 0.8 mg/100 kJ (8) to 3.0 mg/100 kJ (9). The current Standard R7 requires a minimum level of taurine of 1.5 mg/100 kJ, which is within the range in human milk, and not greatly in excess of it, as was suggested by CAFTA (no reference was supplied to substantiate this claim).

The advice of the Authority's consultants is that there is no proven clinical or physiological reason for requiring taurine in infant formula.

It has been shown that taurine is present in breast milk irrespective of maternal diet, and there are some indications that it could be important in pre-term infants.

The position of the Expert Panel was as follows:

Taurine should be permitted as an optional ingredient in infant formula, within the range 2.1 - 8.4 mg/100 mL (0.7 - 3.0 mg/100 kJ), the range for human milk

The rationale for the Panel's position was:

- it is normally present in human milk (second highest amino acid);
- no toxicity/adverse interactions have been demonstrated;
- there is some data suggesting that its inclusion in infant formula would be of nutritional benefit to infants;
- the current Standard R7 requires taurine to a level of 1.5 mg/100 kJ (4.2 mg/100 mL)
- the EC Directive for Hydrolysed Protein-based Formula requires a minimum taurine level of 1.25 mg/100 kJ; it is permitted (level unspecified) by Codex, the US and New Zealand.

It is concluded that taurine should be permitted as an optional ingredient in human milk substitutes to a maximum of 3.0 mg/100kJ. For an entry in the nutrition information table, the level must be at least 0.8 mg/100 kJ.

10. Whey-dominant versus casein-dominant formula

Abbott Australasia requested a change to the casein/whey ratio in formula. The DAA stated that it should be reassessed, and Dorothy Francis suggested it should be in the range 50:50 to 60:40 in products for use by infants less than 6 months old.

Standard R7 specifically bans the use of casein-dominant formula designed for feeding infants in the first six months of life. The available data do not provide a scientific basis for this proscription and the regulation has served to perpetuate a myth about the benefits of whey-dominant products, amongst health workers and consumers. This regulation has also excluded a major manufacturer and marketer (Abbott, Ross Division) from the Australian market.

Evaluation

Since it is the amino acid profile rather than the casein to whey ratio that is important for the formula-fed infant, the Authority, on advice of consultants (nutrition and technical), is of the opinion that the casein to whey ratio of products should not be specified. Instead, specifications for protein quality are given in the draft Standard.

11. The inclusion of a follow-on formula category

Abbott requested that more than one category of product be covered in Standard R7. Jane Allen suggested that one such category be "suitable for term infants after 6 months of age" and Wyeth requested that follow-on formulae continue to be identified as part of Standard R7.

Follow-on formulae, or follow-on milks were developed in the 1970's for the feeding of older infants (over 6 months of age) as the liquid component of increasingly mixed diets. The industry claims that these products are better suited to the nutritional needs of growing older infants and has promoted them as the superior way of supplying nutrients in the second part of infancy, and in particular in preference to unmodified cow milk.

WHO, the European Society of Paediatric Gastroenterology and Nutrition (ESPGAN), the American Academy of Pediatrics (AAP) (11,12,13) and other paediatric bodies have stated that there is no nutritional need for these products. Increased nutritional needs of growing infants should and can be met through the addition of appropriate other weaning foods to the infant formula or human milk diet, and eventually suitable table foods.

Codex has recognised the existence of the products in the market-place and developed a standard for them, as has the EC Directive. WHO has classified them as follow-on formulae rather than follow-on milks, so that they can be more strictly regulated. This decision was made because of the inappropriate marketing practices which were used when the products were classified as milks. As formula they are subject to the provisions of the WHO International Code of Marketing of Breast-milk Substitutes.

Abbott Australasia have requested that addition of flavours to follow-on formula be permitted. In both Western Europe and North America, manufacturers and marketers have requested the use in follow-on formulae of certain additives not permitted in infant formulae, including various forms of vanilla. Codex and the EC have allowed these. Australia has not done so, on the grounds that they are unnecessary. Infants do consume formulae and other milks without flavouring, and this is viewed as a marketing practice dictating infant feeding choices.

Originally developed for infants over 6 months of age, these products are now promoted by some manufacturers as suitable for feeding to infants from 3 - 4 months. The 1991 EC Directive on infant formulae and follow-on formulae permitted this after successful petitioning from the industry. Paediatric opinion

in Australia is that if these products are used, they are not appropriate before the age of 6 months, and thus should be labelled accordingly.

Evaluation

The Authority considers that this category of product should remain as part of Standard R7, identified as "follow-on formula", and not simply by the protein or other essential element composition and that the label should include a statement that the product is "suitable only for infants over 6 months". It also concludes that it is inappropriate to permit these products to be flavoured with vanilla.

12. The inclusion of a pre-term formula category and restrictions on the availability of this type of formula

Abbott and Dorothy Francis support the idea of having more than one category of product in Standard R7, and Jane Allen suggested that "pre-term" be one of these categories.

Increasingly in developed societies, more low-birth weight (LBW) and pre-term infants are surviving because of improvements in care, including nutritional management. In addition technological interventions have resulted in the survival of very low birth weight (VLBW) infants who in Australia now contribute significantly to the total number of preterm babies.

These small infants have special nutritional requirements. Many infants are fed pre-term human milk, modified to suit the needs of individual infants. The use of pre-term human milk is encouraged, but nutritional additives are needed to improve growth rates and bone mineralisation.

Term formula is developed for term infants (nutrients based on mature human milk); it is quite unsuitable for pre-term infants. Pre-term formulae have been developed to meet the theoretical needs of pre-term infants with higher protein, energy, mineral and vitamin concentrations. Carbohydrate is also increased, but lactose reduced. Pre-term formulae are usually fed until the infant reaches 2000 g or is discharged from hospital. Follow-on pre-term formulae have been developed and are in use in other parts of the world. Trials to date have shown their usefulness in maintaining improvements in growth and bone mineral content in infancy. They have not yet appeared in Australian neonatal units.

Pre-term formulae are not regulated nor standardised at present in Australia. Currently they are only available to hospital neonatal intensive care units (NICU's) through hospital pharmacies, and feeding protocols are carefully managed by neonatal specialists.

At least one company marketing in Australia is, in other parts of the world, selling pre-term formulae in regular pharmacies or chemists shops both on prescription and as over-the-counter sales. Two recent reports from Europe, describing hypervitaminosis and other adverse effects of feeding pre-term

formula for an extended period after catch-up growth, highlight the need to maintain appropriate strict control on the availability and promotion of these products for pre-term use.

Evaluation

The Authority considers that pre-term formula should be regulated by Standard R7 as a "formula for special dietary use". The essential composition of pre-term formula has been based on the recommendations of the Authority's consultants, who in turn took into consideration the levels recommended by the American Academy of Pediatrics, Committee of Nutrition (AAPCON), the European Society of Paediatric Gastroenterology and Nutrition (ESPGAN) and the consensus recommendations of the authors of Nutritional Needs of the Preterm Infant (10).

Rationales for differences between pre-term formula and standard infant formula, with respect to the levels of essential nutrients, are at Appendix 4.

The Authority recognises that provisions for restricted availability may need to be made in the future, but it is concluded that at present there is not a demonstrated need because pre-term formulae are only used under specialist medical supervision.

13. Iron levels and claims about the iron content of formulae

Abbott Australasia requested that the maximum level for iron be extended. The DAA asked for a reconsideration of the minimum level for iron, as did Dorothy Francis, who suggested a minimum of 7 mg per litre.

The previous recommendation for iron levels in infant formula allowed for the wide range of 2.8 - 13.5 mg per litre. A 1990 amendment, (6)(a), allowed formula containing not less than 0.25 mg per 100 kJ (6.9 mg per litre) to be labelled as "infant formula with iron".

It is considered that this amendment is inconsistent with the principles applied in the development of the Standard. The reasons for specifying this range were based on both public health and safety issues and lack of precise information about the needs of an individual infant. These do not provide justification for special labelling for products at the top end of that range.

The consultants have recommended a range of 6 - 13.5 mg per litre; other workers and the US FDA have recommended an upper limit of 20 mg per litre, on the basis that this prevents depletion of iron stores and protects against iron deficiency anaemia in the second six months of life. However, there is some concern that iron fortification may compromise immunity, and excess iron leads to constipation and inhibition of zinc and copper absorption.

Formulas with iron levels at the lower end of the present range have been criticised for failing to protect iron stores. Insufficient iron in infancy may

produce irreversible deficits in neural function and behaviour. Recommendations have been made to raise the lower end of the range. Such a measure would be consistent with the recommendation from the AAP that there is no place for "low iron" formulae in infant feeding (11). The USFDA does permit them, but requires any formula with an iron level of less than 1 mg per 100 kcal (approx. 0.23 mg per 100 kJ) to be labelled with the following: "additional iron may be necessary".

Evaluation

The current maximum permitted level for iron, 13.5 mg per litre (0.48 mg/100kJ) is that recommended by consultants to the Authority and is consistent with ranges recommended by some international authorities.

It is concluded that the maximum level for iron should remain at the presently prescribed level (because of possible side effects associated with higher levels), that the minimum level for iron should be raised from 2.8 mg per litre to 6 mg per litre (0.1 mg/100kJ to 0.22 mg/100kJ), and that clause (6)(a), relating to a claim on the iron content of formula, should not be included in the draft revised Standard R7.

14. Inclusion of selenium as an essential nutrient

Douglas Pharmaceuticals, Nutritional Division, have requested the addition of selenium as sodium selenite or selenomethionine to infant formulae. The request for selenium to be permitted has also been raised by Abbott Australasia, Mead Johnson Australia, CAFTA, the Paediatric Nutrition Research Unit staff at Flinders Medical Centre, and, by inference, the Dietitians Association of Australia, who asked that all nutrients for which there were RDIs be included in the Standard.

The selenium content of prepared formulae analysed by the neonatal unit laboratory at the Flinders Medical Centre ranged from 2.9 to 23.5 µg per litre. A recent extensive literature search by workers investigating selenium in breast milk found it contained levels of 15 - 25 µg per litre in countries where the diet is similar to that in Australia and the soils are not selenium deficient. The Authority's consultant advised that, since limited data demonstrate that selenium is absorbed as well from formula as from human milk, the level of supplementation should not differ significantly from the level in human milk.

Selenium-deficient infant formula had not been an issue until formula from New Zealand entered the Australian market. Both Douglas Pharmaceuticals and Mead Johnson Australia manufacture from the same milk pool (indeed the same plant) in New Zealand, and together make up a significant market share in Australia. Douglas have advised that Karitane Infant Formula, which is marketed in New Zealand, is fortified with selenomethionine to a selenium level of 24 µg per litre. New Zealand is a recognised low selenium area and selenium is already added to two formulae in New Zealand.

Although selenium is scheduled in the Standard for the Uniform Scheduling of Drugs and Poisons (SUSDP), this does not prohibit its use in foods. To be permitted in infant formula however, there must be specific permission given in the Code.

Evaluation

Infant formula being the sole source of nutrition for infants, by definition must contain safe and adequate amounts of all nutrients for which recommended intakes have been established. Submissions requesting an appropriate level of selenium in the Standard have been made in recognition of infants' requirement for this nutrient. In addition unpublished reports from New Zealand (7) have identified low selenium status as a risk factor for broncho pulmonary displasia, especially in premature infants. As increasing amounts of formula are being imported into Australia from New Zealand, there is a need to permit supplementation in order to prevent selenium deficiency and also to remove a trade barrier.

Ranges for selenium should be set such that infants can receive the recommended dietary intake for selenium (10 µg for infants up to 6 months and 15 µg for infants from 6 to 12 months). For infants up to 6 months, this means a minimum level of 0.42 µg/100 kJ in infant formula (based on a daily consumption of 850 mL); for infants from 6 to 12 months, this means a minimum level of 0.79 µg/100 kJ in follow-on formula, (based on a daily consumption of 675 mL). There is no RDI for preterm infants, but since their plasma levels of selenium are especially low and this potentially enhances their susceptibility to oxygen toxicity and chronic lung disease, the minimum level should be higher than for standard formula (0.53 µg/100 kJ). The maximum level for all formulae should be 0.89 µg/100 kJ, equivalent to 25 µg/L, the upper level for human milk. This exceeds the RDI for selenium, but is based on sound, recent, Australian data which will be referred to the NHMRC.

It is concluded that revised standard R7 should provide for the listing of Se as an essential nutrient within the range 0.53 µg per 100 kJ to 0.89 µg per 100 kJ in pre-term formula, 0.42 µg per 100 kJ to 0.89 µg per 100 kJ in infant formula, and 0.79 µg per 100 kJ to 0.89 µg per 100 kJ in follow-on formula.

It is also concluded that since in Standard A12 there are entries for selenium which cover human milk substitutes (i.e. "beverages and all other liquid foods" and "foods not containing a food otherwise specified"), there is a need to amend A12 as follows:

insert in column 2 of the Table
'Foods standardised by Standard R7'

and in column 3 of the Table
'must not exceed the levels specified for that food in Standard R7'.

15. Levels of antioxidants

Mead Johnson have requested that mixed tocopherol concentrates and L-ascorbyl palmitate be permitted at a total level of 10 mg per litre, when added as antioxidants and not as sources of vitamin E and C respectively.

Evaluation

Both substances are to be permitted as forms of vitamins in the revised draft Standard R7, and the maximum level being recommended for each is sufficient, in the opinion of the Authority's consultant and an industry representative, to cover nutritional and antioxidant requirements.

Having within the Standard two different maximum permitted levels based on different functions for the one substance is considered to be a potential source of confusion.

It is concluded that no additional permission for antioxidants should be given, and that the permission already in Standard R7 to add α-tocopherol to a maximum level of 10 mg per litre should be deleted, on the basis that it is unnecessary.

EVALUATION AND ASSESSMENT OF OTHER IMPORTANT ISSUES

1. Fluoride - the need to ensure that the consumption of infant formula does not put infants at risk of developing fluorosis

Fluoride is a constituent and natural contaminant of all foods and diets. It is of benefit to humans because of its valuable effects on dental health. It may also play a role in controlling certain enzymatic reactions in some organs. Retention sites for fluoride ions are teeth, bone and calcified cartilage.

At high or excessive levels of intake, fluoride appears toxic. Chronic exposure to high intakes of fluoride over many years may lead to skeletal fluorosis, whilst dental fluorosis may result from excessive fluoride ingestion during the period of tooth calcification.

The US National Research Council (National Academy of Sciences) has estimated that the following levels of fluoride are "safe and adequate" for infants:

Age	daily dietary intakes
Birth to 6 months	0.1 - 0.5 mg
6 months to 12 months	0.2 - 1.0 mg

The NHMRC has suggested that as an interim measure Australia should use these as recommended levels of intake.

An Australian infant consuming 850 mL of formula would receive approximately 0.85 mg of fluoride from water alone, if the formula was reconstituted with water containing 1.0 mg fluoride/litre. (Target levels for drinking water in Australia are 0.7 - 1.0 mg fluoride/litre). This is considerably above the "safe and adequate" intake for infants below the age of six months.

Figures in Table 1 (at Attachment 2 of item 6.6, NFA 26 - a decision paper about establishing an expert panel to assist with the revision of Standard R7) suggest that formula-fed Australian infants may be at risk for the potential consequences of excessive intakes of fluoride, such as dental fluorosis. An examination of these figures for fluoride intake, in terms of mg/kg body weight, shows that the threshold for dental fluorosis could be exceeded as much as threefold if certain formulae were reconstituted with tap water. Both the level of fluoride and the duration of use of infant formula have been cited as risk factors for dental fluorosis. It should be noted however that:

- there are no reports in the Australian literature of healthy term infants with signs or symptoms of chronic fluoride toxicity due to the use of powdered formula made up according to directions; and

- free fluoride as it exists in water is more available than the protein-bound fluorine in foods. There are research findings (15) which indicate that, in the case of young adults, the absorption of fluoride from reconstituted infant formula is considerably less than it is from water.

Since there are apparently no Australian data which suggest that the fluoride levels in infant formula are causing serious fluorosis problems, despite total fluoride ingestion often being above the recommended levels, the amounts previously assumed to be absorbed from infant formula should be reassessed.

Public health authorities, consumer groups and the general public have recently voiced concerns about the amounts of fluoride ingested by infants and young children. It has been suggested by the NHMRC (letter at Attachment 2 of item 6.6, NFA 26) that the NFA, through Standard R7, should control the amount of fluoride in infant formula and require the level of fluoride to be shown in the nutrient panel. The latter would seem impractical since a significant proportion (in one case 96%) of the fluoride in reconstituted infant formula comes from the added water.

Evaluation

The Authority's Expert Panel discussed the issue of safe and adequate levels of fluoride in infant formula. Their position was:

- formula reconstituted with water (fluoridated or non-fluoridated) provides adequate fluoride for infants aged 0 - 6 months;

- there should be a maximum fluoride level imposed on infant formulae, consistent with the highest level of fluoride in formulae currently available in the Australian marketplace - a value which is considered safe; and

- there should be no other course of action taken, such as advice about reconstituting formula with fluoridated or non-fluoridated water.

The rationale for the Panel's position was as follows:

- infants do not need fluoride until they have teeth. Fluoride is therefore considered a non-essential element for infants aged 0 - 6 months.;

- imposition of an upper limit will force manufacturers to monitor their product for fluoride; and

- although there is an increased risk of dental fluorosis by consuming formula made up with fluoridated water, the risk of minor dental fluorosis is outweighed by the benefit to the public as a whole of having fluoridated water to help prevent caries.

Whilst this information could be referred to relevant health professionals for dissemination to parents, it was not considered necessary to include such instructions within the labelling provisions of the Standard.

Available data on fluoride levels in infant formulae show that in general the levels in soy-based products are significantly higher than those in milk-based products.

It is concluded that Standard R7 should specify an upper limit for fluoride of 2.0 mg/L for soy-based human milk substitutes and 0.5 mg/L for all other human milk substitutes in ready-to feed form, or when reconstituted from powder or liquid concentrate using fluoride-free water.

2. Aluminium - the need to set an upper limit for aluminium in infant formula

Aluminium has no known physiological function in humans, is toxic to brain and bone and may also accumulate in other organs. Aluminium interferes with reactions involving calcium, magnesium and iron and with a number of proteins and co-factors concerned with intermediary metabolism.

Because it is the third most common element and the most abundant mineral in the earth's crust, aluminium is a contaminant of practically all foodstuffs. Foods of plant origin will contain relatively greater concentrations, since plants lack an excretory mechanism for aluminium. The amounts occurring in vegetables and animals will vary according to local environmental conditions and the geology of the region through which water flows.

Aluminium has a wide variety of uses, many of which are in food applications. Aluminium salts are permitted food additives and have uses in medical and cosmetic products.

Only a small amount of ingested aluminium is absorbed through the wall of the gastro-intestinal tract. When absorbed, aluminium is bound extensively to protein (transferrin) and the blood plasma aluminium is excreted through the kidneys. If absorption is increased due to a diseased or immature gastrointestinal tract, or excretion is limited due to disease or immaturity of the kidney, aluminium will be retained. Resulting adverse effects on bone and brain and disturbance in iron status have been reported.

Dr Simmer reported that, although the level of contamination of infant formula is probably not clinically significant in infants with normal renal function, it may result in toxicity in infants with renal failure. Infants, especially preterm and the very young, may be at particular risk of aluminium toxicity because of their immature gastro-intestinal tracts and limited ability to excrete the element through normal renal clearance.

There have been reports of high levels of aluminium in infant formulae, particularly those which are soy protein based. No aluminium is added to formulae: it occurs as a 'natural' contaminant of raw ingredients and the manufacturing processes. Analysis by the Australian Government Analytical Laboratories (AGAL) of 10 different infant formula powders on the Australian market (1986) produced the following results:

non-soy formulae (7 samples)	0.7 - 5.8 mg Al/kg
soy formulae (3 samples)	7.0 - 16.0 mg Al/kg

Aluminium levels measured in infant formula powders in the 1992 Australian Market Basket Survey (AMBS) were:

non-soy formulae (18 samples)	0.3 - 5.0 mg Al/kg
soy formulae (9 samples)	4.5 - 7.0 mg Al/kg

All formulae have levels of aluminium that are considerably higher than in human milk, where the level is of the order of 0.05 mg/litre. Although the estimated dietary intake of aluminium by an infant is well below the Provisional Tolerable Weekly Intake (PTWI), whatever the type of milk or formula consumed (AMBS, 1992), concern has been raised by both paediatric researchers and consumers that these levels may be harmful to infants. Recommendations have been made (from paediatric bodies and researchers in Australia, the USA, Canada and the UK) to keep aluminium levels to a minimum. It should be noted that the Sydney Water Board in 1994, made a decision to replace alum (aluminium sulphate) with ferric chloride at all four new plants treating 92% of Sydney's water supply. They concluded that research findings around the world

on the use of alum and its effects on the brain, although not conclusive, provided enough evidence for them to decide to avoid its use.

No standard developed for infant formula at present sets a limit on aluminium contamination. The industry in Australia rejected this measure when the matter was considered by NHMRC in 1988. Since that time, manufacturers have been successful in reducing the level of aluminium in infant formula, as shown by a comparison of the 1986 and 1992 figures quoted. It is necessary, however to monitor levels, as they can be quite variable, and to establish a limit on the permitted level of contamination.

The Authority's consultants advised that a level of contamination no greater than 2 mg /L reconstituted formula is achievable, based on data available a few years ago. Since more recent data indicate that there has been a considerable decrease in the aluminium levels in these products, a more stringent limit can now be applied.

Levels of aluminium in tap water around Australia are usually well under the NHMRC recommended level of 0.2 mg/L (a level set on aesthetic grounds, there being no limit based on health grounds). In reconstituted formula, the proportions are, on average, 130g powder to 900 mL water, or 500 mL liquid concentrate to 500 mL water.

Evaluation

Available data on aluminium levels in infant formulae, from the AMBS and from industry, show that in general the levels in soy-based products are significantly higher than those in milk-based products.

It is concluded that Standard R7 should specify an upper limit for aluminium of 1.0 mg/L for soy-based human milk substitutes and 0.2 mg/L for all other human milk substitutes in ready-to feed form, or when reconstituted from powder or liquid concentrate using aluminium-free water. Almost all formulae on the market in Australia have aluminium levels below these limits.

3 Hydrolysed protein formulae - whether formula containing partially hydrolysed and extensively hydrolysed protein should be included in Standard R7

Several products are now available which, it is claimed, are antigen-reduced or hypoallergenic. The products available are of two types- one in which the cow's milk protein is extensively hydrolysed, and more recently, one in which the protein is only partially hydrolysed. The latter is now widely available in the USA and Western Europe. The use of partially hydrolysed product has become controversial because claims for allergy prevention have not been well supported by clinical trials to date.

Evaluation

In the Authority's consultant's report (at Appendix 5), it is recommended that formulae containing modified protein (hydrolysed protein or synthetic amino acids), and/or modified carbohydrate and/or modified lipid be included in Standard R7. Such formulae play an important role in the management of malabsorption and/or protein allergy. Since they are nutritionally complete, and most of the provisions for standard infant formula are applicable to them, it was concluded that they should be accommodated in Standard R7 as "Proximate-modified Human Milk Substitutes" under the division of "Human Milk Substitutes for Special Dietary Use".

4. Lactose free and low lactose human milk substitutes - whether formulae which are lactose modified or lactose free should be included in Standard R7

There are formulae in the marketplace which are compositionally similar to infant formula, except that they do not satisfy the requirement for lactose. In formulae derived from milk, the lactose has been either hydrolysed or removed. In soy formulae, no lactose is present in the constituents.

Evaluation

To qualify as a "low lactose" food, there must be a lactose reduction of at least 95% ((5)(b)(i) of Standard R1). A "low lactose" human milk substitute is one which complies with this requirement. A "lactose free" human milk substitute must contain no detectable lactose when examined by any method.

The Authority received expert paediatric advice that formulae with less than 1% lactose are suitable for all lactose intolerant infants except those with galactosemia, who may be unable to tolerate even minute amounts of lactose. Since any milk-based formula is unsuitable for galactosemics, even if its level of lactose is so low that it cannot be detected, and any formula with less than 1% lactose is suitable for non-galactosemic lactose intolerant infants, there is no advantage in prescribing a method of lactose analysis with a limit of detection of 0.1%.

It is concluded that:

i) lactose free and low lactose human milk substitutes should be regulated by Standard R7 under the division of "Human Milk Substitutes for Special Dietary Use";
ii) no method of analysis should be specified in conjunction with the claim "lactose free"; and
iii) a warning statement should be required on milk-based, lactose free formula, to the effect that it is unsuitable for galactosemic infants.

5. Carrageenan - whether it should continue to be permitted as an additive in liquid concentrate and ready-to-feed formulae.

Under the current Standard R7, infant formula may contain not more than 0.3 g per litre of carrageenan, in the case of liquid milk-based and soy-based varieties, and not more than 1.0 g per litre of carrageenan, in the case of liquid hydrolysed protein-based and amino acid-based types. Carrageenan improves the stability of the milk system, increasing homogeneity and thus making the liquid smoother.

The toxicology report on carrageenan noted the following:

i) In 1992, the Food Advisory Committee of the UK Ministry of Agriculture, Fisheries and Food (MAFF), recommended that carrageenan should not be permitted in infant formula in the UK. Concern had initially been raised about possible immunological consequences following absorption of carrageenan, particularly by the immature gut. When a subsequent study found that guinea pigs and newborn rabbits absorbed small amounts of carrageenan, the Committee elected to take the previously mentioned action.

ii) The EC Scientific Committee for Food (SCF), in its 1994 report, made a similar recommendation.

Evaluation

Inquiries made to those manufacturers who sell liquid formula products, revealed that all such formulae on the Australian market are imported. Withdrawing permission to add carrageenan could therefore have trade implications. However since the UK and EU constitute a significant proportion of the global market, it may be that other regulatory authorities around the world will move to exclude carrageenan from their infant formula products in order to be able to sell them in Britain and Europe.

One industry representative expressed the view that no single gum could be used as a replacement for carrageenan, although he said that a blend of gums might serve the same function.

It is concluded that since safety concerns have been expressed and human milk substitutes may be the sole source of nutrition for infants, the Authority should act cautiously in this matter and remove permission to add carrageenan until a convincing case is presented to refute the safety concerns.

6. Carnitine, medium chain triglycerides and oligosaccharides - whether each of these should be permitted as optional ingredients

There are differing opinions in the scientific community as to the relative merits of permitting each of these substances to be added to infant formula.

Evaluation:

The Expert Panel's position on the addition of carnitine, medium chain triglycerides and oligosaccharides to infant formula as optional ingredients, and the rationale for the decisions, are as follows:

i) Carnitine

- carnitine should be permitted as an optional ingredient in infant formulae, with the minimum and maximum level based on human milk values, i.e. 0.6 - 1.2 mg/100 mL (0.21 - 0.42 mg/100 kJ).

The rationale for this decision was:

- carnitine is normally present in human milk;
- there is no safety concern;
- there are some data suggesting that its addition to infant formulae (especially soy formulae) could be of nutritional benefit to infants;
- the current Standard R7 permits carnitine to a level of 0.27 mg/100 kJ (0.76 mg/100 mL); and
- the EC Directive requires a minimum carnitine level of 0.29 mg /100 kJ; and it is permitted (level unspecified) by Codex, the US and New Zealand.

ii) Medium Chain Triglycerides (MCTs)

- Medium Chain Triglycerides (MCTs) should not be permitted to be added to infant formulae.

The rationale for this decision was:

- they are not normally present in human milk;
- the long term effects of infants consuming a high percentage of saturated fats are unknown; and
- there is no convincing evidence that the inclusion of MCTs in formula has conferred any benefit to infants.

iii) Oligosaccharides

- Oligosaccharides should not be permitted to be added to infant formulae.

The rationale for this decision was:

- Although various oligosaccharides are present in significant levels in human milk (3 - 6 g/L), and there is reasonable evidence of beneficial

effects in *in vitro* studies, there have been no clinical trials carried out where oligosaccharides have been added to infant formula, therefore no demonstration of efficacy;

- their safety is in question - there has been some research suggesting that they may have adverse interactions with yeast lactase; and
- a decision as to which particular oligosaccharides should be permitted and in what amounts could not be made at this stage, because insufficient research has been done.

It is concluded that carnitine should be permitted to be added to human milk substitutes as an optional nutrient to a maximum of 0.42 mg/100kJ. For an entry in the nutrition information table, the level must be at least 0.21 mg/100 kJ. Neither MCTs nor oligosaccharides should be permitted.

EVALUATION REPORTS:

1. Microbiology Report

Comments on microbiological requirements for infant formula

In setting the microbiological requirements for infant formula products, the effects of the following factors need to be assessed:

- nature of the material - dry, liquid, liquid concentrate;
- packaging employed - single use sachets, multi-use container;
- composition of the material - presence of known risk components;
- nature of the consumer - potential for consumption by risk group(s);
- features in common with other Code entries;
- recommendations by other regulatory or scientific groups; and
- industry manufacturing practices that may affect product quality.

Since the gazettal of the current Standard R7 in July 1988, the only factor that has changed dramatically has been the improvement in dairy industry practices, both at the farm and factory level. This is illustrated by the fact that large companies such as Bonlac have implemented bonus schemes based on farmer's bulk milk cell counts (BMCC) - the lower the BMCC, the higher the bonus.

BMCCs are the number of lymphocytes (pus cells) present in a given volume of milk. Large BMCCs are an indication of active mastitis, in which case the milk is rejected by the milk factory. Lower levels are an indirect, although accurate

measure, of the number of pathogens present in milk, and hence the overall hygiene level on the farm and in the milking shed. The rationale is that a "cleaner" primary product will present less problems within the factory and the final product. Research findings support this rationale. This has been a world wide phenomenon.

In order to address their own concerns regarding microbiological contamination, the dairy industry has been at the forefront of the introduction of Hazard Critical Control Point (HACCP) principles and adjunct quality systems. This includes comprehensive quality control and quality assurance procedures. The measures they have put in place are far advanced of those currently operating in other food industries such as the red meat and poultry industries.

Based on the positive changes that have occurred in the dairy industry there is no discernible need to change the current microbiological requirements in the revised Standard R7.

Note: It has been brought to the attention of the Authority that the prescribed method for the detection of coliform organisms (Australian Standard 1766, *Methods for the Microbiological Examination of Food*) may be not be as efficient as alternative methods. This apparent deficiency has been brought to the attention of the relevant committee within the Standards Association of Australia (SAA). Until the issue is investigated and resolved either way, there is no obvious reason to adopt the alternative method. Prescribed methods, including suggested changes, are subject to intensive investigation and analysis before adoption and subsequent recommendation to the full SAA committee. This process has been established and is under the scrutiny of a panel of expert microbiologists.

2. Toxicology Report

Permitted forms of vitamins, minerals, electrolytes and other nutritional factors that may be added to infant formula

There are no toxicological concerns with regard to any of the chemicals listed under this heading when they are present in the amounts and forms specified. With the exceptions of sodium selenite and seleno methionine, all are approved by the EC Commission Directive of 24 May 1991 (91/321/EEC) or by the CODEX Advisory List of Mineral Salts and Vitamin Compounds for Infants and Children (72-1981). The levels of sodium selenite and seleno methionine in infant formula which were requested by Douglas Pharmaceuticals are considered below.

Sodium selenite and seleno methionine

New Zealand soils are naturally low in selenium which can result in low levels of selenium in food, including infant formula. As a consequence, Douglas Pharmaceuticals New Zealand, requested that the addition of selenium as sodium selenite or seleno methionine to infant formula be permitted in the Code up to a maximum level of 30 µg/L. On average, infants consume 850 mL of

formula per day which would lead to an intake of 25.5 µg selenium/day. This however exceeds the Australian RDI for selenium in infants which is 10 - 15 µg/day. Consequently a maximum level of selenium in infant formula of 15 µg/L is recommended. However this recommendation should be considered in light of the nutrition report.

Additives listed in Standard R 7, (3)(c)(v)(A)

There are no toxicological concerns with any of the chemicals listed in this section. However, it should be noted that carrageenan is not permitted as an additive to infant formula in the United Kingdom (UK).

Carrageenan. Carrageenan is approved by the Codex Standard for Infant Formula (72-1981) and concerns about its safety were addressed in the 1984 JECFA report. This report emphasised the importance of differentiating between native and degraded carrageenan. In addition, the EC Report of the Scientific Committee on Food (23rd series, 1988) approved the use of carrageenan in infant formula.

In an undated report, the UK Ministry of Agriculture, Fisheries and Food (MAFF) raised concern about possible immunological consequences following absorption of carrageenan, particularly by the immature gut. The results of a single, subsequent study were included in a report by the UK Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment (1991). This study found that guinea pigs and newborn rabbits absorbed small amounts of carrageenan. The Committee concluded that although absorption from the human gut was likely to be very slight, it could not be excluded. In 1992, the Food Advisory Committee (MAFF), recommended that carrageenan should not be permitted in infant formula in the UK.

The EC Scientific Committee for Food (SCF) in its 1994 report expressed further concern with regard to carrageenan. New information was provided with regard to the degradation of carrageenan at a pH similar to that found in the human stomach and also of its hydrolysis by artificial gastric juice. Although the EC SCF did not consider it appropriate to adjust the present acceptable daily intake (ADI) for adults until further studies have been completed, they did recommend that carrageenan should not be permitted in infant formula which could constitute almost the entire food supply for the infant at that age period.

Carrageenan is currently permitted in infant formula within Standard R7 (3)(c)(v) of the Code. However, in the light of the concerns raised by MAFF and the EC SCF, the permission for carrageenan in infant formula should be withdrawn. It should be noted, however, that there are other gums permitted under Standard R7 which possibly could be substituted for carrageenan in infant formula.

ASSESSMENT AGAINST OBJECTIVES OF THE NFA

Protection of Public Health and Safety

The revision of Standard R7 provides for the protection of public health and safety of the most vulnerable group in the Australian population, that is, infants routinely fed human milk substitutes.

In order to satisfy this objective, revised Standard R7 strictly stipulates the nutritional composition of human milk substitutes to provide fully for the nutritional needs of infants at all stages of growth and development. For nutrients considered as essential, a range of contents within minimum and maximum levels is prescribed to ensure that the amounts of nutrients available from formula products are both safe and adequate to support health. Where there is sufficient evidence of a sustainable health benefit from consumption of human milk substitutes containing other nutritional factors found in human milk, these factors are considered as optional additions to formula products and are permitted to be added up to a specified maximum level. In addition, the permitted additives and the microbiological specifications have been carefully assessed so that the infant population would not be put at risk.

Provision of Adequate Information to Consumers to Enable Informed Choice and Prevent Fraud and Deception

The provisions for the labelling of human milk substitutes are revised to ensure that carers of infants are given detailed information about the contents of the products as well as clear directions for appropriate use. The relevant labelling provisions of the WHO Code of Marketing Breast Milk Substitutes are also reflected within the Standard. These include a reference to breast milk as the optimum source of nourishment for infants so that potential purchasers of formula products can be informed of the full range of feeding options.

Promotion of Fair Trade

This standard provides for fair trade of formula products, within the confines of the agreement between the formula manufacturers and the Federal Bureau of Consumer Affairs that they will implement the WHO Code within Australia, thus restricting promotion of human milk substitutes.

Promotion of Trade and Commerce in the Food Industry

Human milk substitutes are one of the few food products for which national and international health objectives (that is, promotion of breast feeding) may be in direct conflict with this objective. The global health aim is to reduce the amount of human milk substitute used in infant feeding. The revised Standard R7 does however ensure uniform standards within Australia and harmonisation as far as possible within the international market-place so that there will not be an impediment to trade.

Promotion of Consistency Between Domestic and Overseas Food Standards

The essential elements of this Standard are aligned with the standards of Codex, the European Union, the USA and New Zealand. This will assist the industry, as there is a significant trade of product, both as imports and exports, between Australia and other countries.

REFERENCES

(1) WHO 1981. *International Code of Marketing of Breast-milk Substitutes.* WHO Geneva.

(2) Cunningham AS, Jelliffe DB and Jelliffe PEF (1991) Breast-feeding and health in the 1980's: a global epidemiological review. *The Journal of Paediatrics* 118(5): 659-666.

(3) Woolridge MW and Baum JD (1993) Recent advances in breast feeding. *Acta Paediatrica Japonica* 35: 1-12.

(4) The Breastfed Infant: a model for performance. *Report of the 91st Ross Conference on Pediatric Research,* 1986.

(5) Leach J, Baxter J, Molitor B, Ramstack M and Masor M (1995). Total potentially available nucleosides of human milk by stage of lactation. *Am J Clin Nutr* 61: 1224-30.

(6) Gil A & Sanchez-Medina F (1982). Acid-soluble nucleotides of human milk at different stages of lactation. *J Dairy Res* 49: 301-306.

(7) Janas L & Picciano M (1982). The nucleotide profile of human milk. *Ped Res* 16: 659-662.

(8) Pamblanco M, Portoles M, Paredes C, Ten A and Cumin J (1989). Free amino acids in preterm and term milk from mothers delivering appropriate or small for gesttional age infants. *Am J Clin Nutr* 59: 778-81.

(9) Fomon S (1993), ed. Craven L. *Nutrition of Normal Infants,* Mosby, St Louis, p122-123.

(10) Forbes AL, Falce JK and Cheney MC (1993). Table A2 (Appendix) in *Nutritional Needs of the Preterm Infant.* Tsang TL, Lucas A, Uauy R and Zlotkin S eds., Williams and Wilbius, Baltimore 1993.

(11) American Academy of Pediatrics, Committee on Nutrition. Position Paper. The Use of Whole Cow's Milk in Infancy. *Pediatrics* 89 (6): 1105 - 1109. June 1992.

(12) European Communities Commission. Reports of the Scientific Committee for Food (thirty first series) 1993. *Nutrient and Energy Intakes for the European Community. Office for the Official Publications of the European Communities.* Luxembourg.

(13) National Health and Medical Research Council 1991. *Recommended Dietary Intakes for Use in Australia.* AGPS Canberra.

(14) National Research Council 1989. *Recommended Dietary Allowances. 10th edition. National Academy Press.* Washington DC.

(15) Spak CJ, Ekstrand J, Zylberstein D. 1982. Bioavailability of fluoride added to baby formula and milk. *Caries Res.* 16: 249-256.

CONCLUSIONS

It is concluded that Standard R7 should be revised to align it with current scientific knowledge and opinion, to make its interpretation easier for the user and for the purposes of harmonisation. Pre-market clearance is regarded as unnecessary for human milk substitutes that would be regulated by the proposed Standard R7.

It is intended that the draft revised Standard R7 will -

- be harmonised as far as possible with the infant formula standards of Codex, the US Food and Drug Administration and the European Community's Directive with respect to essential elements;

- retain those labelling and advertising requirements in the current Standard R7 which specifically reflect the provisions of the WHO International Code of Marketing of Breast-milk Substitutes and ensure that all labelling requirements are clear and unambiguous.

- ensure that human milk substitutes sold in Australia -

  - include all nutrients whose essentiality for infants has been established and for which recommended dietary intakes have been developed;

  - are categorised, according to their appropriateness for specific groups of users, with each type of formula being clearly defined; and

  - have safe levels of aluminium and fluoride.

It is further concluded that consequential amendments should be made to Standards A1, A11 and A12 in order to:

- regulate claims about the suitability of foods (other than those complying with Standard R7) as a sole or principal source of nutrition for infants;
- ensure that new additives which have been permitted are listed in the Schedule in Standard A1 of the Code, together with their food additive code numbers;
- ensure that there are references to specifications in the Code for all substances which are permitted in human milk substitutes;
- provide specifications which permit L-selenomethionine to be used as a source of selenium; and
- ensure that the limits specified in the Table for "selenium" in relation to "beverages and all other liquid foods" and "foods not containing a food otherwise specified" cannot be applied to any human milk substitute;

APPENDICES:

1. Summary of Submissions
2. Report on Meeting of Expert Panel on Infant Formula
3. Table of Comparison between Levels of Vitamins and Minerals in the Present Standard R7 and the Revised Standard R7
4. Table of Comparison between Levels of Vitamins and Minerals in Pre-term and Standard Formula in the Revised Standard R7
5. Consultant's Report "Formulae Based on Modified Protein, Fat and Carbohydrate"

ATTACHMENTS:

1. Draft Variation to Standard R7 of the Food Standards Code
2. Explanatory Notes
3. Draft Gazette Notice

SUMMARY OF SUBMISSIONS

Abbott Australasia Pty Ltd (Parent Company USA)

- Supports need for revision to bring standard into line with current knowledge and scientific opinion; Ross Laboratories (a division of Abbott) undertakes considerable research and development in the area of paediatric research. [Paediatric nutritionists at Ross have provided technical information as well as access to a global literature not readily available in Australia].
- Supports international harmonisation with Codex Alimentarius Commissions standard as the reference.
- Supports clarification of definitions as proposed in an earlier proposal (Proposal 49) ie. more than one category of products within R7.
- Recommends a regulatory procedure which includes a committee of experts.
- Supports pre-market clearance, as required in the USA.
- Recommends changes to compositional aspects of products:
  - protein and amino acids.
  - casein to whey ratios.
  - lipids and fatty acids.
  - vitamin range to be increased.
  - vitamin D maximum limit to be increased.
  - tocopherols, consistent with Codex.
  - iodine, upper limit extend as by FDA.
  - iron, upper limit to be extended.
  - choline to be a required addition as in Codex.
  - inositol to be allowed as an optional ingredient.
  - Selenium to be permitted.
- Requests several additions to the schedule of forms of vitamins, minerals and electrolytes that may be used in infant formula.
- Requests permission to use ascorbyl palmitate in infant formula as in Codex.
- Requests addition of flavours to follow-on formulae as in Codex.
- Requests more flexible labelling requirements for imported products.
- Submission well referenced and with significant supporting documents.

Australian College of Paediatrics (Nutrition Sub-Committee)

- Recommends breast feeding for all infants, but when this is impossible, formula should be as similar in nutrient composition as human milk as possible.
- Ranges of nutrients as advised by the American Academy of Paediatrics is recommended.
- Pre-market clearance of new or modified products is supported.
- References attached supporting; documentation provided.

Australian Consumers Association

- Supports the need for compositional standards to be consistent with current scientific knowledge and opinion. Requests NFA convene a committee with consumer representation for the purpose.
- Requests labelling and advertising be consistent with WHO International Code of Marketing of Breast-milk Substitutes.
- Supports concept of pre-market clearance.
- Requests categorisation of products be consistent with provisions of WHO Code above (ie definitions).

Australian Institute of Environmental Health

- No specific comments on standard.
- Supports pre-market clearance.
- Requests a system or registration of products (unnecessary in Australia because of Food Standards Code).

CAFTA

- Concerned about lack of detail in proposal.
- Supports concept of scope of standard for routine and modified feedings.
- Concerned about access to products and sales and advice about use (as in Australian agreement on Marketing in Australia of Infant Formulas); this issue is of no relevance to the standard.
- Concerned about level of taurine; could not provide reference to support their claim - which is incorrect.
- Request that list of vitamins and minerals allowed (schedule) be expanded to that developed by WHO/Codex and include sources of all essential nutrients, e.g. selenium and manganese.
- Levels of 'tocopherols' to be reconsidered.
- Energy value used to express carbohydrate should be reviewed.
- Aspects of Australian Agreement on marketing of Infant Formulas to be taken into consideration in labelling and advertising.
- Pre-market clearance is rejected.

Chief Food Inspector, New South Wales Health

- Definition is inappropriate at present; concerned about additives which could be allowed.
- Sees no reason why exemptions of vitamins and minerals or labelling and claim controls should be different for infants.
- Need clearer definition of products which are developed for a special purpose.
- Opposes pre-market clearance.
- Supports clarification of labelling clause.
- No references attached.

Department of Health and Human Services, FDA, USA

- Considered that insufficient information was in the information summary to enable comment.

Dietitians Association of Australia

- Supports notion that the Codex Standard be used as the basis for Australia, and that the Codex Advisory List of vitamins and minerals be used.
- Agrees that compositional standards be brought into line with current knowledge and scientific consensus. Wants a consultative panel to oversee this process.
  - Iron - minimum needs to be reconsidered.
  - Whey/Casein ratios should be reassessed.
  - Fatty acid profile needs consideration.
  - Levels of vitamins and minerals should be compatible with current recommended dietary intakes.
  - Need for maximum sodium level and limits for trace elements.
  - assessment of contaminant levels.
- Is concerned that compositional standards may become tight and dictatorial leading to lack of market place choice and disincentive to research.
- Recommends specific labelling changes in regard to feeding tables, standardisation of scoops, description of bottles - at 2(c), 5(b)(ii), 5(b)(iv).
- Supports classification of formulae with several categories within R7.
- Supports pre-market clearance.
- No references.

Dorothy Frances, Senior Associate, Department of Paediatrics, University of Melbourne

- Suggests existing R7 is appropriate.
- Supports pre-market clearance (by a specially convened committee).

- Supports the notion of several categories of products under R7.
- Offers suggestions for products for special (medical) use.
- Supports a range for iron levels where lower end of range is 7mg.
- Suggests fatty acid profile needs to be revised.
- Suggests a whey to casein ratio of between 50:50 and 60:40 in products for use by infants under six months of age.
- Recommends standardised scoops for products to be mixed at home and lists the advantages of ready-to-feed formula.
- Promotional material attached as references.

Douglas Pharmaceuticals (New Zealand)

- Selenium as sodium selenite or seleno methionine should be permitted up to a maximum level of 30ug per litre of formula as fed. This is important because of the essentiality of selenium for humans and because New Zealand as a major exporter of infant formulae is also a low selenium area.
- Significant bibliography and supporting papers attached.

Flinders Medical Centre, Paediatric Nutrition Research Staff

- Definition of R7 is non specific.
- Revised R7 should define formulae with particular indications
- Compositional aspects regarding essential nutrients needs revision, e.g. iron and the fatty acid profile.
- Bioavailability of nutrients, e.g. iron, should be addressed.
- Should be a mechanism for pre-market clearance, especially as demands may be made in the absence of long term clinical trials or assessment.
- A paediatric nutrition committee should be established to assess efficacy and other aspects of products.
- No references attached.

Food Advisory Committee, New South Wales Health

- Exactly same issues as raised by Chief Health Inspector.
- No references attached.

Jane Allen, Research Dietitian

- Suggests R7 covers 3 categories of product - preterm, term from birth, and suitable for term infants after 6 months of age.
- Definition should suggest product will contain nutrients to promote normal growth and development.

Mead Johnson Australia (Parent Company USA)

- Requests that the Australian Recommended Dietary Intakes, the USA provisions for infant formula (FDA & Infant Formula Act) and the Codex Alimentarius standard be used as references for R7.
- Energy value for carbohydrate should be 17Kj per gram.
- Essential nutrients or necessary nutritional factors should be added to the standard and to the Schedule of forms of nutrients (eg. Selenium choline).
- That section of Codex Alimentarius Part 11 - Optional Ingredients should be taken into account.
- Inositol should be permitted as an optional ingredient.
- The role of antioxidants should be recognised in determining levels of "tocopherols".
- A revised Schedule based upon the Codex Standard should be adopted.
- Minimal changes should be made to the labelling provisions and Mead Johnson Australia supports existing prescriptive labelling clauses.
- Requests the addition of a clause to exempt "advertising and promotional material pertaining to infant formulae and their use and directed only to health professionals from clauses (6)(a)(d) and (e).
- Requests clearer product definition and declaration of protein, fat and carbohydrate sources.
- Rejects pre-market clearance.
- Recommends reference ranges for values for micronutrients.
- References and attachments provided.

Nursing Mothers Association of Australia

- Standard should conform to the provisions of the WHO International Code of marketing of Breast-milk substitutes.
- Supports concept of pre-market clearance.
- Is critical of statement in the Information Summary issued by the Authority, that "infant formula should have all the characteristics necessary for the **optimal** growth of this special population group" in that it is misleading.

Queensland Health, Environmental Health Branch

- No specific comments on products.
- Supports notion of pre-market clearance and need for review.

Queensland State Committee, Australian College of Paediatrics

- Need for clarity of terms and definitions
- All essential nutrients, eg. selenium should be included

- Because of the uniqueness of infant formulae as the sole source of nutrition, expert paediatric advice should be used in the development of R7.
- no references attached.

Wanda Oram-Miles, Parent

- requests mixing and preparation instructions be retained as in existing standard.

Wyeth Australia Pty Ltd (Parent company USA)

- The submission from this company consisted of five separate parts which dealt with:
  - follow-on formulae (follow-on milks).
  - CAFTA recommendations or concerns.
  - the addition of nucleotides to infant formulae.
  - amendments to the levels of nucleotides earlier proposed for infant formula.
  - the use of calcium glycerophosphate as a source of calcium in products for use by preterm infants.
- Requests that follow-on formulae continue to be identified as part of the Standard R7 - however notes, erroneously, that Codex, EEC and ESPGAM have recognised their need [All these organisations and WHO have stated that there is no nutritional need for such products, but because they were already in the market-place, a standard needed to be developed].
- All the CAFTA issues were shared by Wyeth, except that the aspects of the Australian Agreement on Marketing of Infant Formulas has been interpreted differently [due possibly to the fact that Wyeth sells through pharmacy only in Australia].
- A major portion of the Wyeth submission is concerned with the addition of nucleotides to infant formulae. It is claimed that five of these substances are essential and confer benefits to the formula fed infants receiving them. Extensive documentation purporting to support the benefits of nucleotides (cytidine, guanosine, uridine, inosine and adenosine) added to infant formulae is provided, along with the claim that this would make it "more like human milk".
- A separate submission requests considerably different amounts of the five nucleotides as the additive to those initially submitted; no reason is given for these changes.

APPENDIX 2

REPORT ON MEETING OF EXPERT PANEL ON INFANT FORMULA

15 March 1995 - Flinders Medical Centre, Adelaide

Introduction

Members of the Panel attending this meeting were:

Dr David Briggs (Chairperson), Robin Dobson, Vicki Gallard-Schulz, Dr Robert Gibson, Dr Paul Riordan, Michael Sharpe, Dr Karen Simmer

Terms of Reference

The Panel was convened in order to:

i) determine criteria for permitting the addition of substances to all infant formula regulated by Standard R7;

ii) identify substances which meet the criteria for permitting addition to infant formula; and

iii) ensure that reconstituted formula do not put infants at risk of fluoride toxicity and or inadequacy.

Matters for Discussion

Presentations and discussion of reports on the following topics took place:

- the development of criteria for permitting the addition of essential and optional nutrients to infant formula;
- evaluation of the addition of the following substances to infant formula:

  choline

  inositol

  nucleotides

  oligosaccharides

  taurine

  medium chain triglycerides (MCTs)

  carnitine; and

- the safe and adequate levels of fluoride in infant formula.

Recommendations and rationale

The Panel came to agreement on each of the issues under consideration. The position of the Panel, the reasons in support of their decisions and the relevant scientific evidence are presented in this report. Papers on each of the issues are at Appendix 1 to this document.

1. The development of criteria for permitting the addition of substances to infant formulae

Panel's position:

i) Regarding essential nutrients -

- nutrients for which there is an Australian RDI are to be considered essential;
- essential nutrients **must** be added to infant formula;
- essentiality can be assumed if a deficiency disorder has been demonstrated; and
- new substances should only be regarded as essential if there has been an unequivocal demonstration of their efficacy through long term, controlled, randomised clinical trials on healthy term infants (demonstration of growth alone will not be deemed sufficient).

ii) Regarding optional nutrients -

- optional nutrients **may** be added to infant formula; and
- to qualify as optional nutrients substances must be normally present in human milk; lack of toxicity or adverse interactions must have been demonstrated and there must also be some data suggesting that their inclusion in infant formula would benefit infants.

Rationale:

- Infant formulae should provide nutrients in amounts that support normal growth and development and ideally result in formula-fed infants having biochemically equivalent plasma and tissue levels to breast-fed infants.
- The safety and tolerance of all substances added to formulae must have been clearly demonstrated in human clinical studies.

With regard to claims for optional nutrients, the Panel expressed the opinion that an entry for such a nutrient in the nutrition information table on the label of a formula should not be permitted unless the total amount of that nutrient in the formula is at least equal to the minimum level of the specified range.

2 The issue of permission to add particular substances to infant formulae

2.1 Choline

Panel position:

- the addition of choline to infant formula should be permitted in the range 48 -150 mg/L (1.7 - 5.4 mg/100kJ); and
- the minimum and maximum levels should relate to total choline, i.e. added choline plus any which may come from other ingredients, such as the phosphatidyl choline in lecithin (permitted as an emulsifying agent).

The minimum level for choline corresponds to the lower end of the range in human milk, and the maximum level to the amount of choline which would be supplied by 5 g/L of lecithin (the maximum permitted level for lecithin in infant formula). Based on a value of 23% for the level of phosphatidyl choline in commercial lecithin, and 13% for the choline content of phosphatidyl choline, 5 g/L of lecithin is the equivalent of 150 mg/L of choline.

Rationale:

- choline is normally present in breast milk;
- toxicity/adverse reactions have not been reported, and there are no known safety issues;
- there is some data to suggest that inclusion of choline in infant formula would benefit infants;
- choline is permitted by the EC and New Zealand, and **required** in non-milk based formulae by the US and Codex (1.7 mg/100 kJ) (48 mg/ L) and Canada 2.9 mg/100kJ (80 mg/L); and
- it is important to have a maximum level, because of concern over interactions of choline with methionine and folate.

Report Summary (V G-S):

There are a number of studies which suggest that choline is an essential nutrient for humans, and there is considerable evidence to suggest that some vulnerable populations, including growing infants, are at increased risk of choline deficiency. On the other hand, choline has long been considered a dispensable non-essential nutrient for humans because - i) they are capable of *de novo* synthesis from phosphatidyl ethanolamine, ii) choline deficiency in healthy

humans has been difficult to identify and iii) there is only one study where experimental choline deficiency has been induced in humans.

Based on currently available evidence, humans deprived of choline are not necessarily able to make up the deficit by *de novo* synthesis. Demand for choline has been shown to be influenced by the availability of methionine and folate, and it may be that choline is an essential nutrient when excess methionine and folate are not available in the diet.
Although there is an increasing body of evidence to suggest that choline may be a conditionally essential nutrient for infants, the author recommended that until further trials have been able to demonstrate the efficacy of choline, it should be an optional substance in infant formula. Suggested future directions for research include: the total concentration of choline in human milk (currently in dispute), characterisation of the actual choline components of human milk and the influence of methionine and folate levels on the requirement for choline.

2.2 Inositol

Panel position:

Most formula-fed infants would be receiving some inositol from the cow's milk and/or added lecithin in formula. The effects of inositol-deficient diets on infants are not known.

Although there is no evidence from clinical studies that addition of inositol to formula confers any benefit to normal formula-fed infants, and researchers in the field are not advocating the addition of inositol to formula, it was agreed that:

- the addition of inositol to infant formula should be permitted in the range 3 - 15 mg /100 mL (1.0 - 5.4 mg/100 kJ).

The minimum value represents the level of inositol in cow's milk, and the maximum is at the lower end of the range in human milk, 14 - 45 mg/100mL.

Rationale:

- inositol is normally present in human milk;
- there is no evidence of toxicity or adverse effects in humans;
- there is strong evidence that dietary inositol is beneficial under certain circumstances, especially for premature infants with respiratory problems;
- the relatively high levels of serum inositol in neonates and in colostrum suggest that this substance is of importance, particularly in the first week of life; and
- its addition to infant formula is permitted by several significant overseas food regulatory agencies, and **required** by the US in non-milk based formulae, albeit to only 2.7 mg/100 mL (0.96 mg/100 kJ), approximately the level in cow's milk.

Report Summary (RD):

Evidence about the role of inositol in humans and other animals was examined, to determine whether there is a case for supplementing infant formula with inositol, and if it would be safe to do so. Healthy humans are able to synthesise more inositol than they need, but in circumstances where endogenous synthesis of inositol is inadequate, such as in some disease conditions, dietary inositol has been shown to be beneficial. There are also indications that inositol is particularly important in the first week of life. Its addition to infant formulae is permitted by several significant overseas agencies, but because of a lack of evidence that the addition of inositol would confer any benefit to normal formula fed infants, uncertainty as to optimal levels of addition for growth and development, and the fact that researchers in the field are not advocating such a course of action at this stage, the author recommended against permitting its addition to infant formulae at this stage.

Note:
The Panel adopted the position that it should be permitted.

2.3 Nucleotides

Panel position:

Nucleotides specified in the following list should be permitted in infant formula, within the given ranges:

nucleotide	mg/100 kJ
cytidine 5'-monophosphate	0.22 - 0.60
uridine 5'-monophosphate	0.13 - 0.42
adenosine 5'-monophosphate	0.14 - 0.38
guanosine 5'-monophosphate	0.04 - 0.12
inosine 5'-monophosphate	0.08 - 0.24

with the total concentration of nucleotides not exceeding 1.2 mg/100 kJ (33.7 mg/L). The ranges are based on the levels in human milk, the maxima corresponding to the maximum levels stated in the European Communities Preliminary Draft amending Directive 91/321/EEC.

Rationale:

- nucleotides are normally present in human milk;
- there is no evidence of toxicity or adverse effects and they have been components of some infant formulae for 20 years; and
- there are some clinical trials which suggest they could be helpful.

Report Summary (RG):

Nucleotides are the monomeric units of DNA and RNA and in their phosphorylated forms are major sources of chemical energy for cellular activities. Functional roles proposed for nucleotides include: enhancement of immune function, greater iron bioavailability, modifications in intestinal microflora, changes in plasma lipids and fatty acids and promotion of gut growth and maturation.

Many studies have been carried out in animal and cellular models. Whilst supportive results have been obtained in randomised clinical trials involving formulae supplemented with nucleotides, no clear benefit has been shown. Nucleotide-supplemented formulae have been used for many years, and no deleterious effects have been reported, however there is no known clinical deficiency which can be attributed to nucleotides. Without clear clinical benefits being established, their widespread inclusion in formulae is not encouraged.

2.4 Oligosaccharides

Panel position:

Oligosaccharides should not be permitted to be added to infant formulae.

Rationale:

- Although various oligosaccharides are present in significant levels in human milk (3 - 6 g/L), and there is reasonable evidence of beneficial effects in *in vitro* studies, there have been no clinical trials carried out where oligosaccharides have been added to infant formula, therefore no demonstration of efficacy;
- their safety is in question - there has been some research suggesting that they may have adverse interactions with yeast lactase; and
- a decision as to which particular oligosaccharides should be permitted and in what amounts could not be made at this stage, because insufficient research has been done.

Report Summary (DB & KS):

Oligosaccharides of various chain lengths and combinations of monomers have been identified in human milk.The total oligosaccharide content of human milk ranges from 13 to 21 g/L; only trace levels of oligosaccharides have been reported in cow's milk.

Biologically significant attributes of oligosaccharides include their use in the synthesis of glycoproteins and glycolipids; N-acetylglucosamine-containing oligosaccharides have been shown to stimulate the growth of *Bifidobacterium bifidus* var *pennsylvanicus* ; *in vitro* studies have demonstrated that some oligosaccharides inhibit the adhesion of bacteria to epithelial surfaces. Human milk oligosaccharides have been found to inhibit the hydrolysis of lactose by yeast lactase *in vitro* .

Until more information is available on the biological and other properties of specific oligosaccharides, carbohydrate sequences, and monomers, the activity of the free and bound forms of these compounds and their dose/activity relationships, it is not possible to be assured either of the safety or efficacy associated with the addition of human milk oligosaccharides or their monomers to infant formula. Further work is needed to determine the significance to health of yeast lactase inhibition by human milk oligosaccharides, but it is indicative that, at this time, oligosaccharides should not be added to formula. The authors advised that this recommendation should be kept under close review.

2.4 Taurine

Panel position:

While the current Standard R7 requires a minimum taurine level of 1.5 mg/100kJ (4.2 mg/100 mL), the Panel recommended that taurine should be permitted as an optional ingredient in infant formula, within the range 2.1 - 8.4 mg/100 mL (0.7 - 3.0 mg/100 kJ), the range for human milk.

Rationale:

- it is normally present in human milk (second highest amino acid);
- no toxicity/adverse interactions have been demonstrated;
- there is some data suggesting that its inclusion in infant formula would be of nutritional benefit to infants;
- the EC Directive for Hydrolysed Protein-based Formula requires a minimum taurine level of 1.25 mg/100 kJ; it is permitted (level unspecified) by Codex, the US and New Zealand.

Report Summary (MS):

Taurine, is synthesised endogenously in man from methionine. The major role of taurine in the body is in conjugation with bile acids to promote lipid absorption, but if taurine is in short supply, the system can still function, albeit less efficiently, by substituting glycine for taurine. To date, adverse clinical signs resulting from taurine deficiency in humans have not been identified. There is some evidence that adsorption of fat-soluble vitamins, calcium and cholesterol may be less efficient when low taurine formula is used, but there is no evidence that adding taurine to formula produces increases in the growth of infants.

The author recommends that taurine be regarded as an optional nutrient in infant formula on the basis that there has been no evidence of toxicity or adverse effects, it has already been added to infant formula in Australia for the past five years, there is no Australian RDI or US RDA for it, taurine has not been unequivocally demonstrated to be necessary for the maintenance of normal growth, and there appear to be nutritional benefits from the addition of taurine to formula.

2.5 Medium Chain Triglycerides (MCTs)

Panel position:

Medium Chain Triglycerides (MCTs) should not be permitted to be added to infant formulae.

Rationale:

- they are not normally present in human milk;
- the long term effects of infants consuming a high percentage of saturated fats are unknown; and
- there is no convincing evidence that the inclusion of MCTs in formula has conferred any benefit to infants.

Report Summary (RG):

MCT (C6-C10) are triglycerides (oils) composed chiefly of caprylic (C8, 75%) and capric (C10, 21%) acids with a small amount (C6, 4%) of caproic acid. The rationale for their use in human nutrition is based on reported unique characteristics such as -
i) more complete intestinal hydrolysis and absorption relative to long chain triglycerides (LCT) (C16-C18),
ii) direct absorption of MCT and hydrolysis products into the portal vein,
iii) subsequent mitochondrial uptake of medium chain (MC) fatty acids via a carnitine-independent mechanism and
iv) rapid catabolism and limited esterification of MC fatty acids compared with LC fatty acids.

MCT are currently included in some preterm formula where absorption of normal fats is thought to be limiting, however only marginal improvement or no difference in fat absorption was found in preterm infants fed formula containing MCT compared with those fed formula containing LCT. In a recent study, low birth weight infants fed formula with 4 different levels of MCT oil did not differ in their weight gain, gastrointestinal tolerance or absorption of fat. Thus there appears to be little advantage with respect to fat absorption by including MCT in preterm formula.

Since MCT have also been reported to cause perturbations in plasma fatty acids, plasma ketone bodies, glucose oxidation and calcium absorption, it is questionable whether it is advisable to use them in infant formula.

2.6 Carnitine

Panel Position

Whilst the current Standard R7 permits carnitine to a level of 0.27 mg/100 kJ (0.76 mg/100 mL), the Panel recommended that carnitine should be permitted as an optional ingredient in infant formulae, with the minimum and maximum level based on human milk values, i.e. 0.6 - 1.2 mg/100 mL (0.21 - 0.42 mg/100 kJ).

Rationale:

- carnitine is normally present in human milk;
- there is no safety concern;
- there is some data suggesting that its addition to infant formulae (especially soy formulae) could be of nutritional benefit to infants;
- the EC Directive requires a minimum carnitine level of 0.29 mg /100 kJ; and it is permitted (level unspecified) by Codex, the US and New Zealand.

Interim Summary (pending receipt of report):

L-Carnitine plays a major role in the metabolism of fat. Requirements for carnitine are met by endogenous synthesis and by diet. Newborn infants appear to have reduced stores of carnitine as well as a low capacity for synthesising it. When normal infants are fed carnitine-free diets, plasma carnitine decreases to low levels, there is an increase in the concentration of free fatty acids in plasma and there is increased urinary excretion of medium-chain dicarboxylic acids. It is not known whether having a low plasma carnitine has demonstrable functional consequences.

3 The issue of safe and adequate levels of fluoride in infant formula.

Panel position

- formula reconstituted with water (fluoridated or non-fluoridated) provides adequate fluoride for infants aged 0 - 6 months;
- there should be a maximum fluoride level imposed on infant formulae, consistent with the highest level of fluoride in formulae currently available in the Australian marketplace - and which is considered safe; and
- there should be no other course of action taken, such as advice about reconstituting formula with fluoridated water or fluoride-free water.

Rationale

- infants do not need fluoride until their teeth have erupted. Fluoride is therefore considered a non-essential element for infants aged 0 - 6 months;
- imposition of an upper limit will require manufacturers to monitor their product for fluoride;
- although there is an increased risk of dental fluorosis by consuming formula reconstituted with fluoridated water, the risk of minor dental fluorosis is outweighed by the benefit to the public as a whole of having fluoridated water to help prevent caries.

Report Summary (PR):

All fluoride intake by infants presents a risk of causing mild dental fluorosis. Although undesirable, this entails, at the most, minor cosmetic and no functional disadvantages, and should be seen in the light of the individual and community advantages offered by the use of fluoride to prevent dental caries. Infant formula reconstituted with fluoridated water seems to lead to substantial fluoride intake by infants, but too little is known about the mechanism of causation of fluorosis to determine exact limits for fluoride intakes.

Factors relevant to the development of fluorosis from ingested fluoride include - i) the age of the child (the risk for fluorosis is greatest between 22 and 45 months), ii) whether or not fluoride deposited in mineralising tissue at the time of formula ingestion is released years later,
iii) the pattern of fluoride ingestion, (the risk is lower when the fluoride intake is shared over several episodes rather than taken in one dose), and
iv) the bioavailability of the fluoride, (absorption is 10 - 25% less from formula than from water).

The author suggested that the fluoride intake of formula-fed infants could be reduced by:

- using bottled water provided that its fluoride concentration is less than 0.7 mg/L, and the levels of other substances are satisfactory;
- using a domestic water purifying device to eliminate or reduce the concentration of fluoride (reverse osmosis and distillation being more effective than activated charcoal types).

Whilst this information could be referred to relevant health professionals for dissemination to parents, it was not considered necessary to include such instructions within the labelling provisions of the Standard.

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COMPARISON BETWEEN LEVELS OF VITAMINS AND MINERALS IN THE PRESENT STANDARD R7 AND THOSE PROPOSED FOR THE REVISED STANDARD R7

(Key and references on last page of document)

substance	level in current R7 (per 100 kJ)	proposed level (per 100 kJ)	rationale for change
vitamin A	18 - 37 µg as retinol equiv.	17 - 54 µg as retinol equiv.	Proposed max > current max..The range covers most formulae on the Australian market and harmonises with FDA. Codex 18-37, EU 14-43. Wharton, max 28, Olsen, max. 72. Basis for setting max.: Safe, well below the lowest chronic intake of vit A in infants that manifested in hypervitaminosis (143 - 215). A safety factor was applied and Olsen (1989) concluded an upper limit might well be set between 53 and 71 µg RE/100 kJ. Proposed R7 max. (53) is conservative and harmonises with FDA.
thiamin B1	10 µg min.	10 - 22 µg	No max. in current Std. The range covers most formulae on the Australian market (except Delact & Digestelact) and harmonises with others wrt min. None of the main regulations has a max.; Wharton, max. 21.4. (HM = 5.7) Basis for setting max.: (Mc Cormick, 1989) The therapeutic dosage tolerated by infants with vit B responsive inherited disorders, plus a safety factor, giving a max. equivalent to approx 5 times RDA (62.8). Proposed R7 max., as recommended by Wharton, is more conservative.
riboflavin B2	14 µg min.	14 - 86 µg	No max. in current Std. The range covers most formulae on the Australian market and harmonises with others wrt min. None of the main regulations has a max.; Wharton, max 85.4 (HM =14.2). Basis for setting max.: as for thiamin. Proposed R7 max. is similar to Mc Cormick's recommended value of 83.8.
niacin B3	60 µg min.	60 - 700 µg	No max. in current Std. The range covers most formulae on the Australian market and harmonises with others wrt min. None of the main regulations has a max.. (HM = 70) Basis for setting max.: as for thiamin. Proposed R7 max is in between that proposed by Mc Cormick, (1260) and that proposed by the editors of the symposium where his paper was presented (356)

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folate	1 µg min.	1.7 - 7.9 µg	Min. higher than in current Std, and there is no max. The range covers most formulae on the Australian market and harmonises with others wrt min. Wharton, max 2.5. (HM =1.78). Mc Cormick upper limits, 6.3 (0-6 mths); 9.4 (6-12 mths). Basis for setting max.: as for thiamin.Proposed R7 max. is intermediate between the lower level proposed by Mc Cormick, (6.3) and his editors (5.86), and Mc Cormick's upper limit (9.4).
pyridoxine B6	9 µg min. at least 15 µg/g protein if > .6 g protein/100kJ	8.9 -36 µg	No max. in current Std. Proposed R7 omits the minimum requirement above a protein level of 0.6 g/100 kJ*. The range covers most formulae on the Australian market and harmonises with others wrt min. None of the main regulations has a max. Wharton, max. 35.6. Basis for setting max.: Recommendation by Wharton. (Proposed R7 max. is lower than that recommended by Mc Cormick, (62.8) and his editors (41.9)) *A rationale for prescribing a maximum rather than a minimum ratio of B_6 to protein is supported by the findings of a recent study.(Heiskanen et al, 1994). These suggest that infants may be getting too much B6, because certain biochemical markers of vit B6 status were found to be at much higher levels in formula fed infants than in breast fed infants. The ratio of B6 to protein in the study was approx 40 µg/g protein. Wharton cautions that nutrient concentrations leading to biochemical values in body fluids or tissues very different from breast fed infants should be avoided.
cyanocobal-amin B12	0.04 µg min.	0.04 - 0.13 µg	No max. in current Std. The range covers most formulae on the Australian market (except Digestelac) and harmonises with others wrt min., except EU, = 0.025. None of the main regulations has a max., Wharton, max. 0.12, (HM = 0.011) Basis for setting max.: as for thiamin. Proposed R7 max is in between that proposed by Mc Cormick, (0.11) and that proposed by the editors of the symposium where his paper was presented (0.21)
vitamin C	1.9 mg min.	1.7 - 5.4 mg	No max. in current Std. The range covers most formulae on the Australian market and harmonises with others wrt min., except v. slightly lower. None of the main regulations has a max.. Wharton, max. 2.4. Basis for setting max.: as for thiamin. Proposed R7 max is intermediate between that proposed by Wharton (2.4) and that proposed by Mc Cormick, (7.33) and by the editors of the symposium where his paper was presented (11.5). A max. of 2.4 would result in a very narrow range between min. and max.

vitamin D	0.25 - 0.48 µg	0.25 - 0.61 µg	The range covers most formulae on the Australian market and harmonises with others wrt min. (HM=0.04; CM=0.029) Basis for setting max.: The proposed max (approx 2.5 times the min level) is higher than the value in the current Std. This is because there are no tox. concerns at such a level and it enables Std R7 to harmonise better with the US (0.6) and EU (0.65). Although there are cardiovascular and renal consequences of hypercalcaemia from excess Vit D, even at intakes as high as 100 µg/day, only a few hundred out of thousands were affected during the British overdose "epidemic" in the 1940s.
vitamin E	0.15 mg min.	0.11 - 1.07 mg. min. of 0.5 mg/g PUFA	No max. in current Std. The range covers most formulae on the Australian market and although the min. is lower than in the current Std, it harmonises with FDA, EU and Codex. Bell, max. 2.4 mg, Wharton 0.18. Basis for setting max.: Many neo natal units routinely supplement with 17mg/day and vit E status and side effects have been well documented in supplemented pre term infants. Bell (1989) states that formulae with vit E <4.8 mg/100 kJ will not produce any tox. problems and allows a 50% safety margin on top of this to give a recommended max. of 2.4 mg/100 kJ, a level accepted by the editors of the symposium where his paper was presented. The Authority's consultant considered Bell's max. too high, given the RDI (3 mg/day; 0.13 mg/100 kJ).
vitamin K	1.0 µg min.	1.0 - 3.6 µg	No max. in current Std. The range covers most formulae on the Australian market (except Isomil) and harmonises with others wrt min. Olsen, max 4.8, Wharton 3.6. (HM = 0.05 - 0.08) Basis for setting max.: There is very little evidence of vitamin K toxicity in infants. Supplementation above 4.8 mg/100 kJ is not justified on nutritional grounds, and if there is no upper limit, excess supplementation might occur. Upper limit needs to be 2-3 times the min. to cover soybean products (either soy formula, or formulae containing soy oil as a fat source) which may carry intrinsic high levels of vit K (Olsen, 1989). The max. for preterm formula is 3.6 and since the needs of preterm infants for vit K are likely to be higher than those of term infants, this was regarded as a sufficiently high max. for standard formula.
biotin	0.4 µg min	0.36 - 2.7 µg	No max. in current Std. The range covers most formulae on the Australian market and harmonises with others wrt min. Wharton, max 1.18 (HM = 0.07)kJ. Basis for setting max.: as for thiamin. Proposed R7 max is lower than that proposed by Mc Cormick, (7.33) and slightly higher than that proposed by the editors of the symposium where his paper was presented (2.09).

pantothenic acid	70 µg min	71 - 360 µg	No max. in current Std. The range covers most formulae on the Australian market and harmonises with others wrt min. Wharton, max 178; Mc Cormick max 419. Basis for setting max.: as for thiamin. Proposed R7 max lies between the max levels recommended by Wharton and Mc Cormick.
calcium	12 mg min. (Ca:P >1.2 & <2)	12 mg min. Ca:P not less than 1.1 and not more than 2	Most formulae on the Australian market are in the range 16-24. The R7 Standard harmonises with others wrt min. Greer, max 21 (HM = 11) Maximum: Although there is no max. value set down for Ca, its max is defined by virtue of the fact that there is a max for P and a max Ca:P ratio. Infants fed on cow's milk formula have higher serum P and lower serum Ca than breast fed infants, regardless of the Ca/P ratio of the formula. This indicates that it is the absolute amount of P in the formula that is more important than the Ca/P ratio in the etiology of hypocalcemic tetany (Greer, 1989) . Hypercalcemia cannot be produced in normal individuals by increasing the Ca intake, owing to the inverse relationship between Ca intake and absorption, and to the compensatory rise in Ca excretion when plasma Ca rises (Nordin, 1990). In cow's milk based formulae there are micelles saturated with Ca and P, with a fixed Ca/P ratio, so although the content can be lowered by dilution, the ratio can only be changed by adding Ca or P to an already saturated solution. Mineral "fall-out" then becomes a problem, as does the increased osmolality and renal solute load. Ratio: The range has been extended slightly to harmonise with the US and to include formulae on the Australian market.
chloride	14 - 35 mg	14 - 35 mg	
copper	14 µg min.	14 - 36 µg (milk-based formula) 21 - 43 µg (soy-based formula) Zn:Cu, not more than 10:1	No max. in current Std. The range covers most formulae on the Australian market (except Digestalac) and harmonises with others wrt min., except EU, 4.8. Absorption from milk based formula is similar to abs. from human milk, but need min. Cu in soy formulae to be 21.4 to get similar absorption to that from human milk. None of the main regulations has a max.,except the EU (19). Max., Hambidge & Krebs 47.8 (HM = 7.1 - 10.7). Basis for setting max.: There are potential adverse effects from quite small excesses on a chronic basis. No info on toxic levels, but prems have received Cu at a level of 72 mg/100 kJ for a month without evidence of adverse effects. Recommended max.: twice the min. level needed in soy formulae, i.e. 42.8 (Lonnerdal, 1989).

iron	0.1 - 0.48 mg	0.2 - 0.5 mg	Proposed min. > current min. and is higher than the EU (0.12) and FDA (0.04). R7 max. is higher than UK (0.25), EU (0.36) and Dallman (1989), (0.43), and lower than US (0.71). (HM = 0.01 - 0.018) (CM = 0.018) Basis for increasing min. level (i.e requiring all formulae to be "iron-fortified"): * the use of iron-fortified formula is credited with a declining prevalence of anaemia in US infants; *there is a lack of side effects (at this level), such as constipation and inhibition of Zn and Cu absorption; * even mild iron deficiency may result in impaired cognitive and behavioural development, and the deleterious effects may be permanent; and * the amount of iron absorbed from commercial iron-fortified cereal is low, and the amount of iron-fortified cereal consumed by infants is small. The reason that the proposed minimum level is higher than in the US Std is that in the US, 0.04 mg/100kJ is regarded as a basic level to which more iron can be added giving a formula which is permitted to make the claim "with added iron". Basis for retaining current max.: Some max. may be too high, e.g. US (0.71). There are concerns that high levels of dietary iron inhibit the absorption of trace metals and lower resistance to infection, therefore it is important not to add more than is necessary to prevent deficiency. Iron content also has a major influence on gut flora, fortified formula increasing the levels of pathogenic bacteria (e.g. E.coli) and decreasing the levels of beneficial types (e.g. bifidus), compared with unfortified formula (Dallman, 1989). In Dallman (1989), Senterre and the eds. recommend a max. of 0.43, slightly lower than the proposed R7 max. This value harmonises with the EU values for follow-on formula.
iodine	1.2 - 10 µg	1.2 - 18 µg ? 2.1 in view of ICCIDD recs.	Proposed max > current max. Harmonises with others wrt min. Max. same as USFDA. (HM = 1.4 - 2.9; Ares (1994), 3.6). Minimum level: ICCIDD (1994) recommended a min. daily intake of 90 mg for 0-12 months infants (= 850 mL at 3.8 mg/ 100 kJ) Basis for setting max.: Max. of 17.8 recommended by a task force of AAPCON (1985). Seems reasonable in the light of recent studies which suggest 100g/kg as a safe upper limit for normal term infants. Proposed R7 max is the same as that recommended by Fisher (1988), and is higher than that proposed by the editors of the symposium where this paper was presented (12).

magnesium	1.4 - 3.6 mg	1.4 - 3.6 mg	Harmonises with others wrt min., except EU and FDA (1.2). Same max as EU. Wharton, max. 4.8 (HM = 1.0). Basis for setting max.: Mg toxicity is rare. Rel. poor retention compared to Ca and P. Mg may decrease the absorption of Ca and P. Max. rec (Greer, 1989)= 4.3 mg/100 kJ, the level in cow's milk. The proposed R7 max is lower than that recommended by Greer (1989) and is higher than that proposed by the editors of the symposium where this paper was presented (2.9, approx twice the min.)
manganese	1.2 µg min.	1.2 - 13 µg	No max. in current Std. Harmonises with others wrt min. None of the main regulations has a max.; Krebs & Hambidge, max. 12 (HM = 0.11 - 0.21) (CM = 3.6). Basis for setting max.: Breast-fed neonates are in negative Mn balance with no evidence of suboptimal Mn intake. Upper levels have been recommended on the basis of 2.5 times the level required to achieve positive Mn balance (2.4 - 4.8). Whilst there have been no reports of adverse effects from excess Mn intake by infants, there is no good evidence that careful studies have been undertaken. Mn absorption is reported to be higher in premature infants than in adults, and in early life a significant proportion of absorbed Mn is retained by the brain, the main target organ for Mn toxicity. Lonnerdal suggests a max of 21.4 to ensure that soy formulae, which are high in Mn, are covered. The proposed R7 max is lower than that recommended by Lonnerdal. The Authority's consultant believes that the max. should not be set at an inappropriately high level in order to accommodate some soy formulae.
potassium	20 - 50 mg	20 - 50 mg	
phosphorus	6 - 25 mg (Ca:P >1.2 & <2)	6 - 22 mg Ca:P not less than 1.1 and not more than 2	The range covers most formulae on the Australian market (7.5 - 11), harmonises with others wrt min. and with the max. recommended by the EU, Zeigler & Fomon (1989), and Senterre (1989). (HM=5.3). Basis for setting max.: A max. is necessary because of the risk of neonatal hypocalcemia and increased renal solute and acid loads. Proposed R7 max is similar to that proposed by Greer, (21.5) and higher than that proposed by the editors of the symposium where his paper was presented (16).
sodium	5 mg min.	5 - 14 mg	No max. in current Std. Harmonises with others wrt range. (HM = 4.9) Basis for setting max.: Upper limit needed to limit potential renal solute load, and in line with recs. of Senterre in Lonnerdal, 1989. (max of 16.4 with 0.72 g/100 kJ protein; equivalent to 15.6 with 0.7 g/100 kJ protein). The proposed R7 max is slightly lower than that recommended by Senterre.

selenium	n/a	0.42 - 0.89 µg	Although Se is an essential nutrient, there has to date been no stated requirement for it in infant formula standards. However, this matter is under consideration by the EU and USFDA. Currently, the amount found in infant formula is governed by chance, depending on the level of Se in the raw materials. Formulae on the market in Australia have a Se content ranging from 2.9 - 23.5 µg/L. Basis for setting min.: Infants should receive the RDI of selenium (10 µg /day for 0-6 mths). A level of 0.42 µg/100 kJ will supply 10 µg/day, assuming consumption of 850 mL. Se is absorbed as well from formula as from breast milk, but there is some evidence that the Se compounds in breast milk are more bioavailable than those in formulae. Bioavailability may also vary with the form of Se used in the formula. (Smith, Chen and Thomas (1995) found similar plasma Se concentrations in infants, irrespective of whether they were breast fed or consumed formula supplemented with selenate to the same level as breast milk. They showed that selenate is absorbed and incorporated into glutathione peroxidase more efficiently than selenite or selenomethionine, and that the apparent absorption of selenate from soy formula is 94%, compared with selenite, 62%.) Litov, max 0.89 , Wharton 1.92. Basis for setting max.: One possibility is to set it at the max. level in human milk (0.89 µg/100kJ corresponds to a level of 25 µg/L). A recent survey (Alaejos & Romero, 1995) showed a range of 5.6-26.7 mg/L for Se in mature human milk in some 13 countries worldwide. Consumption of human milk at a level of 60 µg/L has resulted in no recognised cases of human selenosis. Levander (1989) recommended a max. based on extrapolating from toxicity data for adults to infants, on a body weight basis . Levels of 75 - 90 µg/day would hypothetically lead to toxic effects in a 6 kg infant. A safety factor was introduced and the suggestion made that formula contribute a maximum of 45 µg/day (1.9 µg/100 kJ). Editorial comment from the symposium where he delivered the paper advised a more conservative max. (between 0.77 and 0.96). The proposed R7 max (0.89) is within this range.

zinc	0.12 min.	0.12 - 0.36 mg (milk-based formula) 0.18 - 0.43 mg (soy-based formula) Zn/Cu ≤ 10/1	No max. in current Std. The range covers most formulae on the Australian market, harmonises with others wrt min. and with the max. recommended by EU. Most of the main regulations do not have a max.. Krebs & Hambidge, max. 0.36, Lonnerdal 0.43, France 0.19, & Netherlands 0.24. (HM = 0.07 - 0.11). Basis for setting max. and specifying a max. Zn/Cu ratio Milk-based formulae: Trace element absorption may be impaired because of imbalances in the ratios between trace elements (Fe/Zn, Zn/Cu, Fe/Mn) or as a result of trace elements sharing absorptive pathways and thus competing for uptake. These factors need to be take into account when setting maxima. Max., Lonnerdal (1989), 0.43, based on recommended upper limit for Cu level of 0.04 mg/100 kJ and a Zn:Cu ratio of 10:1. The proposed R7 max for Zinc has been taken as 10 times the proposed upper limit for Cu (35.6 mg/100 kJ), ie 0.36 mg/100 kJ. Soy based formulae Zn bioavailability from soy formula has been shown to be considerably lower than from milk-based formula (25%, compared with 45 - 60%), largely due to the presence of phytate. Level needs to be 0.25 to provide as much Zn as early human milk, with a max. of 0.43. (Lonnerdal, 1989). If a special range was given for Cu in soy formulae (21.4 - 42.8 mg/100 kJ suggested) and a ratio of 10:1 for Zn:Cu prescribed, proposed R7 could have a range of 0.21-0.43 mg/100 kJ for Zn in soy formulae.

KEY:

FDA, USFDA, US	US Food and Drug Administration
EU	European Union
HM	Human milk
CM	Cow's milk
ICCIDD	International Committee for the Control of Iodine Deficiency Disorders
AAPCON	American Academy of Pediatrics, Committee on Nutrition
vit	vitamin
PUFA	polyunsaturated fatty acids
info	information
wrt	with respect to
max	maximum
min	minimum
RE	retinol equivalents
tox	toxicological
Std	Standard
RDI	recommended dietary intake

REFERENCES:

Alaejos MS & Romero CD (1995). *Food Chemistry* 52: 1-18

Ares S, Quero J, Duran S, Presas MJ, Herruzo R & de Escobar GM (1994). *Archives of Diseases in Childhood* 71: F184-191

Bell EF (1989). Upper limit of vitamin E in infant formula. *J Nutr* 119: 1829-1831

Dallman PR (1989). Upper limits of iron in infant formula. *J Nutr* 119: 1852-55

Greer FR (1989). Calcium, phosphorus and magnesium: how much is too much for infant formula? *J Nutr* 119: 1846-1851

Hambidge & Krebs (1989). Upper limits of zinc, copper and manganese in infant formulas. *J Nutr* 119: 1861-64

Heiskanen K, Salmenpera L, Perheentupa J & Siimes M (1994). Infant vitamin B-6 status changes with age and with formula feeding. *Am J Clin Nutr* 60: 907-910

Levander OA (1987). A global view of human selenium nutrition. *Ann Rev Nutr* 7: 227-250

Levander OA (1989). Upper limit of selenium in infant formula. *J Nutr* 119: 1869-1873

Lonnerdal B (1989). Trace element absorption in infants as a foundation to setting upper limits for trace elements in infant formula. *J Nutr* 119: 1839-1845

Mc Cormick (1989). Water-soluble vitamins: Bases for suggested upper limits for infant formulas. *J Nutr* 119: 1818-19

Olsen JA (1989). Upper limits of vitamin A in infant formulas, with some comments on vitamin K. *J Nutr* 119: 1820-24

Smith AM, Chen LW & Thomas MR (1995). *Am J Clin Nutr* 61: 44-7

Nordin BEC (1990). Calcium, in Truswell AS (ed.) *Recommended Nutrient Intakes - Australian Papers*. Australian Professional Publications, Mosman NSW, 213

Wharton BA (1989). An approach to setting maxima in infant formulas. *J Nutr* 119: 1768-1772

Zeigler EE & Fomon JJ (1989). Potential renal solute load of infant formulas. *J Nutr* 119: 1785-88

COMPARISON BETWEEN LEVELS OF VITAMINS AND MINERALS IN PRE TERM AND STANDARD FORMULA IN THE REVISED STANDARD R7

Nutrients listed are those where the levels are different in pre-term and standard formula
(Key and References at the end of the document)

substance	level in pre term formula (per 100 kJ)	level in standard formula (per 100 kJ)	rationale for difference
vitamin A	20 - 36 µg as retinol equiv.	17 - 54 µg as retinol equiv.	PT min. > Std min. The range covers most formulae on the Australian market and essentially harmonises with ESPGAN. AAPCON, 5.4-16; Forbes, 42-90. Basis for higher PT min.: Preterm infants have low plasma levels of retinol, suggesting low body stores at birth, and they are at risk of developing deficiency (Bremer & Wharton, 1987). PT max > Std max. Basis for higher PT max.: Whilst there is increasing evidence that vit A may improve the status of infants with chronic lung disease, the consultant advised that rather than permit very high levels of Vit A for all, it would be preferable to set a lower max. in PT formula and supplement individuals with special needs.
thiamin vitamin B1	10 - 48 µg	10 - 36 µg	PT max > Std max. The range covers most formulae on the Australian market, and harmonises with AAPCON wrt min. and Forbes wrt max.. Basis for higher PT max.: The higher metabolic rate of vlbw infants and the fact thatthere is no evidence of toxicity at this level. Thiamin is inactivated by heat, consequently the amount received by the infant may vary with the method used for feed preparation and may be lower than expected (Bremer & Wharton, 1987).

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niacin vitamin B3	0.18 - 0.89 mg	0.06 - 0.7 mg	PT min. > Std min. and PT max. > Std max. The range covers most formulae on the Australian market, and harmonises with ESPGAN wrt min. Forbes, 0.72-0.96; FDA, >0.06; ESPGAN max., 1.2. Basis for higher PT min & max.: In general, preterm infants have increased nutritional requirements compared with term, and they tolerate a smaller volume, therefore it is necesssary to increase the range of most nutrients, including vitamins.
folate	5.0 - 10 µg	1.7 - 7.2 µg	PT min. > Std min. and PT max. > Std max. The range covers most formulae on the Australian market, and harmonises with Forbes. AAPCON, 7.9; ESPGAN, >14.3. Basis for higher PT min & max.: Limited body reserves at birth and rapid post-natal growth and cell division probably increase the need for folate in lbw infants. The fact that a test dose of folate disappears from the blood of new born more rapidly than in older subjects, without any increased amount in the urine, has been interpreted as evidence for increased need. Deficiency in preterms causes megaloblastic anaemia. The literature suggests that the ESPGAN recommended min of 14.3 may not be possible due to technical difficulties, such as destruction by heat treatment and storage, and that supplementation may be necessary to reach this level (Bremer & Wharton, 1987).
pyridoxine vitamin B6	8.9 - 42 µg	8.9 -36 µg	PT max. > Std max. The range covers most formulae on the Australian market, and harmonises with Forbes wrt max.. ESPGAN, 8.4-60; AAPCON, > 8.4. Basis for higher PT max: PT formula may need to contain a higher level than in breast milk (8.4), due to the rapid growth rate of lbw infants (Bremer & Wharton, 1987).
vitamin C	3.5 - 9.6 mg	1.7 - 5.4 mg	PT min. > Std min. and PT max. > Std max. The range covers most formulae on the Australian market, and harmonises with Forbes wrt min. and ESPGAN wrt max.. Basis for higher PT min & max.: LBW infants fed a high protein, casein-dominant formula develop transient elevations of plasma and urinary tyrosine, phenylalanine and their metabolites, due to low activity of the enzyme tyrosine amino transferase. Formula-fed lbw infants require higher amounts of vitamin C to prevent hypertyrosinaemia, and for optimal iron absorption (Bremer & Wharton, 1987).
vitamin D	0.75- 2.0 µg	0.25 - 0.61 µg	PT min. > Std min. and PT max. > Std max. The range covers most formulae on the Australian market, and harmonises with Forbes. AAPCON >1.6; ESPGAN 4.8-9.6. Basis for higher PT min & max.: PT infants need 500 IU vit D/day, as opposed to term, who need 400 (20 - 40 mg higher). Reasons: faster growth rate, stores deficient and bio transformation pathways not fully developed (esp. < 32 wks) (Bremer & Wharton, 1987).. Infants of <25 wks need more Vit D per kg than those >34 wks

vitamin E	0.18 - 1.6 mg min. of 0.9 mg/g PUFA	0.11 - 1.1 mg. min. of 0.5 mg/g PUFA	PT min. > Std min. and PT max. > Std max. The range covers most formulae on the Australian market, and harmonises with AAPCON wrt min. and ESPGAN and Forbes wrt max. Basis for higher PT min & max.: Vit E has a role in the prevention of anaemia of prematurity (involved in synthesis of haem) and as an anti oxidant protects against retinopathy of prematurity, bronchopulmonary dysplasia and intra ventricular haemorrhage (Bremer & Wharton, 1987). Basis for higher vit E/PUFA ratio: This ratio is higher than in Std formula because of the relatively greater concentration of Vit E in PT formula.
pantothenic acid	240 - 360 µg	71 - 360 µg	PT min. >> Std min.. The range covers most formulae on the Australian market, and harmonises with Forbes wrt min and max. ESPGAN and AAPCON both have >72. HM = 89, CM = 124. Basis for higher PT min: Increased nutritional requirements compared with term and smaller volume of formula consumed.
calcium	17 - 34 mg (Ca:P , 1.4 -2)	12 mg min. (Ca:P , 1.2 - 2)	PT min. > Std min. The range covers most formulae on the Australian market, and harmonises with ESPGAN. AAPCON, 41.7; Forbes 24-46. Basis for higher PT min: Formulas specifically designed for LBW infants generally contain more minerals than conventional infant formulae. Peak Ca accretion is at the fetal weight of 1800g (150mg/kg/day). Most preterm formulae do not contain enough Ca and P to allow preterm infants to accumulate these elements at the intra uterine rate. Basis for higher Ca/P ratio: Some preterm formulae which have been designed to approach the Ca and P requirements for LBW infants (as estimated by the factorial method) have Ca:P = 2, and no PT formulae on the Australian market has Ca:P <1.4. Ca:P ratio should be increased when the calcium content is high; 1.4 -2 recd. by ESPGAN. Basis for setting max.: There is a need for an upper limit because of: the possible complications of very high Ca intake; the problem of precipitation; and the lack of evidence that such concentrations are beneficial (Bremer & Wharton, 1987).

chloride	14 - 22 mg	14 - 35 mg	PT max. < Std max. The range covers most formulae on the Australian market, and harmonises with ESPGAN and Forbes.. AAPCON, 20.4 for 800 -1200 g infants; 17 for 1200-1800 g infants - both these are within the recd. range. Basis for lower PT min: Preterm infants (especially those less than 1 kg) are more prone to hypernatremic dehydration.
copper	23 - 30 µg	14 - 36 µg	PT min. > Std min. PT max. < Std max..The range covers most formulae on the Australian market, and essentially harmonises with Forbes and ESPGAN. AAPCON, 21.5; HM, 28.7. Basis for higher PT min: Cases of copper deficiency have been reported in preterm infants. Plasma levels in pre-term infants tend to be low (35 µg/dL at 30 wks cf 50-60 µg/L at 40 wks) (Greene et al, 1988). Basis for lower PT max: PT infants have negative copper balance until the fifth week of life. The ability to make the Cu-carrying protein ceruloplasmin is low in preterm infants, and this limits the ability of the infant to utilise extra copper. Immature infants, especially if stressed, may be unable to handle a copper load. Since unbound copper is potentially toxic, a more cautious max. level for copper in PT formula seems prudent.
iron	0.01 - 0.4 mg	0.21 - 0.48 mg	PT min < Std min. The range covers most formulae on the Australian market, and harmonises with ESPGAN, AAPCON and Forbes in that the R7 max. is the same as their min. AAPCON, 0.41-0.6; ESPGAN, 0.36; Forbes 0.36. Basis for lower PT min: Preterm infants don't need iron for the first 4 to 6 weeks - it may even be deleterious. For this reason some PT formulae don't have iron added - it can be given as a supplement. (Simmer, 1994)
iodine	2.4 - 11 µg	1.2 - 18 µg	PT min > Std min. PT max. < Std max. The range covers most formulae on the Australian market, and harmonises with ESPGAN and with Forbes wrt max. AAPCON, 1.2 Basis for higher PT min: Prem. infants are unable to accumulate the amount of iodine found in term newborns (Ares, 1994) Basis for lower PT max: Iodine intake may be excessive from absorption via the skin of iodine in antiseptics (Greene et al, 1988; Simmer, 1994). 4% of individuals are sensitive to iodine excess, which can cause hypothyroidism.

magnesium	1.5 - 3.6 mg	1.4 - 3.6 mg	PT min. > Std min. The range covers most formulae on the Australian market, and essentially harmonises with Forbes and ESPGAN wrt min.. Max level is slightly higher (Forbes, 2.9; ESPGAN, 3). Basis for higher PT min: Minimum mineral content of PT formulae should be a little higher than that recd. for term formulae (ESPGAN).
manganese	1.2 - 1.8 µg	1.2 - 13 µg	PT max. << Std max..The range covers most formulae on the Australian market, and harmonises with AAPCON wrt min. and ESPGAN wrt max. Forbes, 1.5. Basis for lower PT max: The max. level for Std formula is relatively high to accommodate the levels of Mg in soy formulae. This is not necessary with PT formula because there are no soy varieties.
potassium	20 - 36 mg	20 - 50 mg	PT max. < Std max..The range covers most formulae on the Australian market, and essentially harmonises with ESPGAN. Forbes, 16-24; AAPCON, 16-23. Basis for lower PT max: Extremely preterm infants develop hyperkalaemia, but this occurs rarely. PT infants have immature renal function initially and are often exposed to drugs which may further impair renal function, therefore it is prudent to avoid potassium overload (potentially fatal).
phosphorus	12 - 22 mg (Ca:P, 1.4 - 2)	6 - 22 mg (Ca:P, 1.2 - 2)	PT min. > Std min. The range covers most formulae on the Australian market, and harmonises with ESPGAN and with Forbes wrt min. and AAPCON wrt max.. Basis for higher PT min: Formulae specifically designed for lbw infants generally contain more minerals than conventional infant formulae. Peak P accretion is at the fetal weight of 1800g (80 mg/kg/day). Basis for higher Ca/P ratio: Some preterm formulae designed to approach the Ca and P requirements for lbw infants (as estimated by the factorial method) have Ca:P = 2, and none on the Australian market has Ca:P <1.4 (Bremer & Wharton, 1987).
sodium	9.1 - 14 mg	5 - 14 mg	PT min. > Std min.. The range covers most formulae on the Australian market, and harmonises with Forbes. ESPGAN, 5.5 -13; AAPCON. 12-16. Basis for higher PT min: Preterm infants, esp. >1500 g, do not have well developed renal sodium conservation mechanisms. The fractional excretion of Na is high for up to 14 days after birth, thus preterm formulae require higher levels of Na than term, to prevent hyponatremia (Forbes, 1985).

selenium	0.53 - 0.89µg	0.42 - 0.89 µg	PT min > Std min.. Formulae on the Australian market are within the range 0.1 - 0.84. Forbes, 0.26-0.6; Expressed breast milk (EBM), average 0.57. Other countries have not yet permitted Se in infant formulae, although this is currently being considered by the EU and US. Basis for higher PT min: Plasma Se levels are especially low in pre-term infants. Pre-term infants are at risk of Se depletion which potentially enhances susceptibility to oxygen toxicity and chronic lung disease (Daniels, 1994).

KEY:

ESPGAN	Committee on Nutrition of the Preterm Infant, European Society of Paediatric Gastroenterology and Nutrition
AAPCON	American Academy of Pediatrics, Committee on Nutrition
Forbes	Consensus recommendations by the authors Forbes Al, Falce JK & Cheney MC (1993) in Table A2 (Appendix) "Comparison of Enteral Intake Recommendations for Stable Growing Preterm Infants" in *Nutritional Needs of the Preterm Infant*. Tsang TL, Lucas A, Uauy R & Zlotkin S eds., Williams & Wilbius, Baltimore
HM	Human milk
CM	Cow's milk
lbw	low birth weight
vlbw	very low birth weight
PT	pre-term
vit E/PUFA	vitamin E/polyunsaturated fatty acids
info	information
wrt	with respect to
max	maximum
min	minimum

REFERENCES

Ares S, Quero J, Duran S, Presas MJ, Herruzo R, de Escobar GM (1994). Iodine content of infant formulas and iodine intake of premature babies: high risk of iodine deficiency. *Archives of Disease in Childhood* 71: F184-F191

Bremer HJ & Wharton BA (1987). Committee on Nutrition of the Preterm Infant, European Society of Paediatric Gastroenterology and Nutrition *Nutrition and Feeding of Preterm Infants*. Blackwell Scientific Publications, Oxford.

Daniels L(1995). Selenium status in term and preterm infants. *Conference Proceedings "South-West Pacific Regional Dietitians' Conference"*, Brisbane, p93

Committee on Nutrition, Forbes GB (ed) (1985). Nutritional Needs of Preterm Infants. In *Pediatric Nutrition Handbook*, American Academy of Pediatrics, p 66-82

Greene HJ, Hambidge KM, Schanler R, Tsang RC (1988). Guidelines for the use of vitamins, trace elements, calcium, magnesium, and phosphorus in infants and children receiving total parenteral nutrition: Report of the Subcommittee on Pediatric Parenteral Nutrient Requirements from the Committee on Clinical Practice Issues of the American Society for Clinical Nutrition. *Am J Clin Nutr* 48: 1324-42

Simmer (1994) Professional advice to NFA

APPENDIX 5

CONSULTANT'S REPORT

Karen Simmer **February 1995**

FORMULAE BASED ON MODIFIED PROTEIN, FAT AND CARBOHYDRATE

There are a group of infants who require a special formula as part of their management. These formulae are designed to meet well recognised dietary requirements and contain modified protein, fat and carbohydrate. They have been used successfully in the management of malabsorption due to exocrine pancreatic insufficiency, short bowel syndrome, enteropathies and cow's milk protein allergy. They are often referred to as hypoantigenic. More recently, formulae based on partially hydrolysed protein have been marketed in some countries as hypoallergenic for the prevention of atopic disease, but their effectiveness without other dietary intervention has not been proven.

The ESPGAN Committee recommends that the nutritional efficacy of protein hydrolysate formulae be demonstrated by longitudinal studies including weight and length for at least 3 months duration in at least 20 term infants. The ESPGAN Committee also recommends that information be provided on the properties of the hydrolysate, the procedures for preparation, and the infant plasma concentrations of albumin, prealbumin, transferrin and retinol binding protein achieved. They also recommend that all claims made during marketing be based on clinical randomised trials including groups fed standard formula for at least four months (ESPGAN Report on Antigen-Reduced Infant Formula. *Acta Paediatr* 1993; 82: 314-19).

In Australia, it is well recognised amongst health professionals that formulae marketed for special dietary needs are sometimes marketed and used for irritable and colicky infants without confirmation of a special need such as cow's milk protein allergy or lactose intolerance (This is despite little evidence demonstrating an effect.). The widespread use of these specialised formulae make it particularly important that the composition of these formulae be closely regulated by R7 Standard. Formulae not covered by the R7 Standard in future should only be those designed for infants with congenital defects in amino acid or carbohydrate metabolism, or for infants with urea cycle disorders.

The nutritional compositions of formulae for infants with special needs used in Australia are listed in the Table 1 (Alfare, Pregestemil, Nutramegen, Portagen, Neocate). Portagen is

probably only used for infants with chylothoraces, lymphangiectasia or liver disease. There are some additional formulae marketed by Scientific Hospital Supplies (Generaid Plus, Kindergen). The manufacturers are forwarding the relevant information.
(References on Generaid Plus & Kindergen: Charlton CPJ et al. (1992). *Arch Dis Childh*; 67: 603 - 607; Chin SE et al (1992). *Am J Clin Nutr*; 56: 158 - 163; Chin SE et al (1990). *J Gastro & Hepat.*; 5: 568 - 574)

The nutrients and amounts suggested for formulae for infants with special dietary needs are listed below. Additional substances, and changes in concentration outside the range specified for standard term formula, are discussed.

1. Energy value

2700 kJ/L - 3000 kJ/L

2. Osmolality

< 325 mOsmol/kg

The use of a protein hydrolysate formula with higher osmolalities (500 - 600 mOsmol/kg) has been associated with necrotising enterocolitis (Book LS, Herbst JJ, Atherton SO, Jung AL. NEC in LBW infants fed an elemental formula. *J Ped* 1975;87:602-5). Neocate has an osmolality of 353 mOsmol/L at 70 cal/100 mL. The manufacturers (Scientific Hospital Supplies) need comment on how difficult it would be to get the osmolality within current recommendations, otherwise the range could be increased to < 400 mOsmol/kg.

3. Protein

A non antigenic nitrogen source for allergic infants is achieved by predigesting protein to provide nitrogen as amino acids and peptides which are small enough to have no interaction with the immune system (Table 2).

Table 2.

nitrogen source	average MW	ratio free N:total N
protein	> 20,000	<0.01
peptone	1000-6000	0.1-0.5
peptide/aa mix	200-500	0.5-0.8
aa mix	75-200	0.8-0.9

Protein hydrolysis is achieved by treatment with proteolytic enzymes which simulate intestinal food processing. The hydrolysate is clarified by filtration and centrifugation, and then treated with activated charcoal. The MW is calculated and the antigenicity measured. Formulae based on protein hydrolysates may taste unpleasant and bitter.

Casein hydrolysates have been used for over 40 years. Hydrolysates of whey and soy protein have been introduced in some countries over the last few years. As mentioned, formulae with lower degree hydrolysates of bovine whey proteins and caseins have been introduced and are sometimes referred to as formula containing partially hydrolysed protein.

The protein compositions of formulae used in Australia are given in Table 3. Earlier studies demonstrated that the nitrogen balance of term and preterm infants fed protein hydrolysate formulae was adequate (Graham GG, Klein GL, Cordano A. Nutritive value of elemental formula with low osmolality. *Am J Dis Child* 133, 1979; Moran JR, Terry A, Dunn GD, Greene HL. A hydrolysed formula for feeding infants < 1250g: a controlled clinical trial *Abstr Am Fed Clin Res* 1979; Vanderplas Y et al. The nutritional value of a whey hydrolysate formula compared with a whey predominant formula in healthy infants. *J Ped Gastroenterology & Nutrition* 1993; 17: 92-96). However, more recent studies suggest that the nutritional safety of fully hydrolysed protein formulae is yet to be fully demonstrated. Infants fed a hydrolysed whey formula have reduced total protein concentrations at one month of age, with a higher plasma threonine concentration, a lower plasma tyrosine concentration and a higher ratio of essential to total amino acids (Rigo J, Salle BL, Cavero E, Richard P, Putet G, Senterre J. Plasma amino acid and protein concentrations in infants fed human milk or a whey protein hydrolysate formula during the first month. *Acta Paediatr* 1994; 83: 127-31). Abnormal growth and biochemical indices in infants fed some whey protein hydrolysate formulae have been documented compared with infants fed human milk (Rigo J, Salle B, Putet G, Senterre J. Nutritional evaluation of various protein hydrolysate formulae in term infants during the first month of life. *Acta Paediatr* Suppl 402:100-4, 1994). The growth reduction reached 50% for weight, 15% for length and 30% for head circumference for one formula. In addition, the amino acid profiles of infants fed protein hydrolysate formulae were different to those of infants fed human milk. This may not be desirable, as amino acids are not only protein precursors, but important for neurotransmission.

Formulae based on amino acids are marketed for the combined intolerance of cows' milk protein, soy protein and protein hydrolysates. The amino acids are synthetically produced and not derived from a protein source. The amino acid profile is based on the profile of human milk. Published data on the efficacy of formula based on amino acids is sparse. Intestinal peptide

uptake is greater than amino acid uptake and it has been recommended that peptide-containing solutions only be used for malnourished infants (Silk et al. Use of a peptide rather than a free amino acid nitrogen source in chemically defined elemental diets. *J Parent Ent Nutr* 4; 548-553. 1980; Guandalini S, Rubino A. Development of dipeptide transport in the intestinal mucosa of the rabbit. *Pediatr Res* 16, 99-103, 1982).The more rapid and even absorption of amino acid residues from protein hydrolysates than from equivalent mixtures of free amino acids alone may promote more efficient use of the amino acid residues for protein synthesis (Silk et al. Jejunal absorption of an amino acid mixture simulating casein prepared for oral administration to normal adults. *Br J Nutr* 1975; 33:95-100).

However recently, amino acid derived formulae have been shown to be well tolerated and safe in a small group of children with cows' milk allergy (Sampson HA et al. Safety of amino acid derived formula in children allergic to cow milk. *Paediatrics* 1992; 90: 463-465 19). In another study, 18 infants with late onset adverse reactions to soy and extensively hydrolysed casein and whey formulae underwent a double blind placebo-controlled challenge; an amino acid based formula (Neocate) was demonstrated to have a role in the management of infants with multiple food protein intolerances including intolerance to protein hydrolysates (Hill D, Cameron JSC, Francis DEM, Gonzaley-Andaya AM, Hosking CF. Challenge confirmation of late onset reactions to extensively hydrolysed formulae in infants with multiple food protein intolerance. *J Allergy and Clinical Immunology* 1995, in press). Amino acid based formulae have also been demonstrated to be useful in weaning children with short gut syndrome from parenteral nutrition (Francis D, Hills D, Bines J. Amino acid enteral formula reduces TPN requirement in three young children with short gut syndrome. Abstract *AUSPEN* 1994).

Therefore, formulae based on amino acids have a role in the management of a small group of children with specific dietary requirements. There is no evidence to support their use in the management of colic although, anecdotally, this is becoming more common. One reason for this is that a PBS prescription will suffice for Neocate, which is simpler than the Authority Prescription required before protein hydrolysate formulae are available at a price similar to standard term formula.

Protein content: The protein content recommended for standard formula is 1.26-1.97 g/100 mL but in protein hydrolysate formulae on the Australian market, protein content ranges to 2.5 g/100 mL (Alfare). This is within the Codex regulations (1.2 - 2.7g/100 mL), and the R7 regulation for follow-on formula (< 2.8 g/100 mL). Considering the limited data suggesting a fall in plasma protein if fed whey protein hydrolysed formula with a protein content of 1.6 g/100 mL (Rigo et al 1994), and the possibility of protein losing enteropathy in some conditions for which a protein hydrolysed formula may be prescribed, it seems appropriate to increase the upper limit for protein allowable in these formula.

Recommendation:

Protein content: **1.26 - 2.7 g/100 mL.**

Protein source: **casein hydrolysate, whey hydrolysate, amino acids.**

Soy hydrolysates are not included as there is no scientific reason to include them, and clinical studies demonstrate that infants fed a soy hydrolysate formula have reduced weight and length gain, and reduced plasma protein and transferrin concentrations (Rigo et al 1994).

Comment

A chemical grading of the quality of a protein can be made by comparing its amino acid content with that of a reference protein (mg aa in 1g test protein/mg aa in 1g reference protein). The revised R7 states that the amino acid score should be 1 for infant formula based on cow's milk protein and 0.8 for all others. The chemical score of Neocate is 1.1, therefore a recommendation for formulae for use in children with special dietary needs should include a range of amino acid scores of 0.8 - 1.2. The higher level is reasonable as the protein source may be less bioavailable. The reference protein (human milk) should be stated.

There is concern not only over the protein source in these "modified" formulae, but also over the fat source. The poorer growth documented in some studies of infants fed protein hydrolysate formula may not be due to the protein composition - the fatty acid composition may result in less energy being absorbed.

4. Lipid

Unlike protein, there are no fat hydrolysates in use to overcome fat malabsorption. This is probably due to problems of stability of the free fatty acids liberated by lipases. In general, manufacturers have opted for the use of MCTs (medium chain triglycerides) in formula for infants with special needs. Since MCTs are reputed to be directly absorbed into the portal system without prior enzymatic hydrolysis by digestive enzymes, their use in infants with fat malabsorption appears justified. The effect of a large dose of MCT, directly into the portal vein, is unknown. However it must be recognised that MCTs contain only medium chain length saturated fatty acids (<C8=6%, C8=67%, C10=23%, >C10=4%) and thus the essential fatty acid requirements must be met from other fats in the formula. There is no reason for varying the R7 recommendation for essential fatty acids in standard formula for this group of infants.

The lipid content of one protein hydrolysate formula on the Australian market (Nutramigen) is lower than that recommended for standard formula. However, the carbohydrate content is relatively high, achieving a nutritional profile which may be desirable in infants with fat malabsorption. Therefore it is probably not unreasonable to reduce the minimal requirement to embrace this formula (**2.60 - 3.93 g/100 mL**). The sources of lipid currently used in commonly used formula for children with special needs are listed in Table 3.

Recommendation:

The lipids of infant formulae for infants with special needs-

(a) must not be derived from -

(i) sesame oil

(ii) cotton seed oil

(iii) rapeseed oil with an erucic acid content greater than 5g/L;

(b) must have a ratio of linoleic acid to a-linolenic acid of not less than 4:1 and not more than 10:1; and

(c) if specified in Column 1 in Table 4, must comply with the limits specified in Columns 2 and 3 in Table 4.

It is reasonable to extend the range of allowable saturated fatty acids to include products currently on the Australian market. Amounts of lauric acid and myristic acid should continue to be restricted, as they are known to be atherogenic. LC PUFA (C>=20) are not considered essential, but are classified as optional substances.

Table 4.

Column 1 **Fatty acids**	**Column 2** **Minimum % total fatty acids**	**Column 3** **Maximum % total fatty acids**
Saturated fatty acids Lauric acid (12:0) Myristic acid (14:0) Fatty acids (C>=18)		88 15 15 15
cis-Monounsaturated fatty acids		60
cis-Polyunsaturated fatty acids Linoleic acid (18:2) α–Linolenic acid (18:3) Long chain omega 6 series fatty acids (C>=20) Arachidonic acid (20:4) Long chain omega 3 series fatty acids (C>=20) Eicosapentaenoic acid (20:5) Docosahexaenoic acid (22:6)	 8 1	 20 4 2 0.5 2 0.2 0.6

Trans fatty acids Trans-monounsaturated fatty acids		8 6

Neocate has diacetyltartaric and fatty acid esters of glycerol as emulsifiers. "Scientific Hospital Supplies" should comment on this.

5. Carbohydrate

4.78 - 9.55 g/100 mL as per standard formula

All currently available for children with special dietary needs are lactose free or low lactose.

Permissable carbohydrates are:

maltose
maltodextrin
corn syrup solids
glucose syrup or dried glucose syrup
precooked starch
gelatinised starch
lactose hydrolysate
lactose

6. Vitamins, minerals and electrolytes

Vitamins

Recommended levels per 100 mL are the same as for standard term formula. There is no reason for them to be different, and the range (min. - max.) is quite broad.

Vit A	**50 - 150 µg RE**
Vit D	**0.70 - 1.71 µg**
Vit E	**0.31 - 3.01 mg**
Vit K`	**2.81 - 13.48 µg**
Thiamin	**30 - 100 µg**
Riboflavin	**40 - 240 µg**
Niacin	**0.163 - 1.98 mg**
Pyridoxine (B6)	**25 - 100 µg**
Biotin	**1.01 - 7.58 µg**
Folic acid	**5 - 20 µg**

Vit B12	**0.1 - 0.35 µg**
Pantothenic acid	**0.20 - 0.50 mg**
Vit C	**5 - 15 mg**

Minerals

Studies in rhesus monkeys demonstrated that zinc bioavailability was high from formulae based on milk protein hydrolysates but that zinc retention was decreased with some soy hydrolysate formulae (Rudloff & Lonnerdal. Calcium and zinc retention from protein hydrolysate formulas in suckling rhesus monkeys. *Am J Dis Child* 1992; 146: 588-91).

Considering that some infants fed formulae with modified protein, carbohydrate and fat have liver disease, it is recommended that the maximum levels per 100 mL for trace metals be lower than those recommended for healthy infants. However, since the upper limits for trace elements in term formula are already conservative (safe and not too high) they do not need be lowered for formulae for infants with special dietary needs, with the exception of Mn.

Recommended levels per 100 mL:

Zn	0.34 - 1.01 mg
Cu	40 - 100 µg
Mn	**3.4 - 20 µg**
Fe	0.59 - 1.35 mg
I	3.4 - 5.0 µg
Mg	3.9 - 10.0 mg

The addition of selenium, chromium and molybdenum may be considered necessary for formulae with no natural protein or protein hydrolysates (Alexander FW, Clayton BE, Delves HT. Mineral and trace metal balances in children receiving normal and synthetic diets. *Q J Med* 1974; 43: 89-111), therefore recommended ranges are required.

Selenium

It is recognised that the amount of Se is above that consistent with the RDI, however already there are formulae on the Australian market with selenium levels > 2.0 µg/100 mL. Clinical selenium deficiency has been described, but not in Australian infants fed unsupplemented formulae. Selenium is an important antioxidant and theoretically should benefit infants,

especially preterm infants exposed to oxygen. The addition of selenium will make formula fed infants biochemically and possibly functionally more like breastfed infants.
Recommendation: **1.5 - 2.5 µg/100 mL**

Chromium

Chromium has a role in glucose metabolism and possibly lipoprotein lipase activity.
Recommendation: **10 - 40 µg/100 mL**, similar to human milk.

Molybdenum

Molybdenum has been implicated in the maintenance of neurological and ocular function.
Recommendation: **1 - 2 µg/100 mL**, similar to human milk.

Sodium may facilitate translocation of the peptide carrier complex (data reviewed by Burston D and Matthews DM. The effects of sodium replacement on peptide uptake by the small intestine. In : *Nutrition for special needs in infancy*. Ed F. LLifshitz Marcel Dekker Inc, New York 1985, pp23-35). One formula on the Australian market contains sodium in amounts above that recommended in R7. Alfare has a sodium content of 43 mg/100 mL, higher than other protein hydrolysate formula (26-32) and R7 (14-39). The manufacturers comment that Alfare is designed to play a part in the rehydration of infants after diarrhoea when the sodium content is appropriate.

Theoretically calcium absorption and retention may be impaired from protein hydrolysate formulae because calcium is provided exclusively in the form of various calcium salts, without the presence of organic calcium caseinate, as in conventional formulae (Lee YS, Nogushi LT, Naito H. Intestinal absorption of calcium in rats given diets containing casein or amino acid mixtures: the role of casein phosphopeptides. *Br J Nutr* 1983; 49: 67-76). However, studies in rhesus monkeys have demonstrated that calcium bioavailability is relatively good from protein hydrolysate formulae.

Recommendations for sodium content should be extended from that for standard term formula, but recommendations for calcium should remain the same.

Recommended levels per 100 mL:

Na	**14 - 45 mg**
P	17 - 62 mg (Ca : P; 1.1 - 2)
Ca	min. 34 mg
Mg	3.9 - 10.0 mg
Cl	39 - 98 mg
K	56 - 140 mg

Aluminium

The level of contamination of reconstituted formula should be kept **< 1.5 mg/L**, as for formula for healthy term infants. The level of contamination is likely to be higher in the more refined formulae for infants with special dietary needs, however all on the market have concentrations less than 1.5 mg/L, and infants receiving these formulae for medical indications may be at increased risk of accumulation of aluminium because of increased absorption or decreased excretion.

7. Optional ingredients

Nucleotides

Recent evidence suggests that dietary nucleotides may be conditionally essential for newborns. They may enhance normal development of the gastrointestinal tract and immune function, promote recovery from gut injury, improve liver function after damage, increase protein accretion after stress, and improve host resistance in immuno-compromised patients. A term breastfed infant receives 10-20 mg/d as free nucleotides, and 100-150 mg/d as nucleic acids. The calculated daily requirement is 480 mg/d, and a formula fed infant must therefore synthesise over 95% of his requirement de novo. The safety of adding nucleotides to formula has been demonstrated in long-term controlled clinical trials. There is some evidence to suggest that nucleotide fed infants are more like breast fed infants with respect to fecal flora and plasma lipid profile, and this area is well reviewed and referenced (Uauy-Dagach R, Quan R. Significance of nucleic acids, nucleotides and related compounds in infant nutrition. In : *Protein Metabolism during Infancy*. Ed: Raiha NCR. Raven Press, New York 1994. pp194-210; Editorial Quan, Barnes & Uauy. Do infants need nucleotide supplemented formula for optimal nutrition. *J of Pediatric Gastroenterology & Nutrition* 11:429-437, 1990). Others have reported that formula supplemented with nucleotides does not result in faecal flora similar to breast milk. (Balmer, Hanvelf & Wharton. Diet and fecal flora in the newborn: nucleotides. *Arch Dis Childh* 1994; 70:F137-140). A recent clinical trial of formula supplemented with nucleotides at 14.2 mg%, compared with unsupplemented formula, suggested that the addition of nucleotides reduces the incidence of diarrhoeal disease in infancy (Brunser et al. Effect of dietary nucleotide supplementation on diarrhoeal disease in infants. *Acta Paediatr* 83:188-91, 1994).

Recommendation:

Nucleotides (CMP, UMP, AMP, GMP & IMP) be optional ingredients in formulae designed for children with special needs who are likely to benefit most from their role. The recommended range would be that found in human milk and specified in the revised R7 standard for term formula.

The addition of choline and inositol may be considered necessary for formulae with no natural protein or protein hydrolysates, therefore recommended ranges are required. The rationale for allowing these substances in formula is discussed in detail in the Report of the Expert Panel on Infant Formula (15.3.95)

Choline is in breast milk (50-140 mg/L), and is usually present in formula as phosphatidyl choline, which is often added as an emulsifier. The maximum should be consistent with recommendations for lecithin (7 - 250 mg/100 kcal).
Recommendation: **50 - 150 mg/L**

Inositol is permitted at levels of **30 - 150 mg/L**, which are less than the levels in human milk (140 - 450 mg/L). The minimum is equivalent to the level of inositol in cow's milk. Infants fed on cow's milk based formulae would be receiving this much inositol from the milk base in the unsupplemented cow's milk formula and/or the added lecithin.

Taurine is thought to be important as a growth modulator, inhibitory neurotransmitter and a membrane stabiliser.
Recommendation: **21 - 84 mg/L**, as in human milk

Carnitine is involved in energy metabolism and the transport of long chain fatty acids to oxidation sites.
Recommendation: **6 - 12 mg/L**, as in human milk.

8. Labelling and Advertising

Formula containing modified protein or synthetic amino acids, and modified carbohydrate/-lipid, have an important role in the management of malabsorption (due to such conditions as exocrine pancreatic insufficiency, short bowel syndrome and enteropathies) and in the management of protein intolerance. The use of such formulae should be restricted to these conditions and these indications should be clearly displayed on the label, together with a recommendation that they be used only under medical supervision. Standard term formulae (based on recommendations in R7 for healthy term infants) are more appropriate for healthy infants. The benefits of large amounts of MCT probably outweigh any risks in preterm infants or infants with GIT pathology, but the long-term effects of such a high intake of saturated fat remain unknown, and such an intake is certainly very different to that of breastfed infants, and therefore cannot be recommended.

Any claims that such formulae will benefit healthy term infants with or without irritability or colic should **not** be made unless substantiated by properly controlled, blinded, randomised, clinical studies.

Table. 1. Nutritional Composition of Formulae for Children with Special Dietary Needs.

Nutrient / 100 ml	Pregestimil	Nutramigen	Alfaré	Neocate	Portagen
Energy Kj (Kcal)	285 (68)	280 (67)	300 (72)	292 (70)	280 (67)
Protein (gm)	1.9	1.9	2.5	1.95	2.4
Fat (gm)	3.8	2.6	3.6	3.5	3.2
% total sats	86	14.5	69.2	32	88 – check
% total monos	4.1	26.5	17.5	48.5	4.5
% 18:2ω6	9.7	58	12.6	17.6	7.3
% 18:3ω3	0.2	1	0.6	1.8	0.2
CHO (gm)	7.0	9.3	7.8	8.1	7.8
Na (mg)	26	32	43	18	32
Ca (mg)	63	63	60	49	63
P (mg)	42	42	37	35	48
Mg (mg)	7.4	7.5	9.0	5.1	14
Cl (mg)	58	60	75	44	58
K (mg)	74	74	90	63	85
Zn (mg)	0.6	0.5	0.5	0.7	0.6
Mn (μg)	21	44	5.0	90	200
Cu (μg)	63	74	40	70	97
Fe (mg)	1.3	1.5	0.9	1.0	1.3
Vit A (μg RE)	75	51	72	79	158
Vit D (μg)	1.3	0.9	1.1	1.3	1.3
Vit E (mg)	2.5	0.74	0.9	0.7	1.4
Vit K (μg)	12.7	11	5.9	3.2	10.2
Thiamin (μg)	53	53	40	60	100
Riboflavin (μg)	63	63	100	90	130
Niacin (mg)	0.8	1.2	0.5	0.7	1.8
Pyridoxine (B_6) (μg)	42	51	50	80	140
Biotin (μg)	5.3	5.2	1.6	3.9	5.1
Folic Acid (μg)	10.5	11	6.5	5.7	10.6
Vit B_{12} (μg)	0.2	0.3	0.2	0.2	0.4
Pantothenic Acid (mg)	0.3	0.3	0.3	0.4	0.7
Vit C (mg)	7.9	5.5	5.8	6.0	5.5
Osmolality (mOsm/kg H_2O)	350	340	195	353(70) 325(65)	220

Table 3 Formulae for Children with Special Dietary Needs.

	FAT SOURCES	CHO SOURCES	PROTEIN SOURCES
Pregestimil	55% MCT 20% corn oil 12.5% soy oil 12.5% high oleic acid safflower oil	61% corn syrup solids 20% modified corn starch 19% dextrose	casein hydrolysate + amino acids (cystine, tyrosine, tryptophan, taurine, carnitine)
Nutramigen	corn oil	83% corn syrup solids 17% modified corn starch	casein hydrolysate + amino acids (cystine, tyrosine, tryptophan, taurine, carnitine)
Alfaré	48% MCT 29% milk fat 19% corn oil 4% soy lecithin	86% maltodextrin 12% potato starch 2% lactose	whey hydrolysate
Neocate	hybrid safflower oil refined vegetable oil (coconut, soy)	maltodextrin	synthetic amino acids (based on amino acid composition of human milk)
Portagen	86% MCT 12% corn oil 2% soy lecithin	73% corn syrup solids 25% sucrose 2% starch	casein

ATTACHMENT 1

DRAFT REVISED STANDARD R7 - HUMAN MILK SUBSTITUTES

Omit Standard R7 and substitute -

"STANDARD R7 - Human Milk Substitutes

PURPOSE

This Standard provides for the compositional, microbiological and labelling requirements of foods intended for use as a substitute for human milk. This Standard also provides for human milk substitutes intended for infants with special nutritional requirements.

The Standard applies to human milk substitutes, in powder, liquid concentrate and ready-to-feed forms.

TABLE OF PROVISIONS

PART 2 - HUMAN MILK SUBSTITUTES FOR NORMAL USE

Division 1 - Infant Formula

Division 2 - Follow-On Infant Formula

PART 3 - HUMAN MILK SUBSTITUTES FOR SPECIAL DIETARY USE

Division 1 - Pre-term Human Milk Substitute

Division 2 - Lactose free and Low Lactose Human Milk Substitute

Division 3 - Proximate-Modified Human Milk Substitute

SCHEDULES

PART 1 - GENERAL PROVISIONS

Division 1 - Interpretation

Definitions

1. In this Standard -

'amino acid score' means the lowest of the ratios between the quantity in the human milk substitute of the L-amino acid listed in column 1 of Schedule 1 and the quantity for the corresponding L-amino acid listed in column 2 of Schedule 1.

'carbohydrate-modified' means low lactose or lactose free.

'extensively hydrolysed protein' means protein which has been hydrolysed to the extent that it contains no protein fragments with a *molecular weight fraction greater than 5000 daltons*.

'partially hydrolysed protein' means protein which has been hydrolysed but which contains protein fragments with a *molecular weight fraction greater than 5000 daltons*.

'fat-modified' means that the food contains medium chain triglycerides.

'follow-on infant formula' means a human milk substitute represented as being suitable as the principal source of food for healthy infants aged over six months.

'glucose polymers', in pre-term human milk substitutes, means medium length polymers (less than 10 glucose units) prepared from partially hydrolysed starch.

'human milk substitute' means a food that is represented as being suitable as the principal source of food for infants and includes all foods standardised in this Standard.

'infant' means a child under the age of 12 months.

'infant formula' means a human milk substitute represented as being suitable as the principal source of food for healthy infants.

'lactose free human milk substitute' and **'low lactose human milk substitute'** mean a human milk substitute represented as being suitable to satisfy the special dietary needs of lactose intolerant infants.

'medium chain triglycerides' are oils formed through the esterification of glycerol with medium chain fatty acids (8 to 12 carbon atoms).

'modified cows' milk protein' means cows' milk protein in which there has been an alteration of the ratio between casein protein content and whey protein content.

'partially hydrolysed protein' has fragments large enough to induce allergenic reactions in children who are sensitised.

'pre-term human milk substitute' means a human milk substitute represented as being suitable as the principal source of food for infants of less than 37 weeks gestation.

'protein equivalent' means the amount of nitrogen from peptides and amino acids expressed as protein.

'protein-modified' means that the food contains either extensively or partially hydrolysed protein, or synthetically produced amino acids.

'protein substitute' for the purpose of clause (39) is one or more of casein hydrolysate, whey hydrolysate and L-amino acids.

'proximate-modified human milk substitute' is a human milk substitute represented as being suitable as the principal source of food for infants with-

(a) malabsorption due to exocrine pancreatic insufficiency, short bowel syndrome or enteropathies; or

(b) protein allergy.

'soy-based human milk substitute' is a human milk substitute in which soy protein isolate is the sole source of protein.

References to human milk substitute

2. (1) A reference to a human milk substitute is also a reference to a powdered or concentrated form of the human milk substitute reconstituted according to directions.

(2) The label on or attached to a powdered or concentrated form of a human milk substitute must include everything required to be included in a label on or attached to the human milk substitute when reconstituted according to directions.

Calculation of energy

3. The energy value of a human milk substitute, expressed in kilojoules (kJ), must be calculated as follows:

1 g fat yields	37 kJ
1 g protein yields	17 kJ
1 g carbohydrate yields	16 kJ.

Calculation of protein

4. The protein content of a human milk substitute, must be calculated as follows:

(i) For cow or goat milk protein

Protein content = nitrogen content x 6.38

(ii) For soy protein isolate and protein hydrolysates.

Protein content = nitrogen content x 6.25

Division 2 - General Compositional Requirements

Prohibition on gluten

5. A human milk substitute, when examined by the method prescribed by subclause 3(h) of Standard R1, must not contain any detectable gluten.

Restriction on vitamins, minerals and electrolytes

6. A vitamin, mineral or electrolyte must not be added to a human milk substitute unless expressly permitted by this Standard.

Permitted optional ingredients

7. (1) Any nutrient listed in column 1 of the Table to this clause may be added to a human milk substitute provided that-

(a) the nutrient is in one or more of the forms specified in column 2 of the table to this clause in relation to that nutrient;

(b) after addition, the total amount of that nutrient in the human milk substitute is not more than the amount, if any, specified in column 4.

(2) An entry in a nutrition information table in relation to a nutrient specifeid in the Table to this clause may only be made if the total amount of the nutrient in the food, after addition, is not less than the amount specified in column 3 of the Table to this clause.

TABLE TO CLAUSE 7

Column 1 Substance	Column 2 Permitted Forms	Column 3 Minimum Amount for Claim (mg/100 kJ)	Column 4 Maximum Permitted Amount (mg/100 kJ)
Choline	choline chloride choline bitartrate	1.7	5.4
Inositol	inositol	1.0	5.4
Taurine	taurine	0.8	3
L-carnitine	L-carnitine	0.21	0.42

Cytidine 5′-monophosphate	Cytidine 5′-monophosphate Cytidine 5′-monophosphate sodium salt	0.22	0.6
Uridine 5′-monophosphate	Uridine 5′-monophosphate Uridine 5′-monophosphate sodium salt	0.13	0.42
Adenosine 5′-monophosphate	Adenosine 5′-monophosphate Adenosine 5′-monophosphate sodium salt	0.14	0.38
Guanosine 5′-monophosphate	Guanosine 5′-monophosphate Guanosine 5′-monophosphate sodium salt	0.04	0.12
Inosine 5′-monophosphate	Inosine 5′-monophosphate Inosine 5′-monophosphate sodium salt	0.08	0.24

Limit on nucleotide 5′-monophosphates

8. The total amount of nucleotide 5′-monophosphates in a human milk substitute must not exceed 1.2 mg/100 kJ.

Limit on aluminium

9. (1) A human milk substitute, other than a soy-based human milk substitute, must not contain more than 0.2 mg of aluminium per litre.

(2) A soy-based human milk substitute must not contain more than 1.0 mg of aluminium per litre.

(3) For the purposes of this clause, a human milk substitute in a concentrated or powdered form is to be reconstituted according to directions and using aluminium-free water.

Limit on fluoride

10. (1) A human milk substitute other than a soy-based human milk substitute must not contain more than 0.5 mg of fluoride per litre.

(2) A soy-based human milk substitute must not contain more than 2.0 mg of fluoride per litre.

(3) For the purposes of this clause, a human milk substitute in a concentrated or powdered form is to be reconstituted according to directions and using fluoride-free water.

Division 3 - General Labelling and Packaging Requirements

Requirement for a measuring scoop

11. A package containing human milk substitute in a powdered form, other than a single serve sachet, must contain a scoop suitable for use in accordance with the directions contained in the label on or attached to the package.

Suitability for bottle feeding

12. A human milk substitute must be free of lumps and coarse particles and suitable for feeding through a soft teat.

Names

13. (1) The names by which human milk substitutes are defined in this Standard are not prescribed names except for 'INFANT FORMULA' and 'FOLLOW-ON INFANT FORMULA'.

(2) The appropriate designation of a human milk substitute standardised in Part 3 of this Standard must contain the term 'INFANT FORMULA'.

Required statements

14. (1) Subject to subclauses (2) and (3), the label on or attached to a package containing a human milk substitute must contain the following statements-

(a) 'ATTENTION - BREAST MILK IS BEST FOR BABIES. BEFORE YOU DECIDE TO USE AN INFANT FORMULA, CONSULT YOUR DOCTOR OR CHILD HEALTH CLINIC FOR ADVICE.'

'WARNING - UNBOILED WATER, UNBOILED OR UNSTERILISED BOTTLES AND TEATS CAN MAKE YOUR BABY ILL. PREPARE ONLY ONE BOTTLE AT A TIME. FOLLOW INSTRUCTIONS EXACTLY.'

'USING MORE OR LESS [POWDER or LIQUID CONCENTRATE use whichever is applicable] THAN INDICATED MAY EITHER LEAD TO DEHYDRATION OR DEPRIVE YOUR BABY OF PROPER NUTRITION. DO NOT CHANGE PROPORTIONS WITHOUT MEDICAL ADVICE.';

'FOR INFANTS OVER THE AGE OF 6 MONTHS, IT IS ADVISABLE TO INTRODUCE OTHER FOODS';

(b) 'IF CORRECTLY STORED AND MADE UP IN ACCORDANCE WITH THE DIRECTIONS CONTAINED IN THE LABEL, NO FURTHER VITAMIN OR MINERAL SUPPLEMENTS ARE NECESSARY'; and

(c) where a package containing a human milk substitute is required to contain a measuring scoop -

'USE ONLY THE ENCLOSED SCOOP'.

(2) Where a human milk substitute is in a package having a net weight of 1 kg or more, the statements required by subclause (1) must be in standard type of 3 mm.

(3) The statement specified in paragraph (1)(b) of this clause must not be included on or attached to a package containing pre-term human milk substitute.

Nutrition information table

15. The label on or attached to a package containing a human milk substitute must include a statement of the minimum energy value and the minimum amount of nutrients per 100 mL in the following form-

NUTRITION INFORMATION

	Minimum amount per 100 mL
Energy	kJ
Protein	g
Fat	g
Carbohydrate	g
Vitamin A	µg
Vitamin B_6	µg
Vitamin B_{12}	µg
Vitamin C	mg
Vitamin D	µg
Vitamin E	µg
Vitamin K	µg
Biotin	µg
Niacin	mg
Folate	µg
Pantothenic acid	µg
Riboflavin	µg
Thiamin	µg
Calcium	mg
Copper	µg
Iodine	µg
Iron	mg
Magnesium	mg
Manganese	µg
Phosphorus	mg
Selenium	µg

Zinc	mg
Chloride	mg
Potassium	mg
Sodium	mg

Storage instructions

16. The label on or attached to a package containing a human milk substitute must contain storage instructions for the periods before and after opening of the package.

Statement of protein source

17. The label on or attached to a package containing a human milk substitute other than a proximate-modified human milk substitute must contain a statement of the source of protein in the product.

Prohibited representations

18. The label on or attached to a package containing a human milk substitute must not contain -

(a) a picture of an infant;

(b) a picture that idealises the use of human milk substitute;

(c) the word 'humanised' or 'maternalised' or any word or words having the same or similar effect;

(d) words claiming that the product is suitable for all infants;

(e) information relating to the nutrient content of human milk;

(f) a reference to the presence of any nutrient, except for a reference to a nutrient in-
  (i) the appropriate designation of a proximate-modified human milk susbstitute;
  (ii) a statement of ingredients; or
  (iii) in the nutrition information table.

Division 4 - General Microbiological Requirements

Microbiological standards

19. A human milk substitute -

(a) in powdered form, when examined by the methods prescribed in Schedule 2 of this Standard, must -

(i) have a standard plate count not exceeding 1000 micro-organisms per gram;
(ii) be free from coliforms in 1 g;
(iii) be free from coagulase-positive staphylococci in 0.1g;
(iv) be free from *Salmonella* in 25 g;
(v) have a *Bacillus cereus* count not exceeding 100 micro-organisms per gram;

(b) in liquid concentrate form or ready-to-feed form must not exhibit any detectable microbial growth when examined by the method prescribed in paragraph (a) of Schedule 2 to this Standard.

PART 2 - HUMAN MILK SUBSTITUTES FOR NORMAL USE

Division 1 - Infant Formula

Composition

20. Infant formula-

(a) must have an energy value of not less than 2700 kJ/L and not more than 3000 kJ/L;

(b) must have an osmolality value of not greater than 325 mOsm/kg;

(c) must contain an amount of each nutrient specified in column 1 of the Table to this paragraph which is not less than the amount specified in column 2 and not greater than the amount specified in column 3.

TABLE TO PARAGRAPH 20(c).

Column 1	Column 2	Column 3
Nutrient	Minimum amount per 100 kJ	Maximum amount per 100 kJ
protein	0.45 g	0.7 g
lipid	1.1 g	1.4 g
carbohydrate	1.7 g	3.4 g

Protein

21. (1) The protein in infant formula -

(a) must be one or more of the following-

(i) unmodified cows' milk protein;
(ii) modified cows' milk protein;
(iii) unmodified goats' milk protein;

(iv) soy protein isolate;

(b) must have an amino acid score of at least -

(i) 1.0 when the protein in the food is modified cows milk protein;

(ii) 0.8 in all other cases.

(2) L-amino acids may be added solely for the purpose of achieving the minimum amino acid score specified in subclause (1).

Lipid

22. The lipids in infant formula-

(a) must not be derived from-

(i) sesame oil
(ii) cotton seed oil;

(b) must not contain medium chain triglycerides;

(c) must have a ratio of linoleic acid to α–linolenic acid of not less than 4:1 and not more than 10:1;

(d) if specified in column 1 of the Table to this paragraph, must comply with the limits, if any, specified in columns 2 and 3 .

TABLE TO PARAGRAPH 22(d)

Column 1	Column 2	Column 3
Fatty Acids	**Minimum % total fatty acids**	**Maximum % total fatty acids**
Saturated fatty acids		50
Lauric acid (12:0)		15
Myristic acid (14:0)		15
Fatty acids (C>=18)		15
cis-Monounsaturated fatty acids	30	60
cis-Polyunsaturated fatty acids		
Linoleic acid (18:2)	8	20
α-Linolenic acid (18:3)	1	4
Long chain omega 6 series fatty acids (C>=20)		2
Arachidonic acid (20:4)		0.5
Long chain omega 3 fatty acids (C>=20)		2

Eicosapentaenoic acid (20:5)		0.2
Docosahexaenoic acid (22:6)		0.6
Trans fatty acids		8
Trans-monounsaturated fatty acids		6

Carbohydrate

23. (1) The carbohydrate content of infant formula must be at least 80% lactose.

(2) Any carbohydrate other than lactose in infant formula must be one or more of the following -

(a) maltose
(b) sucrose
(c) maltodextrin
(d) corn syrup solids
(e) glucose syrup or dried glucose syrup
(f) precooked starch
(g) gelatinised starch.

Vitamins, minerals and electrolytes

24. (1) Infant formula must contain the vitamins, minerals and electrolytes specified in column 1 of Schedule 3 provided that, in relation to each vitamin, mineral or electrolyte -

(a) the added vitamin, mineral or electrolyte is in a form specified in column 2;
(b) the food contains at least the quantity specified in column 3; and
(c) the food contains not more than the quantity specified in column 4.

(2) The ratio of-

(a) calcium to phosphorus in infant formula must be not less than 1.1 and not more than 2.0;
(b) zinc to copper in infant formula must not be greater than 10:1.

(3) There must be at least 0.9 mg of d-α-tocopherol equivalents for each gram of polyunsaturated fatty acid.

Other permitted additions

25. Infant formula may contain -

(a) citric acid

(b) L(+)-lactic acid;

(c) nutrients specified in column 1 of the Table to this paragraph provided that the total amount of the nutrient, after addition, does not exceed the amount specified in column 2.

TABLE TO PARAGRAPH 25(c)

Column 1 Nutrient	Column 2 Maximum Amount per litre
Lecithin	5 g
Mono- and di-glycerides of fat-forming fatty acids	2 g in total
Guar gum and locust bean gum	1 g in total
In the case of soy-based infant formula only, acetylated distarch phosphate, distarch phosphate and phosphated starch phosphate	5 g in total

Labelling

26. The label on or attached to a package containing infant formula must include-

(a) in standard type of 3mm, and immediately following the prescribed name, the statement

'SUITABLE FROM BIRTH';

(b) in the case of infant formula in a powdered or liquid concentrate form, directions in words and pictures as to its preparation;

(c) directions in words and pictures as to its use;

(d) in the case of infant formula in the powdered or liquid concentrate form, a feeding guide in the form specified in Table 1 of Schedule 5;

(e) in the case of ready-to-feed infant formula, a feeding guide in the form specified in Table 2 of Schedule 5.

Division 2 - Follow-On Infant Formula

Composition

27. (1) Subject to subclause (2), clauses 20 to 25 of this Standard apply to follow-on infant formula.

(2) Follow-on infant formula must contain an amount of each nutrient specified in column 1 of the Table to this subclause which is not less than the amount specified in column 2 and not greater than the amount specified in column 3 .

TABLE TO SUBCLAUSE 27(2)

Column 1	Column 2	Column 3
Nutrient	**Minimum amount per 100 kJ**	**Maximum amount per 100 kJ**
protein	0.7 g	1.0 g
lipid	0.9 g	1.4 g
selenium	0.79µg	0.89µg
zinc	0.18 mg	0.43 mg

Labelling

28. The label on or attached to a package containing follow-on infant formula must include-

(a) in standard type of 3mm, and immediately following the prescribed name, the statement

'SUITABLE ONLY FOR INFANTS OVER 6 MONTHS';

(b) directions in words and pictures as to its preparation and use;

(c) in the case of follow-on infant formula powder or follow-on liquid concentrate, a feeding guide in the form specified in Table 3 to Schedule 5 of this Standard;

(d) in the case of ready-to-feed follow-on infant formula, a feeding guide in the form specified in Table 4 to Schedule 5 of this Standard.

PART 3 - HUMAN MILK SUBSTITUTES FOR SPECIAL DIETARY USE

Division 1 - Pre-term Human Milk Substitute

Composition

29. (1) Pre-term human milk substitute-

(a) must have an energy value of not less than 2720 kJ/L and not more than 3556 kJ/L;

(b) must have an osmolality value of not greater than 325 mOsm/kg;

(c) must contain an amount of each nutrient specified in column 1 of the Table to this paragraph which is not less than the amount specified in column 2 and not greater than the amount specified in column 3.

TABLE TO PARAGRAPH 29(1)(c)

Column 1 Nutrient	Column 2 Minimum amount per 100 kJ	Column 3 Maximum amount per 100 kJ
protein for infants of <1 kg for infants of ≥1 kg	 0.72 g 0.6 g	 0.76 g 0.72 g
lipid	1.1 g	1.4 g
carbohydrate	1.7 g	3.4 g

Protein

30. (1) The protein in pre-term human milk substitute -

(a) must be one or more of the following-

(i) unmodified cows' milk protein;
(ii) modified cows' milk protein;
(iii) unmodified goats' milk protein.

(b) must have an amino acid score of at least -

(i) 1.0 when the protein in the food is modified cows milk protein;
(ii) 0.8 in all other cases.

(2) L-amino acids may be added solely for the purpose of achieving the amino acid score specified in subclause (1).

Lipid

31. The lipids in pre-term human milk substitute-

(a) must not be derived from-

(i) sesame oil
(ii) cotton seed oil;

(b) must have a ratio of linoleic acid to α–linolenic acid of not less than 4:1 and not more than 15:1;

(c) must not contain medium chain triglycerides;

(d) if specified in column 1 of the Table to this paragraph, must comply with the limits specified in columns 2 and 3 .

TABLE TO PARAGRAPH 31(d)

Column 1 Fatty Acids	Column 2 Minimum % total fatty acids	Column 3 Maximum % total fatty acids
Saturated fatty acids Lauric acid (12:0) Myristic acid (14:0) Fatty acids (C>=18)		50 15 15 15
cis-Monounsaturated fatty acids	30	60
cis-Polyunsaturated fatty acids Linoleic acid (18:2) α-Linolenic acid (18.3) Long chain omega 6 series fatty acids (C>=20) Arachidonic acid (20:4) Long chain omega 3 fatty acids (C>=20) Eicosapentaenoic acid (20:5) Docosahexaenoic acid (22:6)	8 1	20 4 2 0.5 2 0.2 0.6
Trans fatty acids Trans-monounsaturated fatty acids		8 6

Carbohydrate

32. Any carbohydrate in pre-term human milk substitute must be one or more of the following-

(a) lactose
(b) lactose hydrolysate
(c) glucose
(d) glucose polymers
(e) maltodextrin
(f) corn syrup solids.

Vitamins, minerals and electrolytes

33. (1) Pre-term human milk substitute must contain the vitamins, minerals and electrolytes specified in column 1 of Schedule 4 provided that, in relation to each vitamin or mineral -

(i) the added vitamin or mineral is in a form specified in column 2;

(ii) the food contains at least the quantity specified in column 3; and

(iii) the food contains not more than the quantity specified in column 4.

(2) The ratio of calcium to phosphorus in pre-term human milk substitute must be not less than 1.4 and not more than 2.0.

(3) There must be at least 0.9 mg of d-α-tocopherol equivalents for each gram of polyunsaturated fatty acid.

Labelling

34. (1) The label on or attached to a package containing pre-term human milk substitute must include-

(a) in standard type of 3 mm, and immediately following the prescribed name, the statement -

'SUITABLE ONLY FOR PRE-TERM INFANTS
UNDER SPECIALIST MEDICAL SUPERVISION';

(b) directions in words and pictures as to its preparation and use;

(c) a feeding guide in the form specified in Table 5 of Schedule 5.

(2) The words 'pre-term' must appear as part of the appropriate designation of a food standardised in this Division.

Division 2 - Lactose Free and Low Lactose Human Milk Substitutes

Lactose levels

35. (1) Lactose free human milk substitute must not contain any detectable lactose.

(2) Low lactose human milk substitute, when prepared in accordance with directions for use as the case may be, must not contain more than -

(a) 2.4 g/kg of lactose in the case of human milk substitute based on cows' milk protein or modified cows' milk protein; or

(b) 1.8 g/kg of lactose in the case of human milk substitute based on goats' milk protein.

Composition

36. (1) A lactose free or low lactose variety of a human milk substitute must, except for the lactose content, comply with the compositional and labelling requirements which apply to the human milk substitute of which they are a variety.

(2) Lactose free human milk substitute and low lactose human milk substitute may contain lactose hydrolysate.

Labelling

37. (1) The words 'lactose free' or 'low lactose', as the case may be, must appear as part of the appropriate designation of a food standardised in this Division.

(2) The label on or attached to package containg a lactose free human milk substitute in which the protein is milk protein must include, in type of 3mm, the statement-

"NOT SUITABLE FOR INFANTS WITH GALACTOSEMIA".

Division 3 - Proximate-Modified Human Milk Substitute

Composition

38. (1) A proximate-modified human milk substitute-

(a) must have an energy value of not less than 2700 kJ/L and not more than 3000 kJ/L;

(b) must have an osmolality value of not greater than 360 mOsm/kg;

(c) must contain an amount of each nutrient specified in column 1 of the Table to this paragraph which is not less than the amount specified in column 2 and not greater than the amount specified in column 3.

TABLE TO PARAGRAPH 38(1)(c)

Column 1	Column 2	Column 3
Nutrient	Minimum amount per 100 kJ	Maximum amount per 100 kJ
protein or protein equivalent	0.45g	1.4 g
lipid	0.93 g	1.4 g

carbohydrate	1.7 g	3.4 g

Protein

39. (1) The protein in a proximate-modified human milk substitute -

(a) must be one or more of
(i) unmodified cows' milk protein
(ii) modified cows' milk protein;

or must be

(iii) a protein substitute; and

(b) must have an amino acid score between 0.8 and 1.2.

(2) L-amino acids may be added solely for the purpose of achieving the amino acid score specified in subclause (1).

Lipid

40. The lipids in a proximate-modified human milk substitute-

(a) must not be derived from-

(i) sesame oil
(ii) cotton seed oil;

(b) must have a ratio of linoleic acid to α–linolenic acid of not less than 4:1 and not more than 10:1; and

(c) if specified in column 1 of the Table to this paragraph, must comply with the limits specified in columns 2 and 3.

TABLE TO PARAGRAPH 40(c)

Column 1	Column 2	Column 3
Fatty Acids	**Minimum % total fatty acids**	**Maximum % total fatty acids**
Saturated fatty acids		88
Lauric acid (12:0)		15
Myristic acid (14:0)		15

Fatty acids (C>=18)		15
cis-Monounsaturated fatty acids		60
cis-Polyunsaturated fatty acids Linoleic acid (18:2) α-Linolenic acid (18.3) Long chain omega 6 series fatty acids (C>=20) Arachidonic acid (20:4) Long chain omega 3 fatty acids (C>=20) Eicosapentaenoic acid (20:5) Docosahexaenoic acid (22:6)	 8 1	 20 4 2 0.5 2 0.2 0.6
Trans fatty acids Trans-monounsaturated fatty acids		8 6

Carbohydrate

41. Any carbohydrate in a proximate-modified human milk substitute must be one or more of the following-

(a) maltose
(b) glucose syrup
(c) lactose
(d) precooked or gelatinised starch
(e) maltodextrin
(f) corn syrup solids.

Vitamins, minerals and electrolytes

42. (1) Subject to subclause (4), a proximate-modified human milk substitute must contain the vitamins, minerals and electrolytes specified in column 1 of Schedule 3 provided that, in relation to each vitamin or mineral -

(i) the added vitamin or mineral is in a form specified in column 2;

(ii) the food contains at least the quantity specified in column 3; and

(iii) the food contains not more than the quantity specified in column 4.

(2) The ratio of calcium to phosphorus in a proximate-modified human milk substitute must be not less than 1.1 and not more than 2.0.

(3) There must be in a proximate-modified human milk substitute at least 0.5 mg of d-α-tocopherol equivalents for each gram of polyunsaturated fatty acid.

(4) Notwithstanding Schedule 3, a proximate-modified human milk substitute must contain the minerals specified in column 1 of the Table to this subclause provided that, in relation to each mineral -

(i) the food contains at least the quantity specified in column 2;

(ii) the food contains not more than the quantity specified in column 3; and

(iii) where the mineral is specified in Schedule 3, it is added in a form specified in column 2 of that Schedule.

TABLE TO SUBCLAUSE 42(4)

Column 1	Column 2	Column 3
Mineral	Minimum Amount per 100 kJ	Maximum Amount per 100 kJ
Manganese	1.2 ug	7.2 ug
Sodium	4.9 mg	16 mg
Selenium	0.53 ug	0.89 ug

(5) A proximate-modifed human milk substitute may contain the minerals specified in column 1 of the Table to this subclause provided that, in relation to each mineral -

(i) it is in a form specified in column 2;

(ii) the food contains at least the quantity specified in column 3; and

(iii) the food contains not more than the quantity specified in column 4.

TABLE TO SUBCLAUSE 42(5)

Column 1	Column 2	Column 3	Column 4
Mineral	Permitted forms	Minimum Amount per 100 kJ	Maximum Amount per 100 kJ
Chromium	chromium sulphate*	3.5 ug	15 ug
Molybdenum	sodium molybdate (VI) dihydrate*	0.36 mg	0.71 mg

Drafting Note - * subject to satisfactory toxicological assessment

Labelling

43. (1) The label on or attached to a package containing a proximate-modified human milk substitute must include-

(a) in standard type of 3mm, and immediately following the appropriate designation, the statement -

"THIS PRODUCT HAS BEEN SPECIFICALLY FORMULATED FOR INFANTS WITH SPECIAL DIETARY NEEDS AND SHOULD BE USED UNDER MEDICAL SUPERVISON".

(b) directions in words and pictures as to its preparation and use;

(c) a feeding guide in the form specified in Table 1 of Schedule 5.

(2) The appropriate designation of a food standardised in this Division must include a statement indicating-

(a) the conditions for which the food has been specially formulated-
i) malabsorption;
ii) protein allergy; and

(b) the nutrient modifications which apply to the food-
i) protein modified;
ii) carbohydrate modified;
iii) fat modified.

(3) The label on or attached to a package containing a proximate-modified human milk substitute must not inlcude the word 'HYPOALLERGENIC' unless the food does not contain any protein fragments with a *molecular weight fraction greater than 5000 daltons.*

CONSEQUENTIAL AMENDMENTS

Standard A1 is varied by-

(a) inserting after clause (32) -

"(33) A food must not be represented as being suitable as a sole or principal source of nutrition for infants unless it complies with Standard R7."; and

(b) inserting in Parts 1 and 2 of the Schedule, in columns 1 and 2 respectively-

"Nicotinic Acid	375";
"Sodium gluconate	576"; and
"Sodium lactate	325".

Standard A11 is varied by-

(a) inserting after paragraph (ze)-

"(zf) 'USP (1990)' means the United States Pharmacopeia, 22nd Revision. Official from January 1, 1990. United States Pharmacopeial Convention Inc. Rockville, Md (1989);"

(b) inserting in the Schedule the following entries in columns 1 and 2 respectively -

"L-arginine	FCC p26
L-histidine	FCC p143
L-isoleucine	FCC p154
L-lysine	FCC p176
L-methionine	FCC p193
Nicotinic acid	FCC p205
L-phenylalanine	FCC p224
L-Selenomethionine	Addendum 3
Sodium gluconate	FCC p286
Sodium lactate	FCC 3rd suppl p144
Sodium selenite	USP (1990) p1773"
L-threonine	FCC p326
L-tyrosine	FCC p341
L-valine	FCC p341

(c) inserting after Addendum 2, -

DRAFTING NOTE - this specification is also proposed for VLED - one or other can be dropped depending on which is gazetted first.

"ADDENDUM 3
SPECIFICATION FOR L-SELENOMETHIONINE

Formula: $C_5H_{11}NO_2Se$

Formula Weight	196.11
Physical Tests	
Appearance:	Crystalline powder
Colour:	White to off-white
Chemical Tests	
Identification:	IR Spectrum conforms to reference standard.
Melting Range:	260° C to 266° C (dec.)
Sodium:	Less than 0.1%
Heavy Metals:	Undetectable
Assay by Titration:	98.0 to 101.0%
Homogeneity:	One spot on TLC plate using UV light, iodine and ninhydrin as detection methods. Solvent systems: 1. Phenol: water (100:20) 2. Butanol: acetic acid: water (80:20:20)
Optical Rotation:	[α]22/D +21.6° (c = 0.5 in 2N HCl)"

Standard A12 is varied by inserting in columns 2 and 3 respectively of the Table in clause (2), in relation to the entry in column 1 for "Selenium" -

"Foods standardised by Standard R7	must not exceed the levels specified for that food in Standard R7".

SCHEDULE 1

REFERENCE AMINO ACID COMPOSITION OF HUMAN MILK[1]

Column 1 Amino Acid	Column 2 g/100 g of protein
Histidine	2.6
Isoleucine	4.6
Leucine	9.3
Lysine	6.6
*Methionine & Cystine	4.2
*Phenylalanine & Tyrosine	7.2
Threonine	4.3
Tryptophan	1.7
Valine	5.5

* The concentrations of i) methionine and cysteine, and ii) tyrosine and phenylalanine should be added together when calculating the amino acid score.

1 Joint FAO/WHO/UNU Expert Consultation. *Energy and Protein Requirements.* WHO Tech. Rept. Ser. No.724. World Health Organisation, Geneva, Switzerland (1985)

SCHEDULE 2

METHODS OF MICROBIOLOGICAL ANALYSIS

The methods set out in this clause are the prescribed methods with respect to the microbiological analysis of infant formula.

(a) *Standard plate count.* Proceed in accordance with the current standard method in AS 1766, Methods for the Microbiological Examination of Foods, save that for the purpose of this method when 5 sample units each consisting of at least 100 g or more of infant formula powder are examined as detailed, the result shall be reported as 'not exceeding 1000 micro-organisms per gram of the food' when at least 3 of the 5 sample units have a standard plate count of not exceeding 1000 micro-organisms per gram and any remaining sample units have a standard plate count not exceeding 10 000 micro-organisms per gram.

(b) *Coliforms.* Proceed in accordance with the current standard method in AS 1766, Methods for the Microbiological Examination of Foods, save that for the purpose of this method when 5 sample units each consisting of at least 100 g or more of infant formula powder are examined as detailed using an incubation temperature of 30°C the result shall be reported as 'coliforms not detected in 1 gram of the food; when at least 3 of the 5 sample units are free from coliforms in 1 g and any remaining sample units are free from coliforms in 0.1 g.

(c) *Coagulase-positive staphylococci.* Proceed in accordance with the current standard method in AS 1766, *Methods for the Microbiological Examination of Foods,* save that for the purpose of this method when 5 sample units each consisting of at least 100 g or more of infant formula powder are examined as detailed, the result shall be reported as 'coagulase-positive staphylococci not detected in 0.1 g of the food' when at least 4 of the 5 sample units are free from coagulase-positive staphylococci in 0.1 g and any remaining sample units are free from coagulase-positive staphylococci in 0.01 g.

(d) *Salmonella.* Proceed in accordance with the current standard method in AS 1766, *Methods for the Microbiological Examination of Foods,* save that for the purpose of this method when 30 sample units each consisting of at least 100 g or more of infant formula powder are examined as detailed, the result shall be reported as '*Salmonella* not detected in 25 g of the food' when no *Salmonella* has been detected in 25 g of each of the 30 sample units. For the purposes of this method, the sample units may be examined individually or pooled.

(e) *Bacillus cereus*. Proceed in accordance with the current standard method in AS 1766, *Methods for the Microbiological Examination of Foods*, save that for the purposes of this method when 5 sample units each consisting of at least 100g or more of infant formula powder are examined as detailed, the result shall be reported as 'not exceeding 100 micro-organisms per gram of the food' when at least 4 of the 5 sample units have a *Bacillus cereus* count not exceeding 100 micro-organisms per gram and the remaining sample unit has a *Bacillus cereus* count not exceeding 1000 micro-organisms per gram.

SCHEDULE 3

PERMITTED FORMS AND REQUIRED LEVELS OF VITAMINS, MINERALS AND ELECTROLYTES IN INFANT FORMULA

Column 1 **Substance**	Column 2 **Permitted Forms**	Column 3 **Minimum Amount per 100 kJ**	Column 4 **Maximum Amount per 100kJ**
Vitamin A	Retinol Forms vitamin A (retinol) vitamin A acetate (retinyl acetate) vitamin A palmitate (retinyl palmitate) Carotenoid Forms beta-carotene	17 µg retinol equivalents	54 µg retinol equivalents
Thiamin (Vitamin B_1)	thiamin hydrochloride thiamin mononitrate	10 µg thiamin	22 µg thiamin
Riboflavin (Vitamin B_2)	riboflavin riboflavin-5'-phosphate, sodium	14 µg riboflavin	86 µg riboflavin
Niacin	niacinamide (nicotinamide) nicotinic acid	0.06 mg niacin	0.71 mg niacin
Folate	folic acid	1.7 µg folic acid	7.9 µg folic acid
Vitamin B_6	pyridoxine hydrochloride	8.9 µg pyridoxine	36 µg pyridoxine
Vitamin B_{12}	cyanocobalamin hydroxocobalamin	0.04 µg cyanocobalamin	0.13 µg cyanocobalamin

Column 1 **Substance**	Column 2 **Permitted Forms**	Column 3 **Minimum Amount per 100 kJ**	Column 4 **Maximum Amount per 100kJ**
Vitamin C	ascorbic acid ascorbyl palmitate calcium ascorbate potassium ascorbate sodium ascorbate	1.7 mg in total of L-ascorbic acid and dehydroascorbic acid	5.4 mg in total of L-ascorbic acid and dehydroascorbic acid
Vitamin D	vitamin D_2 (ergocalciferol) vitamin D_3 (cholecalciferol)	0.25 µg cholecalciferol	0.61 µg cholecalciferol
Vitamin E α-tocopherol	dl-α-tocopherol d-α-tocopherol concentrate tocopherols concentrate, mixed d-α-tocopheryl acetate dl-α-tocopheryl acetate d-α-tocopheryl acid succinate	0.11 mg d-α–tocopherol equivalents, with a minimum of 0.5 mg per g PUFA	1.1 mg d-α–tocopherol equivalents, with a minimum of 0.5 mg per g PUFA
Vitamin K	vitamin K_1, as phylloquinone (phytomenadione, phytonadione)	1.0 µg vitamin K	3.6 µg vitamin K
Biotin	d-Biotin	0.36 µg biotin	2.7 µg biotin

Column 1 **Substance**	Column 2 **Permitted Forms**	Column 3 **Minimum Amount per 100 kJ**	Column 4 **Maximum Amount per 100kJ**
Pantothenic acid	calcium pantothenate dexpanthenol	71 µg pantothenic acid	360 µg pantothenic acid
Calcium	calcium carbonate calcium chloride calcium citrate calcium gluconate calcium glycerophosphate calcium hydroxide calcium lactate calcium oxide calcium phosphate, dibasic calcium phosphate, monobasic calcium phosphate, tribasic calcium sulphate	12 mg calcium	Not specified
Chloride	calcium chloride magnesium chloride potassium chloride sodium chloride	14 mg chloride	35 mg chloride

Copper	copper gluconate cupric sulphate	14 µg copper for formula other than soy-based formula 21 µg for soy-based formula	36 µg copper for formula other than soy-based formula 43 µg for soy-based formula

Column 1 **Substance**	Column 2 **Permitted Forms**	Column 3 **Minimum Amount per 100 kJ**	Column 4 **Maximum Amount per 100kJ**
Iron	ferric ammonium citrate ferric pyrophosphate ferrous citrate ferrous fumarate ferrous gluconate ferrous lactate ferrous succinate ferrous sulphate	0.2 mg iron	0.5 mg iron
Iodine	potassium iodate potassium iodide sodium iodide	1.2 µg iodine	18 µg iodine
Magnesium	magnesium carbonate magnesium chloride magnesium gluconate magnesium oxide magnesium phosphate, dibasic magnesium phosphate, tribasic magnesium sulphate	1.4 mg magnesium	3.6 mg magnesium

Column 1 **Substance**	Column 2 **Permitted Forms**	Column 3 **Minimum Amount per 100 kJ**	Column 4 **Maximum Amount per 100kJ**
Manganese	manganese chloride manganese gluconate manganese sulphate	1.2 µg manganese	13 µg manganese
Potassium	potassium bicarbonate potassium carbonate potassium chloride potassium citrate potassium glycerophosphate potassium gluconate potassium hydroxide potassium phosphate, dibasic potassium phosphate, monobasic potassium phosphate, tribasic	20 mg potassium	50 mg potassium
Phosphorus	calcium glycerophosphate calcium phosphate, dibasic calcium phosphate, monobasic calcium phosphate, tribasic	6 mg phosphorus	22 mg phosphorus

Column 1 **Substance**	Column 2 **Permitted Forms**	Column 3 **Minimum Amount per 100 kJ**	Column 4 **Maximum Amount per 100kJ**
	magnesium phosphate, dibasic potassium phosphate, dibasic potassium phosphate, monobasic potassium phosphate, tribasic sodium phosphate, dibasic sodium phosphate, monobasic sodium phosphate, tribasic		
Sodium	sodium bicarbonate sodium carbonate sodium chloride sodium citrate sodium gluconate sodium hydroxide sodium iodide sodium lactate sodium phosphate, dibasic sodium phosphate, monobasic	5 mg sodium	14 mg sodium

Column 1 **Substance**	Column 2 **Permitted Forms**	Column 3 **Minimum Amount per 100 kJ**	Column 4 **Maximum Amount per 100kJ**
	sodium phosphate, tribasic sodium sulphate sodium tartrate		
Selenium	sodium selenite seleno methionine	0.42 µg selenium	0.89 µg selenium
Zinc	zinc acetate zinc chloride zinc gluconate zinc oxide zinc sulphate	0.12 mg zinc for formula other than soy-based formula 0.18 mg zinc for soy-based formula	0.36 mg zinc for formula other than soy-based formula 0.43 mg zinc for soy-based formula

SCHEDULE 4

PERMITTED FORMS AND REQUIRED LEVELS OF VITAMINS, MINERALS AND ELECTROLYTES IN PRE-TERM INFANT FORMULA

Column 1 **Substance**	Column 2 **Permitted Forms**	Column 3 **Minimum Amount per 100 kJ**	Column 4 **Maximum Amount per 100 kJ**
Vitamin A	Retinol Forms vitamin A (retinol) vitamin A acetate (retinyl acetate) vitamin A palmitate (retinyl palmitate) Carotenoid Forms beta-carotene	20 µg retinol equivalents	36 µg retinol equivalents
Thiamin (Vitamin B_1)	thiamin hydrochloride thiamin mononitrate	10 µg thiamin	48 µg thiamin
Riboflavin (Vitamin B_2)	riboflavin riboflavin-5'-phosphate, sodium	14 µg riboflavin	86 µg riboflavin
Niacin	niacinamide (nicotinamide) nicotinic acid	0.18 mg niacin	0.89 mg niacin
Folate	folic acid	5.0 µg folic acid	10 µg folic acid
Vitamin B_6	pyridoxine hydrochloride	8.9 µg pyridoxine	42 µg pyridoxine
Vitamin B_{12}	cyanocobalamin hydroxocobalamin	0.04 µg cyanocobalamin	0.13 µg cyanocobalamin

Column 1 Substance	Column 2 Permitted Forms	Column 3 Minimum Amount per 100 kJ	Column 4 Maximum Amount per 100 kJ
Vitamin C	ascorbic acid ascorbyl palmitate calcium ascorbate potassium ascorbate sodium ascorbate	3.5 mg in total of L-ascorbic acid and dehydroascorbic acid	9.6 mg in total of L-ascorbic acid and dehydroascorbic acid
Vitamin D	vitamin D_2 (ergocalciferol) vitamin D_3 (cholecalciferol)	0.75 µg cholecalciferol	2.0 µg cholecalciferol
Vitamin E α-tocopherol	dl-α-tocopherol d-α-tocopherol concentrate tocopherols concentrate, mixed d-α-tocopheryl acetate dl-α-tocopheryl acetate d-α-tocopheryl acid succinate	0.18 mg	1.6 mg
Vitamin K	vitamin K_1, as phylloquinone (phytomenadione, phytonadione)	0.96 µg vitamin K	3.6 µg vitamin K
Biotin	d-Biotin	0.37 µg biotin	2.7 µg biotin

Column 1 Substance	Column 2 Permitted Forms	Column 3 Minimum Amount per 100 kJ	Column 4 Maximum Amount per 100 kJ
Pantothenic acid	calcium pantothenate dexpanthenol	0.24 mg pantothenic acid	0.36 mg pantothenic acid
Calcium	calcium carbonate calcium chloride calcium citrate calcium gluconate calcium glycerophosphate calcium hydroxide calcium lactate calcium oxide calcium phosphate, dibasic calcium phosphate, monobasic calcium phosphate, tribasic calcium sulphate	17 mg calcium	34 mg calcium
Chloride	calcium chloride magnesium chloride potassium chloride sodium chloride	14 mg chloride	22 mg chloride
Copper	copper gluconate cupric sulphate	23 µg copper	30 µg copper

Column 1 Substance	Column 2 Permitted Forms	Column 3 Minimum Amount per 100 kJ	Column 4 Maximum Amount per 100 kJ
Iron	ferric ammonium citrate ferric pyrophosphate ferrous citrate ferrous fumarate ferrous gluconate ferrous lactate ferrous succinate ferrous sulphate	0.01 mg iron	0.4 mg iron
Iodine	potassium iodate potassium iodide sodium iodide	2.4 µg iodine	11 µg iodine
Magnesium	magnesium carbonate magnesium chloride magnesium gluconate magnesium oxide magnesium phosphate, dibasic magnesium phosphate, tribasic magnesium sulphate	1.5 mg magnesium	3.6 mg magnesium
Manganese	manganese chloride manganese gluconate manganese sulphate	1.2 µg manganese	1.8 µg manganese

Column 1 Substance	Column 2 Permitted Forms	Column 3 Minimum Amount per 100 kJ	Column 4 Maximum Amount per 100 kJ
Potassium	potassium bicarbonate potassium carbonate potassium chloride potassium citrate potassium glycerophosphate potassium gluconate potassium hydroxide potassium phosphate, dibasic potassium phosphate, monobasic potassium phosphate, tribasic	20 mg potassium	36 mg potassium
Phosphorus	calcium glycerophosphate calcium phosphate, dibasic calcium phosphate, monobasic calcium phosphate, tribasic magnesium phosphate, dibasic potassium phosphate, dibasic potassium phosphate, monobasic	12 mg phosphorus	22 mg phosphorus

Column 1 Substance	Column 2 Permitted Forms	Column 3 Minimum Amount per 100 kJ	Column 4 Maximum Amount per 100 kJ
Phosphorus continued	potassium phosphate, tribasic sodium phosphate, dibasic sodium phosphate, monobasic sodium phosphate, tribasic		
Sodium	sodium bicarbonate sodium carbonate sodium chloride sodium citrate sodium gluconate sodium hydroxide sodium iodide sodium lactate sodium phosphate, dibasic sodium phosphate, monobasic sodium phosphate, tribasic sodium sulphate sodium tartrate	9.1 mg sodium	14 mg sodium
Selenium	sodium selenite seleno methionine	0.53 µg selenium	0.89 µg selenium

Column 1 Substance	Column 2 Permitted Forms	Column 3 Minimum Amount per 100 kJ	Column 4 Maximum Amount per 100 kJ
Zinc	zinc acetate zinc chloride zinc gluconate zinc oxide zinc sulphate	0.13 mg zinc	0.36 mg zinc

SCHEDULE 5

FEEDING GUIDES

TABLE 1

INFANT FORMULA POWDER OR INFANT FORMULA LIQUID CONCENTRATE

FEEDING GUIDE			
		To prepare one feed	
Age	Number of feeds per day	Cooled, boiled water in mL	Level scoops of powder, or number of sachets, or volume of liquid concentrate in mL (as the case may be)
0 - 2 weeks			
2 - 4 weeks			
1 - 2 months			
2 - 3 months			
3 - 4 months			
4 - 5 months			
5 - 6 months			
6-12 months			

TABLE 2

READY-TO-FEED INFANT FORMULA

FEEDING GUIDE		
Age	Number of feeds per day	Volume of feed in mL
0 - 2 weeks		
2 - 4 weeks		
1 - 2 months		
2 - 3 months		
3 - 4 months		
4 - 5 months		
5 - 6 months		
6 - 12 months		

TABLE 3

FOLLOW-ON INFANT FORMULA POWDER
OR
LIQUID CONCENTRATE

FEEDING GUIDE			
		To prepare one feed	
Age	Number of feeds per day	Cooled boiled water in mL	Level scoops of powder, or number of sachets, or volume of liquid concentrate in mL (as the case may be)
over 6 months			

TABLE 4

READY-TO-FEED FOLLOW-ON INFANT FORMULA

FEEDING GUIDE		
Age	Number of feeds per day	Volume of feed in mL
over 6 months		

~~46~~ 45

TABLE 5

PRE-TERM INFANT FORMULA

FEEDING GUIDE				
Weight of infant in grams	Total daily quantity of cooled boiled water in mL	Total daily quantity of powder in grams	Total daily level scoops of powder, or number of sachets, or volume of liquid concentrate in mL (as the case may be)	Total daily quantity of prepared formula in mL
1000 - 1200				
1200 - 1400				
1400 - 1600				
1600 - 1800				
1800 - 2000				
2000 - 2200				
2200 - 2400				
2400 - 2600				

~~47~~ 46

2/8/95

Changes to P93 Drafting

clause 1	delete "fraction" from the definitions for both partially and extensively hydrolysed protein, and change from italics to normal
	delete the second definition of partially hydrolysed (p4)
clause 7(2)	"specified" misspelt
clause 14	change (4) to (3) and for (3) insert:
	"The statement 'Prepare only one bottle at a time.' in paragraph (1)(a) of this clause is not required for pre-term human milk substitutes unless a feeding table giving quantities per bottle is included in the label."
	(or words to that effect)
clause 17	add "in terms of 21(1)(a)." (or words to that effect)
clause 18	para (f)(i), "substitute" is misspelt.
	Add "or a lactose free or low lactose human milk substitute."
clause 21	(1)(b)(i) cows' (apostrophe missing)
clause 22	the entry in the table to para 22(d) for α-linolenic acid (18:3) should be 2 not 1
clause 30	(1)(b)(i) cows' (apostrophe missing)
clause 31	the entry in the table to para 31(d) for α-linolenic acid (18:3) should be 2 not 1
clause 35	(2)(a) 2.4 g/L **not** /kg
	(2)(b) 1.9 g/L **not** 1.8 g/kg
clause 37	(2) "containing" is misspelt
clause 40	the entry in the table to para 40(c) for α-linolenic acid (18:3) should be 2 not 1
clause 41	(d) delete "or gelatinised" insert (e) "gelatinised starch" (e) becomes (f) (f) becomes (g)

clause 43 renumber (43) to (44) and insert sub heading "**Other permitted additions**" after clause 42, followed by

"43. A proximate-modified human milk substitute which is protein modified may contain -

25 g/L in total of acetylated distarch phosphate, distarch phosphate and phosphated starch phosphate."

new clause (44), formerly (43) In (1)(a) the word "SUPERVISION" has been misspelt

In (2)(b) amend as follows:

(b) the nutrient modifications which apply to the food-

(i) extensively hydrolysed protein
(ii) partially hydrolysed protein
(iii) amino acid based
(iv) carbohydrate modified
(v) fat modified

Delete (3)

Schedule 5 Feeding Tables

In Tables 1,2,3 &4, replace "6-12 months" with 2 separate entries

"6-9 months"

"9-12 months".

DRAFT GAZETTE NOTICE

NOTICE PURSUANT TO SECTION 24

Infant Formula (P93)

The National Food Authority has prepared a proposal (P93) to amend the Australian Food Standards Code to revise the provisions for human milk substitutes intended for normal infants and to include provisions for those with special nutritional requirements.

The Authority has completed a full assessment of the proposal, has prepared draft variations to Standards R7, A1, A11 and A12 - and will now conduct an inquiry to consider the draft variation.

To assist in this process, the Authority invites written submissions on matters relevant to the purpose of the inquiry.

EXPLANATORY NOTES - DRAFT

PROPOSAL P93

REVIEW OF STANDARD R7 - INFANT FORMULA

In February 1993 the National Food Authority prepared a proposal (P93) to review Standard R7 - Infant Formula. This proposal was one outcome of investigations into the regulation of special infant formula. Seventeen submissions were received in response to the Authority's call for public comment. During full assessment, an expert panel was established to advise on specific compositional aspects of the revision. Members of the Panel included a paediatrician/neonatologist, a paediatric nutritionist/dietitian, a representative from the infant formula industry, a biochemist (chief hospital scientist) heading an infant nutrition research group and a specialist in paediatric dentistry.

The draft revised Standard R7 has been named "Human Milk Substitutes", because the scope of the draft Standard will cover a variety of human milk substitutes, of which infant formula is but one category. The draft revised Standard is intended to make provision for all human milk substitutes which are nutritionally complete. It is divided into three parts:

- general provisions, including definitions;
- human milk substitutes for normal use (infant and follow-on infant formula); and
- human milk substitutes for special dietary use (pre-term, lactose free and low lactose, and proximate-modified).

Lactose reduced, lactose free and proximate-modified human milk substitutes are included because they are essentially similar to infant formula, with modifications to the protein and/or carbohydrate and/or fat content, for infants with special dietary requirements. In the draft revised Standard all the compositional and labelling requirements are grouped together for each category of human milk substitute.

Where possible, information in the draft Standard has been tabulated, to assist comprehension. For example, some compositional information previously distributed throughout the existing Standard has been compiled into tabular form in Schedules 3 and 4.

Definitions

The definition of "infant formula" in the current standard has been revised, for improved clarity of meaning and to remove ambiguity; other definitions included in the revised Standard serve to categorise the different types of human milk substitute, or to clarify the meaning of terms used within the Standard.

Composition

The composition of infant formula was determined according to the following rationale:

i) The formula should provide nutrients in amounts that support normal growth and development and ideally result in formula-fed infants having biochemically equivalent plasma and tissue levels to breast-fed infants; and

ii) the safety and tolerance of all substances added to formulae must have been clearly demonstrated in human clinical studies.

The draft revised Standard requires that essential nutrients (which include all those for which there is an Australian Recommended Dietary Intake (RDI), must be present within specified ranges, and other so-called "optional" ingredients are permitted to be present up to specified maximum levels.

Addition of the following nucleotides, cytidine (CMP), adenosine (AMP), guanosine (GMP), inosine (IMP) and uridine (UMP) has been permitted in the draft revised Standard, but in a recent report on nucleotides, the authors suggested that IMP may not normally be present in human milk, and that it may be a sample-preparation artefact. If further evidence substantiates this claim, the Authority would review its decision to permit the addition of IMP to infant formula. Public comment is particularly sought on this issue.

Protein, lipid and carbohydrate requirements are specified for each category of human milk substitute, whilst those for vitamins, minerals and electrolytes are given in Schedule 3 (infant formula) and Schedule 4 (pre-term human milk substitute).

The amino acid profile, rather than the casein-to-whey ratio of formula, was considered as the prime indicator of protein quality. Protein quality is to be determined by calculation of the amino acid score. this is consistent with the requirement of the EC Directive on Infant Formula. The reference amino acid profile, that of human milk, is provided in Schedule 1, and is based on a FAO/WHO reference. No accepted Australian reference for the amino acid composition of human milk was available.

The requirements for lipids in the draft revised Standard are more prescriptive than in the current Standard, so that the lipid profile is aligned more closely with that of human milk. These changes reflect recent research findings in this area. Medium chain triglycerides (MCT) are prohibited on the basis that they are not normally present in human milk. In addition, the long term effects of infants consuming a high percentage of saturated fats is unknown and there is no convincing evidence that the inclusion of MCT in human milk substitutes has conferred any benefit to infants.

A general prohibition on gluten is included in the draft revised Standard because permission has been given to use precooked and gelatinised starch as a source of carbohydrate in some human milk substitutes.

The range of permitted forms of vitamins, minerals and electrolytes in the draft revised Standard has been extended for the purpose of harmonisation. Selenium is required to be present (on the basis that it has an Australian RDI), whereas previously it was not permitted to be added. Although selenium is scheduled in the Standard for the Uniform Scheduling of Drugs and Poisons, this does not prohibit its use in foods, as long as specific permission is given.

Compositional requirements were established on the basis of the consultants' recommendations. There are variations from the levels prescribed in the current Standard for infant formula, and additional maxima have been introduced on the basis that infant formula is designed to be the sole source of nourishment for infants and therefore it is prudent to be cautious when setting compositional parameters. Reasons for setting maxima include the following:

- the toxicity of some nutrients;
- it is likely that the effects of a high dose of a particular nutrient on a group of infants has not been exhaustively tested; and
- to take account of synergistic and antagonistic nutrient interactions (e.g. the inhibiting effect of zinc on copper absorption).

The main considerations in setting nutrient levels were based on:

- as far as possible, covering formulae already on the market in Australia;
- as far as possible, harmonising with the USFDA, the EU and Codex; and
- research findings reported in the current literature, especially recommendations from a 1988 symposium in Iowa (USA) on "Upper Limits of Nutrients in Infant Formulas".

Labelling

Most of the labelling provisions of the current Standard have been retained. Those which apply to provisions of the WHO Code have been included, while

others have been modified to improve clarity. It was considered inappropriate to remove any of the current restrictions on labelling or advertising. The changes made to mixing and preparation instructions and feeding table requirements were intended to make them either more comprehensive or easier to understand or to remove ambiguity. The exemption for iron claims on labels was removed because of changes in the compositional requirements for iron.

In the draft revised Standard, the declaration of nutrient content in the Nutrition Information Table (NIT) is the minimum amount of that nutrient present in 100 mL of the human milk substitute. Currently there is no such specification, and some confusion exists as to whether the claim relates to the actual, average or minimum amount present. With optional ingredients, it is required that at least the minimum level of the range specified for each must be present in order for an entry to be permitted in the NIT.

A warning statement:

'NOT SUITABLE FOR INFANTS WITH GALACTOSEMIA'

is required on the label of milk-based human milk substitutes which claim to be "lactose free". This has been included on the advice of health professionals, because of the extreme sensitivity of these infants to very low levels of lactose

The statement:

'SUITABLE ONLY FOR PRE-TERM INFANTS UNDER SPECIALIST MEDICAL SUPERVISION'

is required on the label of pre-term human milk substitutes. This recognises the need to maintain strict control on the availability and promotion of these products to avoid adverse effects which could result from their inappropriate use.

The statement:

'THIS PRODUCT HAS BEEN SPECIFICALLY FORMULATED FOR INFANTS WITH SPECIAL DIETARY NEEDS AND SHOULD BE USED UNDER MEDICAL SUPERVISION'

is required on the label of proximate-modified human milk substitutes, to discourage the use of these products by healthy infants for whom standard infant formula would be more appropriate.

The requirement that proximate-modified human milk substitutes which are protein modified must state, as part of the appropriate designation, the nature of the modification, i.e. extensively hydrolysed, partially hydrolysed or amino acid based is intended to ensure that those concerned about allergens have sufficient information about the product to enable them to make an informed choice.

There has been no provision made for a claim of "hypoallergenic" in relation to protein-modified formulae. The reason for this is the apparent lack of a suitable criterion to be used as a basis for the claim, such as a test which could be applied. The Authority would appreciate advice on this issue.

Contaminants

Upper limits for aluminium and fluoride have been included in draft revised Standard R7. In each case, the upper limit for soy-based formulae is higher than that for milk-based formula because, in general, the soy-based products have significantly higher aluminium and fluoride levels. Most formulae on the market in Australia have aluminium and fluoride levels below the prescribed limits.

Fluoride

A maximum level for fluoride was introduced to minimise the risks of formula-fed infants developing fluorosis. Whilst it is recognised that the water used to reconstitute formula contributes a significant amount of the total fluoride, it is nevertheless considered desirable that manufacturers should have to monitor the fluoride levels of their products. In a letter to the NFA in 1994, the NHMRC suggested that Standard R7 be amended to control the amount of fluoride in infant formula and also to require the level of fluoride to be shown in the NIT.

Aluminium

A maximum level for aluminium was introduced because of concerns that infants, especially preterm and the very young, may be at particular risk of aluminium toxicity as a consequence of their immature gastro-intestinal tracts and limited ability to excrete the element through normal renal clearance. Recommendations have been made from paediatric bodies and researchers in Australia, the USA, Canada and the UK to keep aluminium levels to a minimum.

Additives

Permissions for additives are the same in the draft revised Standard as in the current Standard R7, with the following exceptions:

- the level of mono- and diglycerides of fat-forming fatty acids has been halved, consistent with the basis for revision of the lipid profile;

- additional tocopherols are not permitted as antioxidants because the maximum permitted level of d-α-tocopherol as a source of vitamin E is sufficiently high to cover nutritional and antioxidant requirements; and

- carrageenan is no longer permitted. Permission has been withdrawn on the basis of concerns over possible immunological consequences following absorption of carrageenan, especially from the immature gut. The ministry

for Agriculture, Fisheries and Food (United Kingdom) in 1992, and the European Scientific Committee for Food, in 1994, recommended that carrageenan should not be permitted in infant formula.

Microbiological Requirements

These have remained unchanged in the draft revised Standard. Based on the positive changes that have occurred in the dairy industry, there is no discernible need for change.

Concerns over Soy Formulae

Since June 1994, the Authority has been aware of reports from New Zealand, of certain alleged hazards associated with the consumption by infants of soy-based formula. These concerns relate principally to the levels of certain phytoestrogens which infants are receiving, at a time when significant hormonally-driven developmental changes are still occurring. It is believed that the phytoestrogens could cause oestrogenic effects such as disturbances in reproductive functions, development of sex organs, sexual behavioural patterns and the predisposition of certain tissues to the development of cancers.

The Authority is seeking comment on the issue, particularly advice as to whether any additional measures, such as warning statements on soy-based formulae, should be considered.

Consequential Amendments

Requiring the addition of selenium and extending the range of permitted forms of certain nutrients have necessitated consequential amendments to other Standards as follows:

- to Standard A11, to provide specifications which permit L-selenomethionine to be used as a source of selenium and to ensure that there are references to specifications for all permitted substances;

- to Standard A1, to list new additives together with their food additive code numbers in the appropriate schedule; and

- to Standard A12, to ensure that ranges specified for "selenium" in Standard R7 are the only ones applicable to human milk substitutes.

A further consequential amendment has been made to Standard A1, to regulate claims about the suitability of foods (other than those complying with Standard R7) as a sole or principal source of nutrition for infants.

WORLD TRADE ORGANISATION (WTO) NOTIFICATION

This matter may be notified to the WTO as either a Sanitary and Phytosanitary Measures (SPS) notification or a Technical Barriers to Trade (TBT) notification

to enable other members of the WTO to assess this matter and make comments on it.

INVITATION FOR PUBLIC SUBMISSIONS

The Authority has completed a full assessment of the proposal, prepared a new draft standard to the Food Standards Code and will now conduct an inquiry to consider the new draft standard.

Written submissions containing technical or other relevant information which will assist the Authority in undertaking the inquiry are invited from interested individuals and organisations. Where possible, technical information should be presented in sufficient detail to allow independent scientific assessment.

The processes of the Authority are open to public scrutiny, and any submissions received will ordinarily be placed on the public register of the Authority and made available for inspection. If you wish any confidential information contained in a submission to remain confidential to the Authority, you should clearly identify the sensitive information and provide justification for treating it in confidence. The *National Food Authority Act 1991* requires the Authority to treat in confidence trade secrets relating to food and any other information relating to food, the commercial value of which would be or could reasonably be expected to be, destroyed or diminished by disclosure.

Submissions should be received by the Authority by 10 November 1995.

All correspondence and submissions on this matter should quote the full title, Proposal No. P93, and be addressed to:

Standards Liaison Officer
National Food Authority
Box 7186
Canberra Mail Centre ACT 2610

Tel (06) 271 2219