codex alimentarius commission

FOOD AND AGRICULTURE ORGANIZATION OF THE UNITED NATIONS

WORLD HEALTH ORGANIZATION

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Agenda Item 6 **CX/NFSDU 03/6-Add.2**
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JOINT FAO/WHO FOOD STANDARDS PROGRAMME

CODEX COMMITTEE ON NUTRITION AND FOODS FOR SPECIAL DIETARY USES
Twenty-fifth Session
Bonn, Germany, 3- 7 November 2003

PROPOSED DRAFT REVISED STANDARD FOR INFANT FORMULA

Working Group on Essential Composition of Infant Formula (Section 3.1), Bonn, 1 November 2003

INTRODUCTION

The Codex Committee on Nutrition and Foods for Special Dietary Uses (CCNFSDU) agreed in 1995 that a revision of the Standard for Infant Formula was necessary. After approval by the Codex Alimentarius Commission, a Proposed Draft Revised Standard for Infant Formula was presented to the 20th session of the CCNFSDU in 1996. This proposal has been discussed during all subsequent sessions in 1998, 2000, 2001 and 2002 without being advanced beyond step 4 of the acceptance procedure.

Because discussion was limited by time constraints, particularly of section 3.1 Essential Composition, a first electronic working group under the leadership of the United States was instituted in 2000 and prepared a detailed revised proposal for section 3.1 for the 23rd session in 2001. Again, there was no time for discussion and the paper was circulated for comments which were the basis for a working group meeting immediately prior to the 24th session 2002. The report of that working group was again not discussed in detail during the session and was therefore circulated for comments as CL 2003/4-NFSDU. Another working group coordinated by the United States and Germany (other participants France, Netherlands, Norway, Tanzania, EC, ENCA, IBFAN, ISDI, and CIAA) was established to work electronically between the 24th and the 25th session and produce a draft proposal for section 3.1, which would be discussed during the meeting of a working group to take place before the 25th session, on 1 November 2003.

The attached paper is the product of that electronic working group and presented to the participants to serve as a basis for the discussion.

The paper has two parts:

Annex I deals with the General Principles for Establishing Minimum and Maximum Values for the Essential Composition of Infant Formula. When the proposed text is accepted by the participants of the working group, it will be presented to the plenum of the CCNFSDU, which will have to decide on their future fate.

Annex II contains the proposals and comments of members of the electronic working group and of CCNFSDU on section 3.1 and the contents of energy, protein, fat, carbohydrates, vitamins, minerals and choline. The working group will have to decide if the presented data are of sufficient scientific strength to be used for a revised proposal for section 3.1.

The report on the discussions and decisions of the working group will be presented as a Conference Room Document (CRD 1) to the plenary.

The coordinators of the electronic working group wish to express their concern on the delay in the revision of the Standard for Infant Formula which dates from 1981 with only minor revisions since that time, and they wish to stress the need for progress in updating the Standard in accordance with current science.

ANNEX I

REVISED GENERAL PRINCIPLES FOR ESTABLISHING MINIMUM AND MAXIMUM VALUES FOR THE ESSENTIAL COMPOSITION OF INFANT FORMULA (CL 2003/4-NFSDU)	**General Principles for Establishing Minimum and Maximum Values for the Essential Composition of Infant Formula** *Text as proposed by the electronic Working Group. (Changes are indicated).*
Section 1	**The Working Group proposes to include the finalised "General Principles" into the Revised Standard for Infant Formula as an annex, to clearly identify the basis for establishing essential composition in order to document past decision-making, guide future decision-making, and support the goal of transparency.**
1. *The goal of establishing minimum and maximum values is to provide safe and nutritionally adequate infant formula products that meet the normal nutritional requirements of healthy infants.*	**1.** *The goal of establishing minimum and maximum values is to provide safe and nutritionally adequate infant formula products that meet the normal nutritional requirements of infants.* Justification: This wording corresponds to the definition for "infant formula" in the International Code of Marketing of Breast-milk Substitutes. **Comments from outside the WG were received from Australia and CRN (CRD 2):** Australia proposes to combine No 1 and No 3: *The goal of establishing minimum and maximum values for those substances that are essential to infant formula, is to provide safe and nutritionally adequate infant formula that meets the normal nutritional requirements of healthy infants.* CRN proposes to delete "nutritionally adequate" and "normal"
2. *A nutritional adequate infant formula product will promote growth and development* **consistent with science based standards** *and meet the nutritional requirements of infants when fed as a sole source of nutrition* **during the first months of life up to introduction of appropriate complementary feeding.**	**2.** *A nutritionally adequate infant formula will promote growth and development consistent with science based standards and meet the nutritional requirements of infants when fed as a sole source of nutrition during the first months of life up to* ***the*** *introduction of appropriate complementary feeding.* Justification: There is little scientific evidence for the nutritional adequacy of exclusive infant formula feeding during the first six months of life. Therefore, no indication for the duration of infant formula feeding should be given. WHO has proposed a new wording for the definition of infant formula in section 2.1.1 of the Revised Standard for Infant Formula (CX/NFSDU 03/6), which even leaves out "the first months of life" : *Infant formula means a breast-milk substitute specially manufactured to satisfy, by itself, the nutritional requirements of infants up to the introduction of appropriate complementary feeding.* **Comments from outside the WG were received from CRN (CRD 2):** *A nutritionally adequate infant formula will promote growth and development consistent with the growth and development of healthy breast-fed or formula-fed infants when fed as the sole source of nutrition to at least the first 4-6 months of life up to introduction of appropriate complementary feeding*

[3. *The values to be established are for those substances that are essential to infant formula.*]	**3.** *The values to be established are for those **nutrients** that are essential to infant formula.* Justification: No.3 is not covered already by No.2 and No.4 and ,therefore, should be retained. **Comments from outside the WG were received from Australia (**see under No. 1) **and from CRN (CRD 2):** CRN proposes the same change as the WG.
4. *These values are based on an evaluation,* **in particular of the scientific evidence of the amounts needed to meet the nutritional requirements of infants, considering relevant human infant studies and the composition of breast-milk.**	**4.** *These values are based on an evaluation, in particular of the scientific evidence of the amounts needed to meet the nutritional requirements of infants, considering relevant human infant studies and the composition of breast-milk.*
5. **In addition to the principles set out in No. 4, when setting minimum and maximum values, consideration will also be given to evidence of adverse health effects.**	**5.** *In addition to the principles set out in No. 4, when setting minimum and maximum values, consideration will also be given to evidence of adverse health effects.* **Comments from outside the WG were received from Australia and New Zealand (CRD 2):** Both support the setting for maximum values only for those nutrients with evidence of adverse effects or the potential of an increased renal solute load. For nutrients for which no such evidence exists non-mandatory guideline maximum values for manufacturers are considered acceptable. **[** ***Maximum values for nutrients with a documented risk of adverse health effects will be determined using a science-based risk assessment approach.. Maximum values for those nutrients without evidence of adverse effects serve as guidance levels for manufacturers. The approach to setting maximum levels for guidance purposes shall be made transparent and comprehensible.*** **]**
6. When establishing minimum and maximum amounts, the following should be taken into account:	**6.** *When establishing minimum and maximum amounts, the following should be taken into account:*
a) bioavailability, processing losses and shelf-life stability from the ingredients and formula matrix.	**a)** *bioavailability, processing losses and shelf-life stability from the ingredients and formula matrix,* **Comments from outside the WG were received from Australia (CRD 2):** Australia proposes to add "added nutrients" between "ingredients" and "and formula matrix".
b) preparations according to directions for use.	**b)** *preparation according to directions for use,*
c) total levels of a nutrient in infant formula, taking into account both naturally occurring nutrients in the ingredients and added nutrients.	**c)** *total levels of a nutrient in infant formula, taking into account both naturally occurring nutrients in the ingredients and added nutrients,* **Comments from outside the WG were received from CRN (CRD 2):** CRN proposes to add "recognizing that bioavailability may differ for these"

[*d) the inherent variability in ingredients* **[***and in water***]** *that may be added to the infant formula product before of after it is purchased.***]**	**d)** *the inherent variability* ***of nutrients*** *in ingredients and in water that may be added to the infant formula* ***during manufacture*** **Comments from outside the WG were received from Australia, Czech Republic, Denmark, New Zealand and CRN (CRD 2):** They all agree that the water added after manufacture to powdered infant formula is not under the control of the manufacturer but falls under the responsibility of governments.
[*e) overages for certain nutrients at appropriate levels to ensure that minimum levels are met throughout the expected shelf-life of the formula.***]**	**[e)** *overages for certain nutrients at appropriate levels to ensure that minimum levels are met throughout the expected shelf-life of the formula* ***but shall not exceed maximum levels*****].** Justification: When both minimum and maximum values for all essential nutrients are established the manufacturer is responsible for a dosage that guarantees the minimum value throughout the shelf-life and that does not exceed the maximum value. Therefore, the declared nutrient content may differ to a certain degree from the analysed content **Comments from outside the WG were received from Australia (CRD 2):** Australia proposes to delete this principle here and to link the minimum levels mentioned in section 3.1.2 of the Standard to the shelf-life .
[*7. In establishing minimum or maximum amounts of nutrients per 100 ml (or per 100 kcal) of infant formula based on consideration of reference nutrient values expressed as units per daily intake or per kilogram of body weight, the following assumptions will be used:*	**7.** *In establishing minimum or maximum amounts of nutrients per 100 ml (or per 100 kcal) of infant formula based on consideration of reference nutrient values expressed as units per daily intake or per kilogram of body weight, the following assumptions will be used:*
a) The mean intake of prepared formula for infants from birth to six months of age is 750 ml per day. This is based on the following assumptions:	**a)** *The mean intake of prepared formula for infants from birth to six months of age is 750 ml per day. This is based on the following assumptions:*
i) a representative body weight for an infant over this period would be 5 kg and a representative caloric intake would be 500 kcal per day (or 100 kcal/kg/day over the first six months); and	***i)*** *a representative body weight for an infant over this period would be 5 kg and a representative caloric intake would be 500 kcal per day (or 100 kcal/kg/day over the first six months); and*
ii) prepared formulas provide about 67 kcal/100 ml.	***ii)*** *prepared formulas provide about 67 kcal/100 ml.*

*Modifications of the approach may be needed when there is justification for deviating from one or more of these assumptions with regard to the specific formula product or specific infant population group.***]**	*Modifications of the approach may be needed when there is justification for deviating from one or more of these assumptions with regard to the specific formula product or specific infant population group* Justification: The proposed values for a daily volume intake, for a reference body weight over the period of the first half year of life and for a daily energy intake as well as for the representative energy value of an infant formula are not meant to be considered as representing actual means of data, particularly not of data on body weight and energy requirement throughout this period. The proposed values allow a simple calculation to convert nutrient reference values, given as amounts per daily intake or per daily intake per kg body-weight, into amounts per energy value or per volume of an infant formula. The choice of a relatively low body weight throughout the first six months of life (which is lower than the reference body weight for boys at the age of 2 months (5.3 kg) and than the reference body weight of girls at the age of 3 months (5.5 kg)) together with the choice of a relatively high energy intake per kg of body-weight (which is higher than the estimated energy requirement of boys and girls over the age of 2 months (95 kcal/kg/day) according to the Institute of Medicine's Dietary Reference Intakes (2002) results in micro-nutrient intakes that correspond to 87 % (girls at the age of 1 month) to 140 % (boys at the age of 6 months) of the daily nutrient reference value for infants 0-6 months of age. The practicality of this simplified approach can, therefore, be considered as proven for micro-nutrients (vitamins and minerals). The suggestion, made by **Norway** and **CRN,** to differentiate between infant formula intended for infants between 0-2 months and 2-6 months of age and to base the calculations on the age-related reference values for body weight for boys and girls and the gender-specific energy requirements, appears, in comparison, too complicated for practical purposes. If it is demonstrated that age-related requirements for e.g. iron and salt are not compatible with the proposed approach, a modification can be introduced for these nutrients.

ANNEX II

REVISED PROPOSAL FOR SECTION 3.1 OF THE PROPOSED DRAFT REVISED STANDARD FOR INFANT FORMULA (CL 2003/4-NFSDU)	**Proposal of the Electronic Working Group for Section 3.1 of the Standard for Infant Formula** ***Proposed changes appear in bold***
3.1 Essential Composition	
3.1.1 Infant formula is a product based on milk of cows or other animals and/or other edible constituents of animal, including fish, or plant origin, which have been proved to be suitable for infant feeding.	**3.1.1** *Infant formula is a product based on milk of cows or other animals and/or other edible* ***ingredients*** *which have been proved to be suitable for infant feeding.* Justification: This wording allows a wide choice of ingredients from local nutritional resources provided their suitability for use in infant feeding has been proven.
3.1.2 Infant formula [**prepared ready for consumption in accordance with instructions of the manufacturer**] shall contain per 100 kcal (or 100 kilojoules) the **following nutrients within the following minimum and maximum levels**:	**3.1.2.1** *Infant formula prepared ready for consumption in accordance with instructions of the manufacturer shall contain* ***per 100 ml not less than 60 kcal (250 kJ) and not more than 75 kcal (315 kJ) of energy.*** **3.1.2.2** *Infant formula prepared ready for consumption shall contain per 100 kcal (100 kJ) the following nutrients within the following minimum and maximum levels.* ***The general principles for establishing these levels are identified in Annex [#] of this standard.*** Justification: The separation of 3.1.2 into two subsections, 3.1.2.1 covering energy and 3.1.2.2 covering the nutrients with a revised sequence from a) protein, b) fat and fatty acids, c) carbohydrates, d) vitamins, e) minerals to f) choline appears to be more logical.
Energy content (- no changes proposed by the working group in 2002 -)	
Protein (- no changes proposed by the working group in 2002) (i) Protein content = nitrogen content x 6.38 for cow's milk proteins and protein partial hydrolysates. Protein content = nitrogen content x 6.25 for soya protein isolates and protein partial hydrolysates. The "chemical index" shall mean the lowest of the ratios between the quantity of each essential amino acid of the test protein and the quantity of each corresponding amino acid of the reference protein (breast-milk, as defined in Annex 1). (ii) The product shall contain protein at a level of not less than 1.8 g/100 kcal (0.45 g/100 kJ) and not more than 3 g/100 kcal (0.7 g/100 kJ). For an equal energy value, the formula must contain an available quantity of each essential and semi-essential amino acid at least equal to that contained in the reference protein (breast-milk, as definded in Annex 1); nevertheless, for calculation purposes, the concentration of methionine and cystine may be added together. [The minimum value set for quality and the maximum for quantity of the protein may be modified by national authorities according to their own regulations and/or	**The WG is unable to propose a revision of the section on protein.** Some valuable comments of members of the WG are included and comments of other delegations can be found in CRD 2 (Australia, Czech Republic, Denmark, Poland) and CX/NFSDU 03/6 (Brazil, Spain, CRN) **Norway**: The quality and quantity of protein in infant formula should be as close as possible to the protein content of human milk. The ratio whey protein to casein should be the same as in breast-milk (1.5). The quality of the protein should be so good that the addition of essential amino acids is unnecessary, except for taurine which should be added to achieve the same content as in breast-milk (27-67μmol/dL). **ESPGHAN**: For all protein sources the protein content should be calculated by multiplying nitrogen content x 6.25, including hydrolysed proteins. The range of protein content for infant formula based on intact cow's milk protein should be 1.8-3.0 g/100 kcal. For infant formula based on soy proteins or on hydrolysed proteins, the minimum protein content should be 2.25 g/100 kcal. **ISDI**: change to read the present (i): "Protein content = nitrogen content x 6.38 for cow's milk proteins and **their** partial hydrolysates. Protein content = nitrogen content x 6.25 for **other** proteins and **their** partial hydrolysates".

local conditions]. (iii) Isolated amino acids may be added to Infant Formula only to improve its nutritional value for infants. Essential amino acids may be added to improve protein quality, only in amounts necessary for that purpose. Only natural L-forms of amino acids shall be used.	Delete the present definition of the "chemical index" in (i), because the chemical index is not mentioned again in the standard. Change to read (ii) para 2: "For an equal energy value, the formula must contain an available quantity **of** each essential and semi-essential amino acid at least equal to that contained in the reference protein (breast-milk, as defined in Annex 1); nevertheless, for calculation purposes, the concentrations of methionine and cystine may be added together, **as well as phenylalanine and tyrosine".** Delete the sentence in square brackets of (ii), para 3, because the nutritional quality of the protein must not be endangered. The result could also be barriers to trade. Delete the word "natural" in the third sentence of (iii), para 1, since the L-forms are the natural forms of amino acids.
Fat and Fatty Acids (- no changes proposed by the working group in 2002 -) The product shall contain: - linoleic acid (in the form of glycerides) at a level of not less than 300 mg/100 kcal (or 70 mg/100 kJ) and not more than 1200 mg/100 kcal (285 mg/100 kJ): - fat at a level not less than 4.4 g/100 kcal (1.05 g/100 kJ) and not more than 6.5 g/100 kcal (1.5 g/100 kJ); - the alpha-linolenic acid content shall not be less than 50 mg/100 kcal (12 mg/100 kJ); - the linoleic/alpha-linolenic acid ratio shall not be less than 5 nor greater than 15; - the trans fatty acid content shall not exceed 4% of the total fat content; - the erucic acid content shall not exceed 1% of the total fat content.	**The WG is unable to propose a revision of the section on Fat and Fatty Acids.** Some valuable comments of members of the WG are included and comments of other delegations can be found in CRD 2 (Czech Republic, Denmark) and CX/NFSDU 03/6 (Brazil, Malaysia, New Zealand, CRN). **Norway**: Upper and lower levels of cholesterol in infant formula should be discussed, because in breast-milk cholesterol is present within a range of 9-41 mg/100ml. The level of trans-fatty acids should be lower than 2%. **ESPGHAN**: The total fat content should be in the range of 4.4-6.0 g/100 kcal. Linoleic acid should contribute 0.5-1.2 g/100 kcal, and alpha-linolenic acid at least 100 mg/100 kcal. The ratio of linoleic acid to alpha-linolenic acid should be in the range of 5-15:1. If docosahexaenoic acid (DHA) (at least 0.2% of fatty acids) and arachidonic acid (AA) are added, the ratio of linoleic acid to alpha-linolenic acid should be in the range of 5-20:1 **ISDI**: There is no need to set a maximum level for linoleic acid, because no adverse effects on e.g. the synthesis of long-chain polyunsaturated fatty acids have been found. A minimum level of 300 mg/100 kcal (70 mg/100 kJ) is supported. The linoleic/alpha-linolenic acid should not be less than **6** nor greater than **16.** The optional addition of long-chain polyunsaturated fatty acids (LCPUFA) not exceeding 1% of total fatty acids content for ω-3-LCP and 2% of total fatty acids content for ω-6-LCP is supported . **ENCA**: AA and DHA should be added to all infant formulae as a global standard should give the best intellectual development potential to all infants. **ESPGHAN**: Trans-fatty acids should not exceed 3% and erucic acid should not exceed 1% of total fatty acids. **ENCA, IBFAN**: Change to read "The trans-fatty acid **level of liquid formula** shall not exceed **2% and the trans-fatty acid level of powdered formula shall not exceed 1.5%"** and "**No erucic acid should be added to infant formula". (Note:** 0.5 to 1% of total fatty acids are erucic acid in breast- milk). **ISDI**: change to read "The trans-fatty acid content shall not exceed **5%** of the total fat content**; and the use of partially hydrogenated oils in infant formula is prohibited".** Because the trans-fatty acid content of cow's milk fat is more variable than previously thought

	and can be higher than 5%, most of which is trans-oleic acid. An upper limit of 4% would restrict unnecessarily the use of milk fat. No adverse effects of trans-fatty acid consumption are expected when the intake of essential fatty acids is appropriate. Human milk can contain up to 17% trans-fatty acids. **ENCA**: No peanut oil should be added because it can still contain substances which can trigger a peanut allergy.
Carbohydrates (- no changes proposed by the working group in 2002 -) The product shall contain carbohydrates at a level of not less than 7 g/100 kcal (1.7 g/100 kJ) and not more than 14 g/100 kcal (3.4 g/100 kJ).	**The WG is unable to propose a revision of the section on Carbohydrates.** Some valuable comments of members of the WG are included. **ISDI**: change the heading of this section into **Digestible Carbohydrates.** **Norway**: Lactose should be the principal carbohydrate in infant formulas. **ENCA, IBFAN**: Lactose is the natural sugar found in breast-milk, therefore the lactose content in infant formula should be as optimal as possible. The addition of other sugars such as sucrose or starches should be restricted. **IBFAN**: the minimum lactose level should be 0.85 g/100 kJ and the maximum sucrose level should be 20% of total carbohydrates. **ESPGHAN**: proposes to change the carbohydrate content to a range between **9 g/100 kcal and** 14 g/100 kcal. The lactose content shall not be less than 4.5 g/100 kcal. **ENCA**: The carbohydrate content should not be fixed in gram/100 kcal but related to their relative sweetness compared to lactose in breast-milk.

The WG is unable to propose a final revision for the table of minimum and maximum values of vitamins and minerals.

Therefore, the values as proposed in Annex II of CL 2003/4-NFSDU are listed for each vitamin and mineral separately, followed by the comments from the WG. Comments and proposals made by other delegations and contained in CRD 2 and CX/NFSDU 03/6 are presented also (in a smaller type). A comparison of all proposals under discussion is given as a table at the end (amounts per 100 kcal only). This table is meant to illustrate the degree of consensus and of dissent with regard to the different vitamins and minerals.

In this table the nutrient names are harmonized with those in the Codex Guidelines on Nutrition Labelling. The amounts of each nutrient are listed in only one unit. Conversion factors to other units that are sometimes used by countries are identified in footnotes to this table. If there is agreement that a minimum or maximum level be established for a nutrient, but little or no data are provided to support a specific level, the table has a notation that the value is “T.B.D.” (i.e. To Be Determined). For all other nutrients without a proposed value, the table has the notation “N.S.” (i.e. Not Specified). All square brackets around numbers in Annex 2 of CL 2003/4-NFSDU are deleted, because the table as a whole is under discussion and considered to be in square brackets. The footnotes to the table have been arranged systematically.

United States: concurs with the values in the table in Annex II of CL 2003/4-NFSDU except for the missing calcium to phosphorus ratio and the values for iron and selenium.

Vitamins

	Unit	Minimum per 100 kcal	Maximum per 100 kcal	Minimum per 100 kilojoules	Maximum per 100 kilojoules
Vitamin A*	µg	60	180	14	43

Norway: The physical forms of retinol and retinylesters should be taken into consideration. Both are absorbed to a greater extent from aqueous emulsions than from oily preparations (References given).

ESPGHAN: The proposed values are accepted under the condition that they refer to preformed retinol or retinylesters. A reliable equivalence factor for the vitamin A activity of β-carotene for infants has not been established.

	Unit	Minimum per 100 kcal	Maximum per 100 kcal	Minimum per 100 kilojoules	Maximum per 100 kilojoules
Vitamin D**	µg	1	2.5	0.25	0.63

Norway: To ensure formula-fed infants sufficient intake of vitamin D it is appropriate to add vitamin D to infant formula. However, in the table "calciferol" does not distinguish between cholecalciferol (vitamin D_3) and ergocalciferol (Vitamin D_2). Vitamin D_3 has higher biological activity and therefore also toxicity than vitamin D_2. Vitamin D_3 should be the preferred form of vitamin D in infant formula. Moreover, the physical forms of vitamin D with different bioavailability should be taken into account.

Czech Republic: supports the proposed minimum and maximum values and the specification of vitamin D as calciferol to include both vitamin D_2 and vitamin D_3. The footnote would be: Calciferol. 1µg calciferol=40 IU vitamin D.

	Unit	Minimum per 100 kcal	Maximum per 100 kcal	Minimum per 100 kilojoules	Maximum per 100 kilojoules
Vitamin E***	mg	0.5/g polyunsaturated fatty acids[5], but in no case less than 0.5/100 kcal	N.S.	0.5/g polyunsaturated fatty acids[5], but in no case less than 0.1/100 kJ	N.S.

ESPGHAN: suggests to set a maximum level of vitamin E of 5 mg alpha-tocopherol equivalent/100 kcal, to avoid accumulation in body tissues, antagonistic actions of vitamin E against vitamin K as well as anticoagulative effects, and prooxidant action of vitamin E when intakes grossly exceed requirements.

CRN: proposes to increase the minimum value to 0.77 mg/100 kcal in order to reach the nutrient reference value for alpha-tocopherol and suggests to not establish a maximum value and to put square brackets around the minimum value per energy unit and around the footnote proposed by the European Community.

	Unit	Minimum per 100 kcal	Maximum per 100 kcal	Minimum per 100 kilojoules	Maximum per 100 kilojoules
Vitamin C**	mg	8	N.S.	1.9	N.S.

ESPGHAN: proposes to set a minimum level of 10 and a maximum level of 30 mg/100 kcal.

New Zealand: proposes a minimum level of 6 mg/100 kcal, derived from a RDA of 30 mg/day.

	Unit	Minimum per 100 kcal	Maximum per 100 kcal	Minimum per 100 kilojoules	Maximum per 100 kilojoules
Thiamin	µg	40	N.S.	10	N.S.

ESPGHAN: proposes to set a minimum level of 30 and a maximum level of 300 µg/100 kcal.

New Zealand: supports the current minimum level of 40 µ/100 kcal.

	Unit	Minimum per 100 kcal	Maximum per 100 kcal	Minimum per 100 kilojoules	Maximum per 100 kilojoules
Riboflavin	µg	60	N.S.	14	N.S.

ESPGHAN: proposes a minimum level of 80 and a maximum level of 400 µg/100 kcal.

	Unit	Minimum per 100 kcal	Maximum per 100 kcal	Minimum per 100 kilojoules	Maximum per 100 kilojoules
Niacin	mg	0.6	N.S.	0.14	N.S.

ESPGHAN: supports a minimum level of 0.3 and a maximum level of 1.2 mg/100 kcal.

ISDI: proposes to add a footnote to niacin "**as preformed niacin**".

	Unit	Minimum per 100 kcal	Maximum per 100 kcal	Minimum per 100 kilojoules	Maximum per 100 kilojoules
Vitamin B_6	µg	15/g protein, but in no case less than 35/100 kcal	N.S.	15/g protein, but in no case less than 9/100 kcal	N.S.

ESPGHAN: suggests not to relate the required content to protein but to energy only. A minimum level of 35 µg/100 kcal is supported and a maximum level of 165 µg/100 kcal is proposed.

	Unit	Minimum per 100 kcal	Maximum per 100 kcal	Minimum per 100 kilojoules	Maximum per 100 kilojoules
Folic acid	µg	11	N.S.	2.6	N.S.

ESPGHAN: supports a minimum level of 10 µg/100 kcal and a maximum level of 30 µg/100 kcal.

ISDI: supports a higher minimum folic acid level than 4 µg/100 kcal and will make a proposal at a later date.

New Zealand: supports a minimum value of 11 µ/100 kcal.

CRN: proposes a minimum value of 7.5 µg/100 kcal, which should be sufficient because of higher bioavailability of added folic acid.

	Unit	Minimum per 100 kcal	Maximum per 100 kcal	Minimum per 100 kilojoules	Maximum per 100 kilojoules
Pantothenic acid	µg	300	N.S.	70	N.S.

ESPGHAN: supports a minimum level of 400 and a maximum level of 2000 µg/100 kcal.

New Zealand: supports a minimum value of 300 µg/100 kcal.

	Unit	Minimum per 100 kcal	Maximum per 100 kcal	Minimum per 100 kilojoules	Maximum per 100 kilojoules
Vitamin B_{12}	µg	0.1	N.S.	0.025	N.S.

ESPGHAN: suggests a maximum value of 0.5 µg/100 kcal.

	Unit	Minimum per 100 kcal	Maximum per 100 kcal	Minimum per 100 kilojoules	Maximum per 100 kilojoules
Vitamin K	µg	4	N.S.	1	N.S.

ESPGHAN: suggests a maximum level of 20 µg/100 kcal.

	Unit	Minimum per 100 kcal	Maximum per 100 kcal	Minimum per 100 kilojoules	Maximum per 100 kilojoules
Biotin	µg	1.5	N.S.	0.4	N.S.

ESPGHAN: suggests a maximum level of 7.5 µg/100 kcal.

New Zealand: supports a minimum value of 1.5 µg/100 kcal.

Minerals

	Unit	Minimum per 100 kcal	Maximum per 100 kcal	Minimum per 100 kilojoules	Maximum per 100 kilojoules
Sodium	mg	20	T.B.D.	5	T.B.D.

Norway: when setting maximum levels for sodium, potassium and chloride the infant's age, that is the maturity of the renal function, should be taken into account. The relation to maximum protein levels and quality of protein must be taken into consideration.

ISDI: believes that there is no need for delaying the setting of maximum levels for Na, K, Cl and P until the report of the FAO/WHO expert consultation on Energy and Protein Requirements becomes available. Model calculations of the potential renal solute load (PRSL) with the highest currently proposed maximum levels for protein (3.4 g/100

kcal) and the highest currently proposed maximum values for sodium (60 mg/100 kcal), potassium (200 mg/100 kcal), chloride 160 mg/100 kcal) and phosphorus (90 mg/100 kcal) show that the PRSL is below 35 mOsm/100 kcal. This value was suggested as upper limit for infant formula (Fomon and Ziegler (1999) Renal solute load and potential renal solute load in infancy. J. Pediatr. 134: 11-14. Fomon (2000) Potential renal solute load: considerations relating to complementary feedings of breastfed infants. Pediatrics 106 (Suppl. 5): 1284).

A maximum sodium level of 60 mg/100 kcal is proposed.

Australia: proposes a maximum level of 60 mg/100 kcal.

Czech Republic: proposes to retain a maximum level of 60 mg/100 kcal.

New Zealand: supports setting a maximum value, 60 mg/100 kcal.

	Unit	Minimum per 100 kcal	Maximum per 100 kcal	Minimum per 100 kilojoules	Maximum per 100 kilojoules
Potassium	mg	60	T.B.D.	14	T.B.D.

ESPGHAN: proposes a maximum level of 160 mg/100 kcal.

ISDI: proposes a maximum level of 200 mg/100 kcal, because the movement of the body's water between the intra- and extracellular compartment depends on the balance between (intracellular) K and (extracellular) Na+Cl. The ratio of K/Na in human milk ranges between 2.5-3.9, average 3.1 (references given). It is proposed to aim for the same ratio in infant formula. Given a maximum sodium level of 60 mg/100 kcal this requires a maximum potassium level of 200 mg/100 kcal.

Australia: proposes a maximum value of 200 mg/100 kcal.

Czech Republic: proposes to retain the maximum value of 200 mg/100 kcal of the Codex Standard 72-1981, in order to achieve a K/Na ratio similar to human milk (3.1)

New Zealand: supports a minimum value of 80 mg/100 kcal and a maximum value of 200 mg/100 kcal as in the Codex Standard 72-1981.

	Unit	Minimum per 100 kcal	Maximum per 100 kcal	Minimum per 100 kilojoules	Maximum per 100 kilojoules
Chloride	mg	50	T.B.D.	12	T.B.D.

ESPGHAN: proposes a maximum level of 160 mg/100 kcal.

ISDI: proposes a maximum chloride level of 150 mg/100 kcal, in order to achieve a similar value for the quotient of potassium and the sum of sodium and chloride as found in human milk (references given).

Australia: proposes a maximum level of 150 mg/100 kcal.

Czech Republic: proposes to retain the maximum value of 150 mg/100 kcal of the Codex Standard 72-1981.

New Zealand: proposes to retain the maximum value of 150 mg/100 kcal of Codex Standard 72-1981

	Unit	Minimum per 100 kcal	Maximum per 100 kcal	Minimum per 100 kilojoules	Maximum per 100 kilojoules
Calcium	mg	50	N.S.	12	N.S.

ESPGHAN: proposes a maximum level of 140 mg/100 kcal.

New Zealand: supports a minimum value of 50 mg/100 kcal and a maximum value N.S.

CRN: proposes a minimum value of 45 mg/100 kcal, which is closer to the calcium content of human milk.

	Unit	Minimum per 100 kcal	Maximum per 100 kcal	Minimum per 100 kilojoules	Maximum per 100 kilojoules
Phosphorus	mg	25	T.B.D.	6	T.B.D.

USA: the footnote on the calcium to phosphorus ratio should be re-included and modified (see below), and an additional footnote on the availability of phosphorus in different kinds of formula should be added (see below).

ESPGHAN: suggests that the minimum for bioavailable phosphorus should be 20 mg/100 kcal and the maximum 70 mg/100 kcal. Either the bioavailability of phosphorus in a given formula has to be measured or an average bioavailability of about 80% from cow's milk protein based formula and of about 70% from soy protein isolate based formula can be assumed. For cow's milk based formula a minimum phosphorus content of 25 mg/100 kcal and a maximum level of 90 mg/100 kcal is recommended, whereas for formula based on soy protein the minimum and maximum phosphorus levels would have to be 30 and 100 mg/100 kcal, respectively.

ISDI: proposes a maximum phosphorus content of 90 mg/100 kcal, because high phosphorus levels are undesirable in infant formula.

Australia: proposes a maximum level of 90 mg/100 kcal and the re-introduction of the footnote on the calcium to phosphorus ratio.

Czech Republic: proposes to retain the maximum level of 90 mg/100 kcal and re-introduce the footnote on the calcium to phosphorus ratio of up to 2.2

New Zealand: supports the proposed minimum value of 25 mg/100 kcal and a maximum calcium to phosphorus ratio of 2.2.

	Unit	Minimum per 100 kcal	Maximum per 100 kcal	Minimum per 100 kilojoules	Maximum per 100 kilojoules
Magnesium	mg	5	N.S.	1.2	N.S.

ESPGHAN: proposes to retain the maximum value of 15 mg/100 kcal.

New Zealand: supports a minimum value of 5 mg/100 kcal and a maximum value N.S.

	Unit	Minimum per 100 kcal	Maximum per 100 kcal	Minimum per 100 kilojoules	Maximum per 100 kilojoules
Iron	mg	0.5	1.5	0.12	0.36

Norway: Separate values for minimum and maximum values of iron should be given for early and late infancy. The bioavailability of the iron source has to be taken into account. Iron requirements of infants 0-6 months of age are estimated to be 0.5 mg/day, for infants 6-12 months of age 0.9 mg/day (Fomon (1993) Nutrition of normal infants. Mosby, St. Louis).

USA: Supports a maximum iron level of 2 to 3 mg/100 kcal based on maximum reported and permitted use in the United States, with no evidence of any problems at these levels. The tolerable upper level of intake (UL) established by the U.S. Institute of Medicine (2001) (i.e. 40 mg/day of supplemental non-heme iron, which corresponds to 8 mg/100 kcal for a representative infant who consumes 500 kcal/day) is considered too high because its establishment did not take into account iron' s interaction with other minerals (e.g., zinc) or its oxidation potential (e.g., with unsaturated fatty acids). Rather, the Institute of Medicine's basis for setting an UL for iron was limited to gastrointestinal adverse side effects. We further considered that a maximum level of 1.5 mg/ 100 kcal is probably too low. Regulations in the United States permit iron concentrations up to 3.0 mg/100 kcal (21 CFR §107.100(a)). Furthermore, iron concentrations for iron-fortified formulas in the United States reportedly range from 0.6 mg/ 100 kcal to 1.8 mg/ 100 kcal (Pediatrics 1999;104:119-123).

ESPGHAN: suggests a minimum of 0.3 mg/100 kcal and a maximum of 1.3 mg/100 kcal for cow's milk protein based formula, and, because of lower bioavailability, a minimum of 0.45 mg/100 kcal and a maximum of 1.9 mg/100 kcal for soy protein based formula.

ISDI: proposes a maximum iron level of 2.5 mg/100 kcal, because the level of 1.5 mg/100 kcal is low if it applies to countries where major iron deficiencies are encountered.

Australia: proposes to increase the maximum level to 2.0 mg/100 kcal.

Czech Republic: proposes to increase the maximum value to 2.5 mg/100 kcal.

New Zealand: supports the proposed minimum and maximum values (CRD 2). It proposes a maximum value of 2 mg/100 kcal (CX/NFSDU 03/6).

	Unit	Minimum per 100 kcal	Maximum per 100 kcal	Minimum per 100 kilojoules	Maximum per 100 kilojoules
Iodine	µg	5	T.B.D.	1.2	T.B.D.

ESPGHAN: suggests a minimum of 10 µg/100 kcal and a maximum of 50 µg/100 kcal.

ISDI: will make a proposal for a minimum level at a later date. A maximum level is difficult to propose, because the iodine content of cow's milk is not constant and depends on seasons and hygienic or agricultural techniques. The maximum level should be given as "N.S." and not as "T.B.D.".

Czech Republic: proposes that the maximum value be N.S., because of seasonal and local variations in the iodine content of cow's milk.

	Unit	Minimum per 100 kcal	Maximum per 100 kcal	Minimum per 100 kilojoules	Maximum per 100 kilojoules
Copper***	µg	60	T.B.D.	14	T.B.D.

ESPGHAN: suggests a minimum of 35 µg/100 kcal and a maximum level of 100 µg/100 kcal.

Australia: supports the removal of the square brackets around the footnote on copper and retaining the text.

New Zealand: supports the current minimum level of 60 µg/100 kcal as it is close to the **level** in breast-milk.

	Unit	Minimum per 100 kcal	Maximum per 100 kcal	Minimum per 100 kilojoules	Maximum per 100 kilojoules
Zinc	mg	0.5	T.B.D.	0.12	T.B.D.

ESPGHAN: suggests a maximum level of 1.5 mg/100 kcal.

Spain: proposes a maximum value of 1.5 mg/100 kcal for formula based on cow's milk protein.

Poland: proposes a maximum value of 1.5 mg/100 kcal.

	Unit	Minimum per 100 kcal	Maximum per 100 kcal	Minimum per 100 kilojoules	Maximum per 100 kilojoules
Manganese	µg	1	T.B.D.	0.24	T.B.D.

ESPGHAN: suggests a maximum level of 100 µg/100 kcal.

	Unit	Minimum per 100 kcal	Maximum per 100 kcal	Minimum per 100 kilojoules	Maximum per 100 kilojoules
Selenium	µg	6	T.B.D.******	1.4	T.B.D.******

USA: proposes the maximum level to be 9 µg/100 kcal (or 2 µg/100 kJ). This maximum value is based on the tolerable upper intake level of 45 µg/day for infants 0-6 months that was established by the U.S. Institute of Medicine (2000), and the assumption that a representative caloric intake would be 500 kcal/day.

A minimum value of 3 µg selenium/100 kcal (0.7 µg/100 kJ) is proposed based on the average concentration of selenium in human milk of 18 µg/L that was reported by the U.S. Institute of Medicine (2000), and on the assumption that infant formula has about 67 kcal per 100 ml. A correction for lower bioavailability of selenium from infant formula is not deemed to be necessary.

ESPGHAN: proposes a minimum value of 3 µg/100 kcal and a maximum value of 9 µg/100 kcal.

ISDI: opposes strongly the setting of a minimum level of selenium and suggests the minimum to be "N.S.". There are no indications of selenium deficiencies in infants fed infant formula for which no minimum level has been set in legislation as it is the case in the European Union. It is questionable whether average levels of selenium found in human

milk represent the minimum requirement of infants. The selenium content of human milk is under the influence of the selenium content of the mother's diet. Average selenium contents of human milk in countries other than the United States and Canada have been significantly lower than the reported 18 µg/L.

It would be more prudent to set a maximum level only if selenium is added.

Australia: is opposed to a minimum selenium level of 6µg/100 kcal, because it is higher than the selenium content in human milk in areas without signs of selenium deficiency in breast-fed infants. A minimum level of 1.5 µg/100 kcal is proposed.

Czech Republic: is opposed to the setting of a minimum level; this should be N.S.. A maximum value should be set if selenium is added (T.B.D and footnote).

New Zealand: considers the proposed minimum level of 6µg/100 kcal as too high and proposes a minimum value of 1.5 µg/100 kcal and a maximum value of 6 µg/100 kcal (CRD 2). It can support a minimum value of 0.8 µg/100 kcal (CX/NFSDU 03/6).

CRN: proposes a minimum level of 1 µg/100 kcal and to retain the square brackets around 6 µg/100 kcal, which is too high .

	Unit	Minimum per 100 kcal	Maximum per 100 kcal	Minimum per 100 kilojoules	Maximum per 100 kilojoules
Choline	mg	7	N.S.	1.7	N.S.

ESPGHAN: suggests a maximum level of 30 mg/100 kcal.

Carnitine

ESPGHAN and **ISDI**: suggest that carnitine should be added in the table to the section with choline. Formula based on soy protein or on hydrolysed protein should have a minimum carnitine content of 1.2 mg/100 kcal (0.3 mg/100 kJ). A minimum carnitine content for formula based on intact cow's milk protein is not necessary. A maximum level should not be specified (N.S.).

CRN proposes to permit L-carnitine as an optional ingredient in all formulas with a minimum value of 1.2 µg/100 kcal and a maximum value N.S.

The following table shows the minimum and maximum values per 100 kcal for vitamins, minerals and choline as given in Codex Standard 72-1981, in ALINORM 03/26A, Appendix II, and in CL 2003/4-NFSDU (square brackets around numbers deleted) in comparison to the proposals made by members of the WG and by members of delegations outside the WG.

		Codex Standard 72-1981		**Alinorm 03/26A, Appendix II**		**CL 2003/4-NFSDU, Annex 2**		**Proposals from WG-members**		**Proposals from delegations outside the WG**	
		Amounts per 100 kilocalories (kcal)									
	Unit	*Minimum*	*Maximum*	*Minimum*	*Maximum*	*Minimum*	*Maximum*	*Minimum*	*Maximum*	*Minimum*	*Maximum*
Vitamins											
Vitamin A[1]	µg	75	150	60	180	60	180			–	–
Vitamin D[2]	µg	1	2.5	1	2.5	1	2.5			1	2.5
Vitamin E[3]	mg	0.7 IU/g linoleic acid, but in no case less than 0.7/100 kcal	N.S.[4]	0.5/g linoleic acid, but in no case less than 0.5/100 kcal	N.S.	0.5/g polyunsa-turated fatty acids[5], but in no case less than 0.5/100 kcal	N.S.	0.5	5	0.77 /100kcal	N.S.
Vitamin C[6]	mg	8	N.S.	8	N.S.	8	N.S.	10	30	6	–
Thiamin	µg	40	N.S.	40	N.S.	40	N.S.	30	300	40	–
Riboflavin	µg	60	N.S.	60	N.S.	60	N.S.	80	400	–	–
Niacin	mg	0.25	N.S.	0.8	N.S.	0.6	N.S.	0.3	1.2	–	–
Vitamin B_6	µg	35	N.S.	15/g protein, but in no case less than 35/100 kcal	N.S.	15/g protein but in no case less than 35/100 kcal	N.S.	35	165	–	–
Folic acid	µg	4	N.S.	4	N.S.	11	N.S.	10	30	7.5-11	N.S.
Pantothenic acid	µg	300	N.S.	300	N.S.	300	N.S.	400	2000	300	N.S.
Vitamin B_{12}	µg	0.1	N.S.	0.1	N.S.	0.1	N.S.	0.1	0.5	–	–
Vitamin K	µg	4	N.S.	4	N.S.	4	N.S.	4	20	–	–

[1] expressed as retinol equivalent (RE). 1 µg RE = 3.33 IU Vitamin A. **ISDI** proposes the folowing conversion factors for Vitamin A: 1 IU Vitamin A = 0.3 µg retinol. 1 µg RE = 1 µg all-trans retinol = 6µg all-trans-β-carotene = 3.33 IU Vitamin A

[2] Calciferol. 1 µg calciferol = 40 IU Vitamin D. **ISDI** proposes to add**:** 1 IU Vitamin D = 25 ng (0.025 µg) cholecalciferol = 25 ng ergocalciferol.

[3] Alpha-Tocopherol-Equivalent (TE).

[4] N.S. = not specified

[5] expressed as linoleic acid. The following factors of equivalence shall be used to adapt the minimal vitamin E content to the fatty acid composition of the formula: 0.5 mg d-α-tocopherol equivalent/ 1 g linoleic acid; 0.75 mg d-α- tocopherol equivalent/ 1g linolenic acid; 1.0 mg d-α-tocopherol equivalent/ 1 g arachidonic acid; 1.25 mg d-α-tocopherol equivalent/ 1 g eicosapentaenoic acid; 1.5 mg d-α-tocopherol equivalent/ 1 g docosahexaenoic acid (proposed by the European Community and supported by Germany and ESPGHAN.

[6] expressed as ascorbic acid

		Codex Standard 72-1981		Alinorm 03/26A, Appendix II		CL 2003/4-NFSDU, Annex 2		Proposals from WG-members		Proposals from delegations outside the WG	
		Amounts per 100 kilocalories (kcal)									
	Unit	*Minimum*	*Maximum*	*Minimum*	*Maximum*	*Minimum*	*Maximum*	*Minimum*	*Maximum*	*Minimum*	*Maximum*
Biotin	µg	1.5	N.S.	1.5	N.S.	1.5	N.S.	1.5	7.5	1.5	
Minerals											
Sodium	mg	20	60	20	60	20	T.B.D.[7]	20	60	20	60
Potassium	mg	80	200	60	145	60	T.B.D.	60	160-200	80	200
Chloride	mg	55	150	50	125	50	T.B.D.	50	150-160	50	150
Calcium[8]	mg	50	N.S.	50	N.S.	50	N.S.	50	140	45	N.S.
Phosphorus[9]	mg	25	N.S.	25	90	25	T.B.D.	25	90-100	25	90
Magnesium	mg	6	N.S.	5	15	5	N.S.	5	15	5	N.S.
Iron	mg	0.15/1	N.S.	0.5	1.5	0.5	1.5	0.3-0.5	1.3-3.0	0.5	2-2.5
Iodine	µg	5	N.S.	5	N.S.	5	T.B.D.	5-10	50/N.S.	5	N.S.
Copper[10]	µg	60	N.S.	20	80	60	T.B.D.	35-60	100	60	N.S.
Zinc	mg	0.5	N.S.	0.5	N.S.	0.5	T.B.D.	0.5	1.5	0.5	1.5
Manganese	µg	5	N.S.	5	N.S.	1	T.B.D.	1	100	–	–
Selenium	µg	–	–	N.S.	3	[6]	T.B.D.[11].	3/N.S.	9	0.8-1.5	6
Choline	mg	7	N.S.	N.S.	N.S.	7	N.S.	7	30		

[7] T.B.D. = to be determined

[8] The calcium to phosphorus (weight to weight) ratio shall not be less than 1.2 and not more than 2.2

[9] Proposed by USA: "The availability of phosphorus in milk-based and soy-protein isolate based formulas differs considerably. All (100%) of the phosphorus in milk-based formulas is available whereas about 70% of phosphorus is available in soy-protein isolate based formulas. Available phosphorus should serve as the basis for addition of calcium to avoid addition of nutritionally unneeded calcium to achieve a calcium/phosphorus ratio within the specified range."

[10] [Adjustments may be needed in these levels for infant formula made in regions with a high content of copper in the water supply]

[11] [if added]