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31 March 2006

ISDI COMMENTS on
Advisory list of nutrient compounds for the use in foods for special dietary uses intended for use by infants and young children at step 3
CL 2005/53-NFSDU (Alinorm 06/29/26 §140 & Appendix V)

General remark on the requested substances

In the table below, the substances ISDI wishes to be included in the advisory list are, for the great majority, defined and authorised already in supranational or national legislation specification.

The advisory list of vitamin formulations, mineral salts, amino acids and other substances should not be considered as a positive (e.g. closed) list for ingredients referred to in sections 3.2.1 and 3.2.2.

Most of these substances are sources of nutrients that are mandatory in Infant Formulae, Follow-Up-Formulae, Processed Cereal-Based Foods for infants and young children Canned Baby Foods and Foods for Special Medical Purposes.

They have been shown to have good technological and nutritional characteristics. They allow flexibility in the formulation of the variety of foods specifically designed for infants and young children.

All dietetic foods, manufactured for infants and adults, contain additives and ingredients which are classified as food grade, often even pharmaceutical grade materials, which have been approved for use by international expert bodies. The materials used must comply with assigned specific purity criteria, to ensure that no lower or chemical grade materials can find their way into dietetic foods.

Specific remark on Foods for Special Medical Purposes

FSMPs play a vital part in the dietary management of those infants and young children who have special nutritional requirements. Products intended for infants and young children not in good health are highly specific and are designed to meet the particular nutritional requirements resulting from a disease, disorder or medical condition. They are designed to be used for the dietary management of infants suffering from a particular disease e.g. phenylketonuria, galactosemia and other inborn errors of metabolism, malabsorption, allergies.

In some medical conditions, protein requirements cannot be met using whole protein due to intolerance, inability to metabolise etc. To supply the protein requirements to such patients, a range of amino acids must be used, to provide the body protein in its simplest form, while satisfying the specific daily requirements.

In many cases, the products are used as the only source of nutrition and are, in fact, substitutes for normal food. Thus a full complement of nutrition in the form of carbohydrate, protein, fat, vitamins, minerals and trace elements must be supplied. It is vital that the vitamins and minerals sources and sources of other nutrients requested by ISDI for use in FSMPs are accepted, to allow the formulation of these much needed products.

The following tables summarise ISDI proposals (addition in bold, deletion stroke out) and comments on the document prepared by the delegation of Germany.

A: ADVISORY LIST OF MINERAL SALTS AND TRACE ELEMENTS FOR USE IN FOODS FOR SPECIAL DIETARY USES INTENDED FOR USE BY INFANTS AND YOUNG CHILDREN

Nutrient Source	Purity Requirements by		Use in Food Categories for Infants and Young Children					ISDI Comments
	CAC[2]	international and/or national bodies	IF	FUF	PCBF	CBF	FSMP	
1. Sources of Calcium								
New Zealand, Malaysia, ISDI: ~~[~~1.13 Calcium sulphate~~]~~	√ (1979)	JECFA (1975), Ph Int, FCC, Ph Eur (dihydrate), DAB, MP	**√**	-	-	-	~~[~~√~~]~~	Authorised in EU (Directive 2001/15 amended by Directive 2004/5) following positive opinion from the European Food Safety Authority on this usage, 10 Dec. 2003
2. Source of Iron (Fe)								
2.13 Ferric orthophosphate		FCC**, Affirmed GRAS (21CFR184.1301)**			**√**			
EU, ISDI: ~~[~~2.14 Sodium ferric diphosphate~~]~~		FCC	-	-	~~[~~√~~]~~	~~[~~√~~]~~	~~[~~√~~]~~	Authorised in EU(Directive 2001/15), for this usage, following positive opinion from the EU Scientific Committee on Food dated 12 May 1999
ISDI: ~~[~~2.15 Ferrous citrate~~]~~		FCC, **Affirmed GRAS (21CFR184.1307c)**	~~[~~√~~]~~	~~[~~√~~]~~	~~[~~√~~]~~	~~[~~√~~]~~	~~[~~√~~]~~	**Martindale - The Extra Pharmacopoeia**, 29th edition, 1989, ed. JEF Reynolds, The Pharmaceutical Press, London, UK.
New Zealand: ~~[~~2.16 Ferrous succinate~~]~~		MP, MI			**√**			ISDI supports the addition of ferric orthophosphate, sodium ferric diphosphate, ferrous succinate and ferrous bisglycinate as sources of iron in cereal products for children but not in infant formulas or FSMP products. These iron sources can have taste and stability advantages and have been shown to be bioavailable.
South Africa: ~~[~~2.17 Ferrous bisglycinate~~]~~		JECFA (2003)			**√**			
4. Source of Sodium (Na)								
~~New Zealand: [4.11 Sodium chloride(iodised)]~~		~~USP, Ph Eur, BP, JP~~	~~?~~	~~?~~	~~?~~	~~?~~	~~?~~	Delete this section Iodine levels in foods for special dietary should be tightly controlled and should therefore be added specifically rather than through iodised salt.
8. Source of Zinc (Zn)								

EU, ISDI: ~~[~~8.6 Zinc carbonate~~]~~		BP (hydroxide carbonate)	-	-	-	-	~~[~~√~~]~~	Authorised in EU (Directive 2001/15) for this usage, following positive opinion from the EU Scientific Committee on Food dated 12 May 1999
10. Source of Selenium (Se)								
10.1 Sodium selenate		MI	√	√	NZ: ~~[~~√~~]~~	-	√	ISDI supports the addition. Authorised in EU (Directive 2001/15), used with no safety concerns in the EU for many years.
10.2 Sodium selenite		DAC, MP, MI	√	√	NZ: ~~[~~√~~]~~	-	√	ISDI supports the addition. Authorised in EU (Directive 2001/15), used with no safety concerns in the EU for many years
11. Chromium (Cr III)								
11.2 Chromium (III) chloride		USP, MI	√				√	ISDI supports the addition.
12. Molybdenum (Mo VI)								
12.1 Sodium molybdate		Ph Eur (dihydrate), BP, DAB	√				√	ISDI supports the addition.
13. Fluoride (F)								
ISDI: [13.3 Calcium fluoride]		DAB	-	-	-	-	~~[~~√~~]~~	

B: ADVISORY LIST OF VITAMIN COMPOUNDS FOR USE IN FOODS FOR SPECIAL DIETARY USES INTENDED FOR USE BY INFANTS AND YOUNG CHILDREN

Nutrient Source	**Purity Requirements by**		**Use in Food Categories for Infants and Young Children**					ISDI Comments
	CAC[2]	**international and/or national bodies**	**IF**	**FUF**	**PCBF**	**CBF**	**FSMP**	
2. Provitamin A								
~~ISDI: [2.2 Provitamin A other than beta-carotene: [2.2.1 apo-8-carotenal]~~	~~√ (1991)~~	~~JECFA (1984), FCC~~	~~[√]~~	~~[√]~~	~~[√]~~	~~[√]~~	~~[√]~~	Delete. ISDI had already withdrawn this request in 2004
4. Vitamin E								
ISDI, EU, New Zealand: ~~[~~4.5 D-alpha-Tocopheryl acid succinate~~]~~		FCC, NF	-	-	-	-	~~[~~√~~]~~	Authorised in EU(Directive 2001/15) for this usage, following positive opinion from the EU Scientific Committee on Food dated 12 May 1999

C: ADVISORY LIST OF AMINO ACIDS AND OTHER NUTRIENTS FOR USE IN FOODS FOR SPECIAL DIETARY USES INTENDED FOR USE BY INFANTS AND YOUNG CHILDREN

Nutrient Source	Purity Requirements by		Use in Food Categories for Infants and Young Children		ISDI Comments			
	CAC[2]	international and/or national bodies	IF	FUF	PCBF	CBF	FSMP	
1. Amino acids[31]								
1.23 L- Glutamic acid		JECFA (1987), FCC, USP, Ph Eur	~~ISDI: [√]~~	~~ISDI: [√]~~			√	Glutamine is no longer considered as an (semi) essential amino acids and therefore can be deleted except for FSMP.
1.24 L- Glutamine		FCC, USP, DAB	~~ISDI: [√]~~	~~ISDI: [√]~~			√	
1.30 Guanosine 5-monophosphate (GMP)		**JECFA (1985)**	**√**	**ISDI: [√]**	**-**	**-**	**√**	ISDI proposes to move those two substances from the nucleotides section to the amino acids section.
1.31 Inosine 5-monophosphate (IMP)		**JECFA (1974)**	**√**	**ISDI: [√]**	**-**	**-**	**√**	
1.32 Magnesium aspartate		**Ph Eur**					**√**	
2. Carnitine								
2.1 L-Carnitine		FCC, USP, Ph Eur	√	√	ISDI: [√]	ISDI: [√]	√	Authorised in EU(Directive 96/5) for this usage, following positive opinion from the EU Scientific Committee on Food dated 27 Oct. 1989
ISDI: [2.2 L-Carnitine tartrate]		FCC, Ph Eur	-		-	-	√	Authorised in EU (Directive 2001/15 amended by Directive 2004/5) following positive opinion from the European Food Safety Authority on this usage, 3 Nov 2003
3.1 Taurine		USP, JP	√	ISDI: [√]	-	-	√	
~~**6. Nucleotides**~~								
~~6.1 Guanosine 5-monophosphate (GMP)~~		~~JECFA (1985)~~	~~√~~	~~ISDI: [√]~~	-	-	~~√~~	ISDI proposes to move those two substances from the nucleotides section to the amino acids section.
~~6.2 Inosine 5-monophosphate (IMP)~~		~~JECFA (1974)~~	~~√~~	~~ISDI: [√]~~	-	-	~~√~~	

[1] ISDI: As far as applicable, also the sodium, potassium calcium and magnesium salts of the amino acids as well as their hydrochlorides may be used.

6. Antioxidants								
6.1 Xanthophyll/Lutein		**US GRAS (2004), JEFCA (2004) Lutein from *Tagetes erecta***	√	√			√	ISDI supports the addition of lutein and mixed carotenes, carotenoids with anti-oxidant functions, to foods intended for infants and children including infant formula. A growing body of evidence suggests that human milk contains a wide variety of carotenoids that may provide antioxidant benefits to infants. Lutein has been recently recognized as GRAS by the US government and has been listed by JEFCA. The US FDA has recently recognized lycopene as GRAS. Mixed carotenes, a synonym for carotenes (vegetable), have been widely approved for use in infant formula in many markets and is listed by JEFCA.
6.2 Mixed carotenes		**EU dir 95/45/EC: E 160a(ii) and JEFCA (FNP 52 Add 6(1998): Carotenes (vegetable)**	√	√			√	
7. Other Compounds								
7.1 ARA		**US GRAS (2001), FSANZ**	√	√			√	ISDI supports the addition of ARA (arachidonic acid-rich single cell oil) derived from the soil fungus *Mortierella alpina* and DHA (docosahexanoic acid-rich single cell oil) derived from the microalgael species *Crypthecodinium cohnii.* These oils have been granted GRAS status for use in infant formula by the US FDA. Additionally, these oil sources have been approved for use in many countries including China, Mexico and Saudi Arabia. Numerous clinical studies suggest that the addition of these sources of polyunsaturated fatty acids to formulas for infants and young children improve both visual and mental development.
7.2 DHA		**US GRAS (2001), FSANZ**	√	√			√	

LIST OF NUTRIENT COMPOUNDS THAT LACK OFFICIAL PURITY REQUIREMENTS

Nutrient Source	Purity Requirements by		Use in Food Categories for Infants and Young Children					ISDI Comments
	CAC[2]	international and/or national bodies	IF	FUF	PCBF	CBF	FSMP	
LIST A:								
~~[Calcium citrate malate]~~	~~?~~	~~?~~	~~-~~	~~-~~	~~-~~	~~-~~	~~[√]~~	ISDI withdraws this request
~~[Calcium enriched yeast]~~	~~?~~	~~?~~	~~-~~	~~-~~	~~-~~	~~-~~	~~[√]~~	ISDI withdraws this request
~~[Calcium pyruvate monohydrate]~~	~~?~~	~~?~~	~~-~~	~~-~~	~~-~~	~~-~~	~~[√]~~	ISDI withdraws this request
~~[~~Cupric carbonate~~]~~	?	?	~~[√]~~	~~[√]~~	~~[√]~~	~~[√]~~	~~[√]~~	Although there are no purity criteria, these substances have been authorised and used in the European Union for many years and is currently used in some formulations in Asia and in Latin America.
~~[~~Cupric citrate~~]~~	?	**USP**	~~[√]~~	~~[√]~~	~~[√]~~	~~[√]~~	~~[√]~~	
~~[~~Sodium iodate~~]~~	?	**FCC**	-	-	~~[√]~~	~~[√]~~	~~[√]~~	Martindale, 29th edition, 1989
~~[~~Sodium hydrogen selenite~~]~~	?	?	ISDI: ~~[√]~~	ISDI: ~~[√]~~	ISDI: ~~[√]~~	ISDI: ~~[√]~~	~~[√]~~	Although it lacks official purity criteria. It is used as a source of selenium in FSMPs for infants and young children and is included in Directive 2001/15/EC as a substance that may be added to foods for specific nutritional uses. It has been used with no safety concerns in the EU for many years.
~~ISDI: [Selenium enriched yeast]~~	~~?~~	~~?~~	~~-~~	~~-~~	~~-~~	~~-~~	~~[√]~~	ISDI withdraws this request
~~ISDI: [Chromium enriched yeast]~~	~~?~~	~~?~~	~~-~~	~~-~~	~~-~~	~~-~~	~~[√]~~	ISDI withdraws this request
~~[~~Potassium fluoride~~]~~	?	**FCC**	-	-	-	-	~~[√]~~	These substances have been used for many years. Martindale, 29th edition, 1989

LIST B:								
[DL-alpha-Tocopheryl acid succinate]		**FCC**	-	-	-	-	[√]	Martindale, 29th edition, 1989
[DL-alpha-Tocopheryl polyethylene glycol 1000 succinate]	?	**USP**	-	-	-	-	[√]	The rationale is based on the addition of water soluble vitamin E (tocopheryl polyethylene glycol 1000 succinate) to the diet of children with cholestatic disorders, as a result of altered absorption of fat and vitamins that occurs in cholestasis. Intraluminal bile acid deficiency causes defects in fatty acid emulsification. Steatorrhea is a constant occurrence in cholestasis and fat malabsorption also includes fat soluble vitamin malabsorption and deficiency. In particular vitamin E deficiency causes ataxia, hyporeflexia and polyneuropathy. The water-soluble form of vitamin E is an important gain in the management of cholestasis, allowing an avoidance of repeated intramuscular injections in these patients. This benefit cannot be obtained with the classical fat-soluble vitamin E (tocopherol) even given at high doses.
[Potassium-L-ascorbate]	?	**FCC**	[√]	[√]	[√]	[√]	[√]	These substances have been used for many years. Martindale, 29th edition, 1989
[Pyridoxal 5-phosphate]	?	**USP, FCC**	[√]	[√]	[√]	[√]	[√]	These substances have been used for many years. Martindale
[Pyridoxal dipalmitate]	?	?	[√]	[√]	[√]	[√]	[√]	Although there are no purity criteria, these substances have been used for many years.
LIST C:								
[L-Isoleucine hydrochloride]	?	**USP, FCC**					[√]	Martindale, 29th edition, 1989 Source of Isoleucine in FSMPs for infants and young children. Isoleucine hydrochloride is permitted as a source of Isoleucine in foods for specific nutritional uses in the EU (2001/15/EC).

~~L-Leucine hydrochloride~~		**FCC, USP**					~~√~~	Allowed in USA (21CFR172.320) Martindale, 29th edition, 1989 Source of Leucine in FSMPs for infants and young children. Leucine hydrochloride is permitted as a source of Leucine in foods for specific nutritional uses in the EU (2001/15/EC).
~~L-Lysine acetate~~		**FCC, USP**	ISDI: ~~√~~	ISDI: ~~√~~	ISDI: ~~√~~	ISDI: ~~√~~	~~√~~	Martindale, 29th edition, 1989 It is currently used in FSMPs for infants and young children as a source of lysine and is a permitted nutrient source for use in foods for particular uses in the EU (2001/15/EC)
~~L-Lysine L-Aspartate~~	?	?			-		~~√~~	Both lysine aspartate and lysine glutamate are produced from the salification individual monographed amino acids. These amino acid salts are permitted under EU legislation and detailed product specification data was submitted to the SCF to support inclusion of these amino acids in 2001/15/EC.
~~L-Lysine L-Glutamate dihydrate~~	?	?			-		~~√~~	
~~L-Ornithine~~	?	**FCC**			-		~~√~~	Martindale, 29th edition, 1989
Ornithine monohydrochloride		**DAB**					√	Included as a source of ornithine in FSMPs for infants and young children. Ornithine monohydrochloride is permitted a source of ornithine in foods for specific nutritional uses in the EU (2001/15/EC).
~~L-Carnitine hydrochloride~~		**FCC**	~~√~~	~~√~~	ISDI: ~~√~~	ISDI: ~~√~~	~~√~~	Martindale, 29th edition, 1989
~~Choline~~		**FCC, USP, US GRAS (21CFR182.8252)**	~~√~~	~~√~~	~~√~~	~~√~~	~~√~~	Martindale, 29th edition, 1989
~~Cytidine 5-monophosphate~~	?	**FSANZ, Jap Food Std**	~~√~~	ISDI: ~~√~~	-	-	~~√~~	Food Standards Australia New Zealand (Std 1.3.4) Japan's Specifications and Standards for Food Additives, 7th ed (2000)
~~Disodium Uridine 5-monophosphate~~	?	**FSANZ, Jap Food Std**	~~√~~	ISDI: ~~√~~	-	-	~~√~~	Food Standards Australia New Zealand (Std 1.3.4) Japan's Specifications and Standards for Food Additives, 7th ed (2000)
~~Adenosine 5-monophosphate~~	?	**FSANZ, FCC**	~~√~~	ISDI: ~~√~~	-	-	~~√~~	Food Standards Australia New Zealand (Std 1.3.4) Martindale, 29th edition, 1989
~~Disodium Guanosine 5-monophosphate~~		**FCC, JECFA, FSANZ, Jap Food Std**	~~√~~	ISDI: ~~√~~	-	-	~~√~~	FCC 5th ed (2005), JECFA, Food Standards Australia New Zealand (Std 1.3.4), Japan's Specifications and Standards for Food Additives, 7th ed (2000)

~~Disodium Inosine 5-monophosphate~~		**FCC, JECFA, FSANZ, Jap Food Std**	~~√~~	ISDI: ~~√~~	-	-	~~√~~	FCC 5th ed (2005), JECFA, Food Standards Australia New Zealand (Std 1.3.4), Japan's Specifications and Standards for Food Additives, 7th ed (2000)
ISDI: ~~Creatine monohydrate~~	?	?					~~√~~	Positive opinion from EFSA 17 Feb 2004
Calcium Glutamate							√	Permitted nutrient sources in the foods for particular nutritional uses in the EU (2001/15/EC).
Potassium Glutamate							√	Permitted nutrient sources in the foods for particular nutritional uses in the EU (2001/15/EC).
Lycopene		**US GRAS (2005)**	√	√			√	ISDI supports the addition of lycopene with anti-oxidant functions, to foods intended for infants and children including infant formula. A growing body of evidence suggests that human milk contains a wide variety of carotenoids that may provide antioxidant benefits to infants.

D: ADVISORY LIST OF FOOD ADDITIVES FOR SPECIAL NUTRIENT FORMS

ISDI maintains its request to amend the introductory paragraph as follows:

> For reasons of stability and safe handling, some vitamins **and nutrients** have to be converted into suitable preparations, e.g. stabilised oily solutions, gelatine or gum arabic coated products, fat embedded preparations, dry rubbed preparations. For this purpose, the ~~edible materials and the additives included~~ **substances permitted in the** ~~respective~~ **specific Codex standards may be used**. **In addition, the following food additives may also be used**:

	INS no.	Additive/Carrier	Maximum Level in Ready-to-use food [mg/kg]	ISDI Comments
(e)	301	**EC**: Sodium L-ascorbate (in coatings of nutrient preparations containing PUFAs)	~~75~~ **250**	This number needs to be increased. Some powders are 2.8% encapsulated LCPUFA and 5% of the encapsulated LCPUFA is sodium ascorbate. A number like 250 ppm is more reasonable
(g)		**Costa Rica**: Fish gelatine		ISDI supports the addition.
(j)		**Costa Rica:** Glycyl Tristearate		ISDI supports the addition.
(m)		**Costa Rica**: Saccharose (in formulae with lactose as only carbohydrate)	10	This number needs to be increased since it is exceeded by sucrose diluted carrageenan which although not used in Europe, it is used in Latin America and Asia. Also encapsulated LCPUFA contain some sucrose.
(u)	420	**ISDI:** Sorbitol (carrier in L-Ascorbic Acid)		Carrier in L-Ascorbic acid

ANNEX 1: REFERENCES & ABBREVIATIONS

ISDI references:

- "Opinion on substances for nutritional purposes which have been proposed for use in the manufacture of foods for particular nutritional purposes ('Parnuts')." Expressed 12 May 1999 by the European Scientific Committee on Food (http://europa.eu.int/comm/food/fs/sc/scf/out31_en.pdf)

- Opinion of the Scientific Panel on Food Additives, Flavourings, Processing Aids and Materials in Contact with Food (AFC) on a request from the Commission related to Calcium sulphate for use in foods for particular nutritional uses. Expressed 10 December 2003 (http://www.efsa.eu.int/science/afc/afc_opinions/193/opinion_afc_03_en1.pdf)

- Report on the essential requirements for weaning foods. Adopted 27 October 1989 and 30 March 1990by the the European Scientific Committee on Food (http://europa.eu.int/comm/food/fs/sc/scf/reports/scf_reports_24.pdf)

- Commission Directive 2001/15/EC of 15 February 2001 on substances that may be added for specific nutritional purposes in foods for particular nutritional uses, as amended by Directive 2004/5 (http://europa.eu.int/eur-lex/en/consleg/pdf/2001/en_2001L0015_do_001.pdf)

- Commission Directive of 16 February 1996 on processed cereal-based foods and baby foods for infants and young children (http://europa.eu.int/eur-lex/en/consleg/pdf/1996/en_1996L0005_do_001.pdf)

Abbreviations:

IF	Infant Formula
FUF	Follow-Up Formula
PCBF	Processed Cereal-Based Food
CBF	Canned Baby Food
FSMP	Food for Special Medical Purposes
BP	British Pharmacopoeia
BPC	British Pharmaceutical Codex
DAB	Deutsches Arzneibuch
DAC	Deutscher Arzneimittel-Codex
FCC	Food Chemicals Codex
FSANZ	Food Standards Australia New Zealand
FU	Farmacopoea Ufficiale della Republica Italiana
JP	The Pharmacopeia of Japan
Jap Food Stan	Japanese Food Standard
NF	The National Formulary/USA
Ph Eur	Pharmacopoeia Europaea
Ph Franç	Pharmacopée Française
Ph Helv	Pharmacopoea Helvetica
Ph Int	International Pharmacopeia
USP	The United States Pharmacopeia