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SCIENTIFIC COMMITTEE ON FOOD

SCF/CS/ADD/NUT/20/Final
12/05/99

OPINION ON SUBSTANCES FOR NUTRITIONAL PURPOSES WHICH HAVE BEEN PROPOSED FOR USE IN THE MANUFACTURE OF FOODS FOR PARTICULAR NUTRITIONAL PURPOSES ('PARNUTS')

(expressed on 12/5/99)

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Terms of reference

To advise on the establishment of a list of substances with specific nutritional purposes, such as vitamins, minerals, trace elements, amino acids and other substances intended to be added to foodstuffs for particular nutritional uses, and, where appropriate, the conditions under which they should be used.

Background

Article 4.2 of Council Directive 89/398/EEC[1] relating to foodstuffs intended for particular nutritional uses (FPNUs) provides that the Commission shall adopt a list of substances with specific nutritional purposes which may be added to these products. The same article states that conditions of use should also be adopted, where appropriate. Annex 1 of Directive 89/398/EEC lists groups of FPNUs for which specific provisions are to be laid down by specific Directives. Such Directives have now been adopted for infant formulae and follow-on formulae,[2,3] processed cereal-based foods and baby foods,[4] and foods intended for use in energy-restricted diets for weight reduction.[5] In the two Directives relating to foods intended for infants and young children, appropriate substances for inclusion for nutritional purposes have been listed, together with any necessary conditions of use. For the remainder of the groups of FPNUs for which specific Directives were to be adopted, the Commission, after consultation with the Scientific Committee for Food (SCF), opted to draw up a framework list of nutritional substances which could be used in all remaining groups of FPNUs, including FPNUs not belonging to the groups listed in Directive 89/398/EEC.

In making recommendations, the Committee has considered information on current practices on the addition of substances for nutritional purposes in FPNUs as well as technological and biological data on such substances supplied by industry,[6] together with a proposed list of nutritional substances. This proposed list included substances that had already been approved by the Committee for use in the manufacture of foods intended for infants and young children in good health.[7-14] Some of the nutritional substances considered in this opinion have been proposed only for use in foods for special medical purposes (FSMPs), which are a sub-category of FPNUs. The Committee was aware that certain FPNUs contain, or may contain, essential fatty acids such as linoleic acid, arachidonic acid or other long chain polyunsaturated fatty acids . Food ingredient sources of these fatty acids, such as vegetable oils, fish oils and egg lecithin, were not included in the lists of nutritional substances intended for foods for infants and young children and similarly they will not be included in the framework list. The Committee also does not think it necessary to list substances that could be classified as dietary fibre. The Committee notes that a number of such substances, which are used for technological purposes, are already regulated by appropriate Directives.

Nutritional considerations

The Committee wishes to stress that the fact that a substance is deemed acceptable for inclusion in a framework list does not imply that the Committee considers it is necessary or appropriate to add that substance to all FPNUs. The Committee considers that all nutritional substances presently permitted in foods intended for infants and young children should be included in the framework list for use in any category of FPNUs, including semi-essential nutrients presently permitted in infant formulae and weaning foods to fulfil specific physiological requirements. Further, any nutrient deemed to be essential in the opinion of the Committee, and for which a Population Reference Intake (PRI) or an "acceptable range of intakes" has been established in an earlier report,[15] should be included in the framework list of nutritional substances.

Amino acids presently permitted in foods intended for infants and young children to enhance the biological value of protein should be included in the framework list. However, the list of permitted amino acids must be extended for FSMPs given that different amino acids may be necessary in specific medical conditions.

Toxicological considerations

From the list of nutritional substances requested, the Committee considered the toxicological aspects of those substances that have not already been approved for use in foods for infants and young children. The Committee was provided with few specifications for the nutritional substances requested and thus has not considered the issue of purity criteria in relation to the requested substances as it understands that this issue will be addressed separately by the Commission. Similarly, while PRIs or acceptable ranges of intake have already been set for many of the nutrients requested,[15] the Committee has not considered the question of upper levels for nutrients that may be present in FPNUs. The issue of upper levels for vitamins and minerals is currently under separate review by the Committee. This work may provide the Commission with the scientific elements to stipulate upper levels for vitamins and minerals in FPNUs, where necessary, in the relevant specific Directives. The Committee has already advised on upper levels for vitamins, minerals and trace elements in FSMPs.[16] The views expressed in this opinion are therefore limited to consideration of the toxicological aspects of the particular chemical form of each requested nutritional substance.

Vitamins

D-alpha-tocopheryl acid succinate

D-α-tocopherol, DL-α-tocopherol and their acetates have been approved by the SCF as nutrient substances in foods for infants and young children and in FSMPs.[8,10,14,16] The SCF has also accepted the use of tocopherols as antioxidants for foods in general[17] and as additives in nutrient preparations for use in infant formulae, follow-on formulae and weaning foods,[18] but considered it was not appropriate to establish an ADI. The Joint FAO/WHO Expert Committee on Food Additives (JECFA) has allocated DL-α-tocopherol and D-α-tocopherol concentrate a group ADI of 0.15 – 2 mg/kg b.w..[19] However, neither body has evaluated the succinic acid ester of D-α-tocopherol.

Toxicological studies available on D-α-tocopheryl acid succinate are limited to acute oral toxicity in the rat (low), skin and eye irritation tests. Clinical studies, primarily designed to assess the efficacy of D-α-tocopheryl acid succinate as a source of vitamin E in the

therapy of angina pectoris and muscular dystrophy,[20-23] reported no adverse effects apart from transient diarrhoea and intestinal cramps, which have also been reported following high doses of other forms of vitamin E.[15] These studies are of limited value for safety evaluation of the succinate. Bioavailability studies indicate that D-α-tocopheryl acid succinate is hydrolysed to tocopherol and succinic acid, but the extent to which it is hydrolysed prior to systemic absorption is uncertain. While no systematic toxicological studies are available for succinic acid and its salts, succinate ion is a normal intermediary in human metabolism in the citric acid cycle and in glucose and fatty acid synthesis. The Committee established a group ADI "not specified" for succinate in 1991.[24]

Since the absorption of some unhydrolysed D-α-tocopheryl acid succinate cannot be excluded at present, clarification of the extent of hydrolysis is desirable for all uses, but particularly because of potential high dose intake in food supplements. Pending this clarification, which should be submitted within one year of publication of this opinion, the Committee considers the use of D-α-tocopheryl acid succinate to be temporarily acceptable.

Minerals

Magnesium acetate

The Committee considered that the bioavailability of magnesium from magnesium acetate would be comparable to that from other magnesium salts and that use of magnesium acetate as a nutrient source for FPNUs was acceptable.

Zinc carbonate

Zinc carbonate itself has not been tested toxicologically. However, toxicological data are available on other zinc salts and on zinc in general. The SCF has also established a PRI for zinc.[15] There is no reason to expect that zinc carbonate would behave any differently from other zinc salts since it can be assumed that it will dissolve in gastric fluids to release zinc and carbon dioxide. It can therefore be considered comparable to other soluble zinc salts already approved for FPNUs. The use of zinc carbonate as a source of zinc for FPNUs is acceptable.

Selenium-containing substances

In the SCF report on essential requirements for infant formulae and follow-on formulae,[12] the Committee agreed that the use of sodium selenate, sodium selenite, selenomethionine and selenium enriched yeast was acceptable as a source of selenium in infant formula. The Committee was subsequently asked in 1994 to reconsider the acceptability of selenomethionine and selenium enriched yeast as sources of selenium following the submission of scientific evidence casting doubts on their acceptability. The Committee revised its earlier view in the light of this evidence and recommended, by way of prudence, that organic selenium compounds should not be used in the manufacture of infant formulae until their acceptability has been established.[25] In the case of *selenomethionine*, the Committee considered that information was needed on the significance of differing rates of renewal in plasma and tissues for selenomethionine compared with inorganic selenium compounds. This was because there is evidence that selenomethionine has a much quicker turnover in plasma, liver, pancreas and peripheral tissues with a slower rate of renewal than does selenite. However, it stays about 5 times longer in the body as a whole than in the compartments with the lowest rate of renewal, implying a substantial re-use of the selenium from organic forms. This could be an

advantage if recycled selenium is well incorporated into metabolically active proteins, but a disadvantage in cases of excessive exposure to selenium. In the case of *selenium enriched yeast*, the Committee considered that information was needed on the distribution of the various selenium-containing compounds and their selenium content.

For the present opinion, the Committee considered its earlier views and the following information. All forms of selenium, both inorganic and organic, are considered to be well absorbed and bioavailable, with the exception of metal selenides. There is a consensus that the organic form, selenomethionine, is less toxic than the inorganic forms, sodium selenite and selenate.[26] However, it is also clear that different forms of selenium are differently distributed in organs and tissues (see later).[26] In humans selenomethionine, for example, has a longer half-life than inorganic forms of selenium. It is diverted into pathways of methionine metabolism as selenomethionine and, although incorporated into protein, it is less available for immediate selenoprotein synthesis than inorganic selenium.[27] Selenomethionine can be directly metabolised into selenocysteine or first catabolised and the selenium released used for the synthesis of selenocysteine. It is this ability to be "recycled" which probably accounts for its longer half-life.

The reservations expressed by the SCF in 1994[25] concerning the proposed use of *selenomethionine* in infant formulae would equally apply to use in foods other than infant formulae. Its proposed use cannot therefore be evaluated until the required information specified by the Committee in 1994 is supplied.

Sodium hydrogen selenite is chemically similar to sodium selenite and similarly readily bioavailable.[28] It is likely to have the same biological activity as sodium selenite. Clinical assessments of selenium status in infants and children with phenylketonuria or maple syrup urine disease, given foods for special medical purposes containing sodium hydrogen selenite, confirm that plasma selenium concentrations were restored to normal in infants and children.[29] As sodium selenite has already been considered acceptable by the SCF for use in infant formulae, the use of sodium hydrogen selenite as a source of selenium for nutrient purposes can also be accepted in FPNUs.

Selenocystine is the oxidised form of selenocysteine which is considered to be highly oxidisable. The selenium forms of these two amino acids occur naturally and are found at the active site of certain enzymes in prokaryotic and eukaryotic organisms.[28] Like other organic selenium compounds, selenocysteine and selenocystine are retained longer in the body than inorganic selenium. However, the lack of information about its bioavailability, absorption and subsequent behaviour in the body (e.g. it is readily catabolised by selenocysteine β-lyase) suggest that the Committee's earlier reservations about the use of organic selenium compounds[25] should apply to selenocystine as well.

No information on *Lactobacillus enriched in selenium* has been submitted and the Committee's earlier reservations about the use of organic selenium compounds similarly apply.[25]

Selenium enriched yeasts are obtained by cultivation of *Saccharomyces cerevisiae* in a beet molasses medium, enriched with sodium selenite, followed by heat inactivation and drying.[6] It has been suggested that the relative toxicities of commercial selenium enriched yeast products are likely to vary, depending on source materials, growth medium, methods of manufacture and selenium content.[26,30] It has also been suggested that the amount of selenium present as selenomethionine in selenium enriched yeasts may vary between 20 and 50% and that this depends on the concentration of selenium present; when selenium concentration is low the proportion of selenium covalently bound

as selenomethionine is likely to be proportionately high and *vice versa*.[30] The same authors have suggested that some selenium in selenium enriched yeasts is organically bound in selenotrisulphides.[30]

Limited animal studies comparing selenium enriched yeast with an inorganic form, sodium selenite, indicate that for a given selenium intake, selenium enriched yeast is less toxic than sodium selenite, perhaps due to less rapid absorption and less immediate bioavailability. However, tissue retention of selenium administered as selenium enriched yeast is longer.[30,31]

Human supplementation studies indicate that selenium enriched yeast is effective at raising plasma selenium levels[32,33] and that it raises plasma and platelet glutathione peroxidase activity levels by greater amounts than does supplementation with an equivalent amount of selenium given as sodium selenite.[34] Renal plasma clearance of selenium is lower and plasma selenium levels are higher after supplementation with selenium enriched yeast compared with an equivalent amount of selenium given as sodium selenate.[35] In those given selenium enriched yeast, the majority of the selenium is incorporated into haemoglobin, whereas in those given selenate it is equally distributed between glutathione peroxidase and haemoglobin. [35] Another study has also shown that selenium enriched yeast increases selenium levels in red blood cells and plasma, whereas selenium as sodium selenite or selenate preferentially increases platelet glutathione peroxidase content.[36] Plasma and erythrocyte selenium levels continue to increase if selenium enriched yeasts are given over time whereas with selenate, they hardly increase or level off rapidly. There are also differences in the time course of depletion of platelet glutathione peroxidase once selenium supplementation is stopped, with more rapid depletion after cessation of selenate than after selenium enriched yeast.

In view of the above information, which indicates uncertainty about the range of selenium enriched yeast preparations which could be used and the range of selenium compounds they may contain, and differences in the way in which the body handles organic compared with inorganic forms, the Committee's earlier reservations about the use of organic selenium compounds still apply.[25] It is noted, however, that organic forms are generally less toxic than inorganic forms.

Chromium-containing substances

For c*hromium (III) chloride, chromium (III) sulphate* and their corresponding *hexahydrates* no information about their bioavailability, hydrolysis, metabolism or toxicity was submitted. However, data available on other trivalent chromium salts indicate that absorption and toxicity are low.[15] It can be reasonably assumed that chromium (III) chloride, chromium (III) sulphate and their hexahydrates are absorbed in the gastrointestinal tract in a similar manner to other chromium (III) salts. The use of chromium (III) chloride, chromium (III) sulphate and their hexahydrates in FPNUs is therefore acceptable. It should be noted, however, that the absorption of chromium (III) salts from FSMPs given orally to infants and children with diseases affecting permeability of the gut may be enhanced and their use would need to be carefully managed.[37]

Chromium tripicolinate, an organic complex of chromium with picolinic acid (a metabolite of tryptophan) is stated to have higher bioavailability than inorganic chromium salts.[38] However, no data on bioavailability or metabolism were submitted. Toxicity data on chromium tripicolinate indicated it was negative in mutagenicity

studies, of low acute toxicity in the rat and without obvious toxicity in a 20-week oral study in rats.[38-41] A human study examining the possible beneficial effects of chromium tripicolinate on serum triglyceride levels reported no adverse effects following administration of 1000 μg/day.[42] Since the degree of bioavailability of chromium is critical to its toxicity, evaluation of the acceptability of chromium tripicolinate as a nutrient source of chromium in FPNUs is not possible unless data on bioavailability in humans are provided.

Chromium(III) from *chromium (III) enriched yeasts* is stated to be bioavailable but no detailed information was submitted by the petitioner.[6] Since the degree of bioavailability of chromium is critical to its toxicity, evaluation of the acceptability of chromium (III) enriched yeasts as a nutrient source of chromium in FPNUs is not possible unless data on bioavailability in humans are provided.

Molybdenum-containing substances

Molybdenum (VI) from *ammonium molybdate* (available in its tetrahydrate form) and *sodium molybdate* (available in its dihydrate form) is efficiently and rapidly absorbed from the gastrointestinal tract, with 40-100% being absorbed in the duodenum and proximal jejunum.[43-45] The use of molybdates has been requested for FPNUs to correct deficiencies of molybdenum which have been found in cases of prolonged total parenteral nutrition,[46] inborn errors of molybdenum metabolism[45] and in children with severe digestive pathologies.[47] In short bowel syndrome and Crohn's disease molybdenum losses in the faeces can be very high, up to 600μg/day.[43] In view of the evidence of bioavailability of molybdenum from these two salts and the absence of any concern about the cations, ammonia and sodium, the use of both ammonium molybdate and sodium molybdate in FPNUs is acceptable.

Fluorine-containing substances

The toxicity of fluoride was recently evaluated by the Committee in the context of its occurrence in natural mineral waters.[48] The bioavailability of fluorine from sodium or potassium fluoride in water is around 100%. In the absence of any concern about the sodium and potassium cations, the use of *sodium fluoride* and *potassium fluoride* in FPNUs is acceptable.

Amino acids and their derivatives and peptides

The Committee considered that the use of individual amino acids, including those specifically requested for use in FSMPs, i.e. *L-alanine, L-aspartic acid, L-citrulline, L-glutamic acid, L-glutamine, glycine, L-ornithine* and *L-proline*, their sodium, potassium, calcium and magnesium salts and their hydrochlorides to be acceptable.

The Committee considered the request to use the following amino acid derivatives in FSMPs:-

L-cysteine ethylester hydrochloride
L-cysteine methylester hydrochloride
N-acetyl-L-cysteine
N-acetyl-L-cystine
L-glutamine α-keto glutaric acid
N-acetyl-L-glutamine
N-acetyl-L-methionine

L-ornithine α-keto glutaric acid
L-4-hydroxyproline
N-acetyl-4-hydroxyproline
N-acetyl-L-tryptophan
N-acetyl-L-tyrosine

The Committee has been informed that N-acetyl derivatives of amino acids are preferred in some cases to the amino acids themselves because they prevent bitter taste and/or unpleasant odours and give more stability against Maillard browning reactions during food processing.[6] The Committee noted and agreed with the petitioner's comment that in order to limit the formation of nitrosamines, N-acetyl derivatives should not be used in infant foods containing significant amounts of nitrate or nitrite. The Committee was also informed that α-keto acid derivatives of amino acids are more stable during heat treatment and in aqueous solutions than the amino acids themselves. However, in the case of all the amino acid derivatives listed above, no information was submitted by the petitioner on bioavailability in humans, hydrolysis, metabolism or toxicological safety. The Committee is therefore unable to evaluate these amino acid derivatives until the above-mentioned information is provided.

The Committee considered the use of *L-lysine acetate* to be acceptable in all FPNUs as it is a salt which is soluble in aqueous solution. L-lysine would therefore be bioavailable and there is no concern about the anion, acetate.

The Committee recognises that some dipeptides, tripeptides and oligopeptides are important ingredients in the manufacture of certain types of FSMPs. Their diversity is such that it would be unrealistic to try to list them individually. Some of these peptides are produced by hydrolysis of normal food proteins and others are synthesised de novo. It is possible that either of these processes could produce atypical, cross-linked or bioactive peptides with pharmacological or toxicological properties. The Committee therefore wishes to give further consideration to the issue of peptide preparations and will report on this at a later date, once it has obtained and considered information on methods of production and composition of peptide preparations.

Other nitrogen-containing compounds

No biological information has been submitted concerning *L-carnitine-L-tartrate*. No evaluation is therefore possible of the acceptability of its use in FPNUs.

Conclusions

The Committee considered the list of substances for nutritional purposes proposed for use in the manufacture of foods for particular nutritional uses. It was noted that many of these substances had been approved previously by the Committee for use in the manufacture of foods for particular nutritional uses intended for infants and young children. The Committee considered that the latter substances should be included in the framework list for use in any category of FPNUs. In this opinion, the Committee has evaluated a number of new substances requested for use in the manufacture of all FPNUs other than those intended for infants and young children and a number of new substances requested specifically for FSMPs.

The nutritional substances considered acceptable for use in all FPNUs or in FSMPs only are listed in the Annex. For clarity, the Annex also includes the substances previously approved for use in foods for particular nutritional uses intended for infants and young children that should be included in the framework list. The Committee wishes to stress that the fact that a substance is deemed acceptable for inclusion in the framework list does not imply that the Committee considers it necessary or appropriate to add that substance to all FPNUs.

In the case of *D-alpha tocopheryl acid succinate*, the Committee considered that it was temporarily acceptable pending submission of information on the extent of hydrolysis prior to systemic absorption, within one year of publication of this opinion.

In addition to the substances listed in the Annex as acceptable for use, the Committee was requested to evaluate the following substances:

Selenomethionine
Selenocystine
Lactobacillus enriched in selenium
Selenium enriched yeast
Chromium tripicolinate
Chromium enriched yeast
L-cysteine ethylester hydrochloride
L-cysteine methylester hydrochloride
N-acetyl-L-cysteine
N-acetyl-L-cystine
L-glutamine α-keto glutaric acid
N-acetyl-L-glutamine
N-acetyl-L-methionine
L-ornithine α-keto glutaric acid
L-4-hydroxyproline
N-acetyl-4-hydroxyproline
N-acetyl-L-tryptophan
N-acetyl-L-tyrosine
L-carnitine-L-tartrate
Dipeptides
Tripeptides
Oligopeptides

In the case of these substances listed above, the Committee considered that the data submitted by the petitioners were insufficient for an evaluation. The Committee requires further information on these substances as detailed earlier in this opinion.

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ANNEX

SUBSTANCES FOR NUTRITIONAL PURPOSES ACCEPTABLE FOR USE IN THE MANUFACTURE OF FOODS FOR PARTICULAR NUTRITIONAL USES

For the purpose of this table:

- **"All FPNU" means foods for particular nutritional uses including FSMPs except those intended for infants and young children in good health**
- **"FSMP" means foods for particular nutritional uses intended for special medical purposes**

SUBSTANCE	CONDITIONS OF USE	
	All FPNU	FSMP
1. Vitamins		
VITAMIN A		
- retinol	x	
- retinyl acetate	x	
- retinyl palmitate	x	
- beta-carotene	x	
VITAMIN D		
- cholecalciferol	x	
- ergocalciferol	x	
VITAMIN E		
- D-alpha-tocopherol	x	
- DL-alpha-tocopherol	x	
- D-alpha-tocopheryl acetate	x	
- DL-alpha-tocopheryl acetate	x	
- D-alpha-tocopheryl acid succinate	x	Temporarily acceptable
VITAMIN K		
- phylloquinone (phytomenadione)	x	
VITAMIN B1		
- thiamin hydrochloride	x	
- thiamin mononitrate	x	
VITAMIN B2		
- riboflavin	x	
- riboflavin 5'-phosphate	x	
NIACIN		
- nicotinic acid	x	
- nicotinamide	x	
PANTOTHENIC ACID		
- D-pantothenate, calcium	x	
- D-pantothenate, sodium	x	
- dexpanthenol	x	

ANNEX (continuation)

SUBSTANCE	CONDITIONS OF USE	
	All FPNU	**FSMP**
VITAMIN B6		
- pyridoxine hydrochloride	x	
- pyridoxine 5'-phosphate	x	
FOLIC ACID		
- pteroylmonoglutamic acid	x	
VITAMIN B12		
- cyanocobalamin	x	
- hydroxocobalamin	x	
BIOTIN		
- D-biotin	x	
VITAMIN C		
- L-ascorbic acid	x	
- sodium-L-ascorbic acid	x	
- calcium-L-ascorbic acid	x	
- potassium-L-ascorbic acid	x	
- L-ascorbyl 6-palmitate	x	
2. Minerals		
CALCIUM		
- carbonate	x	
- chloride	x	
- salts of citric acid	x	
- gluconate	x	
- glycerophosphate	x	
- lactate	x	
- salts of orthophosphoric acid	x	
- hydroxide	x	
- oxide	x	
MAGNESIUM		
- acetate	x	
- carbonate	x	
- chloride	x	
- salts of citric acid	x	
- gluconate	x	
- glycerophosphate	x	
- salts of orthophosphoric acid	x	
- lactate	x	
- hydroxide	x	
- oxide	x	
- sulphate	x	

ANNEX (continuation)

SUBSTANCE	CONDITIONS OF USE	
	All FPNU	FSMP
IRON		
- ferrous carbonate	x	
- ferrous citrate	x	
- ferric ammonium citrate	x	
- ferrous gluconate	x	
- ferrous fumarate	x	
- ferric sodium diphosphate	x	
- ferrous lactate	x	
- ferrous sulphate	x	
- ferric diphosphate	x	
- ferric saccharate	x	
- elemental iron	x	
COPPER		
-cupric carbonate	x	
-cupric citrate	x	
-cupric gluconate	x	
-cupric sulphate	x	
-copper lysine complex	x	
IODINE		
- potassium iodide	x	
- potassium iodate	x	
- sodium iodide	x	
- sodium iodate	x	
ZINC		
- acetate	x	
- chloride	x	
- citrate	x	
- gluconate	x	
- lactate	x	
- oxide	x	
- carbonate	x	
- sulphate	x	
MANGANESE		
- carbonate	x	
- chloride	x	
- citrate	x	
- gluconate	x	
- glycerophosphate	x	
- sulphate	x	

ANNEX (continuation)

SUBSTANCE	CONDITIONS OF USE	
	All FPNU	FSMP
SODIUM		
- bicarbonate	x	
- carbonate	x	
- chloride	x	
- citrate	x	
- gluconate	x	
- lactate	x	
- hydroxide	x	
- salts of orthophosphoric acid	x	
POTASSIUM		
- bicarbonate	x	
- carbonate	x	
- chloride	x	
- citrate	x	
- gluconate	x	
- glycerophosphate	x	
- lactate	x	
- hydroxide	x	
- salts of orthophosphoric acid	x	
SELENIUM		
- sodium selenate	x	
- sodium hydrogen selenite	x	
- sodium selenite	x	
CHROMIUM (III)		
- chloride	x	
- sulphate	x	
MOLYBDENUM (VI)		
- ammonium molybdate	x	
- sodium molybdate	x	
FLUORINE		
- potassium fluoride	x	
- sodium fluoride	x	

ANNEX (continuation)

SUBSTANCE	CONDITIONS OF USE	
	All FPNU	FSMP
3. Amino acids		
- L-alanine		x
- L-arginine	x	
- L-aspartic acid		x
- L-citruline		x
- L-cysteine	x	
- L-cystine	x	
- L-histidine	x	
- L-glutamic acid		x
- L-glutamine		x
- glycine		x
- L-isoleucine	x	
- L-leucine	x	
- L-lysine	x	
- L-lysine acetate	x	
- L-methionine	x	
- L-ornithine		x
- L-phenylalanine	x	
- L-proline		x
- L-threonine	x	
- L-tryptophan	x	
- L-tyrosine	x	
- L-valine	x	

For amino acids, as far as applicable, also the sodium, potassium, calcium and magnesium salts as well as their hydrochlorides may be used.

4. Other nitrogen compounds	
- L-carnitine	x
- L-carnitine hydrochloride	x
- taurine	x
5. Nucleotides	
- adenosine 5'-phosphoric acid (AMP)	x
- sodium salts of AMP	x
- cytidine 5'-monophosphoric acid (CMP)	x
- sodium salts of CMP	x
- guanosine 5'-phosphoric acid (GMP)	x
- sodium salts of GMP	x
- inosine 5'-phosphoric acid (IMP)	x
- sodium salts of IMP	x
- uridine 5'-phosphoric acid (UMP)	x
- sodium salts of UMP	x

ANNEX (continuation)

SUBSTANCE	CONDITIONS OF USE	
	All FPNU	**FSMP**
6. Others		
- choline	x	
- choline chloride	x	
- choline bitartrate	x	
- choline citrate	x	
- inositol	x	

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