

**CODEX COMMITTEE ON NUTRITION AND FOODS FOR SPECIAL
DIETARY USES**

**Forty fourth Session – Dresden, Germany
2-6 October 2024**

European Union comments on

Agenda item 8

**Discussion paper on use of fructans, beta-carotene, lycopene in
*Standard for Infant Formula and Formulas for Special Medical
Purposes Intended for Infants (CXS 72-1981)*
(CX/NFSDU 24/44/8)**

*European Union Competence
European Union Vote*

The European Union (EU) thank the United States as chair of the Electronic Working Group (EWG) for the work carried out on this subject and the presentation of the discussion paper.

beta-carotene

The EU does not support recommendation i., the EU does not support that CCNFSDU44 informs CCMAS that beta-carotene is a suitable optional ingredient as defined in CXS 72-1981 and listed in the *Advisory Lists of Nutrient Compounds for use in Foods for Special Dietary Uses Intended for Infants and Young Children (CXG 10-1979)*, and request CCMAS to endorse AOAC 2016.13 / ISO DIS 23443 (beta carotene and lycopene) for use with beta-carotene in the CXS 72-1981 as a Type II method.

The EU considers that the Terms of Reference (ToR) of the EWG on item 8 of the agenda for CCNFSDU44 are not met regarding the use of beta-carotene as optional ingredient in CX 72-1981. According to the ToR, the EWG was requested to

"Review the use of [...] beta-carotene [...]",

and to (emphasis added)

*"Develop recommendations to CCNFSDU44 regarding the **safety and suitability** of these ingredients as **optional ingredients** in CXS 72-1981 [...]"*.

In CX/NFSDU 24/44/8, the chair of the EWG concluded that beta-carotene is a suitable optional ingredient as defined in CXS 72-1981, that it is listed in the Advisory Lists of nutrient compounds for use in foods for special dietary uses intended for infants and young children (CXG 10-1979) (Advisory Lists (CXG 10-1979)), and that CCMAS should therefore be requested to endorse AOAC 2016.13 / ISO DIS 23443 (beta-carotene and lycopene) for use of beta-carotene in the CXS 72-1981 as a Type II method.

The justification provided for this conclusion was the support by 11 (of 13) EWG members who stated that beta-carotene is a safe and suitable ingredient and that it is listed in the Advisory Lists (CXG 10-1979). However, neither CX/NFSDU 24/44/8 nor the EWG Consultation Paper prepared by the USA as EWG Chair as of October 27, 2023, provide any information regarding the safety, suitability and/or benefits of using beta-carotene in infant formula or in formula for special medical purposes (FSMP) for infants. To the EU's understanding, it would have been within the ToR of the EWG to review scientific data on the safety and suitability of beta-carotene for infants. Moreover, as beta-carotene is listed in the Advisory Lists (CXG 10-1979) only as provitamin A, the EWG should have presented data showing that beta-carotene can be efficiently converted into vitamin A in infants and is therefore a safe source of vitamin A.

In the above-mentioned Consultation Paper, it is indicated that beta-carotene (together with lycopene) are the most abundant carotenoids in human milk and that breastfed infants are therefore exposed to beta-carotene, whereas infants who consume infant formula have little or no intake of beta-carotene. However, the presence of a substance in human milk does not provide sufficient cause for this substance to be used in infant formula. Thus, it seems that the fact that beta-carotene is listed in the Advisory Lists (CXG 10-1979) has been taken by the EWG as the only reference for the appropriateness of beta-carotene as an optional ingredient in infant formula.

The EU notes that the current listing of beta-carotene as provitamin A in the Advisory Lists (CXG 10-1979) might be a mistake. The EU considers that it is questionable whether the criteria for including nutrient compounds in the lists (Section 2.1 in CXG 10-1979) have ever been critically reviewed in the case of beta-carotene.

With respect to the criterion 2.1 a) that nutrient compounds must be safe and appropriate for the intended use, the EU is of the opinion that there is a lack of knowledge on the rate of conversion of beta-carotene to vitamin A in infants.

The EU notes that carotenoids have so far not been considered as sources of vitamin A in infants, neither in Codex, as reflected in the footnotes to the provisions for vitamin A in the Infant formula and Follow-up formula Standards (CXS 72-1981 and CXS 156-1987):

“[...] Retinol contents shall be provided by preformed retinol, while any contents of carotenoids should not be included in the calculation and declaration of vitamin A activity.”

nor at EU level (EFSA, 2014¹).

¹ Emphasis added, page 56: “Retinol sources authorised for use in IF and FOF are retinol and two forms of retinyl esters, i.e. retinyl palmitate and retinyl acetate. **Carotenoids are not considered as a source of vitamin A in infants owing to a lack of knowledge on the bioconversion of carotenoids in infants.**” and page 56/58: “Recommendations Assuming an average energy intake of an infant below six months of age of 500 kcal/day and taking as a basis the intake levels of vitamin A considered adequate by the Panel for this age group of 350 µg RE/day **based on pre-formed vitamin A intakes from breast milk**, this converts into a required minimum vitamin A content of formula of 70 µg RE/100 kcal. [...] The vitamin A activity in IF and FOF **should be provided by retinol or retinyl esters. In view of the existing uncertainties as to the relative equivalence of β-carotene and retinol in infants, any content of carotenes should not be included in the calculation and declaration of vitamin A activity.**”

EFSA NDA Panel (EFSA Panel on Dietetic Products, Nutrition and Allergies), 2014. Scientific Opinion on the essential composition of infant and follow-on formulae. EFSA Journal 12: 3760, 106 pp.
<https://efsa.onlinelibrary.wiley.com/doi/pdf/10.2903/j.efsa.2014.3760>

Moreover, the EU considers that there is currently no scientific evidence that beta-carotene as such is needed for growth, development and health by infants in the first months of life.

According to 2.2 of the Advisory Lists (CXG 10-1979),

"Nutrient compounds shall be deleted from the lists if they are found to no longer meet these criteria. If a country proposes to add or delete a nutrient compound to/from a list, the country should provide information that addresses how the nutrient compound satisfies/does not satisfy the criteria in Section 2.1."

The EU considers that there is insufficient evidence that beta-carotene is appropriate for the intended use as an optional ingredient/source of vitamin A in infant formula and considers that beta-carotene does not fulfil the criteria for being kept in the Advisory Lists (CXG 10-1979). Therefore, the EWG should clarify these aspects for CCNFSDU 45. Alternatively, we suggest that beta-carotene be removed from the Advisory lists (CXG 10-1979), at least regarding its optional use in infant formula, Sec. A and Sec. B.

In addition, generally, the only specific (nutrient) function in the body for beta-carotene is its action as a precursor of vitamin A. Other functions listed in the EWG Consultation Paper relate to lycopene but are assumed to be also valid for beta-carotene (numerous biological effects in humans, including antioxidant, anti-inflammatory and immunomodulatory properties), such effects are non-specific. The addition of beta-carotene to infant formula has not been scientifically demonstrated to lead to additional health benefits compared with formula to which beta-carotene has not been added.

Fructooligosaccharides (FOS), oligofructose (OF), and oligofructan

The EU does not support recommendation ii., the EU does not support that CCNFSDU44 informs CCMAS that

- fructooligosaccharides (FOS), oligofructose (OF), and oligofructan are nutrient compounds consistent with the provisions established in the Advisory Lists (CAC/GL 10-1979)
- FOS, OF and oligofructan are suitable optional ingredients as defined in CXS 72-1981
- requesting CCMAS to endorse AOAC 2016.14/ISO DIS 22579 | IDF 241 (Fructans) for use with CXS 72-1981 as a Type II method.

The EU considers that the ToR of the EWG are not met with regard to the use, safety and suitability of FOS, OF and oligofructan. The use, safety and suitability of specific fructans as an optional ingredient has not been sufficiently demonstrated.

The EU would like to receive clarification about the terms used, the substances under consideration (Fructooligosaccharides (FOS), oligofructose (OF), and oligofructan) and how they relate to one another. The EU notes that for the substances under consideration, FOS, OF and oligofructan, definitions vary and therefore the EU would like to receive clarification which concrete substances are included in those groups. has been provided. It is not possible to evaluate groups of substances without knowing exactly which substances are included.

The substances included in the groups need to correspond to the substances that are measured by a proposed method. Without clearly defining the substances covered, a suitable method cannot be determined. The EU would like to receive clarification about which substances, e.g. chain-length, are measured by the proposed analytical methods AOAC 2016.14/ISO DIS 22579 | IDF 241 (Fructans). The EU would like to receive clarification about how the proposed method differentiates between e.g. FOS and d fructose, e.g. derived from longer chain molecules such as inulin.

The EU notes that the method proposed seems to measure the amount of fructose in the product. However, the *Standard for Infant Formula and Formulas for Special Medical Purposes Intended for Infants* (CXS 72- 1981) lists in relation to Carbohydrates (emphasis added):

“Total carbohydrates⁸⁾

Unit	Minimum	Maximum	GUL
g/100 kcal	9.0	14.0	-
g/100 kJ	2.2	3.3	-

⁸⁾ Lactose and glucose polymers should be the preferred carbohydrates in formula based on cows’ milk protein and hydrolysed protein. Only precooked and/or gelatinized starches gluten free by nature may be added to infant formula up to 30 percent of total carbohydrates and up to 2 g/100 ml.

Sucrose, unless needed, and the addition of fructose as an ingredient, should be avoided in infant formula because of potential life-threatening symptoms in young infants with unrecognized hereditary fructose intolerance”.

The EU would like to receive clarification how the proposed method can distinguish between fructose added as such or as a component of sucrose, which should be avoided, and fructose added as optional ingredient in the form of FOS, OF and oligofructan.

The EU notes that FOS, OF and oligofructan are heterogenous groups and include a wide variety of inulin-type fructans with variable degrees of polymerisation, this heterogenous group is not sufficiently characterised. The ToR of the EWG refer to “fructans (fructo-oligosaccharides and other relevant fructans in human milk)”, however, the EWG Consultation Paper covers substances beyond the terms of reference, the EWG Consultation Paper states that “Unlike HMOs, fructans are not a component of human milk”. As fructans investigated in the EWG are not a component of human milk, this group of substances is outside the ToR of the EWG.

The EU notes that the Advisory Lists (CAC/GL 10-1979) refer to nutrient compounds, which may be used for nutritional purposes in foods for special dietary uses intended for infants and young children. “Nutrients” have been defined in the *Codex Guidelines on Nutrition Labelling* (CXG 2-1985) as

“any substance normally consumed as a constituent of food:

- (a) which provides energy; or
- (b) which is needed for growth, development and maintenance of life; or
- (c) a deficit of which will cause characteristic bio-chemical or physiological changes to occur.”

The EU does not consider that FOS, OF and oligofructan meet this above definition and that therefore, the three substances are not eligible to be added to the Advisory Lists (CAC/GL 10-1979).

Furthermore, in order to include nutrient compounds in the Advisory Lists (CAC/GL 10-1979), the criteria for such inclusion need to be met, however, the EU considers that this is not the case for FOS, OF and oligofructan. The following criteria need to be met (emphasis added):

1. Advisory Lists (CAC/GL 10-1979)

*“Nutrient compounds that are to be added for nutritional purposes to foods for infants and young children may be included in the lists only if: a) they are **shown to be safe and appropriate** for the intended use as nutrient sources for infants and young children; [...] the fulfilment of the above criteria **shall be demonstrated by generally accepted scientific criteria**”*

2. Standard for Infant Formula and Formulas for Special Medical Purposes Intended for Infants (CXS 72-1981)

*“[...] other ingredients may be added **in order to provide substances ordinarily found in human milk and to ensure that the formulation is suitable as the sole source of nutrition for the infant or to provide other benefits that are similar to outcomes of populations of breastfed babies.** [...] **The suitability for the particular nutritional uses for infants and the safety of these substances shall be scientifically demonstrated.**”*

The EU has asked for but not received clarification about evidence of the safety of FOS, OF and oligofructan for infants.

FOS, OF and oligofructan are not found in human milk, therefore FOS, OF and oligofructan are not added to match the composition of human milk. The EU considers that it has not been demonstrated that FOS, OF and oligofructan are needed for growth, development and good health status of infants aged 0 – 6 months. The effects for FOS, OF and oligofructan claimed in the EWG Consultation Paper (to have an influence on the composition of gut microbiota and on stool consistency) alone, even if they would be demonstrated scientifically, do not provide a health benefit. However, a health benefit would need to be substantiated for infants aged 0-6 months in order to be considered as an optional ingredient.

The EU considers that there is no scientific evidence to support that adding FOS, OF and oligofructan is beneficial for infants, that the addition of FOS, OF and oligofructan lead to the formulation being suitable as the sole source of nutrition for the infant or to provide other benefits that are similar to outcomes of populations of breastfed babies.

Finally, the EU notes that the EWG Consultation Paper refers to benefits of human milk oligosaccharides (HMOs), which are different from FOS, OF and oligofructan. However, benefits should be scientifically demonstrated for the specific compounds that are evaluated to whether they meet the criteria for optional ingredients or not, here FOS, OF and oligofructan.