CODEX ALIMENTARIUS COMMISSION

Food and Agriculture Organization of the United Nations

World Health Organization

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Agenda Item 7 **NFSDU/43 CRD 07**

JOINT FAO/WHO FOOD STANDARDS PROGRAMME
CODEX COMMITTEE ON NUTRITION AND FOODS FOR SPECIAL DIETARY USES

Forty-third Session

Düsseldorf, Germany
7 – 10 March with report adoption by virtual mode on 15 March 2023

Prioritization mechanism / emerging issues or new work proposals

Proposal 1.2: Proposal to align the permitted uses of the folic acid source Calcium-L-Methyl-Folate with those of N-Pteroyl-L-Glutamic acid in the advisory list of nutrient compounds for use in foods for special dietary uses intended for infants and young children

Prepared by Switzerland

Summary of the new work proposal, in particular an updated self-assessment against the CCNFSDU Priority setting criteria as outlined in CX/NFSDU 23/43/8

This CRD summarizes the discussion paper submitted by Switzerland in reply to CL 2020/30-NFSDU, and in particular provides the ***updated self-assessment*** against the CCNFSDU Priority setting criteria as outlined in CX/NFSDU 23/43/8. This update was necessary because for the reply to CL 2020/30-NFSDU the decision tree included in Appendix IX of REP 20/NFSDU from the 41st session of the CCNFSDU had to be used which is slightly different, so our arguments had to be re-arranged. This update is also provided because it is understood that the ad-hoc physical working group on priority setting will focus on the priority assessment as such, and **this document is intended to help delegates understand our proposal and assist with the priority assessment**. The arguments presented as such are the same as in our reply to CL 2020/30-NFSDU.

Summary of the Swiss proposal

New scientific evidence as assessed by **EFSA (2020)**, a Codex RASB, concludes that the folic acid nutrient source **Calcium-L-methyl-folate is safe, bioavailable and suitable for use in all foods intended for infants and young children.** This folic acid nutrient source is the natural form as found in human milk. Based on the new scientific finding, the permitted uses for calcium-L-methyl-folate in the Advisory Lists of nutrient compounds in CXG 10-1979, part B can be extended to include also IF Sec A, FUF, PCBF and CBF, in addition to the already existing permissions for the two FSMP. Furthermore, it is proposed that reference to the USP monograph be added as it had been found suitable for the intended use by the RASB as well.

The graph below summarises our work proposal in a visualised way for fast comprehension:

ADVISORY LISTS OF NUTRIENT COMPOUNDS FOR USE IN FOODS FOR SPECIAL DIETARY USES INTENDED FOR INFANTS AND YOUNG CHILDREN (CXG 10-1979)

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

CAC/GL 10 - 1979 15

Nutrient Source	Purity Requirements by		Use in Codex Food Standards Applicable to Infants and Young Children					
	CAC[1]	International and/or national bodies	IF		FUF[4]	PCBF[5]	CBF[6]	FSMP[7] for infants and young children
			Sec. A[2]	Sec. B[3]				

(…)

10. Folic acid								
10.1 N-Pteroyl-L-glutamic acid		Ph Int, FCC, USP, Ph Eur, Jap Food Stan	√	√	√	√	√	√
10.2 Calcium-L-methyl-folate		JECFA (2005)	-	√	-	-	-	√

add USP

add 4 additional checkmarks "√" to allow use in all Infant/Young Children food categories

Graphical representation of the Swiss proposal to extend the use of Calcium-L-methyl-folate based on Codex RASB (EFSA) new scientific evidence

Updated self-assessment against the prioritization mechanism criteria as set in CX/NFSDU 23/43/8.

We understand from para 10 in Appendix I of CX/NFSDU 23/43/8 that the host country secretariat checks new work proposals for the decision tree questions 1-4, so that the focus for the ad-hoc working group can be on question 5 with its four criteria. Nevertheless, we include our answers to question 1-4 in this CRD as well for sake of completeness.

1. **Is the new work proposal coming from CAC, a CAC subsidiary body and/or a member?**

   YES. While this proposal for the use extension for calcium-L-methyl-folate in the Advisory List CXG 10-1979 is not a request from the CAC, it is nevertheless a request from a Codex member country, Switzerland. → proceed to Q2.

2. **Is the new work proposal following the process and criteria outlined in the Procedural Manual?**

   YES. The Swiss discussion paper (see CX/NFSDU 23/43/7) follows all administrative criteria according to the Codex PM. It consists of three parts:

   - Part 1: The project document which follows the Codex Procedural Manual Sec. II Proposal for new work/revision of a standard.
   - Part 2: Appendix IX (Guideline for preliminary assessment of work priorities for CCNFSDU) of the CCNSDU report REP20/NFSDU, including a self-assessment against paragraph 2 of the Appendix IX, now updated with this document to follow CX/NFSDU 23/43/8.
   - Part 3: All information required according to the special procedure in the Advisory list of nutrient compounds (Section 2 in CXG 10-1979). → proceed to Q3.

3. **Does this new work proposal address issues which are consistent with the terms of reference of CCNFSDU?**

   YES. The new work proposal proposes an amendment due to scientific progress to an existing document (CXG 10-1979) under the purview of the CCNFSDU. This document (CXG 10-1979) is also listed as a CCNFSDU related standard on the Codex website, in the CCNFSDU section. → proceed to Q 4.

4. Does the new work proposal contain a self-assessment based on the CCNFSDU prioritization criteria?

YES. The discussion paper submitted by Switzerland in reply to CL 2020/30-NFSDU included a self-assessment against the CCNFSDU Priority setting criteria which at that time had been published in Appendix IX of the CCNFSDU report REP20/NFSDU. This CRD now provides the update to that self-assessment by following CX/NFSDU 23/43/8. We note that our self-assessment against Appendix IX included basically already all answers that are now required for CX/NFSDU 23/43/8. The answers provided here just follow the order as set in CX/NFSDU 23/43/8. → proceed to 5.

5. Proposal is qualified for a case-by-case review

According to the decision tree, a Yes to question 1-4 results in the conclusion that a proposal is qualified for a case-by-case review by an ad-hoc working group. The proposal of Switzerland qualifies for this assessment.

Consequently, here **our case-by-case self-assessment against the criteria of question 5:**

A. Impact on health of target group

The advisory list of nutrient compounds targets food for children aged 0-36 month. This target group of infants and young children is a vulnerable population. It is among others for this reason that this specific advisory list with acceptable nutrient forms exists. As regards the gross size of the target population being principally in scope of the nutrients in the Advisory list, one source of statistical data allowed to conclude that the total number of infants/young children amounts to some 600 million (data from 2015). More details are provided in our proposal in CX/NFSDU 23/43/7.

The proposal does not resolve, mitigate, prevent or significantly reduce a consumer health risk. However, the **calcium-L-methyl-folate is the natural form of the vitamin folic acid** as provided by mother´s milk to infants/young children. As the scientific evidence has been provided (EFSA 2020) now that this nutrient form is not only suitable for FSMPs for infants/young children, but that it is **also safe, bioavailable and suitable for use in IF Sec A, FUF, PCBF and CBF**, the Advisory list should be **updated** in line with Codex principles which require CAC and its subsidiary bodies to ensure **that Codex Standards and related texts are consistent with and reflect current scientific knowledge** (PM, sec I.5).

The new scientific evidence has a positive impact for the target population because the Advisory list CXG 10-1979 can now fully follow the **"gold standard" principle** that those nutrients which are present in mother's milk are expected to be the best candidates for inclusion into foods for infants. Calcium-L-methyl-folate meets this criterion.

Calcium-L-methyl-folate complies with the JECFA (2005) purity criteria. The additional proposal to allow the substance as well when in compliance with the purity criteria of its recent **USP monograph** is equally acceptable and has been **confirmed by EFSA (2020**). The substance is used substitutional for N-pteroyl-L-glutamic acid and thus does not lead to an increased exposure by the target population to the vitamin folic acid. In addition, the standards for the concerned food categories of the Advisory list set maximum levels for vitamins, including folic acid.

In conclusion, the **work proposal has a very positive (high) impact for the health of the target population** because the Advisory list will follow the most recent scientific knowledge and will allow the use of the natural form of folic acid now for all food categories for infants/young children. Note also that the criteria as set in section 2 of the Advisory list itself are also fully met.

B. Impact on food safety

In terms of food safety, the Advisory list CXG 10-1979 sets specific requirements that a nutrient has to meet in order to be eligible for listing in the advisory list. Calcium-L-methyl-folate meets all these criteria: it was shown and confirmed by JECFA (2005) and EFSA (2004, 2020) that it is safe and appropriate for the intended use as a nutrient source for infants and young children, that it is biologically available based on animal and/or human studies, that it meets an appropriate specification for identity and purity (JECFA, USP monographs), that its stability in the infant/young children foods has been demonstrated, and that all those data are based on generally accepted scientific criteria.

Food safety is not compromised by the proposal of Switzerland. Calcium-L-methyl-folate is an already permitted nutrient source for the target population. The substance permitted by the Advisory list complies with the JECFA (2005) purity criteria. The additional proposal to allow the substance to comply with the purity criteria of its recent USP monograph is equally acceptable and has been confirmed by EFSA (2020). Furthermore, the substance is used substitutional for N-pteroyl-L-glutamic acid and thus does not lead to an increased exposure by the target population to the vitamin folic acid. In addition, the standards for the concerned food categories of the Advisory list set maximum levels for vitamins, including folic acid.

A more thorough discussion of all these points is provided in the proposal as shown in CX/NFSDU 23/43/7.

To sum up the safety aspects, we quote from EFSA (2020): *"(…) it was concluded that calcium-L-methyl-folate is non-genotoxic and that sub chronic and embryo toxicity/teratogenicity studies in rats did not reveal any adverse effects up to the highest dose tested. The Panel considered that no additional toxicological studies are required on the nutrient source. The intervention study in healthy infants provided by the applicant did not indicate differences in growth and tolerance parameters in infants who consumed either and infant formula supplemented with calcium-L-methyl-folate or with folic acid, and did not raise concerns regarding formula supplemented with calcium-L-methyl-folate or with folic acid, and did not raise concerns regarding safety or tolerability of the infant formula with the proposed nutrient source. The study also provided further supporting evidence for the bioavailability of calcium-L-methyl-folate. The Panel considers that calcium-L-methyl-folate is a source from which folate is bioavailable and concludes that calcium-L-methyl-folate is safe under the proposed uses and use levels for infants and young children."*

"The Panel considers that the information provided on the specifications of the NS is sufficient and does not raise safety concerns" (CH remark: NS = Nutrient Substance; specifications assessed included JECFA, USP)

"(…) that the data provided sufficient information with respect to the stability (…)"

In conclusion, the **positive impact on food safety is high**. While advancing the Advisory list to reflect most recent nutritional science, no compromise is made on food safety. The safety is well established, and EFSA even concluded that no additional toxicological studies are needed.

C. Impact on trade practices

The extension of use of the already listed nutrient source calcium-L-methyl-folate offers manufacturers an additional choice when selecting a nutrient source for folic acid for use in a food for infants and young children. The presently permitted source of folic acid, N-pteroyl-L-glutamic acid remains listed so that the extension of use for calcium-L-methyl-folate only offers an additional choice. It does not replace the N-pteroyl-L-glutamic acid. However, when a manufacturer decides to use calcium-L-methyl-folate as a folic acid source, its use is substitutional for N-pteroyl-L-glutamic acid. This choice is generic and at the discretion of each manufacturer around the world. Thus, the extension of use of calcium-L-methyl-folate has no negative impact on fair trade practices, but only offers a new choice to manufactures and the possibility to reformulate products. Taking into account that some Codex members already allow the use of calcium-L-methyl-folate in all six food categories for infants and young children, the new work proposal of Switzerland will help at the right point in time to avoid technical impediments to trade.

In conclusion, the **positive impact on reducing potential technical impediments is high**. The proposal comes at the right time to avoid that major technical trade impediments will arise.

D. Global impact

The new work proposal has a positive impact on trade and helps to maintain global harmonization and fair trade because some Codex members already permit the use of calcium-L-methyl-folate not only in IF Sec A, but also FUF, PCBF and CBF. **Switzerland**, the **European Union and the UK[1],** as well as **Argentina[1] and Mexico[1], Morocco[1], Algeria[1] and Egypt[1]** already permit Calcium-L-methyl-folate in all six infant/young children food categories.

If the Advisory list is not amended to reflect current science, trade issues are about to arise. According to our regulatory knowledge, numerous countries, in particular in the Asia/Pacific Area and Africa, follow Codex closely in their jurisdictions and presently only allow Calcium-L-methyl-folate in the two FSMP food categories. Amendments to national regulations in those regions for calcium-L-methyl-folate are expected to follow only after an endorsement by Codex via the Advisory list. Thus, this work proposal is right on time and **prospective by helping to avoid global issues prior to their occurrence**. This is how things actually should be.

We conclude that the **positive overall global impact is high** for the reasons as outlined above.

[1] to the best of our current knowledge