CODEX ALIMENTARIUS COMMISSION

Food and Agriculture Organization of the United Nations

World Health Organization

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Agenda Item 8a **NFSDU/43 CRD 4**

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

Forty-third Session

Düsseldorf, Germany
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Methods of analysis in the *Standard for Infant Formula and Formulas for Special Medical Purposes Intended for Infants* (CXS 72-1981)

Comments by ISDI

EXECUTIVE SUMMARY

This document outlines a proposal to replace and complement methods of analysis for the determination of nutrients in infant formula, which are listed in CXS 234-1999 and referenced in CXS 72-1981 and CXG 10-1979. It is proposed that these new methods be considered during the 43rd Session of the Codex Committee on Nutrition and Foods for Special Dietary Uses (CCNFSDU) in March 2023 and that they either: (1) replace current Type II/III methods which may be outdated, and/or methods that were not validated on all types of infant formula; or (2) serve as Type II or Type III methods where such methods do not currently exist.

These new methods have been developed through the Stakeholder Panel on Infant Formula and Adult Nutritionals (SPIFAN) project, which is managed by AOAC INTERNATIONAL (AOAC). They have also either been developed by the International Organization for Standardization (ISO) and International Dairy Federation (IDF) as ISO or ISO/IDF Standards or are in the process of being adopted as such. It is proposed that these new methods be adopted as Codex Type II or III methods to enable them to be utilized as needed for the purposes of dispute resolution internationally.

ISDI RECOMMENDATION

That the Committee:

- Refer AOAC 2018.06 / ISO 4214 | IDF 254 /AACC 07-50.01 to CCMAS, for review and endorsement with the recommendation of a Type II method.
- Refer AOAC 2017.03 to CCMAS, for review and endorsement with the recommendation of a Type II method.
- Refer AOAC 2014.02 to CCMAS, for review and endorsement with the recommendation of a Type III method.

Please find details below.

INTRODUCTION

The *Standard for Infant Formula and Formulas for Special Medical Purposes Intended for Infants* (CXS 72-1981) was revised in 2007. At the 30th CCNFSDU Session in 2008, the electronic Working Group (eWG) on methods of analysis for infant formula recommended the Committee to periodically review the infant formula methods listed in the *Recommended Methods of Analysis and Sampling* (CXS 234-1999) to keep them updated (ALINORM 09/03/26). In 2009, the Codex Committee on Methods of Analysis and Sampling (CCMAS) endorsed the status of several methods of analysis for nutrients in CXS 72-1981 based on the best available methods in matrices at the time (ALINORM 09/32/23 paras. 45-71). These methods were adopted by the Codex Alimentarius Commission in 2009, including various Type I, I, III and/or IV methods, and are included in CXS 234-1999.

BACKGROUND

Some methods referenced in CXS 72-1981 and CXS 234-1999 are outdated and/or not validated for infant formula. Further, for some required nutrients and many optional ingredients, Codex Type I or Type II methods are lacking.

Since 2015, new methods of analysis for nutrients in infant formula, which were validated by AOAC International, ISO and IDF through the SPIFAN project, have been adopted and published in the *Journal of AOAC INTERNATIONAL,* adopted and published by ISO and IDF as ISO or ISO|IDF Standards, and have been submitted to Codex for review. Methods are introduced by CCNFSDU, referred to CCMAS for technical review, typing and endorsement, and then submitted to the Codex Alimentarius Commission (CAC) for adoption. To date, methods for vitamin A, vitamin C, vitamin B_{12}, vitamin D, vitamin E, vitamin K, thiamin, riboflavin, niacin, pyridoxine, biotin, pantothenic acid, folate, myo-inositol, choline, carnitine, fatty acid profile, total nucleotides, iodine, chloride, calcium, magnesium, phosphorus, potassium, sodium, copper, iron, manganese, zinc, chromium, selenium, and molybdenum have been brought through this process and all have been adopted by CAC as Type II methods for the purpose of dispute resolution. In addition, methods for thiamine, riboflavin, niacin, vitamin B_6, choline, and carnitine were adopted as Type II during the 44th CAC Session in November/December 2021.

PROPOSAL AND RATIONALE

The Committee is requested to consider recommending that the following methods be referred to CCMAS for technical review and typing. The Committee is also requested to recommend that CCMAS review the existing Type II and Type III methods for these nutrients listed in CXS 234-1999, to determine if the methods meet the specifications in CODEX STAN 72. Based on this review, CCMAS may either retain the existing methods, make necessary changes to the method Types, or revoke any methods which do not meet the specifications. Rationale supporting each method is provided below. Table 1 presents the summary of the proposed changes.

It should be noted that methods submitted comply with criteria to propose methods of analysis to CCMAS for endorsement[1].

With regard to potential questions regarding certain technologies, it should be noted that CCNFSDU have previously considered questions from CCMAS related to expensive instrumentation and whether some countries may not have the capacity to run certain methods. It should be noted a Type II method is not required to be used except in the case of resolving a dispute that cannot otherwise be settled, and in all other cases any approved Codex method may be used. The United States supports the desire of countries to use all approved Codex methods for routine nutrient analysis. However, there is a strong need to have one Type II method for each nutrient or group of nutrients in infant formula that will be used as the referee method in the case of a dispute that cannot otherwise be settled. As such, CCNFSDU and CCMAS have endorsed several methods that use the ICP-MS and other sophisticated instrumentation as Type II.[2,3]

Total Amino Acids (minus Taurine and Tryptophan) (AOAC 2018.06 / ISO 4214 | IDF 254 /AACC 07-50.01)

AOAC 2018.06 / ISO 4214 | IDF 254 /AACC 07-50.01 is proposed as Type II for the determination of total amino acids (minus taurine and tryptophan) in infant formula. There is currently no Type II method in CXS 234-1999 for the determination of total amino acids in infant formula.

AOAC 2018.06 is an Official Final Action method which has undergone successful multi-laboratory validation (MLV) using 9 infant, child and adult nutritional formulas covering the fortification range. 15 laboratories in 6 countries participated in the MLV of the UHPLC-UV method, which quantitatively determines the concentration of total amino acids in infant formula. The method has been approved as AOAC Official Final Action and was published[4]. ISO/IDF has published this method as a final ISO and IDF Standard ISO 4214 | IDF 254. The Cereals and Grains Association has published this method as an approved method of analysis as AACC 07-50.01.

Tryptophan (AOAC 2017.03)

AOAC 2017.03 is proposed as Type II for the determination of tryptophan in infant formula. There is currently no Type II method in CXS 234-1999 for the determination of tryptophan in infant formula.

AOAC 2017.03 has undergone successful MLV using 14 infant, child and adult nutritional formulas covering the fortification range. 10 laboratories in seven countries participated in the MLV of the HPLC method, which determines the concentration of tryptophan in infant formula. AOAC 2017.03 has been published as Official Final Action.[5]

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[1] Comprehensive Guidance for the Process of Submission, Consideration and Endorsement of Methods for Inclusion in CXS 234

[2] AOAC 2011.19 | ISO 20649 | IDF 235

[3] AOAC 2012.15 | ISO 20647 | IDF 234

[4] Jaudzems G., Fuerer C. Determination of Total Amino Acids in Infant Formulas, Adult Nutritionals, Dairy, and Cereal Matrixes by UHPLC-UV: Interlaboratory Validation Study, Final Action 2018.06. J AOAC Int. 2022;105(6):1625-1639. https://doi.org/10.1093/jaoacint/qsac083

[5] Draher J. HPLC Determination of Total Tryptophan in Infant Formula and Adult/Pediatric Nutritional Formula Following Enzymatic Hydrolysis, Multilaboratory Testing Study: Final Action 2017.03. J AOAC Int. 2019;102(5):1567-1573. https://doi.org/10.1093/jaoac/102.5.1567

Vitamin B12 (AOAC 2014.02)

AOAC 2014.02 is proposed as Type III for the determination of vitamin B12 in infant formula. AOAC 2014.02 is an Official Final Action method which has undergone successful MLV using 10 infant, child and adult nutritional formulas covering the fortification range. 18 laboratories in 11 countries participated in the MLV of the LC with UV detection method, which determines the concentrations of vitamin B12 in infant formula. AOAC 2014.02 is published as AOAC Official Final Action.[6]

RECOMMENDATION

That the Committee:

- Refer AOAC 2018.06 / ISO 4214 | IDF 254 / AACC 07-50.01 to CCMAS, for review and endorsement with the recommendation of a Type II method.
- Refer AOAC 2017.03 to CCMAS, for review and endorsement with the recommendation of a Type II method.
- Refer AOAC 2014.02 to CCMAS, for review and endorsement with the recommendation of a Type III method.

TABLE 1. AOAC Official Method, ISO/IDF Standards, and AACC approved method validated in Infant Formula

Commodity	Provision	Method	Principle	Proposed Type
Infant Formula	Total amino acids	**AOAC 2018.06 / ISO 4214 | IDF 254 /AACC 07-50.01**	**UHPLC-UV**	**II**
	Tryptophan	**AOAC 2017.03**	**HPLC**	**II**
	Vitamin B12	AOAC 2011.10 / ISO 20634	HPLC	II
		AOAC 986.23	Turbidimetric Method	III
		AOAC 2014.02	**LC-UV**	**III**

[6] Giménez EC, Martin F. Vitamin B12 (cyanocobalamin) in Infant Formula Adult/Pediatric Nutritional Formula by Liquid Chromatography with Ultraviolet Detection: Collaborative Study, Final Action 2014.02. J AOAC Int. 2018;101(4):1112-1118. https://doi.org/10.5740/jaoacint.17-0452