CODEX ALIMENTARIUS COMMISSION

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World Health Organization

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Agenda Item 3 **MAS/37 CRD/6**

JOINT FAO/WHO FOOD STANDARDS PROGRAMME

CODEX COMMITTEE ON METHODS OF ANALYSIS SAMPLING

Thirty-seventh Session
Budapest, Hungary, 22 – 26 February 2016

ENDORSEMENT OF METHODS OF ANALYSIS PROVISIONS IN CODEX STANDARDS

(Information provided by AOAC, ISO and IDF – methods of analysis for nutrients in infant formula)

The Codex Committee on Nutrition and Foods for Special Dietary Uses (CCNFSDU) agreed during its 37th Session to refer the following eight methods for nutrients in infant formula, as presented in CX/NFSDU 15/37/10 (Rev) to the Codex Committee on Methods of Analysis and Sampling (CCMAS) for technical review; vitamin B12; myo-inositol; chromium, selenium and molybdenum; nucleotides; vitamins A and E; fatty acid profile; iodine; and pantothenic acid. This includes typing, endorsement and inclusion in the Recommended Methods of Analysis and Sampling (CODEX STAN 234- 1999) during its 37th Session, as these methods reflect the most recent scientific methods of analysis for these nutrients and were validated on a broad range of infant formula products (Appendix V, Part I).

All methods are published as AOAC Official Methods of Analysis Final Action and as ISO Standards or ISO|IDF Standards. Each method has been collaboratively tested.

AOAC, ISO and IDF recommend swift adoption of these methods as dispute resolution methods (Type II) for nutrients in Infant Formula because:

- Available methods for certain nutrients do not determine the same analyte(s) or what is claimed on the product label (e.g. different forms of vitamin B12, different forms of vitamin E);
- Problems in international trade can be created when different methods are used, which meet agreed criteria but may give different results, therefore, are not suitable for dispute resolution; and
- The Codex criteria approach uses the concentration-based Horwitz-Thompson equation as a predictor for $PRSD_R$ and RSD_R. These values, especially for low-level nutrients, are too wide relative to current fortification practices and guidelines as well as product specification ranges. As such, this approach is not sufficient in resolving disputes.

In paragraph 1 below, the validation data as presented in the ISO Standards or ISO|IDF Standards is given.

Paragraph 2 gives an overview of references to the AOAC Official Methods and publications of collaborative study reports by AOAC INTERNATIONAL.

Paragraph 3 explains how the results obtained with the analytical methods can be expressed in alignment with CODEX STAN 72-1981.

Paragraph 4 explains how the AOAC/ISO/IDF methods perform compared to the methods already listed in CODEX STAN 234.

1. Scope, Principle and Validation data of 8 proposed methods.

ISO 20639:2015 technically equivalent to AOAC 2012.16

Infant formula and adult nutritionals -- Determination of pantothenic acid by ultra-high performance liquid chromatography and tandem mass spectrometry method (UHPLC-MS/MS)

Scope_principle_ISO_20639.pdf

Annex_B_Precision_data_ISO_20639.pdf

ISO 20637:2015 technically equivalent to AOAC 2011.18

Infant formula and adult nutritionals -- Determination of myo-inositol by liquid chromatography and pulsed amperometry

Scope_principle_ISO_20637.pdf

Annex_B_Precision_data_ISO_20637.pdf

ISO 20634:2015 technically equivalent to AOAC 2011.10

Infant formula and adult nutritionals -- Determination of vitamin B12 by reversed phase high performance liquid chromatography (RP-HPLC)

Scope_principle_ISO_20634.pdf

Annex_B_Precision_data_ISO_20634.pdf

ISO 20638:2015 technically equivalent to AOAC 2011.20

Infant formula -- Determination of nucleotides by liquid chromatography

Scope_principle_ISO_20638.pdf

Annex_B_Precision_data_ISO_20638.pdf

ISO 20633:2015 technically equivalent to AOAC 2012.10

Infant formula and adult nutritionals -- Determination of vitamin E and vitamin A by normal phase high performance liquid chromatography

Scope_principle_ISO_20633.pdf

Annex_B_Precision_data_ISO_20633.pdf

ISO 16958|IDF 231:2015 technically equivalent to AOAC 2012.13

Milk, milk products, infant formula and adult nutritionals -- Determination of fatty acids composition -- Capillary gas chromatographic method

Scope_principle_ISO_16958_IDF_231.pdf

Annex_B_Precision_data_ISO_16958_IDF

ISO 20649|IDF 235:2015 technically equivalent to AOAC 2011.19

Infant formula and adult nutritionals -- Determination of chromium, selenium and molybdenum -- Inductively coupled plasma mass spectrometry (ICP-MS)

Scope_principle_ISO_20649_IDF_235.pdf

Annex_B_Precision_data_ISO_20649_IDF

ISO 20647|IDF 234:2015 technically equivalent to AOAC 2012.15

Infant formula and adult nutritionals -- Determination of total iodine -- Inductively coupled plasma mass spectrometry (ICP-MS)


Scope_principle_ISO_20647_IDF_234.pdf


Annex_B_Precision_data_ISO_20647_IDF

2. References to AOAC INTERNATIONAL Official Methods of Analysis – report from collaborative studies.

All references are available in the electronic version of the Journal of AOAC INTERNATIONAL. Six of the references are published in the printed version of the Journal of AOAC INTERNATIONAL. The remaining two are “in press”.

AOAC 2012.16

Martin, F., & Campos Giménez, E. (2015) J. AOAC Int. 98(6), 1697-1701.

http://aoac.publisher.ingentaconnect.com/content/aoac/jaoac/2015/00000098/00000006/art00025

AOAC 2011.18

Butler-Thompson, L. D-B., Jacobs, W.A., & Schimpf, K.J. (2015) J. AOAC Int. 98(6), 1666-1678.

http://aoac.publisher.ingentaconnect.com/content/aoac/jaoac/2015/00000098/00000006/art00023

AOAC 2011.10

Butler-Thompson, L. D-B., Jacobs, W.A., & Schimpf, K.J. (2015) J. AOAC Int. 98(6), 1655-1665.

http://aoac.publisher.ingentaconnect.com/content/aoac/jaoac/2015/00000098/00000006/art00022

AOAC 2011.20

Gill, B.D., & Indyk, H.E. (2015) J. AOAC Int. 98(4), 971-979.

http://dx.doi.org/10.5740/jaoacint.15-050

AOAC 2012.10

McMahon, A. (2016) J. AOAC Int. 99(1), in press.

http://aoac.publisher.ingentaconnect.com/content/aoac/jaoac/pre-prints/content-9901-1

AOAC 2012.13

Golay, P-A., & Moulin, J. (2016) J. AOAC Int. 99(1), in press.

http://aoac.publisher.ingentaconnect.com/content/aoac/jaoac/pre-prints/content-9801-2

AOAC 2011.19

Pacquette, L., & Thompson, J. (2015) J. AOAC Int. 98(6), 1702-1710.

http://aoac.publisher.ingentaconnect.com/content/aoac/jaoac/2015/00000098/00000006/art00026

AOAC 2012.15

Zywicki, R.S., & Sullivan, D.M. (2015) J. AOAC Int. 98(5), 1407-1416

http://aoac.publisher.ingentaconnect.com/content/aoac/jaoac/2015/00000098/00000005/art00030

3. Expression of results by using proposed methods of analysis

Results obtained by using the proposed methods of analysis for nutrients in infant formula are calculated and expressed in amounts per 100g powder, or per 100g Ready to Feed (RTF) product. RTF samples can be from liquid origin. When RTF is reconstituted from powders, 25 grams of powdered infant formula is to be mixed with 200 grams of water.

In the CODEX Standard for Infant Formula (CODEX STAN 72-1981), the essential composition is expressed in amounts per 100 available kilocalories, and amounts per 100 available kilojoules.

By using the amount of kcal and kjoules per 100g powder, or RTF product, on the product label of the sample analyzed, the nutrient concentrations can be calculated and expressed in amounts per 100 kcalories or kjoules as follows:

$$\mathrm{w} = \frac{v}{y}\ x\ 100\ x\ f$$

w = nutrient concentration in mg/100 kcal or kjoules
v = nutrient concentration in mg/100g
y = amount of kcal or kjoules per 100g powder or RTF as indicated on sample package
f = dilution factor:
Example 1: In case of analysis of powders and of liquid Infant formula, f=1
Example 2: In case of reconstituted powders (25 g powder with 200 g of water), f=9.

4. Specificity of the recently published methods

Chromium, Selenium, Molybdenum:

ISO 20649|IDF 235/AOAC 2011.19 has better performance characteristics, improved specificity, and is specifically validated for infant formula according to CODEX STAN-72 and is therefore proposed as type II dispute resolution method. European standards can be kept in CODEX STAN-234 as Type III.

It is proposed to repeal AOAC 2006.03 (current Type III method for Chromium), as its scope is fertilizers. It is suggested that EN 14082 and EN14083 become Codex Type III for Chromium.

It is proposed to repeal AOAC 2006.03 (current Type III method for Molybdenum), as its scope is fertilizers. It is suggested that EN 14083 become Codex Type III for Molybdenum.

It is proposed that EN 14627, the current Type II method for selenium, is kept as Type III method.

Vitamin A/E:

ISO 20633/AOAC 2012.10 is:

- preferable over EN 12823-1 as type II dispute resolution method for vitamin A because:
    - EN 12823-1 was collaboratively studied on milk powder and margarine. These matrices are not representative of current infant formula matrices. As such, product matrix challenges can be observed compromising method performance.
    - ISO 20633/AOAC 2012.10 has been collaboratively studied using 12 infant formula matrices representative of the wide range and diversity of current formulations for these product categories.
    - ISO 20633/AOAC 2012.10 has improved precision and accuracy.
- preferable over EN 12822 as type II dispute resolution method for vitamin E because:
    - EN 12822 was collaboratively studied using milk powder, margarine and oat powder. These matrices are not representative of current infant formula matrices. As such, product matrix challenges can be observed compromising method performance.
    - ISO 20633/AOAC 2012.10 has been collaboratively studied using 12 infant formula matrices representative of the wide range and diversity of current formulations for these product categories.
    - ISO 20633/AOAC 2012.10 has improved precision and accuracy.
    - separates and quantifies alpha-tocopherol and alpha-tocopherol acetate esters further, as required by current regulatory standards.
    - there is no global agreement on the activity of other forms of vitamin E (EFSA, WHO).

- results are converted to tocopherol equivalents as per CODEX STAN-72.
- Note: no method differentiates D from DL isomers.

- Specifically validated for vitamin A and vitamin E in infant formula according to CODEX STAN-72.

Therefore, it is proposed as type II dispute resolution method for vitamin A and vitamin E.

European standards and AOAC 992.03 can be kept in CODEX STAN-234 as type III.

It should be noted that AOAC 992.03 is the current Codex Type III method. However, only for follow-on formula and not for infant formula.

Iodine

ISO 20647|IDF 234/AOAC 2012.15:

- measures total iodine (as stipulated in CODEX STAN 72-1981), where AOAC 992.24 measures only free iodide, and has many interferences;
- has far superior specificity and other performance characteristics to AOAC 992.24;
- is specifically validated for infant formula according to CODEX STAN-72.

Therefore, it is proposed as type II dispute resolution method. It is proposed to repeal AOAC 992.24 (Current Type II method), as the ion-selective electrode does not quantify total iodine and may deliver different results compared to ICP-MS.

Hammer & Andrey. JAOAC INTERNATIONAL Vol 91, No6, 2008: 1397

Vitamin B12

ISO 20634:2015 / AOAC 2011.10 is

- preferable over AOAC 986.23 (Current Type II method) as Type II dispute resolution method for vitamin B12 because:
  - AOAC 986.23, Cobalamin in Milk-Based Infant Formula, 1988, is a relatively old method, validated using only milk based infant formula. This matrix is not representative of current infant formula matrices.
  - ISO 20634:2015 / AOAC 2011.10 has been collaboratively tested using 12 infant formula matrices representative of the wide range and diversity of current formulations for these product categories (milk, soy, hydrolysed protein etc.)
  - ISO 20634 / AOAC 2011.10 has improved precision and accuracy compared to the microbiological method where poor repeatability and a high number of failed results has been observed due to poor growth of the organism and/or contamination. Although the microbiological method shows high sensitivity, enabling the detection of low concentrations other food components can cause interference with the assay. It is also expensive to support in the absence of a minimum level of use.
  - AOAC 986.23 is based on non-specific determination known to respond to substances other than cobalamin, Campos-Giménez et al. JAOAC INTERNATIONAL Vol 91, No4, 2008 : 786
- It is proposed that AOAC 986.23 (Current Type II method) be repealed from the Codex list for infant formula.

Pantothenic acid

It is proposed to keep AOAC 992.07, based on microbiology, as Type III method. Results generated by AOAC 992.07 are not different from results generated by AOAC 2012.16 as confirmed by Andrieux et al.: JAOAC INTERNATIONAL Vol.95, No1, 2012: 143.

Fatty acids

Proposed type II method: ISO 16958 | IDF 231:2015 / AOAC 2012.13.

It is proposed that AOAC 996.06 (Current Type II method) be kept as Type III method. It should be noted that if trans fatty acids need to be determined that this method is not fit for purpose.

It is proposed that AOCS Ce 1h-05 (Current Type III method) be kept as Type III method. It should be noted that if trans fatty acids need to be determined that this method is not fit for purpose.