Infant Formula, AOAC SPIFAN, Harmonization

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1. Why need for standards infant formula?
2. AOAC INTERNATIONAL SPIFAN project
3. Why is it important that Standardization bodies collaborate?
4. Example collaboration between ISO-AOAC-IDF
Agenda

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• In 1963 FAO and WHO created The Joint Food Standards Programme – ‘Codex Alimentarius’ with two main purposes globally
  – protecting health of the consumers; and
  – ensuring fair trade practices in the food trade

• In 1994, WTO Agreement on Sanitary and Phytosanitary (SPS) measures, established Codex Alimentarius as the relevant standard-setting organization for food safety.
STANDARD FOR INFANT FORMULA AND FORMULAS FOR SPECIAL MEDICAL PURPOSES INTENDED FOR INFANTS

CODEX STAN 72 – 1981

SECTION A: REVISED STANDARD FOR INFANT FORMULA

PREAMBLE

This standard is divided into two sections. Section A refers to Infant Formula, and Section B deals with Formulas for Special Medical Purposes Intended for Infants.

1. SCOPE

1.1 This section of the Standard applies to infant formula in liquid or powdered form intended for use, where necessary, as a substitute for human milk in meeting the normal nutritional requirements of infants.

1.2 This section of the Standard contains compositional, quality and safety requirements for Infant Formula.

1.3 Only products that comply with the criteria laid down in the provisions of this section of this Standard would be accepted for marketing as infant formula. No product other than infant formula may be marketed or otherwise represented as suitable for satisfying by itself the nutritional requirements of normal healthy infants during the first months of life.

1.4 The application of this section of the Standard should take into account the recommendations made in the International Code of Marketing of Breast-milk Substitutes (1981), the Global Strategy for Infant and Young Child Feeding and World Health Assembly resolution WHA54.2 (2001).

2. DESCRIPTION

2.1 Product Definition

2.1.1 Infant formula means a breast-milk substitute specially manufactured to satisfy, by itself, the nutritional requirements of infants during the first months of life up to the introduction of appropriate complementary feeding.

2.1.2 The product is so processed by physical means only and so packaged as to prevent spoilage and contamination under normal conditions of handling, storage and distribution in the country where the product is sold.

2.2 Other Definitions

The term infant means a person not more than 12 months of age.

3. ESSENTIAL COMPOSITION AND QUALITY FACTORS

3.1 Essential Composition

3.1.1 Infant formula is a product based on milk of cows or other animals or a mixture thereof and/or other ingredients which have been proven to be suitable for infant feeding. The nutritional safety and adequacy of infant formula shall be scientifically demonstrated to support growth and development of infants. All ingredients and food additives shall be gluten-free.
<table>
<thead>
<tr>
<th>Vitamin A</th>
<th>AOAC 992.04 (retinol isomers)</th>
<th>HPLC</th>
<th>Type II</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vitamin A above 500 IU/l milk after reconstitution</td>
<td>AOAC 992.06 (retinol)</td>
<td>HPLC</td>
<td>Type III</td>
</tr>
<tr>
<td>Vitamin A</td>
<td>EN 12823-1:2000 (all-trans-retinol and 13-cis-retinol) Vitamin A (both natural + supplemental ester forms) aggregated and quantified as individual retinol isomers (13-cis and all-trans)</td>
<td>HPLC</td>
<td>Type III</td>
</tr>
<tr>
<td>Vitamin D</td>
<td>AOAC 992.26 D&lt;sub&gt;2&lt;/sub&gt; measured</td>
<td>HPLC</td>
<td>Type III</td>
</tr>
<tr>
<td>Vitamin D</td>
<td>EN 12821:2000 (D2 and/or D3 measured as single components. Hydroxylated forms not measured.) NMLK 167: 2000</td>
<td>HPLC</td>
<td>Type II</td>
</tr>
<tr>
<td>Vitamin D</td>
<td>AOAC 995.05 D2 and D3 measured</td>
<td>HPLC</td>
<td>Type III</td>
</tr>
<tr>
<td>Vitamin E</td>
<td>AOAC 992.03 Measures all rac-vitamin E (both natural + supplemental ester forms) aggregated and quantified as α-congeners</td>
<td>HPLC</td>
<td>Type III</td>
</tr>
<tr>
<td>Vitamin E</td>
<td>EN 12822: 2000 (Measures Vitamin E (both natural +</td>
<td>HPLC</td>
<td>Type II</td>
</tr>
</tbody>
</table>

**Type II**: Reference Method, chosen from Type III methods, recommended for use in case of dispute and calibration purposes.  
**Type III**: Alternative methods; meets criteria required by CCMAS, may be used for control, inspection or regulatory purposes.
Why need for new Reference Standards?

• Infant formula most heavily regulated food product in the world.
• Most of Codex endorsed Standards originate from the eighties, when Infant Formula act was enabled in the US.
• New products produced over time, e.g. hydrolyzed protein, which may face analytical challenges.
• Existing Standards mostly not validated for infant formula in general and particularly new products.
Agenda

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SPIFAN is a project governed by AOAC INTERNATIONAL and supported by Infant Formula Industry aiming to establish recognized International Reference Standards for infant and adult nutritionals
Governance
Manufacturers
Authorities, technology providers, private laboratories, associations, academia
Communicates on behalf of all manufacturers with AOAC
Process to establish new reference analytical methods

Priority Setting
SMPR

Working Groups

Expert Review Panel

AOAC First Action OM

AOAC Final Action OM
AOAC SMPR 2011.005

Standard Method Performance Requirements for Vitamin B₁₂ in Infant Formula and Adult/Pediatric Nutritional Formula

Approved by: Stakeholder Panel on Infant Formula and Adult Nutritional (SPIFAN)
Final Version Date: April 5, 2011
Effective Date: April 5, 2011

Intended Use:

1. Applicability
Determination of vitamin B₁₂ in all forms of infant, adult, and/or pediatric formula (powder, ready-to-feed liquids, and liquid concentrates). For the purpose of this SMPR, vitamin B₁₂ is defined as cobalamin-containing compounds with the biological activity of cyanocobalamin such as cyanocobalamins (CAS 68-18-9), cobalamins (CAS 13422-02-1), hydroxycobalamins (CAS 13422-51-9), methylcobalamins (CAS 13422-55-4), and adenosylcobalamins (CAS 15870-00-1).

2. Analytical Techniques
Any analytical technique that meets the following method performance requirements is acceptable.

3. Definitions
Adult/Pediatric Formula
Nutritionally complete, specially formulated food, consumed in liquid form, which may contain the sole source of nourishment (AOAC SMPR, 2010), made from any combination of milk, soy, rice, whey, hydrolyzed protein, starch, and amino acids, with and without intact proteins.

Infant Formula
Breast-milk substitutes specially manufactured to satisfy, by itself, the nutritional requirements of infants during the first months of life up to the introduction of appropriate complementary feeding (Codex Standard 72-1981), made from any combination of milk, soy, rice, whey, hydrolyzed protein, starch, and amino acids, with and without intact proteins.

Limit of Detection (LOD)
The minimum concentration or mass of analyte that can be detected as a given matrix with no greater than 5% false-negative risk and 5% false-positive risk.

Limit of Quantitation (LOQ)
The minimum concentration or mass of analyte in a given matrix that can be reported as a quantitative result.

Repeatability
Variation arising when all efforts are made to keep conditions constant by using the same instrument and operator, and repeating during a short time period. Expressed as the repeatability standard deviation (SD), or % repeatability relative standard deviation (RSD).
Process to select methods for AOAC First and Final Action

AOAC 1st Action Method → ERP reviews each method + SLV data, then selects the best procedure → Selected AOAC 1st Action Method → Study director organises MLT → AOAC Final Action method

ERP = Expert Review Panel
SLV = Single laboratory validation
MLT = Multi-laboratory testing
Matrices for Single and Multi Lab Validation

- SRM 1849 (NIST)
- Infant Formula Powder Milk-Based
- Infant Formula Ready to Feed Milk-Based
- Infant Formula Powder Soy-Based
- Infant Formula Powder Hydrolysate Milk-Based
- Infant Formula Powder Hydrolysate Soy-Based
- Infant Formula Powder Elemental (amino acid-based)
- Child Formula Powder
- Adult Nutritional Powder
- Adult Nutritional Powder Low Fat
- Adult Nutritional RTF High Protein
- Adult Nutritional RTF High Fat
### Status Chart as per 2013 SPIFAN nutrients

<table>
<thead>
<tr>
<th>Nutrient</th>
<th>First Action status for</th>
<th>Next steps to prepare for Final Action status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vitamin A/E</td>
<td>AOAC 2012.10</td>
<td>MLT 2013</td>
</tr>
<tr>
<td>Vitamin D</td>
<td>AOAC 2011.11</td>
<td>MLT 2013</td>
</tr>
<tr>
<td>Vitamin B₁₂</td>
<td>AOAC 2011.10</td>
<td>MLT 2013</td>
</tr>
<tr>
<td>Inositol</td>
<td>AOAC 2011.18</td>
<td>MLT 2013</td>
</tr>
<tr>
<td>Nucleotides</td>
<td>AOAC 2011.20</td>
<td>MLT 2013</td>
</tr>
<tr>
<td>Ultra trace (Cr,Se,Mo)</td>
<td>AOAC 2011.19</td>
<td>MLT 2013</td>
</tr>
<tr>
<td>Fatty Acids</td>
<td>AOAC 2012.13</td>
<td>MLT 2013</td>
</tr>
<tr>
<td>Iodine</td>
<td>2 methods</td>
<td>Agenda Sept 2013</td>
</tr>
<tr>
<td>Pantothenic Acid</td>
<td>1 method</td>
<td>Agenda Sept 2013</td>
</tr>
<tr>
<td>Carnitine</td>
<td>1 method</td>
<td>Agenda Sept 2013</td>
</tr>
<tr>
<td>Choline</td>
<td>3 methods</td>
<td>Agenda Sept 2013</td>
</tr>
<tr>
<td>Vitamin C</td>
<td>2 methods</td>
<td>Agenda Sept 2013</td>
</tr>
<tr>
<td>Whey protein</td>
<td>2 methods</td>
<td>Work in progress</td>
</tr>
</tbody>
</table>
SPIFAN II (to be confirmed): Following nutrients included: Minerals [Calcium, Copper, Iron, Magnesium, Manganese, Phosphorus, Potassium, Sodium and Zinc], Biotin, Vitamin K, Vitamin B1, Vitamin B2, Vitamin B5, Vitamin B6, Amino Acids, Oligosaccharides [FOS and GOS], Carotenoids [Alpha Carotene, Beta Carotene, Gamma Carotene, Lutein and Lycopene], Chloride, Fluoride
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Why is it important that Standardization bodies collaborate?

- In international food trade disputes on compliance with regulations may be caused by differences among analytical methods used.
- Adoption of internationally accepted analytical methods may prevent this.
- Standardization bodies need to collaborate to enhance harmonization and avoiding duplication of work.
- Manufacturers, authorities, contract laboratories will have a common understanding on analytical methods to use. This will harmonize compliance testing of products by all stakeholders.
The risk of bias is high!

Harmonisation at international level is required.
FOR IMMEDIATE RELEASE

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ISO and AOAC Sign Cooperation Agreement for Joint Development and Approval of Common Standards

Rockville, Maryland, USA — A cooperation agreement was signed on June 18, 2012, between the International Organization for Standardization (ISO) and AOAC INTERNATIONAL. The new partnership allows for the joint development and approval of common standards.

Rob Steele, Secretary General of ISO, says, “Such harmonization will significantly increase the global relevance and impact of our respective organizations through international promotion and adoption of our harmonized methods.”

“ISO is a very important partner, and we are extremely pleased to enter into this high-level agreement,” says AOAC Executive Director James Bradford. “The new agreement underscores that ISO and AOAC share an effective and efficient approach in development of international standards.”

Erik Konings, AOAC Board Member and one of the SPIFAN (Stakeholder Panel on Infant Formula and Adult Nutritional) stakeholders says, “The ISO/AOAC agreement broadens global acceptance of standards which will facilitate international trade of infant formula and adult nutritional for the benefit of all stakeholders, including consumers.”

Both AOAC and ISO are already internationally recognized and respected, and the collaboration will reinforce the global reputation of both organizations. Under the newagreement, ISO and AOAC can participate in each other’s work to jointly develop and approve standards. Initial priorities will focus on the areas of food, beverage, agri-bio products, and infant formula and adult nutritional products.”
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• TC 34 WG14: Vitamins, carotenoids, and other nutrients
• TC 34 SC5: Milk and Milk products

• Project to be developed in ISO (sub)committee or working group where appropriate expertise is available.
ISO TC34 Working Group on vitamins, carotenoids and other nutrients.
1st meeting on April 25 and 26, 2013 at the Nestlé Research Center, Lausanne, Switzerland. 20 participants from 11 countries

**Agenda:**

- Adoption published horizontal CEN standards as ISO standards.

- New methods for discussion: Stakeholder Panel on Infant Formula and Adult Nutritionals (SPIFAN)
Potential future ISO Standards

- AOAC 2012.10 on vitamin A&E
- AOAC 2011.10 on vitamin $B_{12}$
- AOAC 2011.11 on vitamin D
- AOAC 2012.16 on pantothenic acid

After full collaborative study

- WG14 interested to work on methods for inositol, carnitine, choline, nucleotides and taurine.
• There is a need for up to date Reference Standards in the area of infant formula and adult nutritionals.
• AOAC SPIFAN provides a platform where all stakeholders gather and agree on Standards for analytical methods.
• To prevent disputes on compliance with regulations, standardization bodies have to collaborate to enhance harmonization and avoiding duplication of work.
• The ISO-AOAC agreement broadens global acceptance of standards which will facilitate international trade of infant formula and adult nutritionals for the benefit of all stakeholders, including consumers.