Establishing Globally Harmonized Standards for Analytical Methods for Nutrients in Infant Formula by AOAC/ISO/IDF

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Outline

• Why is there a need for new international standards for analytical methods to ensure compliance of infant formula?
• Stakeholder Panel on Infant Formula and Adult Nutritionals (SPIFAN)
• SPIFAN Process
• Enhancement of global scope through ISO/IDF collaboration
• Endorsement of new methods by Codex Committee on Methods of Analysis and Sampling
• Examples of jointly developed standards, and work in progress
Codex Alimentarius

- 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.
Codex Standard for Infant Formula and Formulas for special medical purposes intended for infants

CODEx Alimentarius

INTERNATIONAL FOOD STANDARDS

CODEX STAN 72 - 1981

Adopted as a worldwide Standard in 1981.
CODEX STAN 234-1999 recommended methods of analysis for dispute resolution

<table>
<thead>
<tr>
<th>Commodity</th>
<th>Method Description</th>
<th>Code</th>
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<tbody>
<tr>
<td>Infant formula</td>
<td>Sodium and potassium, AOAC 984.27, ICP emission spectrometry</td>
<td>III</td>
</tr>
<tr>
<td>Infant formula</td>
<td>Sodium and potassium, ISO 8070</td>
<td>IDF 119:2007, Flame atomic absorption spectrophotometry</td>
</tr>
<tr>
<td>Infant formula</td>
<td>Thiamine, AOAC 985.27, Fluorimetry</td>
<td>III</td>
</tr>
<tr>
<td>Infant formula</td>
<td>Thiamine, EN 14112:2003 (Measures all vitamin B₁ forms (natural and added free, bound and phosphorylated) following extraction and conversion to thiamine), HPLC with pre or post column derivatization to thinchrom</td>
<td>II</td>
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Why is there a need for new Standards?

- Available Official Methods originate from 1980’s
- Official Methods for limited number of parameters: stakeholders using their ‘own’ methods
- Modern products with analytical challenges (e.g. hydrolyzed protein)
- Existing Standards mostly not validated for IF
The current SPIFAN program as designed is dedicated to ...

- Providing a collaborative program driven through a public-private partnership
- Developing consensus Standard Method Performance Requirements (SMPRs)
- Updating current Codex Type II nutrient methods, with methods that are fit-for-purpose and thoroughly vetted against standard criteria
Stakeholder Panel on Infant Formula and Adult Nutritionals (SPIFAN)

Governance

Manufacturers

Authorities, technology providers, private laboratories, associations, academia

Communicates on behalf of all manufacturers with AOAC

100+ Stakeholders
**SPIFAN Process**

| Stakeholder Panel | • Broad and representative group  
|                   | • Governing body, which introduces new nutrients (or contaminants) to be analyzed |
| Technically Focused Working Groups (WGs) | • Led by a chairperson, who proposes method criteria, which are then vetted by full WG and outlined in SMPRs  
|                   | • Consists of technical experts from industry, government, CROs, academia, NGOs and technology providers to develop method performance criteria required for dispute resolution methods |
| Vetted Expert Review Panel (ERP) | • Develop standards and make decisions |
What Defines SMPRs

**Applicability Statement**

**Definitions**

Method Performance Requirements
Could include: analytical range, LOD, LOQ, repeatability (RSDr), recovery, reproducibility (RSDR)

**Other Details**
- Public review and comment period
- Questions resolved by WG chair
- Approval by Stakeholder Panel

Currently 28 approved and published SMPRs (http://stakeholder.aoac.org/SPIFAN/smpr.html)
Voluntary Consensus Standards Development

SPIFAN I (SMPRs)
2011 – 2013
15 Standards Developed

- Vitamin A
- Vitamin B12
- Vitamin D
- Folate
- Inositol
- Vitamin E
- Whey Protein
- Fatty Acids (ISO)
- Carnitine
- Vitamin C (India 2012)
- Choline (India 2012)
- Pantothenate
- Iodine
- Ultra Trace Minerals (Mo, Se, Cr)
- Nucleotides

SPIFAN II (SMPRs)
2013 – 2016
13 Standards Developed

- Vitamin K
- FOS
- GOS
- Biotin
- Minerals
- Amino Acids
- Carotenoids
- Fluoride
- Chloride
- Vitamin B1 (thiamine)
- Vitamin B2 (riboflavin)
- Vitamin B3 (niacin)
- Vitamin B6 (pyridoxine)
SPIFAN Process

SMPR is approved
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AOAC issues a public call for all analytical methods that have potential to meet the SMPR requirements
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A small screening group reviews the methods submitted.
SPIFAN Process

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Methods with greatest promise given access to sample materials representative of many infant formula (IF) products

SPIFAN Single Laboratory Validation (SLV) kit
SLV Kits

• Contain 12-15 sample matrices, produced by infant formula manufacturers
  o Sample matrices include liquid, powder, milk-, soy- and hydrolyzed protein-based IFs child/adult nutritional matrices (with varied fat/carbohydrate composition) and a NIST SRM 1849a
Methods with greatest promise given access to sample materials representative of many infant formula (IF) products

SPIFAN Single Laboratory Validation (SLV) kit

Method authors who wish to participate in the SPIFAN process are provided with SLV kits

Must be followed by method authors for SLV matrix analysis

SMPR is approved

AOAC issues a public call for all analytical methods that have potential to meet the SMPR requirements

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Methods with greatest promise given access to sample materials representative of many infant formula (IF) products SPIFAN Single Laboratory Validation (SLV) kit Method authors who wish to participate in the SPIFAN process are provided with SLV kits Must be followed by method authors for SLV matrix analysis SLV data submitted to AOAC and reviewed by the AOAC-vetted ERP

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Methods with greatest promise given access to sample materials representative of many infant formula (IF) products SPIFAN Single Laboratory Validation (SLV) kit

Method authors who wish to participate in the SPIFAN process are provided with SLV kits

Must be followed by method authors for SLV matrix analysis

SLV data submitted to AOAC and reviewed by the AOAC-vetted ERP

ERP may choose to recommend one or more methods for a particular nutrient (or contaminant) as AOAC Official First Action

SMPR is approved

AOAC issues a public call for all analytical methods that have potential to meet the SMPR requirements

A small screening group reviews the methods submitted
Multi-Laboratory Testing (MLT) Process

First Action methods go through multi-lab testing (MLT) process to establish robustness

Process is similar to IUPAC/ISO/AOAC Harmonized Protocol for design, conduct and interpretation of collaborative studies and follows the International Standards

| ERP selects one method per nutrient (or contaminant) to proceed to a MLT study | MLT study data from a minimum of eight labs is used to establish method reproducibility (RSDR) |
| MLT study chaired by a Study Director (typically the method author) |
Enhancing global scope

Building on AOAC’s strong base

• Infant formula industry drove joint agreement in 2012 with ISO to further enhance global scope of the SPIFAN program

• With focus on milk, milk products and infant formula also involved collaboration with IDF through the existing agreement between ISO and IDF relating to their joint programme of work on methods of analysis and sampling for milk and milk products
AOAC/ISO/IDF alignment of Standard Development Processes

AOAC

- Stakeholder Panel, Analyte prioritization, SMPR, call for methods
- ERP designates AOAC Official Method
  - First Action
- ERP designates AOAC Official method
  - Final action

ISO/IDF

- New Work Item proposal in TC ISO/IDF agreed by members
- Draft International Standard
- Member consultation on final DIS and integrate comments received
EXISTING
AOAC-ISO/IDF cooperative agreement (2012) to jointly develop/approve SPIFAN standards

CURRENT
Joint AOAC/IS/IDF nutrient methods being considered

RECOMMENDATION
Same methods being proposed to the Codex Committee on Methods of Analysis and Sampling (CCMAS)
Goal is to become/replace current Codex Type II nutrient methods for dispute resolution
First Set of New Globally Harmonized Standards

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<tr>
<th>Analyte</th>
<th>AOAC</th>
<th>ISO/IDF</th>
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<tbody>
<tr>
<td>Vitamin B$_{12}$</td>
<td>AOAC 2011.10</td>
<td>ISO 20634:2015</td>
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<tr>
<td>Myo-inositol</td>
<td>AOAC 2011.18</td>
<td>ISO 20637:2015</td>
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<tr>
<td>Nucleotides</td>
<td>AOAC 2011.20</td>
<td>ISO 20638:2015</td>
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<tr>
<td>Vitamins A and E</td>
<td>AOAC 2012.10</td>
<td>ISO 20633:2015</td>
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<td>Fatty acid profile</td>
<td>AOAC 2012.13</td>
<td>ISO 16958</td>
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<tr>
<td>Iodine</td>
<td>AOAC 2012.15</td>
<td>ISO 20647</td>
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<tr>
<td>Pantothenic acid</td>
<td>AOAC 2012.16</td>
<td>ISO 20639:2015</td>
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AOAC/ISO/IDF, and ISDI representatives supported joint methods at CCMAS February 22-26, 2016, Budapest, Hungary
Recommendations CCMAS to CAC

- Adopt as Type II (dispute resolution) methods: vitamin B12, pantothenic acid, total nucleotides, iodine, fatty acids including trans fatty acids, vitamin A
- Adopt methods for vitamin E and myo-inositol as Type II, provided that CCNFSFU 2016 confirms that the forms to be analyzed according to CODEX STAN 72 match those analyzed by the respective methods.
- Adopt the analytical method for Chromium, Molybdenum, and Selenium as Type III (alternative method). CCMAS proposed criteria to CCNFSDU
N1077: Determination of Chloride in milk, dairy products, infant formula and adult/pediatric nutritional formulaby potentiometric titration

N1078: Determination of minerals and trace elements in milk, dairy products, infant formula and adult/pediatric nutritional formulaby - ICP/AES method

N1079: Determination of minerals and trace elements in milk, dairy products, infant formula and adult/pediatric nutritional formulaby - ICP/MS method
Collaboration with CAIQ Beijing on development of common **AOAC/ISO/IDF/GB method for Chloride**

**Status:** Agreed MLT protocol to collaboratively test Chloride in infant formula, adult nutritionals, milk, milk powder, whey powder, butter, cheese

**Among 10-12 laboratories.**
N1837: Determination of trans vitamin K₁ in infant formula and adult nutritionals by a normal phase HPLC method with post-column reduction and fluorescence detection.

N1838: Determination of free and total choline and carnitine in infant formula and adult nutritionals by a liquid chromatography and tandem mass spectrometry.

N1839: Determination of vitamin B₁, B₂, B₃ and B₆ content in infant formula and adult nutritionals by liquid chromatography and tandem mass spectrometry.
Summary

• Since 2011 a public/private partnership is driving replacement of methods of analysis for nutrients in infant formula.
• New standards have been jointly developed by AOAC, ISO and IDF through the Stakeholder Panel on Infant Formula and Adult Nutritionals (SPIFAN) project.
• It is proposed that these new methods be adopted as Codex Type II Methods to enable them to be utilized as needed for the purposes of dispute resolution internationally.