



## JOINT FAO/WHO FOOD STANDARDS PROGRAMME

### CODEX COMMITTEE ON NUTRITION AND FOODS FOR SPECIAL DIETARY USES

Thirty-seventh Session  
Bad Soden a.T. – Germany  
23 – 27 November 2015

#### REVIEW OF THE STANDARDS FOR FOLLOW-UP FORMULA (CODEX STAN 156-1987)

*Comments of ISDI*

#### ISDI – International Special Dietary Foods Industries

##### I. Introduction

As part of the revision in 2007 of the Codex Standard for Infant Formula (Codex STAN 72-1981), the principles for the establishment of minimum and maximum or upper nutrient values were discussed and are defined in Annex II of this Standard.

The principles lay down the criteria to be considered when developing infant formulas that are safe for use and are nutritionally adequate, namely that meet the normal nutritional requirements of infants. In view of the current exercise to revise the Codex Standard for Follow-up Formula (Codex STAN 156-1987) reviewing and establishing minimum and maximum or upper nutrient levels for follow-up formula is extremely relevant considering new scientific data on both nutritional requirements as well as more knowledge regarding technological aspects of manufacturing follow-up formula.

To this aim the following aspects are to be considered when establishing these nutrient level recommendations.

- A nutritionally adequate follow-up formula needs to promote adequate growth and development consistent with science based standards and meet the nutritional requirements of older infants when fed a follow-up formula as part of the complementary feeding diet.
- The nutrient values to be established are to be based on an independent evaluation, in particular of the scientific evidence of the amounts needed to meet the nutritional requirements of older infants, considering relevant human infant studies as well as the composition of breast-milk or other relevant food sources.
- In setting minimum and maximum or upper nutrient values, consideration will also be given to the safety of such values.

For nutrients with a documented risk of adverse health effects the upper levels to be taken into account will be determined using a science-based risk assessment approach. Where scientific data are not sufficient for a science-based risk assessment, consideration should be given to an established history of apparently safe use of the nutrient in older infants and young children, as appropriate. Values derived on the basis of meeting the nutritional requirements of older infants or young children and an established history of apparently safe use should be considered as interim guidance upper levels. The approach to setting maximum and upper guidance values shall be made transparent and comprehensible.

- When establishing minimum and maximum amounts, the following should also be taken into account:
  - bioavailability, processing and shelf-life stability from the ingredients and formula matrix,
  - total levels of a nutrient in follow-up formula, taking into account both naturally occurring nutrients in the ingredients and added nutrients,
  - the inherent variability of nutrients in ingredients and in water that may be added to the follow-up formula during manufacture.

- Overages for individual nutrients, as appropriate, to ensure that the required minimum levels are met throughout the shelf-life of the formula, will be included in the maximum value.

ISDI members have conducted a review of the actual nutrient levels of currently available follow-up formulas for older infants and evaluated the technological aspects that influence the nutrients levels to inform the discussions on these aspects which must be considered in order to achieve revised nutrient levels which can be achieved in practice.

The present report will review these technological aspects and provide data for those nutrients that may be more technologically challenging for follow-up formula for older infants (6-12 months). It aims to contribute to the discussion regarding the composition criteria for follow-up formulas for older infants during the 37<sup>th</sup> CCNFSDU meeting.

This report is to be considered preliminary as more data are still being collected. A final report will be made available and shared with the Codex Secretariat and the electronic Working Group (eWG) to complete the current review on nutrient levels of follow-up formula for older infants.

ISDI proposes to similarly review data for follow-up formula for young children (12-36 months).

## **II. Technological aspects influencing the nutrient level ranges in follow-up formula:**

As highlighted previously by ISDI several factors influence the management of nutrient levels in follow-up formula:

### Variability of endogenous nutrients in the ingredients:

There is considerable variability in endogenous nutrient levels of the ingredients used to manufacture formulas. The same ingredient is almost always obtained from different suppliers in different regions of the world, which may result in considerable variation in the endogenous contribution of nutrients to the follow-up formula for older infants. This is particularly true for the endogenous contribution coming from major ingredients such as protein sources (e.g., iodine and potassium) and vegetable oils (e.g., linoleic and  $\alpha$ -linolenic acids).

### Variability of manufacturing & processing:

There is considerable variability that results from manufacturing and processing conditions. Manufacturing and processing conditions are different across various manufacturing sites, but they all consist of heat, mixing and packaging elements that may affect nutrient levels.

### Variability due nutrient losses over shelf life:

Some nutrients are more sensitive to losses over shelf-life due to oxidation, light, temperature, or format. Losses over shelf life will depend on type of product, its form (liquid vs. powder), type of packaging and container and the length of shelf life. Processing losses were not specifically examined because those losses occur prior to the release. They do account, however, for some of the variability of release values for some nutrients

### Variability associated with the analytical methodology used to determine nutrient levels:

When setting maximum and minimum levels, particularly for those nutrients with higher analytical variability (e.g., vitamin B<sub>12</sub>, folic acid), the analytical variability ought to be taken into account. Indeed as several regulatory bodies do apply the minimum and maximum nutrient levels in the strictest sense, i.e. zero tolerance outside the range, the consequences of the analytical variability inevitably reduce the range of practically applicable nutrient levels.

## **III. Review of nutrient levels in available follow-up formulas for older infants**

Members of ISDI collected and analysed data for nutrient levels in currently available follow-up formulas. Our focus was to identify and discuss those nutrients for which the actual nutrient levels are at or above the upper nutrient levels as proposed by the electronic Working Group (eWG) leading the revision of the Standard.

Based on the available preliminary data and experience, ISDI considers that the proposal made by the eWG Chair is technologically achievable for all nutrients except for vitamin A, copper, zinc and iron. Information on those four nutrients will be detailed below.

ISDI made these conclusions based on a survey on analytical data for currently available follow-up formulas for older infants provided by 6 global follow-up formula manufacturers<sup>1</sup>.

### **III.1. Survey details and Management**

#### Products covered in this report:

The data cover follow-up formula as defined by Codex Alimentarius, and more specifically follow-up formulas for older infants (6-12 months). The data are representative for milk-based liquid, milk-based powder, and soy-based powder follow-up formula for older infants.

The preliminary data included in this survey represent approximately 2 million older infants that were fed follow-up formula. This estimate is based on the total number of batches included in the survey, that were analysed over a period of three years and the corresponding total volume of follow-up formula.

#### Geographical origin of products covered in this report:

The survey included analytical data for follow-up formulas for older infants produced in Africa, Asia-Pacific, Europe, Latin America and North America.

These products are available in Africa, Asia-Pacific, Europe, Latin America and, North America.

#### Nutrients covered in this report:

The current draft of the essential composition of nutrients in follow-up formulas for older infants specifies minimum and maximum levels for 31 nutrients. This list includes compositional criteria for 3 macronutrients (including specifications for the essential fatty acids), 13 vitamins, 12 minerals and 3 other nutrients.

Nutrient levels in the analysed products were compared with the levels in the current Standard for Follow-up Formula (Codex STAN 156 – 1987), the ENA (Koletzko, 2013) and eWG Chair proposals.

#### Source of Analytical Data:

The analytical data were extracted from the formula manufacturers' quality assurance databases for batches for follow-up formula for older infants (6-12 months).

Analytical values were collected at the time of product release, i.e. represent early shelf life, or at specific shelf-life data points to assess nutrient stability data over shelf-life.

All analytical methods and procedures were officially validated and performed according to Good Laboratory Practices.

### **III.2 Vitamin A**

#### Introduction

Vitamin A in follow-up formula is derived principally from its specific addition at the time of manufacture. Only a small percentage of preformed vitamin A comes from inherent levels in ingredients.

#### Data Collection

##### *Maximum loss over shelf-life*

Nutrient	Maximum % loss at end of shelf-life
Vitamin A	20%

Shelf life degradation data showed that losses can be up to 20%. The losses depend on the form of the product (powder, concentrated liquid or ready to feed), the packaging, filling environment (inert atmosphere or not) and the storage conditions as well as assigned shelf life.

As stated before these are preliminary data that will be confirmed in the final ISDI report.

##### *Variability of the analytical methodology*

Nutrient	Nutrient Variability (RSD)
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<sup>1</sup> These companies provide formulas in more than 1 continent and are representative formula manufacturers.

Vitamin A	24%
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RSD = Relative Standard Deviation

*Comparison of expert recommendation, current regulations and actual nutrient levels.*

Nutrient	Unit per 100 kcal	ENA Max	Codex Standard for Follow-up Formula	eWG Chair proposed MV	Range of Means*	Range of Means +3SD *
Vitamin A	µg RE	180	225	180	98 – 135 (**)	60-180 (**)

\* The wide ranges of actual nutrient levels reflect different formulation used globally due to nutrition requirements and different regulatory standards.

\*\* Preliminary data.

### Conclusion

Based on the preliminary data, it seems that the proposal of the eWG Chair can be accepted. However ISDI's experience based on the previous survey conducted for the revision of the infant formula standard (MacLean, 2010) indicates that caution is needed when establishing the upper level for vitamin A. Therefore ISDI maintains its position for a maximum value of 225 µg RE/100 kcal, pending the collection of more data, which will be shared in the final ISDI report.

### References

Chavez Serva J, (2008) Analysis of vitamins A, E and C, iron and selenium contents in infant milk-based powdered formula during full shelf-life. *Food Chemistry*, 117: 1187-1197.

MacLean Jr W, Van Dael P, Clemens R, *et al.* (2010) Upper levels of nutrients in infant formulas: Comparison of analytical data with the revised Codex infant formula standard. *Journal of Food Composition and Analysis*, 23: 44-53.

## **III.3. Iron**

### Introduction

The iron level in follow-up formula for older infants is determined primarily by the amount of iron specifically added by the manufacturer. Without the addition, most follow-up formulas for older infants would contain no more than ~0.3-0.4 mg/100 kcal.

### Data Collection

#### *Maximum loss over shelf-life*

Nutrient	Maximum % loss at end of shelf-life
Iron	0%

There is no loss of iron over shelf life.

#### *Variability of the analytical methodology*

Nutrient	Nutrient Variability (RSD)
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Iron	7%
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RSD = Relative Standard Deviation

*Comparison of expert recommendation, current regulations and actual nutrient level.*

Nutrient	Unit per 100 kcal	ENA Max	Codex Standard for Follow-up Formula	eWG Chair proposed MV	Range of Means*	Range of Means +3SD *
Iron	mg	1.9, 2.5(soy)	2	2	1.15-1.9 (**)	1.3-2.4 (**)

\* The wide ranges of actual nutrient levels reflect different formulation used globally due to nutrition requirements and different regulatory standards.

\*\* Preliminary data.

#### Scientific evidence and technical constraints

From the perspective of a history of safe use, iron supplemented formulas in the USA have label declarations between 1.5 and 1.8 mg/100 kcal in order to meet a minimum nutrient level for iron of 1.5 mg/100 kcal due to the Special Supplemental Nutrition Program for Women, Infants, and Children (WIC), resulting in actual iron levels being higher than the maximum value proposed by the eWG Chair of 2.0 mg/100 kcal. Historical data reveal that follow-up formulas for older infants (6-12 months) with actual levels at or above 2.0 mg/100 kcal represent approximately 80% of all formulas sold in the US for the past 5-10 years (in the US infant formulas cover 0-12 months of age and as such they are representative of follow-up formulas for older infants). An average of 4 million babies are born each year in the U.S., at least 3 million of whom are fed iron-fortified formulas. Identical formulas with the same iron levels have been available for many years in many other countries around the world as well (e.g., Latin America). Hence these iron levels have a long history of apparent safe use.

#### Conclusion

Based on the totality of the available data, ISDI proposes a GUL of 2.5 mg/100 kcal, which is scientifically and technologically substantiated and enables to accommodate all principles defined by Codex Alimentarius.

### **III.4. Copper**

#### Introduction

The copper level in follow-up formula for older infants is determined primarily by the amount of copper specifically added by the manufacturer. However, copper levels of ready to use follow-up formula for older infants are influenced by the copper level of water used for the formula preparation.

#### Data Collection

*Maximum loss over shelf-life.*

Nutrient	Maximum % loss at end of shelf-life
Copper	0%

There is no loss of copper over shelf life.

*Variability of the analytical methodology*

Nutrient	Nutrient Variability (RSD)
Copper	10%

RSD = Relative Standard Deviation

*Comparison of expert recommendation, current regulations and actual nutrient levels.*

Nutrient	Unit per 100 kcal	ENA GUL	Codex Standard for Follow-up Formula	eWG Chair proposed GUL	Range of Means*	Range of Means +3SD *
Copper	µg	250	-	120	67-125 **	60-150 **

\* The wide ranges of actual nutrient levels reflect different formulation used globally due to nutrition requirements and different regulatory standards.

\*\* Preliminary data.

### Conclusion

Based on the preliminary data, it seems that the proposal of the eWG Chair can be accepted.

However, ISDI maintains its position for a GUL of 250 µg/100 kcal, based on the recommendation of the International Expert Group coordinated by the Early Nutrition Academy (Koletzko, 2013) as well as the need to complete the collection of additional data, which will be shared in the final ISDI report.

### Reference:

Koletzko B, Bhutta ZA, Cai W, *et al.* (2013) Compositional requirements of follow-up formula for use in infancy: recommendations of an international expert group coordinated by the Early Nutrition Academy. *Annals of Nutrition and Metabolism*, 62:44–54.

## **III.5. Zinc**

### Introduction

The zinc level in follow-up formula for older infants is determined primarily by the amount of zinc specifically added by the manufacturer.

### Data Collection

*Maximum loss over shelf-life*

Nutrient	Maximum % loss at end of shelf-life
Zinc	0%

There is no change in zinc content in finished product over shelf life.

*Variability of the analytical methodology*

Nutrient	Nutrient variability (RSD)
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Zinc	9%
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RSD = Relative Standard Deviation

*Comparison of expert recommendation, current regulations and actual nutrient levels*

Nutrient	Unit per 100 kcal	ENA GUL	Codex Standard for Follow-up Formula	eWG Chair proposed GUL	Range of Means*	Range of Means +3SD *
Zinc	mg	1.5	-	1	0.63-1.4 **	1.1-1.6 **

\* The wide ranges of actual nutrient levels reflect different formulation used globally due to nutrition requirements and different regulatory standards.

\*\* Preliminary data.

#### Scientific evidence and technical constraints

The statistical analysis of actual zinc levels suggests that at a GUL of 1.0 mg/100 kcal as proposed by the eWG Chair, several batches would exceed the GUL. Therefore a higher GUL would be appropriate given the fact that GUL for zinc is set in the Codex Standard for Infant Formula at 1.5 mg/100 kcal and that there are actual data to support the history of apparent safe use at a level of 1.5 mg/100 kcal. A higher GUL, such as the one provided for in for infant formulas, would encompass the technological aspects and the history of apparent safe use.

Additionally, the International Expert Group coordinated by the Early Nutrition Academy (Koletzko, 2013) proposed a GUL for zinc at 1.5 mg/100 kcal by based on the totality of safety data for zinc in older infants.

#### Conclusion

Based on the available data, ISDI maintains its proposal for a GUL of 1.5 mg/100 kcal of zinc, which is aligned with the recommendation of the International Expert Group coordinated by the Early Nutrition Academy (Koletzko, 2013), is scientifically and technologically substantiated and enables to accommodate all principles defined by Codex Alimentarius.

#### Reference:

Koletzko B, Bhutta ZA, Cai W, *et al.* (2013) Compositional requirements of follow-up formula for use in infancy: recommendations of an international expert group coordinated by the Early Nutrition Academy. *Annals of Nutrition and Metabolism*, 62:44–54.