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Original Article

Upper levels of nutrients in infant formulas: Comparison of analytical data with the revised Codex infant formula standard

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ABSTRACT

The Codex Alimentarius Commission adopted a revised standard for infant formula in 2007. This standard provides a regulatory framework for infant formula, including provisions for its essential composition. The recommendations for the essential composition specify minimum levels and either maximum values (MVs) or guidance upper levels (GULs) for 31 nutrients. As part of the revision process, the first cooperative survey of levels of nutrients in infant formulas was conducted by several global manufacturers. Whereas formulas met proposed minimum levels of all nutrients, 15 nutrients were identified whose levels were likely to exceed the proposed MV or GUL: vitamins A and K, thiamine, riboflavin, niacin, vitamin B_6, folic acid, vitamin B_{12}, vitamin C, iron, copper, manganese, potassium and iodine. Analytical data were collected for those nutrients from 21,385 batches of milk-based infant formula and 9070 batches of soy-based infant formula, whose total volumes were sufficient to feed more than 33 million infants for periods of three months. The number of batches analyzed ranged from 440 (vitamin K) to 27,920 (vitamin C). Of nutrients with an MV, only levels of vitamin A in some batches exceeded the maximum; no batch contained levels previously reported in the literature to be associated with adverse effects. There were several nutrients with GULs for which there were batches that exceeded the suggested upper limit. Data for some nutrients showed considerable variability, which related to form (liquid vs. powder), inherent levels of nutrients in formula ingredients, protein source, nutrient stability, analytical variability and effects of process, package and container size.

1. Introduction

Codex Alimentarius ("Codex") is a global food standards program sponsored jointly by the Food and Agricultural Organization (FAO) and World Health Organization (WHO). Its goal is to establish standards for various foods that will assure consumer safety and facilitate trade. Codex periodically revises food standards as new scientific data become available. In 1995, the decision was taken to revise the Codex standard for infant formula, which had last been amended in 1987. After 11 years of discussion in the Codex Committee on Foods for Special Dietary Uses (CCNFSDU), a revised standard (Codex STAN 72-1981; revision 2007) was adopted in 2007 (Codex Alimentarius Commission, 2007a). A key part of that standard, the essential nutrient composition of infant formula, had been discussed by the Committee at annual meetings for several years without reaching consensus. In 2004, CCNFSDU requested additional advice from an international expert group of scientific experts in the area of infant nutrition (referred to as the "IEG"). The IEG presented its recommendations (Koletzko et al., 2005) at the 27th session in November 2005, and those recommendations formed the basis for further discussions of compositional criteria.

During those discussions, several issues became apparent:

- For several nutrients the maximum levels recommended by the IEG were close to or lower than levels in current infant formulas.
- The scientific basis for setting maximum levels was variable and inconsistent. This problem resulted in part because for some nutrients the data related to adverse effects from excessive intakes were relatively well documented, which enabled establishing science-based upper nutrient levels, while for other nutrients the database was quite meager, which created uncertainties about how best to set upper levels.

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Table 1
Summary of analytical methods used.

Nutrient	Analytical principle used	Comparable standard reference methods where applicable
Alpha-linoleic acids	All methods converted fatty acids in oils to FAMES that were then measured by GC with FID.	AOAC 992.25, AOAC 991.39, 996.06
Vitamin A	Saponification/extraction/HPLC measurement of retinol (and isomers).	AOAC 992.04, AOAC 992.06, EN 12823-1
Vitamin K	HPLC with fluorescence or UV detection.	AOAC 999.15, AOAC 992.27, EN 14148
Thiamin	All methods relied on conversion of thiamine to thiochrome and then HPLC using fluorescence detection.	AOAC 986.27, EN 14122
Riboflavin	All methods relied on HPLC using fluorescence detection.	EN 14152
Niacin	Two methods were used, either the standard microbiological reference method for infant formula or HPLC.	AOAC 985.34
Vitamin B_{12}	Two methods were used, either microbiological or HPLC.	AOAC 986.23
Folic acid	Three basic methodologies were employed: (1) microbiological, (2) HPLC, (3) BIA.	AOAC 992.05
Vitamin C	Vitamin C analysis was based upon its reduction potential and measured in one of three ways, potentiometrically, coulometrically, or colorimetrically.	AOAC 985.33
Biotin	Three basic methodologies that were employed: (1) microbiological, (2) HPLC, (3) BIA.	Proposed EN 15607
Iron	Atomic absorption spectrometry or ICP	AOAC 984.27, AOAC 985.35
Potassium	Atomic absorption spectrometry or ICP.	AOAC 985.35, AOAC 984.27
Manganese	Atomic absorption spectrometry or ICP.	AOAC 984.27, AOAC 985.35
Iodine	Ion-selective electrode or inverse colorimetric method.	AOAC 992.24
Copper	Atomic absorption spectrometry or ICP.	AOAC 984.27, AOAC 985.35

Abbreviations: GC: gas chromatography; HPLC: high pressure liquid chromatography; UV: ultraviolet; FAMES: fatty acid methyl esters; FID: flame ionization detection; BIA: Biomolecular interaction analysis; AA: atomic absorption; ICP-AES: Inductively-coupled plasma atomic emission spectroscopy; AOAC: AOAC International (Official Methods, 2006); CEN: European Committee for Standarization (Comité Européen de Normalisation); EN: European Norm.

- It was recognized that information on actual nutrient levels in infant formulas historically fed without apparent adverse effects could be used to support the safety of use of the actual nutrient levels.

With the above in mind, the concept of specifying maximum values (MVs) for some nutrients and guidance upper levels (GULs) for others was adopted. For those nutrients for which there were known levels above which adverse effects were a possibility, e.g. vitamin D, an MV would be set. For those nutrients for which elevated intakes had not been associated with adverse effects, e.g. many of the B vitamins, a GUL would be suggested based on knowledge of nutrient requirements of infants, technological and manufacturing considerations, known variability in current formulas and a history of apparent safe use in infant formulas. GULs would not be absolute maximums.

To help in establishing MVs or GULs based on a history of apparent safe use, the International Special Dietary Foods Industries (ISDI), the organization representing the infant formula manufacturers at Codex, proposed submitting global data on the variability of nutrient levels in current products. Those data would reflect the nutrient levels that formula-fed infants were actually consuming. They would also provide perspective on the technological issues that constrain manufacturing infant formulas with levels of certain nutrients within narrow limits. This paper presents data from the survey of the levels of selected nutrients in infant formula manufactured during the period 2000–2005 and compares those levels with the essential composition in the revised Codex standard for infant formula.

2. Materials and methods

At the time the survey was conducted, the draft revised standard specified minimum values and MVs or GULs for 31 nutrients in infant formulas—3 macronutrients (including specifications for the essential fatty acids), 13 vitamins, 12 minerals and 3 other nutrients. Participating infant formula manufacturers compared levels of nutrients in their infant formulas marketed globally with the proposed minimum and upper nutrient levels. This initial assessment determined that the levels of all nutrients met the proposed minimum values. However, in the case of 15 nutrients the data suggested that levels in some batches were expected to be at or above the proposed upper nutrient levels. These included two fat soluble vitamins (vitamins A and K), eight water soluble vitamins (thiamine, riboflavin, niacin, vitamin B_6, folic acid, vitamin B_{12}, vitamin C and biotin) and five minerals/trace elements (iron, copper, manganese, potassium and iodine).

Formal data collection and analysis focusing on those 15 nutrients were completed in a 4-month period between December 2005 and March 2006 in order to meet the Codex agenda. The present paper includes data provided by four global infant formula manufacturers, namely Abbott Laboratories, Mead Johnson Nutrition, Numico (currently Danone Baby Foods), and Wyeth Nutrition.

2.1. Nutrient data collection

The data covered infant formulas as defined by Codex Alimentarius, i.e. "a breast milk substitute specifically manufactured to satisfy, by itself, the nutritional requirements of infants during the first months of life up to the introduction of appropriate complementary feeding." Analytical data were collected for liquid and powder forms of milk-based and soy-based infant formulas from the quality assurance databases for batches produced and released into the market during the period 2000–2005. The nutrient compositions of formulas reflected by these data are representative of formulations that have been manufactured and sold for more than the 5 years specifically covered by the survey and that in most cases continue to be sold today. The analytical data covered globally marketed infant formulas produced in Asia, Europe and the Americas according to Good Manufacturing Practices.

Analytical values were determined shortly after manufacturing. Table 1 summarizes the analytical methods used and shows the comparable standard reference methods, where applicable. All analytical procedures were formally validated and performed under stringent quality control according to Good Laboratory Practices.[1] Because these were surveillance data, not all batches

[1] The recommended analytical methods for infant formulas in Codex standards are still under discussion (Codex Alimentarius Commission, 2008). The methods used to obtain the data reported here generally were equivalent to the currently proposed Type II and Type III methods as defined by the Codex Committee on Methods of Analysis and Sampling (Codex Alimentarius Commission, 2007b).