

The new European regulatory framework for infant and follow-on formulas: Comments from the Committee of Nutrition of the French Society of Pediatrics (CN-SFP)

Short title: The new European regulatory framework for infant and follow-on formulas

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Abbreviations

ALA: alpha-linolenic acid

ARA arachidonic acid

DHA: docosahexaenoic acid

EFSA: European Food Safety Authority

FOF: follow-on formulas

HAF: hypoallergenic formulas

IF: infant formulas

LA: linoleic acid

LC-PUFA: long-chain polyunsaturated fatty acids

TEI: total energy intake

TFA: total fatty acids

YCF: young child formulas

1. Introduction

The composition of infant formulas (IFs) and follow-on formulas (FOFs) on the market in the European Union (EU) has been complying with EU rules since 1991 (Directive 91/321/EEC, replaced by 2006/141/EC). A new regulation (2016/127 of September 25, 2015) [1] was enforced from February 22, 2020, except for formulas containing hydrolyzed proteins for which the date of enforcement is set for February 22, 2021. This regulation is based on prior advice from the European Food Safety Authority (EFSA), relating to the reference values of food intake [2] and the composition of IFs and FOFs [3]. It is part of a wider regulation framework, 609/2013 of June 12, 2013, which also involves foods for special medical purposes and meal substitutes intended for weight control. In order to facilitate the implementation of regulation 2016/127, the sale of stocks is authorized beyond February 2020. There is no European regulation for young child formulas (YCFs), for children aged 1–3 years. However, the nutritional and safety concerns (contaminants, pesticides, etc.) for these preparations have led countries to now consider separate national regulations [4].

2. Main changes for IFs and FOFs

IFs alone have to meet the needs of non-exclusively breastfed infants from birth to the beginning of complementary feeding. FOFs are intended for older infants when complementary feeding has started. The composition of FOFs is close to that of IFs, albeit with a higher protein and a lower fat content, as well as a higher iron content. IFs and FOFs based on dairy proteins (cow, goat) may legally be labeled "infant milk" and "follow-on milk."

2.1 Proteins

The only proteins authorized in IFs and FOFs are cow's milk proteins, soy protein isolates, hydrolyzed proteins (from cow's milk and rice) and, since 2013, goat's milk proteins [5]. Soy-

based preparations have undergone a gradual decline, probably linked to their phytoestrogen content [6] and have not been marketed in France since 2018.

The maximum authorized protein content (g/100 kcal) has been reduced for IFs and FOFs, and the minimum content has been reduced only for FOFs: (1) IFs: 1.8–2.5 instead of 1.8–3; (2) FOFs: 1.8–2.5 instead of 1.8–3.5; (3) IFs containing hydrolyzed proteins: 1.86–2.8 instead of 1.8–3; (4) FOFs containing hydrolyzed proteins: 1.86–2.8 instead of 2.25–3.5; (5) IFs containing soy protein isolates: 2.25–2.8 instead of 2.25–3; (6) IFs containing soy protein isolates: 2.25–2.8 instead of 2.25–3.5. These reductions are related to the common observation of a protein intake above the needs for this age [7].

2.2 Essential fatty acids and long-chain polyunsaturated fatty acids (LC-PUFA)

The lipid content of IFs and FOFs has not changed: 4.4–6.0 g/100 kcal. For all IFs and FOFs, the minimum content of linoleic acid (LA) has been increased from 300–500 mg/100 kcal, without changing the maximum content (1200 mg/100 kcal); the minimum content of alpha-linolenic acid (ALA) has not changed (50 mg/100 kcal) and a maximum value has been introduced (100 mg/100 kcal). The minimum LA and ALA content corresponds to the intakes recommended by the EFSA [2], i.e., 4% and 0.5% of the total energy intake (TEI), respectively. The maximum content corresponds to the maximum content observed in human milk, i.e., 24% and 2% of the total fatty acids (TFA).

The addition of docosahexaenoic acid (DHA), between 20 and 50 mg/100 kcal, or approximately 0.5–1% of TFA, to IFs and FOFs has become mandatory. The minimum level corresponds to the intake recommended by the EFSA in 2013 [3], i.e., 100 mg/day and the maximum level corresponds to the maximum levels observed in human milk, i.e., approximately 1% of TFA. Other LC-PUFA (C20 and C22) can be added, without exceeding in total 2% of TFA for all LC-PUFA ω 6 and 1% for arachidonic acid (ARA).

The absence of a mandatory addition of ARA, in contrast to the opinion of the EFSA [3], is largely debated, especially since ARA is present in human milk and synthesis may be insufficient [8]. According to the *Codex Alimentarius*, the level of DHA should not exceed the level of ARA [9]. The World Health Organization recommended in 2010 a minimum intake of ARA during the first 6 months: ARA: 0.4–0.6% of TFA and DHA: 0.2–0.36% of TFA [10]. Different organizations and scientific societies have considered the importance of a balanced intake between ARA and DHA and have recommended an intake equivalent to 0.5% of TFA for ARA and 0.32% of TFA for DHA [11–13]. The additional cost of supplementation with ARA may explain differences in formula supplementation between manufacturers. For FOFs, the addition of ARA seems less important since complementary feeding, when comprising fish, meat, and egg, is a notable source of ARA, for which, however, the recommended intake has not been established for this age [7].

2.3 Erucic acid

The maximum erucic acid content of IFs and FOFs has been reduced from 1% to 0.4% of TFA. In animals, excessive consumption of erucic acid is associated with the risk of myocardial lipidosis, a reversible condition, and other potential effects have also been observed, in high doses, in the liver, kidneys, and skeletal muscles [14].

2.4 Adding glucose syrup

The glucose content is limited to 0.84 g/100 kcal, instead of 2 g/100 kcal.

2.5 Vitamins

To optimize the vitamin D status, its minimum content in IFs and FOFs has been increased from 1 to 2 µg/100 kcal. The maximum content is still 2.5 µg/100 kcal in IFs and 3 µg in FOFs (1 µg = 40 IU).

The minimum level of vitamin A in IFs and FOFs has been increased from 60 to 70 µg/100 kcal but the maximum has been lowered from 180 to 114 µg/100 kcal. In France, the latest food consumption surveys show average daily intakes that are higher than the recommended nutritional intakes [15,16].

The minimum authorized level of vitamin K has been reduced from 4 to 1 µg/100 kcal in IFs and FOFs.

2.6 Choline

The minimum content of choline, which plays an essential role in brain development, has been increased from 7 to 25 mg/100 kcal in IFs.

2.7 Allegations

Nutrition and health claims not based on randomized, controlled studies are prohibited. The wording "contains DHA" is authorized until February 22, 2025, "lactose only" is used if lactose is the only carbohydrate present in the formula, and "lactose-free" refers to a lactose content of the formula not exceeding 10 mg/100 kcal.

2.8 Other modifications

Some minor modifications to the limits of certain minerals appear in the new regulation (slight increase in the minimum levels of sodium, potassium, chlorides, copper, iodine, and selenium; decrease in the maximum level of zinc, etc.).

3. Preparations containing hydrolyzed proteins

Three types of these preparations appear despite the lack of scientific or regulatory definitions, e.g., partial vs. extensive protein hydrolysate: (1) the so-called hypoallergenic formulas (HAF) contain partial hydrolysates intended for the reduction of the risk of clinical manifestations of allergy in infants at risk (those having a parent or siblings presenting at least one allergic manifestation type: eczema, allergic rhinitis, asthma, proven food allergy [17]); (2) the extensively hydrolyzed proteins (from cow's milk or rice) are intended for infants allergic to cow's milk proteins; (3) IFs and FOFs may contain partial hydrolysates which, according to the manufacturers, could accelerate gastric emptying and intestinal transit.

For all these preparations, the main regulatory changes are as follows:

1. The suitability and safety of each preparation have to be demonstrated by a randomized clinical trial with an appropriate non-inferiority methodology, analyzing the growth in reference with a preparation based on intact proteins. Only a positive assessment by the EFSA will allow the preparation to be launched on the market (this requirement has already been expressed in the EFSA 2014 scientific opinion).

2. Appropriate clinical trials should demonstrate whether, and to what extent, a so-called HAF reduces the risk of development, at least in the short term (up to 1 year of age), of clinical manifestations of allergy in infants who are at risk and not exclusively breastfed. Without a positive evaluation of the results by the EFSA, a claim relating to an allergy risk reduction will not be allowed, even if the product has shown nutritional adequacy and safety (requirement already expressed in the EFSA 2014 scientific opinion). Currently, only one formula, based on hydrolyzed cow's milk whey proteins, meets these criteria, i.e., the reduction of atopic dermatitis and allergic manifestations [18].

These two regulatory requirements will probably lead to a reduction in the market offer of IFs and FOFs containing hydrolyzed proteins.

4. Conclusion

Most changes brought about by this new regulation appear beneficial, such as the reduction of protein intake in IFs and FOFs, the mandatory addition of DHA, the reduction of glucose and vitamins A and K, the increase in vitamin D and choline. The CN-SFP regrets the absence of an increase in the lower limit of the total lipid content, in light of the results from the Nutri-Bébé survey [7], the absence of the mandatory addition of ARA in IFs (which does not prevent its use according to manufacturers), and the lack of any framework for YCFs. The CN-SFP highlights the progress made by requiring scientific evidence before allowing for a claim to be made.

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