

# The basics of prescribing infant formulas

Owens CJW, BScDietetics; Labuschagne IL, BScDietetics; Lombard MJ, PhD  
Nutrition Information Centre, Stellenbosch University

Correspondence to: C Owens, e-mail: nicus@sun.ac.za

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## Abstract

All infant formulas must support the normal growth and development of infants, and this needs to be scientifically demonstrated. Formulas have to contain sufficient amounts of basic nutrients, and so are nutritionally interchangeable, with no evidence indicating that one brand is superior to another.<sup>1,2</sup>

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## Introduction

Regulatory bodies around the world agree that breastfeeding provides the best nutrition for infants.<sup>1</sup> Exclusive breastfeeding is recommended by the World Health Organization (WHO) for the first six months, and supplemental breastfeeding for up to two years, or more. Although breastfeeding provides more benefits than formula feeding, many parents still choose infant formula as an alternative to the former.<sup>3,4</sup> Human milk contains antibodies, hormones, enzymes, and many other components, which cannot be added to formula. However, additives with proven benefits, are added to modern day infant formulas.<sup>5</sup>

This article looks at the basics of prescribing infant formula. Serious medical cases, such as short bowel syndrome and malabsorption, are beyond the scope of this article.

## Components of standard infant formulas

The nutritional composition of all infant formulas must meet the global standards as recommended by the European Society for Paediatric Gastroenterology, Hepatology and Nutrition's (ESPGHAN) international expert group that was commissioned by The Codex Alimentarius Commission in November 2004. All infant formulas must contain sufficient amounts of basic nutrients, and are thus nutritionally interchangeable (Table I). No evidence exists to recommend one brand over another.<sup>1,2</sup>

## Prescribing the correct infant formula

Infant formulas developed as unmodified cows' milk are not recommended for infants younger than 12 months of age, as they pose serious health risks.<sup>6,7</sup>

A wide variety of infant formulas are available, which makes choosing a suitable one difficult for parents and healthcare professionals. The majority of infants who are not being breastfed can use a standard infant formula, but a select few will require a more specialised formula. This will depend on gestational age and the presence of an illness.<sup>1</sup>

Table II provides a guide of available infant formulas, and indication of use. Formulas that are marketed for infants who are older than one year of age are not included, as no evidence exists to promote the use of such milk, or to demonstrate their superiority in terms of growth or development, when compared to whole milk.<sup>6</sup>

## Casein- vs. whey-predominant infant formulas

Manufacturing companies market casein- or curd-predominant formulas to "hungry" babies. However, there is no conclusive evidence that babies sleep longer, or have better quality sleep, if given such milk. These formulas form relatively indigestible curds in the stomach, and are not recommended for young babies.<sup>6</sup>

By comparison, whey-predominant infant formulas are more easily digested. Its composition of whey:casein (60:40) is similar to that found in human milk. For this reason, whey-predominant infant formulas are usually prescribed for newborn infants.<sup>6</sup>

## Additional components added to infant formulas

As more human milk components are discovered, modifications to existing infant formula and new infant formulas are made.<sup>5</sup> The European Society for Paediatric Gastroenterology, Hepatology and Nutrition's (ESPGHAN)

**Table 1:** The European Society for Paediatric Gastroenterology, Hepatology and Nutrition's recommended standards for the macro- and micronutrient composition of infant formula<sup>1</sup>

Component	Minimum	Maximum
<b>Energy:</b> kcal/100 ml	60	70
<b>Protein:</b> g/100 kcal		
Cows' milk	1.8	3
Soy	2.25	3
Hydrolysed	1.8 <sup>a</sup>	3
<b>Lipids:</b> g/100 kcal		
Total fat	4.4	6.0
Linoleic acid	0.3	1.2
$\alpha$ -linoleic acid	50	Not specified
<b>Carbohydrates:</b> g/100 kcal	9.0	14.0
<b>Fat-soluble vitamins:</b> $\mu$ g/100 kcal (unless otherwise specified)	60	180
Vitamin A: $\mu$ g RE/100 kcal (retinol equivalent)	1	2.5
Vitamin D <sub>3</sub>	0.5	5
Vitamin E: mg $\alpha$ -TE/100 kcal ( $\alpha$ -tocopherol equivalent)	4	25
Vitamin K		
<b>Water-soluble vitamins:</b> $\mu$ g/100 kcal (unless otherwise specified)	60	300
Thiamine	80	400
Riboflavin	300	1 500
Niacin	35	175
Vitamin B <sub>6</sub>	0.1	0.5
Vitamin B <sub>12</sub>	400	2 000
Pantothenic acid	10	50
Folic acid	8	30
Vitamin C: mg/100 kcal	1.5	7.5
Biotin		
<b>Minerals and trace elements:</b> mg/100 kcal		
Iron (cows' milk and hydrolysate protein)	0.3 <sup>b</sup>	1.3
Iron (soy-based protein)	0.45	20
Calcium	50	140
Phosphorus (cows' milk and hydrolysate protein)	25	90
Phosphorus (soy-based protein)	30	100
Magnesium	5	15
Sodium	20	60
Chloride	50	160
Potassium	60	160
<b>Minerals and trace elements:</b> $\mu$ g/100 kcal	1	50
Manganese	Not specified	60
Fluoride	10	50
Iodine	1	9
Selenium	35	80
Copper	0.5	1.5
Zinc		
<b>Other substances:</b> mg/100 kcal		
Choline	7	50
Myo-inositol	4	40
L-carnitine	1.2	Not specified

a = If an infant formula is based on hydrolysed protein, and it contains less than 2.25g/100 kcal protein, it should be clinically tested.

b = In areas where iron deficiency is proven, a higher iron content can be approved at national level.

international expert group, commissioned by The Codex Alimentarius Commission in November 2004, reported that the mere fact that a component is found in human milk, does

not justify its addition to formula. Formula milk additives have to demonstrate that they provide a scientifically proven benefit.<sup>2</sup>

### Long-chain polyunsaturated fatty acid supplementation

Alpha-linolenic acid (ALA) is the precursor for docosahexaenoic acid (DHA), more commonly referred to as omega-3 fatty acids. Linoleic acid (LA) is the precursor of arachidonic acid (AA), also known as omega-6 fatty acids. Omega-3 and omega-6 fatty acids are long-chain polyunsaturated fatty acids, important for neurological, cognitive, and visual development in the rapidly growing newborn.<sup>8</sup>

DHA and AA are present in human milk, in variable amounts. However, until recently, infant formulas only contained their precursors, LA and ALA. The addition of LA and ALA to formulas is standard, and they have to be added to all infant formulas on ESPGHAN's recommendation.<sup>1,2,9</sup>

In a recent Cochrane review, it was reported that the supplementation of DHA and AA in formula milk has not shown any beneficial effect with regard to the visual, physical, and neurodevelopment of term infants.<sup>2</sup> Further research is needed before routine supplementation of DHA and AA in infant formulas can be recommended.<sup>2</sup>

### Pre- and probiotics

Prebiotics, mostly in the form of indigestible oligosaccharides, are frequently added to infant formulas. Evidence that prebiotics reduce allergic disease is insufficient. Adding them is optional, providing they do not exceed 0.8g/100 ml.<sup>10,11</sup>

The motivation for adding probiotics to infant formula is that they might have a positive effect on digestion, with regard to the frequency and duration of gastrointestinal infections, including acute rotavirus gastroenteritis. They might reduce the risk of antibiotic-associated diarrhoea developing, as well as improve immunity. When added to infant formulas, *Bifidobacterium lactis* and *Lactobacillus reuteri* showed a significant decrease in the incidence and duration of diarrhoea caused by rotavirus.<sup>12</sup> A systematic review conducted by ESPGHAN indicated that there is not enough evidence to recommend the addition of probiotics to infant formula.<sup>1</sup>

### Nucleotides

A randomised control trial by Singhal et al found that healthy term infants fed nucleotide supplemented formulas experienced a greater weight increase and greater head circumference measurement compared to non-supplemented formulas.<sup>13</sup> ESPGHAN supports the addition of nucleotides to infant formula, provided that they do not exceed the maximum allowed amount of 5 mg/100 kcal.<sup>2,13,14</sup>

**Table II: Infant formula available in South Africa, and indication of use**

Class	Indication of use	Brand name	Kcal/100 ml	Protein source and g/100 ml	Carbohydrates and g/100 ml	Additives
<b>Standard term infant formula 0-6 months of age, but can be used up to 12 months of age</b>	Healthy term infants, of normal birth weight	Nestlé, Nan 1®	67	Demineralised whey, 30:70 whey-dominant, 1.23	Lactose, 7.47	DHA <sup>a</sup> , AA <sup>b</sup> , and nucleotides
		Nestlé, Lactogen 1®	67	Demineralised whey, 55:45 casein-dominant, 1.51	Lactose, maltodextrin, 7.46	-
		Pfizer, S26 1®	67	Skimmed milk 40:60 whey-dominant, 1.5	Lactose, 7.2	-
		Pfizer, S26 Gold 1®	67	Skimmed milk, 40:60 whey-dominant, 1.5	Lactose, 7.2	DHA, AA, and nucleotides
		Pfizer, SMA 1®	67	Skimmed milk, 1.6 80:20 casein-dominant	Lactose, 7.0	-
		Aspen, Infacare 1®	67	Whey protein, 40:60 whey-dominant, 1.5	Glucose, lactose, 7.5	-
		Aspen, Infacare Gold 1®	68	Whey protein, 40:60 whey-dominant, 1.4	Lactose, 7.5	DHA, AA, and nucleotides
		Aspen, Infacare Nurture 1®	67	Whey protein, 40:60 whey-dominant, 1.5	Lactose, 7.5	DHA and AA. Prebiotics and nucleotides
		Pharmac, Novolac 1®	66.1	Demineralised whey, 50:50 whey:casein, 1.5	Lactose, maltodextrin, 7.5	-
		Abbott, Similac Advance with Iron®	68	Whey protein, 1.4	Lactose, 7.3	DHA, AA, and nucleotides
<b>Standard term infant formula 6-12 months of age (not to be used for infants &lt; 6 months of age)</b>	Healthy term infants older than 6 months of age	Nestlé, Nan 2®	67	Demineralised whey, 60:40 casein-dominant, 2.02	Lactose, 7.67	DHA probiotics: <i>Lactobacillus</i> GG and <i>Bifidobacterium longum</i>
		Nestlé, Lactogen 2®	67	Skim milk, 64:35 casein-dominant, 2.03	Lactose, maltodextrin, sucrose, 8.05	Probiotics: <i>Lactobacillus reuteri</i>
		Pfizer, S26 Promil 2®	67	Whey protein, 60:40 casein-dominant, 2.2	Lactose and sucrose, 8.2	Nucleotides
		Pfizer, S26 Gold Promil 2®	67	Whey protein, 60:40 casein-dominant, 2.2	Lactose and sucrose	DHA, AA, and nucleotides
		Aspen, Infacare 2®	66	Whey protein, 65:35 casein-dominant, 2.4	Sucrose and glucose syrup, 8.6	-
		Aspen, Infacare Gold 2®	69	Whey protein, 50:50 casein:whey	Lactose and sucrose	DHA, AA, and nucleotides
		Aspen, Infacare Nuture 2®	67.3	Skim milk, 40:60 casein-dominant	Lactose and sucrose, 8.1	DHA, AA, and nucleotides. Pre-and probiotics
		Pharmaco, Novolac 2®	66	Skimmed milk, 80:20 casein-dominant, 1.6	Lactose and maltodextrin, 7.7	-
<b>Preterm formula</b>	Premature infants < 37 weeks gestation. Birth weight < 2.5 kg	Nestlé, Pre nan powder®	80	30:70 whey, 2.3	Lactose, maltodextrin, 8.57	DHA, AA and nucleotides
		Nestlé, Pre nan ready to drink®	80	100% partially hydrolysed whey protein, 2.9	8.4	DHA, AA and nucleotides
		Abbott, Similac Special Care 24Cal®	81	Skimmed milk, whey protein concentrate, 2.4	Lactose and corn syrup solids 8.4	DHA and AA
		Abbott, Similac Special Care 20Cal®	68	Skimmed milk, whey protein, 2.0	Lactose and corn syrup solids, 7	DHA and AA
<b>Soya formula 0-6 months of age</b>	Primary lactase deficiency. Galactosaemia. Vegetarian diet.	Abbott, Similac Isomil Advance®	68	Soy protein isolate, 1.66	Corn syrup and sucrose, 7.0	DHA and AA
		Abbott, Isomil 1®	68	Soy protein isolate, 1.8	Corn syrup, sucrose, maltose, 6.9	-
		Pfizer, Infasoy 1®	67	Soy protein isolate, 1.8	Corn syrup and sucrose	-
		Aspen, Infacare soya 1®	65	Soy protein isolate, 1.8	Corn syrup solids, 6.6	-
		Aspen, Infacare Gold Soya 1®	67	Soy protein isolate	Corn syrup solids	DHA, AA, and nucleotides

Class	Indication of use	Brand name	Kcal/100 ml	Protein source and g/100 ml	Carbohydrates and g/100 ml	Additives
<b>Soya formula 6-12 months of age</b>	Primary lactase deficiency. Galactosaemia. Vegetarian diet.	Abbott, Isomil 2®	69	Soy protein isolate, 2.3	Corn syrup, sucrose and maltose, 8.0	-
		Aspen, Infacare soya 2®	72	Soy protein isolate, 2.2	Corn syrup solids, 7.7	-
		Aspen, Infacare Gold Soya 2®	-	Soy protein isolate	Corn syrup solids	DHA, AA, and nucleotides
		Pfizer, Infasoy 2®	66	Soy protein isolate, 2.5	Corn syrup and sucrose, 6.9	Nucleotides
<b>Anti-reflux formula</b>	Reflux associated with failure to thrive, respiratory symptoms and esophagitis	Nestlé, Nan AR®	67	Demineralised whey 30:70 casein-dominant, 1.24	Lactose, potato and corn starch, 7.7	-
		Pharmaco, Novolac AR 1 (Also AR 2)®	66	Skim milk, 80:20 casein-dominant 1.7	Lactose and corn starch, 7.4	Long-chain polyunsaturated fatty acids
		Aspen, Infacare AR®	67	Skim milk, 80:20 casein-dominant, 1.6	Corn syrup solids, carob bean gum	-
		Aspen, Infacare Nurture AR®	67	Skim milk, 80:20 casein-dominant, 1.6	Corn syrup solids, 7.0	DHA, AA, and nucleotides
<b>Acidified formula</b>	Infants with an increased risk of developing gastroenteritis	Nestlé, Nan Pelargon®	67	Demineralised whey, 50:50. 1.49	Lactose, maltodextrin, 7.57	Chemically acidified with lactic acid
		Aspen, Melegi®	67	Whey protein, 40:60 whey-dominant, 1.5	Corn syrup solids, lactose, 7.5	Chemically acidified with citric acid
<b>Low-lactose or lactose-free</b>	Galactosaemia. (However, not all of the formulas in this category are suitable for patients with galactosaemia). Acute diarrhoea. Lactose intolerance.	Nestlé, Nan Lactose free®	67	Potassium caseinate, whey protein 40:60, whey-dominant, 1.4	Corn syrup (maltodextrin), 7.8	DHA, AA, and nucleotides
		Aspen, Infacare® Nurture LF® Not for galactosaemia.	67	Calcium caseinate, 1.5	Corn syrup solids, 7.2	DHA and AA. Prebiotics
<b>Hydrolysed cows' milk formula</b>	Limited research on the prevention of cows' milk and other allergies (infants 0-6 months of age)	Nestlé, Nan HA® 1 (new)	67	100% partially hydrolysed whey protein, 1.51	Lactose, maltodextrin, 7.56	DHA and AA
	Limited research on the prevention of cows' milk and other allergies (infants 6-12 months of age)	Nestlé, Nan HA 2®	67	100% partially hydrolysed whey protein, 2.01	Lactose, maltodextrin, 8	DHA and AA. Probiotics: <i>Lactobacillus GG</i> and <i>Bifidobacterium longum</i>
	Limited research on the prevention of cows' milk and other allergies (infants 0-12 months of age)	Abbott, Similac Advanced HA®	71	26% degree of hydrolysis, 1.9	Maltodextrin, 7.9	Nucleotides
		Pharmaco, Novolac HA®	65	16-22% degree of hydrolysis, 1.6	Lactose, starch, glucose syrup, 7.6	-
		Aspen, Infacare Nurture HA Comfort®	67	Hydrolysed whey, 1.5	Corn syrup, lactose, 7.2	DHA and AA. Probiotics
<b>Extensively hydrolysed formula</b>	Diagnosed cows' milk allergy, and other medical conditions	Nestlé, Alfaré®	70	100% whey protein extensively hydrolysed (80% small peptides, 20% free amino acids)	Maltodextrin and potato starch	DHA and nucleotides
		Abbott, Similac Alimentum®	66.7	Extensively hydrolysed casein, supplemented with 60% free amino acids, 1.8	Sucrose, modified tapioca, 6.8	DHA and AA
	Cow's milk protein allergy 0-6 months	Pharmaco, Novolac Allernova®	61.7	39 % degree of hydrolysis, 1.4	Glucose syrup. 6.7	-
	Cow's milk protein allergy	Nutricia, Pepticate®	66	Extensively hydrolysed whey, 1.6	Maltodextrin, 7.1	DHA, AA, and nucleotides

Class	Indication of use	Brand name	Kcal/100 ml	Protein source and g/100 ml	Carbohydrates and g/100 ml	Additives
Free amino acid-based formula	Highly allergic infant. Other conditions where an elemental diet may be indicated.	Nutricia, Neocate®	71	Free amino acids, 1.95	Glucose, syrup, 8.1	-
	Highly allergic infant. Other conditions where an elemental diet may be indicated. Children > 1 year of age.	Nutricia, Neocate advanced®	100	Free amino acids, 2.5	Glucose syrup, 14.6	-

a = docosahexaenoic acid, b = arachidonic acid

## Specialised formulas

In a small percentage of cases, due to feeding intolerances, infants require specialised formulas. This should only be given on the recommendation of a dietitian or physician.<sup>1</sup>

### Protein-modified formula

#### Preventing cows' milk allergies, as well as others

There is no evidence to support giving hydrolysed cows' milk over exclusive breast milk in an attempt to prevent allergies in infants. Limited evidence exists to support giving hypoallergenic (partially hydrolysed or extensively hydrolysed) formula vs. cows' milk formula to infants at high risk of developing allergies.<sup>15</sup>

Evidence indicates that giving soy-based formula, rather than cow's milk formula, does not reduce the risk of the development of allergies such as asthma, eczema, rhinitis, and cow's milk allergy, in later infancy and childhood.<sup>16,17</sup>

#### Treatment of cows' milk allergies

Where exclusive breastfeeding is not possible, extensively hydrolysed cows' milk protein formulas and amino acid-based formulas should be given to treat infants with diagnosed cows' milk protein allergies. Amino acid-based formulas should be given to infants who are highly allergic.<sup>18</sup>

#### Treatment of colic

The authors of a recent Cochrane review concluded that there is some evidence to promote offering hydrolysed cow's milk formula to bottle-fed infants suffering from colic.<sup>19</sup> However, the recommendation is based on a small randomised control trial, and further research is required. Soy infant formulas should not be given to prevent or treat colic.<sup>17</sup>

#### Soy-based infant formula

Cows' milk protein allergy (CMPA) is a major financially driven indication for soy formulas to be given, but giving hydrolysed cow's milk protein formula and amino acid-based

formula has proven to be more effective, and should be the first option in treating CMPA. ESPAGHAN recommends that there should be a transition from hydrolysed cow's milk protein formula to soy-based formula after six months of age, as it is better tolerated by older infants. The viewpoint of the American Academy of Paediatrics (AAP) is as follows: "... for infants with documented CMPA, extensively hydrolysed protein formula should be considered, because 10-14% of these infants will also have a soy protein allergy."<sup>17</sup>

The only medical indication for giving soy infant formulas is galactosaemia and primary lactase deficiency. ESPGHAN and the AAP recommend a lactose-containing formula for realimentation, but a lactose-free formula is better tolerated in infants with secondary lactose intolerance after acute gastroenteritis. This has encouraged the consumption of isolated soy-based infant formula, but research has shown that the use of lactose-free formula is also well tolerated.<sup>17</sup>

#### Carbohydrate-modified formula

The major carbohydrate in breast milk and standard cows' milk formula is lactose. Strong evidence suggests that a lactose-free infant formula is effective in the dietary management of acute diarrhoea.<sup>17</sup> Galactose and glucose make up lactose, and therefore, infants with galactosaemia require a lactose-free infant formula, and cannot be breastfed.<sup>20</sup>

#### Acidified formula

Infant formula can be chemically acidified through the addition of L (+) lactic acid, or biologically through fermentation, which transforms lactose into lactic acid. The method of acidification does not have an effect on the growth of infants. The growth of pathogenic bacteria is inhibited through the use of an acidified formula, leading to a decreased incidence of diarrhoea in infants.<sup>20</sup>

#### Preterm milk

Human milk is the best source of nutrition for all infants, including infants who are born prematurely.<sup>21,22</sup> An

appropriate preterm formula should be prescribed by a neonatologist on an individualised basis, to premature infants who cannot be breastfed. It should be given in the early months, after birth.<sup>23</sup> Continuous nutritional intervention post-discharge must be encouraged, and is of vital importance.<sup>24</sup>

### Anti-reflux formula

Almost half of all infants are affected by symptomatic gastroesophageal reflux (GER). Uncomplicated GER usually resolves spontaneously, and needs no treatment. Infants with GER presenting with failure to thrive, and esophagitis and respiratory complications, typically need pharmacological, or other treatment. Non pharmacological treatment includes giving an infant formula that is pre-thickened with pre-cooked corn starch or locust bean gum, which has been proven to decrease episodes of regurgitation and emesis. Pre-thickened formula is nutritionally safe, and contains adequate amounts of the necessary nutrients.<sup>1,14,25,26</sup>

### Follow-on milk for infants aged six to 12 months

Giving follow-on milk was deemed “not necessary” by the World Health Assembly. The United Nations Children’s Fund’s (UNICEF) position is that parents can continue to give first milk until an infant reaches 12 months of age. First milk, together with complimentary foods, will provide enough nutrients to satisfy a healthy infant’s nutritional needs.<sup>6</sup>

## Conclusion

Breastfeeding is the best source of nutrition for most infants, and should be promoted, supported, and protected at all times. In rare cases, for example, infants with galactosaemia or primary lactase deficiency, or for any other medical reasons where the mother is unable, or unwilling, to breastfeed, it is important to select a suitable infant formula based on the infant’s individual needs, and medical condition.

## Conflict of interest

I declare that I have no financial or personal relationship(s) which may have inappropriately influenced me in writing this paper.

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