Claims made for infant formula, ingredients and formulations.

FIRST STEPS NUTRITION TRUST

Introduction

What information is summarised here?

Over the past few years we have collated some of the claims made on infant formula websites about products and ingredients and reviewed the evidence provided. From February 2020 no health claims are allowed on infant formula labels by law, and depending on how the law is interpreted by the Department of Health and Social Care (guidance notes for the new regulations are pending) this may mean that claims cannot be made on websites or in print advertising. Whilst this has meant a significant reduction in claims made for infant formula, manufacturers maintain claims for follow-on formula knowing that cross-branding will associate all products of the same brand with the claims. This also allows ingredient and formulation names to become familiar so that the 'name' of an ingredient can appear alone without a claim needing to be made where they are disallowed.

We therefore believe that it remains helpful for health workers to be aware of the claims that have been made in the past and to look at some of the evidence that was provided to support these claims. We have therefore summarised statements and claims that were being used for infant formula before the regulatory change. **These have been taken from work we have published over the past three years to demonstrate the sort of claims and evidence that have typically been used by infant formula manufacturers.**

Expert opinion on infant formula composition

In 2014 the European Food Safety Authority (EFSA) reviewed the essential composition of infant formula and follow-on formula (EFSA, 2014[2]). EFSA independently analysed all the evidence available to determine the necessary, and unnecessary, components of infant formula,

Key points made by EFSA about infant formula

Nutrient/component	EFSA (2014) opinion/comment
Can formula milk be 'close' to breastmilk?	Breastmilk is the preferred food for all healthy infants. Whereas the composition of infant formula remains stable over time, breastmilk composition changes continuously and therefore infant formula cannot imitate breastmilk. The mere presence of a substance in human milk does not necessarily indicate a specific benefit of this substance for the infant, nor do the concentrations of nutrients in human milk necessarily reflect infants' dietary requirements because they may mirror maternal intakes rather than infants' needs, or because absorption efficiency of certain nutrients differ between breastmilk and formula.

Can formula milk be 'close' to breastmilk?	Infant formula cannot imitate breastmilk with respect to its energy and protein content. The structure of about 200 human milk oligosaccharides has been identified. The production of oligosaccharides is genetically determined and the individual pattern of oligosaccharides differs between women. The oligosaccharides of human milk are considered to be one of the principal growth factors, for example, for *Bifidobacteria* in the infant gut and are responsible for the composition of the gut microbiota found in breast-fed infants. There is no evidence for health benefits from the addition of prebiotic oligosaccharides (GOS/FOS) to infant or follow-on formula.
Is it safe to add ingredients that are not needed, or in amounts higher than necessary?	Nutrients and substances should be added to formulae for infants *only* in amounts that serve a nutritional or other benefit. The addition in amounts higher than those serving a nutritional or other benefit or the inclusion of unnecessary substances in formulae ***may put a burden on the infant's metabolism or on other physiological functions***, as substances which are not used or stored have to be excreted.
Are there risks when nutrients are added at maximum amounts?	There is a lack of studies designed to investigate the short- or long-term health consequences of consumption of formulae containing the currently permitted maximum amounts of nutrients in infant formula.
Ingredients added to infant formula which are <u>unnecessary</u>	• Arachidonic acid (ARA) • Eicosapentaenoic acid (EPA) • Non-digestible oligosaccharides (prebiotics. GOS/FOS mixtures) • Probiotics • Synbiotics (a mix of prebiotics and probiotics) • Chromium • Fluoride • Taurine • Nucleotides • Phospholipids as a source of long-chain polyunsaturated fatty acids instead of triacylglycerols • Triacylglycerols with palmitic acid predominantly esterified in the *sn*-2 position

[2] EFSA (2014). *Scientific opinion on the essential composition of infant and follow-on formulae.* Parma, Italy: European Food Safety Authority. Available at http://www.efsa.europa.eu/en/efsajournal/pub/3760

Statements and claims made for infant formula, ingredients or formulations.

Here we have grouped the different health conditions or benefits for which statements or claims have been made, detailing how specific manufacturers defend these and reviewing evidence provided.

1. General statements about product composition.
2. Claims made that ingredients/infant formula can support healthy growth.
3. Claims made that ingredients/infant formula can support healthy development.
4. Claims made that ingredients/infant formula can support improved digestion and gut health.
5. Claims made that ingredients/infant formula can reduce the risk of allergies.
6. Claims made that ingredients/infant formula can support the immune system.

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1. General statements about product composition

All infant formula have a similar nutritional composition in order to comply with UK compositional regulations and they are all nutritionally adequate for infants. If a substance was found that was definitely beneficial for infant health that could be added to infant formula, it would be in all products by law.

Here we give examples of statements that have been made by manufacturers for product composition, use of specific combinations of non-essential ingredients, organic ingredients, use of goats' milk or whole cows' milk. We also provide some examples of where manufacturers have contravened regulations by making statements comparing their products to breastmilk or breastfeeding.

1.1 Statements or claims about product composition or formulation

New regulations for infant formula restrict manufacturers from making health claims about specific ingredients but permits them to list ingredients. Below are some examples of statements made by manufacturers about specific product composition.

Danone Nutricia add a number of ingredients to Aptamil First Infant Milk and Follow-on Milk that includes galacto- and fructo-oligosaccharides (GOS/FOS), long chain polyunsaturated fatty acids, and nucleotides. This blend was patented as Pronutra+ and Nutricia made the following statement on their website:

'Contains our unique blend of ingredients.'

These are ingredients found in a number of infant formula and no evidence was provided to explain why this was 'unique'.

Aptamil Profutura also made statements about the use of ingredients, although no specific claims were made about their inclusion, for example:

'Egg lipid has been added.'

'The product uses anhydrous milk fat.'

Danone Nutricia, the manufacturer of this milk said in a letter to First Steps Nutrition Trust that:

"The egg phospholipid in Aptamil Profutura milk RTF is sourced from egg yolk. We are confident that the egg phospholipid does not pose a risk of causing an allergic reaction and our supplier guarantees that the level of egg protein in the egg phospholipid is <0.001ppm per mg."

Apparently of the 11mg/100ml docosahexaenoic acid (DHA) present in the milk, 2.2mg comes from egg phospholipid. The remainder is provided by the fish oil and algal oils used.

Is there any benefit to adding phospholipids to infant formula?

The Aptamil Professional website claimed that Aptamil Profutura First Infant Milk:

'Contains phospholipid-bound LCPs inspired by the complex structure of fats within breastmilk.'

The EFSA 2014 opinion on the essential composition of infant formula stated that, whilst there are phospholipids naturally present in breastmilk:

"There is no convincing evidence for a beneficial effect of using LCPUFA supplied as phospholipids in infant formula."

The manufacturer made no claims specifically about the egg lipid as a source of LCPUFA in this formula, simply stating it was present, so it was not clear why they were using this as a partial source of DHA.

As for the statement regarding the addition of anhydrous milk fat, the Aptamil Professional website claimed that the product:

"Contains milk fat to provide a fatty acid profile closer to that of breastmilk."

And then went on to state that:

"In breastmilk, when palmitic acid is in the beta position it has certain benefits for babies, including better fat absorption, easy digestion, softer stools and reduced constipation."

Anhydrous milk fat is simply milk fat (butter fat) that has had all water removed. The references given to support this type of fat having properties which may aid fat and calcium absorption come from Jensen et al (1978), Carnielli et al (1996) and Kennedy et al (1999). The Jensen et al (1978) study reports on the variable composition of human milk in relation to maternal diet and highlights the lack of reliable data at that time on milk composition. This paper offers no support for the statements made.

The studies by Carnielli et al (1996) and Kennedy et al (1999) have previously been used to support claims that use of synthetic triglycerides with a higher proportion of palmitate in the *sn-2* position improves fat and calcium absorption. They are now being used to support the same claims for the use of anhydrous milk fat, which has a greater proportion of palmitate in the *sn*-2 position than the vegetable oils commonly used in infant formula milks. Both of these studies examined the impact on fat and calcium absorption when infants were fed formula containing higher proportions of palmitic acid in the *sn*-2 position than were present in Aptamil Profutura 1 First Infant Milk as a result of the use of anhydrous milk fat. The Kennedy et al study also reported that a number of parents reported concern about runny stools after feeding formula containing high *sn*-2 palmitate.

The recent EFSA *Scientific opinion on the essential composition of infant and follow-on formulae* (2014) concluded that there was no convincing evidence for a beneficial effect of the use of palmitic acid predominantly esterified in the *sn-2* position in infant or follow-on formula.

1.2 Statements or claims making comparison to breastmilk or breastfeeding

The UK Guidance Notes (Department of Health, 2013) which explained the previous (2007) regulations on infant formula composition, marketing and labelling, stated that:

"Non-mandatory text or pictures on infant formula and follow-on formula labelling must not make reference to 'breastmilk', 'breastfeeding', 'moving on from breastfeeding' or ***'closer to/inspired by breastmilk'****. Use of such terms would not comply with Regulation 17 (2) or 18(2)."*

Despite this there were several instances where manufacturers made claims of this nature. For example, Aptamil Profutura claimed that their product was:

'Nutritionally closer to breastmilk in fat composition and structure than any other brand.'

Aptamil Profutura supported this claim with a chart comparing their milk with others and based the claim on the added phospholipid and the fat composition which we have already reviewed above. They claimed that:

'LCPs in breastmilk come in two different forms: phospholipid-bound and triglyceride-bound.'

The reference given to support this, Harzer et al (1983), looked at changing patterns of human milk lipids in the course of lactation, and clearly made the point that milk composition changes as lactation progresses, and in mothers in different areas. It concludes that, because there are strong intra-individual differences in the composition of breastmilk, care should be taken when taking samples of breastmilk for analysis. This study does not in any way support a feed of consistent composition, or this infant formula, as being 'close to breastmilk'. Just because manufacturers manipulate fat composition to mimic breastmilk components does not make it 'closer to breastmilk' in function.

Hipp Organic Combiotic First Infant Milk also compared their product to breastmilk by making the following claim about their protein content:

…'protein level and profile closer to that found in breastmilk.'

It is important to note that EFSA (2014) clearly state in their opinion that:

"Infant formula cannot imitate breast-milk with respect to its energy and protein content."

The reference given to support the statement from Hipp, Nommsen et al (1991), is from an American study which examined factors associated with concentrations of energy-yielding nutrients in human milk. This study measured the protein in samples of milk from lactating women at different time points over a period of 12 months, but the protein profile was not examined. This study also showed that there was significant variation in breastmilk composition related to a number of maternal factors, and it is important to remember that breastmilk changes composition during and between feeds and over time. The statement that this infant formula has *"a protein level and profile closer to breastmilk*" is therefore not supported by this reference.

Nestlé, who manufacture SMA, have also made comparisons with breastfeeding/breastmilk for their SMA Pro First Infant Formula and SMA Organic First Infant Milk:

'A lower protein content formula has been shown to provide growth rates more like a breastfed baby.'

'Is the only First Infant Milk clinically proven to achieve a growth rate comparable with a breastfed baby.'

Hipp Organic Combiotic First Infant Milk made the following statement:

'Organic – made from milk produced by cows kept to organic standards and fed an organic diet, free from GM ingredients and chemical pesticides.'

Hipp Organic reference a study by Butler et al (2008) to support the statements that organic milk is higher in vitamin E, beta-carotene, lutein and zeaxanthin, but fail to mention what the comparison is. The Butler et al study, which compares concentrations of fatty acids and antioxidants in milk from high-input, conventional farms, low-input organic farms and low-input non-organic farms, reported that milk from the low-input organic *and* low-input non-organic farms had higher concentrations of conjugated linoleic and *α*-linolenic acid, *α*-tocopherol and carotenoids compared with milk from the high-input system. Milk composition differed significantly between the two low-input systems during the second half of the grazing period only, with milk from non-organic cows being higher in antioxidants and conjugated linoleic acid, and that from organic cows being higher in *α*-linolenic acid. This does not necessarily translate into higher levels in infant formula made with organic milk where concentrations of micronutrients are regulated; nor does it suggest any clinical advantage of higher levels of micronutrients.

Hipp also made claims for the benefits of their organic formula milks over milks produced using conventional farming methods:

'All infant and follow on milks are required to meet strict regulations to make sure they are nutritionally adequate for baby - but our Combiotic® range has the added benefits that come from using organic ingredients.'

Some of the benefits claimed for the Combiotic range include:

'…making sure there are no pesticides used on the farms where the cows graze: babies are known to be more susceptible to the effects of pesticide residues so choosing an organic diet for babies is very important'

It is important to note that there are strict limits on the level of any individual pesticide residue that may be present in infant formula and follow-on formula and specific upper limits for toxic pesticides.

'Our milks are tested for purity at every stage of production'

There was however no indication of what the product is tested for or how this compares to the testing of products from other manufacturers that might suggest that their organic product is more beneficial.

It is important to note that whilst these claims were made for the Combiotic range, Hipp Combiotic Growing-up Milk 4 and Hipp Combiotic Comfort Milk are not certified organic.

1.4 Statements or claims made for use of goats' milk

Kabrita Gold First Infant Milk made the following statement:

'It is naturally rich in important nutrients such as Ca and vitamin A and has a high bio-availability of iron.'

'It has a deliciously mild taste.'

No evidence was given on the website to support these statements.

NannyCare First Infant Formula made the following statement:

'The only goat milk formula supported by clinical trials.'

On the manufacturer's website, reference is made to a trial by Zhou et al (2014) which was used as evidence to EFSA (2012) when they reviewed the safety of goats' milk protein as a source of protein in infant formula. Nannycare First Infant Milk was the formula used in that study. The EFSA recommendation was that milk from goats' milk or cows' milk can be a suitable protein source for infant formula provided the final product complies with the composition criteria laid down in the relevant EU Directive. The EFSA panel highlighted that, if goat milk protein is used in infant formula, particular attention has to be given to the amino acid content by adding in appropriate free amino acids to ensure that the profile is adequate.

The following claims were also made by NannyCare:

Goat milk:

'Is an excellent source of high quality, readily digestible proteins.'

'Forms looser, softer and more porous curds in the baby's stomach. (This is particularly helpful to the baby's delicate developing digestive system.)'

'Has a casein profile which is closer to human milk (than cow's milk).'

'Has high levels of medium-chain fatty acids.'

'Has high levels of nucleotides.'

No evidence was provided on the website to support these claims.

In their evaluation of the suitability of goats' milk protein as the protein source in infant formula, EFSA stated that, while they note the differences in the composition of the caseins between goat and cow milk, no difference in digestibility has been observed (EFSA, 2012). In addition they state that there is no convincing evidence to support a lower incidence of allergic reactions in infants fed formula based on goats' milk protein compared with those fed cows' milk protein based formula.

The relevance of high levels of medium-chain fatty acids or nucleotides is not explained, but whether an infant formula is made from cows' or goats' milk protein, the composition has to meet current regulations.

1.5 Statements or claims made for use of whole milk

Kendal Nutricare made the following claims for their Kendamil milks on the company website:

'Milder and more natural taste than formulas made from skimmed milk.'

'Retains all the natural goodness and benefits of full cream nutrients.'

'Formulated to include the essential nutrients your baby needs to complement a balanced weaning diet.'

These claims are not substantiated by reference to scientific evidence. It is important to ensure families do not believe that whole animal 'full-cream' milk is a breastmilk alternative. Claims suggesting that full cream milk is full of natural goodness and more wholesome for infants could be misleading.

The company website stated that the product was made using whole milk**.** Whilst whole milk is used in the product manufacture, after drying, it only accounts for about 16% of the dry weight of the powder, the majority being composed of whey powder, vegetable oils and lactose.

2. Claims made that ingredients/infant formula can support healthy growth

2.1 Reduced protein content

Hipp Organic made the following claim for its first infant formula:

'…the UK's first reduced protein infant formula.'

The difference in protein content was however not sufficiently significant to differentiate it from other brands: in terms of protein content per 100ml of infant formula. Most first formula have had comparable protein contents of about 1.3g/100ml for several years.

Hipp made health claims for its product based on the results of the Hipp-funded BeMIM study (Fleddermann et al, 2014). The aim of this study was to prove the safety and suitability of a reduced-protein formula for healthy term babies. The study compared outcomes related to the intakes of two formula, one with a protein content of 1.3g/100ml, and one with a protein content of 1.5g/100ml.

The claims made by Hipp for their formula were based on findings from this study and include:

'Adequate growth.'

This is to be expected as the low protein test infant formula met compositional recommendations.

'Protein intakes closer to breastfed infants.'

The fact that protein intakes may be similar in breastfed and formula-fed infants does not suggest that this is associated with any clinical advantage. The estimate used for protein intakes of breastfed infants are based on breastmilk composition of 1.2g/100ml (1.7g/100kcal), reported by Nommsen et al (1991). The current estimate of protein content in breastmilk in the UK is 1.3g/100ml (Finglas et al, 2015).

The evidence presented by Hipp to promote their milks on the basis of reduced protein did not confirm that this infant formula had any clinical advantage over other whey-based first infant formula available on the market.

Nestlé made the following statement for SMA Advanced First Infant Milk on their website in 2019:

'The lowest protein infant formula in the UK and Ireland.'

The references given to support this statement were their own datacard and the datacards for other first infant formula products. The datacard for SMA Advanced First Infant Milk stated that the protein content was 1.2g/100mls (1.9g/100kcal). However, SMA Pro First Infant Milk appeared to have a lower protein content per 100kcal (1.85g/100kcal), although the amount per 100mls appeared higher (1.24g/100mls). SMA Organic First Infant Milk listed an equivalent protein content to SMA Advanced per 100kcal (1.9g/100kcal) but appeared to be slightly higher when calculated per 100mls (1.28g/100mls). Hipp Organic Combiotic First Infant Milk also showed a lower protein content than SMA Advanced per 100kcal (1.89g/100kcal), but this appears higher when calculated as per 100mls (1.25g/100mls). These discrepancies are likely to be due to rounding.

Even assuming that the SMA Advanced protein content is not rounded, the difference was not sufficiently significant between it and the other brands; the difference in protein content between SMA Advanced and Hipp Organic was 0.01g/100kcal.

The same claim was previously made by Nestlé for SMA Pro First Infant Milk, which it claimed had the lowest protein content of any infant milk on the market. However, as we have noted above, the difference was not sufficiently significant to differentiate it from all other brands; at the time the difference in protein content between SMA Pro First Infant Milk and the brand with the next lowest protein content was 0.02g/100kcal.

Nestlé also made the following statement regarding SMA Pro First Infant Milk:

'The quantity of protein has been reduced.'

SMA Nutrition claimed to have used a *"new exclusive protein process"* to produce the protein component of their infant milk. No information was given on the website to explain what this process is, but in an email to First Steps Nutrition Trust, Nestlé Nutrition said that:

"This patented process allows SMA Nutrition to reduce the total protein content in SMA PRO First Infant Milk to 1.25g/100ml (1.87g/100kcal) in line with scientific opinion while maintaining a desirable amino acid profile."

The SMA professional website also made claims for SMA Pro First Infant Milk:

'SMA PRO First Infant Milk has lower levels of insulinogenic amino acids compared with other first infant milks.'

'Insulinogenic amino acids are shown to contribute to obesity later in life.'

There were, however, no articles from peer-reviewed journals to support these claims, and the claims were referenced as *"on file at Nestlé".* We asked for this data but it was not provided.

Nestlé also claimed for SMA Organic First Infant Milk:

'A lower protein content formula has been shown to provide growth rates more like a breastfed baby.'

It is established internationally that infant formula-fed infants grow at a different pace to breastfed infants (Garza and de Onis, 2004). It is unclear whether SMA Pro First Infant Milk is the same milk as the one used in the studies which they say support this claim.

Nestlé also claimed that:

'This slower growth rate has been linked to long-term health benefits, including a lower risk of obesity, cardiovascular disease and diabetes.'

This statement was referenced with a review article by Singhal and Lucas (2004) on the association between early nutrition and later risk for cardiovascular disease, obesity and diabetes. Since this time there has been a significant reduction in the protein content of most infant formula milks on the UK market.

SMA linked the claims above to suggest that their lower protein formula leads to slower growth rates than infant formula with a higher protein content, which in turn may reduce later risk for obesity, cardiovascular disease and diabetes, however, the role of protein in

increased growth rate and higher BMI in childhood is still a matter of debate and requires more research (EFSA, 2014).

2.2 Product formulation

Hipp made the following statement regarding the composition of Hipp Organic Combiotic First Infant Formula:

'Hipp gentle organic formula is specially formulated using only the finest organic milk and contains Omega 3 & 6 LCPs (DHA & AA) and PRÆBIOTIK® oligosaccharides (GOS), as well as all the important vitamins, minerals and other nutrients (required by law) that babies need to grow strong and healthy.'

No direct health claims were made for health benefits of either fatty acids or oligosaccharides in Hipp Organic Combiotic First Infant Milk and no evidence was provided to explain why these were added.

3. Claims made that ingredients/infant formula can support healthy development

3.1 The addition of Long Chain Polyunsaturated Fatty Acids (LCP/LCPUFA)

Current regulations (from February 2020) for infant formula specify that docosahexaenoic acid (DHA) is a mandatory ingredient, specifying minimum and maximum amounts. Previous regulations permitted it as an ingredient, but it was not mandatory. Arachiadonic Acid (AA) is a permissible ingredient, but it is not mandatory.

Several of the same references were used by manufacturers to support claims or statements on the addition of LCPUFA to products, including a paper by Koletzko et al (2008), an EFSA paper from 2009, and a study by Willatts et al (1998).

The review article by Koletzko et al (2008) summarised the evidence for the role of DHA and AA in maternal and term infant nutrition as well as infant development and made recommendations concerning their inclusion in the infant diet. The review concluded that the fetus and neonate should receive LC-PUFA in amounts sufficient to support optimal visual and cognitive development. It recommended breastfeeding as the best way to achieve this and that if breastfeeding were not possible, formula supplemented with DHA and AA should be used. DHA supplementation should be at levels between 0.2 and 0.5 weight percent of total fat, with the minimum amount of AA equivalent to the contents of DHA.

In 2009, EFSA approved the claim that *"DHA contributes to the visual development of infants"* (EFSA, 2009). However, the validity of this claim is still debated, as it is argued that visual acuity develops slowly during the early years of life and early observations of visual measurements in infants are not predictive of later visual functions. Studies would have to follow children for seven years or longer to see if small clinical changes observed in early life had any real impact (Chambers et al, 2013).

The study by Willatts et al (1998), funded by Milupa (now Danone Nutricia), considers long chain fatty acid supplementation in term infants through formula supplementation and impact on IQ. Cognitive behaviour was tested at 10 months by a three-step solution to uncovering and retrieving a hidden toy. The authors concluded that there may be some benefit of supplementation with long chain polyunsaturated fatty acids, but whether it is possible to measure cognitive behaviour at this age is debateable.

The EFSA *Scientific opinion on the essential composition of infant and follow-on formulae* (EFSA, 2014) presents a useful summary of all the evidence, including data from these studies, relating to fatty acids in human and artificial milks. EFSA concluded that, whilst they still believe that DHA should be added to infant and follow-on formula in similar amounts as are present in breastmilk as a 'prudent measure':

"The panel notes there is no convincing evidence that the addition of LCPUFA to infant formula or follow-on formula has any benefits beyond infancy on any functional outcomes."

Danone Nutricia used the studies above to support claims and statements for several of their infant formula products, including this claim for their Aptamil 1 First Infant Milk:

'…enriched with LCPs, including DHA (Omega 3), at levels that are scientifically recognised by the European Food Safety Authority (EFSA) to support normal visual development and have a ratio of AA:DHA that meets consensus recommendations..

The references given to support this statement were Koletzko et al (2008), and the EFSA opinion paper (EFSA, 2009).

At the time of the claim, Aptamil 1 First Milk contained 0.01g DHA/100ml (0.32% fatty acids), which was within the range that all milks now have to contain by law for current regulations. The new formulation of the product contains an increased amount, 0.017g DHA/100ml (0.52% fatty acids), as required by new regulations for infant formula composition.

Danone Nutricia also made the following statement regarding their Aptamil Profutura First Infant Milk:

"Contains our highest level of LCPs (long chain polyunsaturated fatty acids)."

The manufacturers claimed that Aptamil Profutura 1 First Infant Milk had increased levels of LCPs. At the time, Aptamil 1 First Milk contained 0.01g DHA/100ml, and Aptamil Profutura 1 First Infant Milk contained 0.011g/100ml (1/1000th g more per 100ml). This was a minimal change that was likely to be insignificant once compositional differences and compositional degradations within infant milk products are considered.

The manufacturers claimed on the website that Aptamil Profutura 1 First Infant Milk:

'Contains our highest levels of DHA to support normal visual development.'

They also supported this claim with the paper by Koletzko et al (2008) and the EFSA paper from 2009, plus the Willatts et al (1998) study.

The claims did not make it clear that an increased amount of LCPs would not be of any greater benefit than the amount already used.

Also on their website, Danone Nutricia made the following statement:

'Cow & Gate Infant Milk contains LCPs.'

The three papers we believe were used to support the addition of LCPs were Willatts et al (1998), Birch et al (1998), and Birch et al (2000).

Birch et al (1998) reported that the supplementation of term infant formula with DHA or with DHA and AA during the first 4 months of life yielded better visual acuity at 6, 17 and 57 weeks of age but not at 26 weeks when acuity development reaches a plateau.

Birch et al (2000) reported a statistically significant developmental age advantage for DHA and DHA+AA supplemented groups in the cognitive and motor subscales of the Bayley Scales of Infant Development compared to the unsupplemented group, but no such increase was observed for the language, psychomotor development index or behaviour rating scale. On the basis of their results, the authors suggested that early dietary supply of DHA was a dietary determinant of improved performance on the mental development index.

None of these conclusions are supported by EFSA (2014).Hipp Organic Combiotic First Infant Milk made the following statement:

'Added LCPs omega 3 & 6 – Docosahexaenoic acid (DHA) and Arachidonic acid (AA), important for the development of the brain, nervous system and eyesigh.'

They supported this statement using the Koletzko et al (2008) paper detailed above.

Nestlé used the same reference to support the following claim on their website for SMA Organic First Infant Milk:

"SMA Organic First Infant Milk contains Omega 3 and 6 LCPs for brain and eye development."

They also made the following claim for SMA Pro First Infant Milk:

"Although LCPs can be made in the body, infants have a high demand for these nutrients. SMA PRO First Infant Milk contains Omega 3 and 6 LCPs."

It is a regulatory requirement that infant formula provides a specific fatty acid profile, and it is not clear how the claim being made here about fatty acids in the milk relates to mandatory versus optional ingredients.

4. Claims made that ingredients/infant formula can support improved digestion and gut health

4.1 The addition of GOS/FOS (prebiotics)

EFSA has repeatedly denied permission for a health claim based on the use of prebiotics in infant formula and follow on formula.

EFSA (2014) states that:

" … there is no evidence for health benefits from the addition of prebiotic oligosaccharides (GOS/FOS) to infant or follow-on formula."

Current and previous regulations for infant formula permit the addition of Fructo-oligosaccharides (FOS) and galacto-oligosaccharides (GOS) but these are not mandatory ingredients.

Several manufacturers made claims that the use of GOS/FOS can support improved digestion and gut health.

Danone Nutricia made the following claim for Aptamil Profutura First Infant Milk:

'Contains our patented blend of GOS/FOS (9:1) bringing the intestinal microflora closer to that of a breastfed infant.'

The manufacturers provided a reference from Moro et al (2002), a study undertaken at the Numico (Danone) Research Centre, to support this statement. In this study, 90 healthy term infants were randomly allocated to receive formula milk supplemented with oligosaccharides at a concentration of 0.4g/100ml, or 0.8g/100ml, or placebo, over a period of 28 days. The formulas used in this study had a different composition to Aptamil Profutura 1 First Infant Milk as they were higher in protein, lower in fat, had a different range of added ingredients and lower osmolality. The infants receiving the formula milk supplemented with oligosaccharides in this study showed a dose-dependent increase in the amount of *Bifidobacteria* in stools, but this alone does not provide evidence of clinical impact.

Evidence from the same study (Moro et al, 2002) was used by Danone Nutricia to support this statement for Aptamil First Infant Milk:

'***Bottlefed babies given a formula containing GOS/FOS also have softer stools than those fed a formula without GOS/FOS.'***

Nestlé also referenced the Moro et al (2002) study to support the following claim for SMA Pro First Infant Milk:

'Contains GOS/FOS for increased gastrointestinal comfort and softer stools similar to that of a breastfed infant.'

The concentration of oligosaccharides which were used in the formula that resulted in greater stool softness in the Moro et al study (2002) was double that used in SMA Pro First Infant Milk at the time the claim was made.

They also provided a reference from another clinical trial to support the statement. This study by Vivatvakin et al (2010) reported that infants fed a whey-based infant formula supplemented with oligosaccharides and long-chain polyunsaturated fatty acids had fewer hard stools and more soft stools than infants fed a casein-based formula with no additional ingredients. Infants fed the whey-based formula also had a microbiota composition and gastric and intestinal transit times closer to those of breastfed infants. The authors concluded that, based on parental reports of regurgitation, vomiting, crying and colic, whey-based formula supplemented with oligosaccharides and LCPs provides superior

gastrointestinal comfort than casein-based formula that does not contain these added ingredients.

This trial was sponsored by Nestlé and does little to support the use of oligosaccharides in infant formula because the parental reported effects could not be attributed solely to the presence of GOS/FOS, as one of the trial formula milks was whey-based and the other casein-based. Current recommendations in the UK are that a first infant formula should be whey-dominant to bring it closer to the whey:casein ratio found in breastmilk.

SMA Pro powdered formula contained GOS/FOS but not the ready-to-feed formula, suggesting that the company itself may not be convinced of the benefit of adding prebiotics: if it was, GOS/FOS would be added to all its infant formula.

Kabrita Gold 1 First Infant Milk also made the following claim regarding the addition of GOS/FOS, but no evidence was given on the website to support it:

'Kabrita also contains prebiotic fibers: GOS / FOS. These fibers have a positive effect on the bacterial composition in the gut by stimulating growth of beneficial bacteria (Bifido- and lactobacilli).'

Hipp Organic Combiotic First Infant Milk made the following statement:

'Added prebiotic oligosaccharides (galacto-oligosaccharides – GOS), extracted from lactose.'

Ben at al (2008) was referenced to support the addition of GOS. This pilot study conducted in China in a relatively small sample of infants (with no intention to treat analysis attempted) looked at levels of *Bifidobacteria* and *Lactobacilli* and stool characteristics in infants fed either formula milk with or without GOS, those having human milk and formula with GOS, or those having human milk only. After three months, the intestinal *Bifidobacteria* and *Lactobacilli*, were somewhat higher in the group fed formula with GOS than in the group given un-supplemented formula. Acetic acid and fecal pH was decreased in infants fed with the GOS-formula or human milk. The formula used in this study was a different type of formula to the Hipp formula for which this evidence is used. This study was reviewed by EFSA (2014) which concluded that there was no significant evidence that the addition of prebiotics are beneficial to infant health.

4.2 Type of milk used

Goats' milk based infant formula manufacturers have made claims that goats' milk is easy to digest. However, in their evaluation of the suitability of goats' milk protein as the protein source in infant formula, EFSA clearly stated that, while they note the differences in the composition of the caseins between goat and cow milk, no difference in digestibility has been observed (EFSA, 2012).

Despite this, Kabrita Gold 1 Infant Milk made the claim that as a goats' milk infant formula it:

'Is naturally easy to digest (due to a unique fat and protein composition).'

And NannyCare First Infant Milk claimed that:

'Goat milk:

Is an excellent source of high quality, readily digestible proteins.

Forms looser, softer and more porous curds in the baby's stomach. (This is particularly helpful to the baby's delicate developing digestive system.)'

No evidence was provided on either website to support these claims.

Claims have also been made by manufacturers for infant milks based on partially hydrolysed protein. In the UK, 'comfort milks' containing partially hydrolysed whey protein have been marketed as being easier to digest than infant formula based on intact protein. There is very little evidence to substantiate this and most manufacturers rely on results from small clinical trials which examine the effect of protein composition on gastric emptying. It is unclear how gastric emptying relates to digestibility, which is itself a poorly defined term. Babies do not need hydrolysed proteins to help make infant formula easier to digest.

Nestlé made the following claim for SMA Advanced First Infant Formula:

'Easy-to-digest (100% whey, partially hydrolysed protein for faster gastric emptying and softer stools).'

Evidence from two different studies was given to support this claim. One small under powered study measuring gastric emptying in infants with and without reflux (Billeaud et al, 1990) and a pooled analysis of seven Nestlé sponsored studies investigating adequate growth, stool consistency and stool frequency in infants fed with standard infant formula or infant formula based on partially hydrolysed whey proteins (Czerkies et al, 2018). This study reported caregiver information on stool consistency as part of a study on growth and tolerance. Despite claiming in the abstract that infants given partially hydrolysed formula had more soft, and fewer hard stools, the authors state in the text that the sensitivity analysis showed that the prebiotic-containing partially hydrolysed formula did not affect stool consistency and that stool frequency was similar between groups at all time points.

Nestlé also made claims about digestion for SMA Organic First Infant Milk:

'..is whey-dominant making it easy to digest.'

And SMA Pro First Infant Milk also claimed to be:

'Easy to digest.'

Both these statements were supported by reference to the then NHS Choices website which states that whey-based formula milks are suitable for new born babies as they are thought to be easier to digest than casein-based infant formula (NHS Choices now replaced by NHS webite but statement still made at https://www.nhs.uk/conditions/pregnancy-and-baby/types-of-infant-formula/). Being whey based is not unique to SMA Pro or SMA Organic first milks as infant formula based on cows' milk available in the UK typically have at least 50% whey protein.

Kendamil First Infant Milk made the following statement regarding the addition of 'full-cream milk' to support infants' digestion:

'Better suited for sensitive babies digestive systems than skimmed milk products.'

This claim was not substantiated by reference to scientific evidence. The company website stated that the product is made using whole milk. Whilst whole milk was used in the product manufacture, after drying, it only accounted for about 16% of the dry weight of the powder, the majority being composed of whey powder, vegetable oils and lactose.

4.2 The addition of specific fat blends

Claims have also been made regarding the addition of structured vegetable oils to support improved digestibility. The EFSA Scientific opinion on the essential composition of infant and follow-on formulae (EFSA, 2014) concluded that:

"There is no convincing evidence for beneficial effects of the use of structured triglycerides with palmitic acid predominantly in the sn-2 position in infant and/or follow-on formula."

Despite this, Kabrita Gold First Infant Milk made the following claim:

Kabrita contains our special DigestX OPO-fat blend (also known as beta-palmitate). Breast milk is known to contain a high amount of beta-palmitate and contributes to the typical breast-fed stools and calcium absorption.

No evidence was given on the website to support this claim.

5. Claims made that ingredients/infant formula can reduce the risk of allergies

5.1 The addition of GOS/FOS (prebiotics)

EFSA (2014) states that:

" … there is no evidence for health benefits from the addition of prebiotic oligosaccharides (GOS/FOS) to infant or follow-on formula."

Danone Nutricia have made claims that the use of GOS/FOS in Aptamil 1 First Infant Milk can reduce the risk of allergies:

'... with our blend of prebiotic galacto- and fructo-oligosaccharides, shown to reduce the risk of allergies up to 5 years.'

The reference given to support this claim, Arslanoglu et al (2012), was a follow-up study from a previous Arslanoglu et al, 2007 study. The authors followed up some of the original cohort to 5 years, but only 42 children remained in the intervention group from the 102 original completers. The original study was reviewed and discounted as evidence by EFSA reviews of efficacy of benefit from oligosaccharide addition to infant formula.

Danone Nutricia also used the Arslanoglu et al 2012 paper to support claims made for the use of their blend of GOS/FOS on the allergy pages of the website:

'...our unique GOS/FOS blend is clinically proven to reduce the risk of developing allergic manifestations and severity of symptoms for up to five years.'

This statement is also referenced by an additional study by Arslanoglu et al published in 2008, plus a paper by Pampura et al (2014). Again, the two Arslanoglu et al studies are from a series of studies which follow the same cohort of children at risk of atopy from the first 6 months of life to 5 years. The original study by Arslanoglu et al (2007) reported on the impact of supplementation of hypoallergenic, hydrolysed whey-based formula milk with either 0.8g/100ml GOS/FOS or 0.8g/100ml maltodextrin as placebo on atopic dermatitis and allergy symptoms in the first 6 months of life. The two Arslanoglu et al (2008) and Arslanoglu et al (2012) studies cited extended the previous (flawed) study published in 2007 to 2 years and 5 years respectively. At 5 years only 42 children remained in the intervention group from the 102 original completers.

The original study (Arslanoglu et al, 2007) was reviewed and discounted as evidence by earlier reviews of efficacy of benefit from oligosaccharide addition to infant formula and was also reviewed by EFSA (2014).

The study by Pampura et al (2014) was a small Russian multicentre study of 51 infants of about 6 months of age with symptoms of atopic dermatitis. The infants were fed hydrolysed Nutrilon containing Nutricias' patented blend of GOS/FOS. The study reports a reduction in symptoms of atopic dermatitis after 4 weeks of feeding with the test formula. As the test formula was based on hydrolysed whey protein, it is not possible to establish links between the inclusion of GOS/FOS and changes in atopic dermatitis.

5.2 Organic ingredients

Hipp Organic Combiotic First Infant Milk made the following claim on their website:

'..babies consuming organic dairy products are less likely to suffer from atopic eczema.'

The authors of the report speculated that a protective effect may be due to a high intake of n-3 fatty acids and/or conjugated linoleic acid from organic dairy products (Kummeling et al, 2008). It is important to point out that this research does not support the use of organic infant milk as protective against eczema as no information other than whether or not the infant received breastmilk was collected for the first year of life, during which time maternal diet was used as a proxy for infant diet. The authors concluded that it was uncertain whether their finding represented a true association and that it should be interpreted with caution (Kummeling et al, 2008).

6. Claims made that ingredients/infant formula can support the immune system

6.1 The addition of GOS/FOS (prebiotics)

EFSA (2014) states that:

" … there is no evidence for health benefits from the addition of prebiotic oligosaccharides (GOS/FOS) to infant or follow-on formula."

Danone Nutricia made the following claim for Aptamil 1 First Infant Milk:

'...contains GOS/FOS, non-digestible carbohydrates that occur naturally in breastmilk. They decrease the presence of pathogens in the gut flora increasing the growth of friendly bacteria such as bifidobacteria and lactobacilli. These friendly bacteria are an integral part of a baby's natural immune system.'

The references given to support this statement were from clinical trials conducted by Knol et al, 2005, Moro et al, 2002 and Costalos et al, 2008. Knol et al (2005) looked at whether or not standard infant formula supplemented with GOS/FOS was able to establish a bifido-dominant microflora, not only in numbers, but also with respect to the metabolic activity in the colon. The authors concluded that the addition of the prebiotic GOS/FOS mixture to an infant formula had a stimulating effect on the growth of *Bifidobacteria* and on the metabolic activity of the total intestinal flora. This study was included in the review commissioned by EFSA (2014) but was not accepted as evidence of benefit from the addition of GOS/FOS to infant formula.

The study by Costalos et al, 2008, used a test formula with a concentration of oligosaccharides different to the currently marketed product and reported a lower percentage of faecal *Clostridia* and a higher percentage of faecal *Bifidobacteria* in the group receiving the test formula with added oligosaccharides. This study was also included in the review by EFSA (2014) but was not accepted as evidence of benefit from the addition of GOS/FOS to infant formula.

The study by Moro et al (2002), was undertaken at the Numico (now Danone Nutricia) Research Centre and included 90 healthy term infants who were allocated to receive formula milk supplemented with oligosaccharides at a concentration of 0.4g/100ml or 0.8g/100ml or placebo, over a period of 28 days. The infant formula used in this study was different to Aptamil 1 First Milk as it had higher protein and fat contents and a different range of added ingredients. The infants receiving the infant formula supplemented with oligosaccharides showed a dose-dependent increase in the amount of *Bifidobacteria* in stools. However, this does not mean that there is any clinical benefit to the addition of oligosaccharides.

The study (Moro et al, 2002) was also used to support the claims made on the feeding problems and allergy pages of Danone Nutricia's website, where great emphasis was placed on prebiotics. The following claims were made on the page for constipation:

'Q6 How can healthcare professionals advise parents who switch between formula milks?

...Choosing one which contains prebiotic oligosaccharides has been shown to increase the growth of friendly bacteria (including bifidobacteria and lactobacilli) - an integral part of an infant's immune system.....'

No direct evidence was provided directly linking growth of 'friendly' bacteria with improved immune function.

Danone Nutricia also made the following claim regarding Aptamil 1 First Infant Milk:

'Babies fed a formula containing GOS/FOS have been shown to have a lower incidence of recurrent upper respiratory tract infections, diarrhoea, infections requiring antibiotics and atopic dermatitis than those fed a formula without GOS/FOS.'

The references given to support these claims were studies sponsored by the manufacturer (Numico, now Danone Nutricia). Arslanoglu et al (2007) and Moro et al (2006) considered the impact of oligosaccharides in infant formula on infections and atopic dermatitis in the first 6 months of life within the same cohort of infants at risk of atopy. Both studies reported reduced incidence of their outcome measures within the test groups compared to the control groups. The infant formula used in both the test and control groups contained extensively hydrolysed proteins supplemented with oligosaccharides, but Aptamil 1 First Milk did not contain hydrolysed proteins.

Another reference given to support the claims above was a study by Bruzzese et al (2009), also sponsored by Numico (now Danone Nutrcia), which looked at the impact of infant formula milk supplemented with GOS/FOS at 0.4mg/100ml on the incidence of intestinal and respiratory infections in a cohort of healthy term infants. This study reported a lower incidence of gastroenteritis and fewer children receiving multiple courses of antibiotics within a year for the group receiving supplemented formula. The study was reviewed by EFSA (2014) as part of the evidence that led to their conclusion that there was insufficient evidence to support claims made about prebiotics in infant formula.

6.2 The addition of prebiotics and postbiotics

Danone Nutricia made the following statement regarding Aptamil 1 First Infant Milk:

'Now, Aptamil powder formulations undergo Nutricia's unique process, producing postbiotics.'

Danone marketed the change as being related mainly to the introduction of a new processing method rather than to a reformulation of the product itself. There was little information about the new process on the website, however it involved the fermentation of milk with the lactic acid producing bacterial *strains Bifidobacterium breve* and *Streptococcus thermophiles.* Approximately a quarter of the milk powder used in the new versions of the milks were derived from milk fermented in this way. A number of claims were made by Danone about the use of postbiotics in combination with their prebiotic GOS:FOS mix in the Aptamil products:

'This combination of prebiotics and postbiotics have been shown to support a healthy gut in infants, important for immune system development and functioning.'

Danone supported these claims by reference to two clinical trials and a review article. The review article by Wopereis et al, (2014), from the Nutricia research centre was used to

support the use of prebiotics combined with postbiotics, however this article did not refer to postbiotics or to the combination of prebiotics and postbiotics in infant formula.

A referenced clinical trial by Rodriguez-Herrera et al (2018), examined the faecal microbiota of infants consuming a test formula with prebiotics and fermented milk or a control formula without prebiotics or fermented milk. This trial reported that in contrast to the infants consuming the control product the infants consuming the test formula showed a saccharolytic fermentation profile (lower pH, higher level of acetic acid, higher level of sIgA). The authors reported that the levels of some bacterial groups changed consistently between the test and control formula and levels in the test arm appeared to be more in line with levels detected in the breastfed reference group.

A further clinical trial by Tims et al, (2018), investigated the effect of partly fermented formula using three different ratios of fermented formula on base powder,15%, 30% and 50% along with prebiotics (GOS/FOS 9:1) on the composition of the infant gut microbiota. These test formulae were compared to three control products, formula with prebiotic only, formula with fermented addition only and a formula without either. A breastfed reference group was included. The authors reported that the faeces of infants consuming one of the experimental products showed similar saccharolytic fermentation profile to infants consuming the control formula with prebiotics and the breastfed infants (lower pH, higher level of acetic acid, higher level of sIgA) compared to those consuming formula without prebiotic. There was no dose response effect noted for the fermented formulae and no clinical benefits were reported (Tims, et al, 2018).

These trials were reported as either abstract or oral presentation at the ESPGHAN conference in May 2018 and not as peer reviewed papers from scientific journals. Neither of the trials reported any benefit for GOS:FOS combined with a proportion of fermented milk compared to formula with GOS:FOS 9:1 only. It is therefore difficult to establish any scientific rationale for the addition of fermented milk to a formula milk containing GOS/FOS. No data was given to support the claims made and it was not clear if the products used in the trials were the same as the marketed product.

6.3 The addition of nucleotides

EFSA (2014) stated that:

"there is no necessity to add nucleotides to infant or follow-on formula."

Danone Nutricia made the following claim regarding the addition of nucleotides to Aptamil 1 First Infant Milk:

'… contains nucleotides, which form the building blocks of every cell in the body, including those of the immune system.'

Whilst no direct claims were made for the addition of nucleotides, Aptamil supported their addition by reference to Pickering et al (1998) and Yau et al (2003). Both of these clinical trials looked at the immune response of infants fed formula milk supplemented with nucleotides at 7.2mg/100ml. The trials had conflicting results. Yau et al (2003) reported that, at 8-28 weeks, infants fed the supplemented formula were shown to have a 25.4% lower risk

of diarrhoea and higher concentrations of serum IgA throughout the study than infants fed the control formula. Both groups had a similar antibody response to hepatitis B immunisation and similar incidence of lower respiratory tract infections, whilst the risk of upper respiratory tract infections was 1.13 times higher in the group fed supplemented formula. Pickering et al (1998) reported that, compared to the control group, at 7 months of age the supplemented group had significantly higher H influenzae type b and diphtheria humoral antibody responses. The antibody responses to tetanus and polio virus were not enhanced by nucleotide fortification.

These studies were reviewed by EFSA (2014) and not accepted as evidence that nucleotides are beneficial.

6.4 The addition of human milk oligosaccharides (HMO)

Nestlé suggested there was evidence for significant health benefits for the addition of the artificially created 'Human Milk Oligosaccharide' (HMO) analogues 2'-fucosyllactose (2'FL) and Lacto-N-neotetraose (LNnT).

In the SMA Nutrition clinical evidence summary the following statements were made about the benefits of artificial HMO added to infant formula:

'Infants who received the test formula (with HMOs) compared to control formula had:

70% lower risk of parent-reported bronchitis through 12 months of age

55% lower risk of parent-reported lower respiratory tract infections through 12 months of age

56% lower use of antipyretics through 4 months of age

53% lower use of antibiotics through 12 months of age

Significantly softer stools at 2 months

Fewer night-time awakenings at 2 months; in a sub-group of infants delivered by caesarean section, colic at 4 months was reported less frequently.'

These claims were based on a single trial conducted by Puccio et al (2017), which enrolled fformula fed infants at 14 days or younger, randomised to either a test or control infant formula for 6 months. The study was sponsored by Nestlé and five of the study authors were employed in Nestlé funded centres. Nestlé also funded editorial assistance for paper preparation.

The test and control formula used in the trial were identical apart from the addition of the two artificial oligosaccharides (1.0g of 2'FL and 0.5g LNnT per litre, replacing lactose).The test formula had 67kcal/100ml, contained long-chain polyunsaturated fatty acids, 1.8g

protein/100kcal (equivalent to 1.2g/100ml) and a whey casein ratio of 70:30. The Nestlé Advanced range of milks for which claims based on this paper were being associated were 100% whey based and not the same as this test formula. Families were given the test and control formula for 6 months and then both groups were given the same unsupplemented follow on formula from 6 months, with complementary foods allowed from 4 months.

The study was conducted between 2012-2015 in Italy and Belgium. There was no breastfed reference group recruited for this study. The study was not powered to have a number of reported variables as primary outcomes. Some outcomes were only reported for small sub-groups or at specific time points. There was no reference group of breastfed babies to compare optimal outcomes with these outcomes in fully formula fed babies.

GI symptoms (flatulence, spitting up and vomiting) showed no significant difference between the two groups. Stool softness showed no significant difference between the two groups at any visit, except a small (but apparently significant) difference reported at two months. The authors reported that a sub-group of infants delivered by caesarean section (about a 1/3 of the sample) were reported to have colic (based on parental report) less frequently at four months and reporting of child waking was suggested by the authors to show a small but significant difference between test and control formula groups in the first two months only.

Within the 'infections and infestations' category the authors claimed statistically significant differences in the parentally reported outcomes of bronchitis, lower respiratory tract infection, and in recorded antibiotic and antipyretic use, but some of these differences were at certain time points only. No significantly different outcomes were reported for other infections. The trial findings do not prove health benefits from the addition of the two artificial HMOs to the test formula, and the authors (Puccio et al, 2017) accept that all these findings need to be properly considered in further studies.

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