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The **gold standard** ingredient
for infant formula

Arla Foods Ingredients

Discovering the wonders of whey 

The vital protein for a healthy infant formula

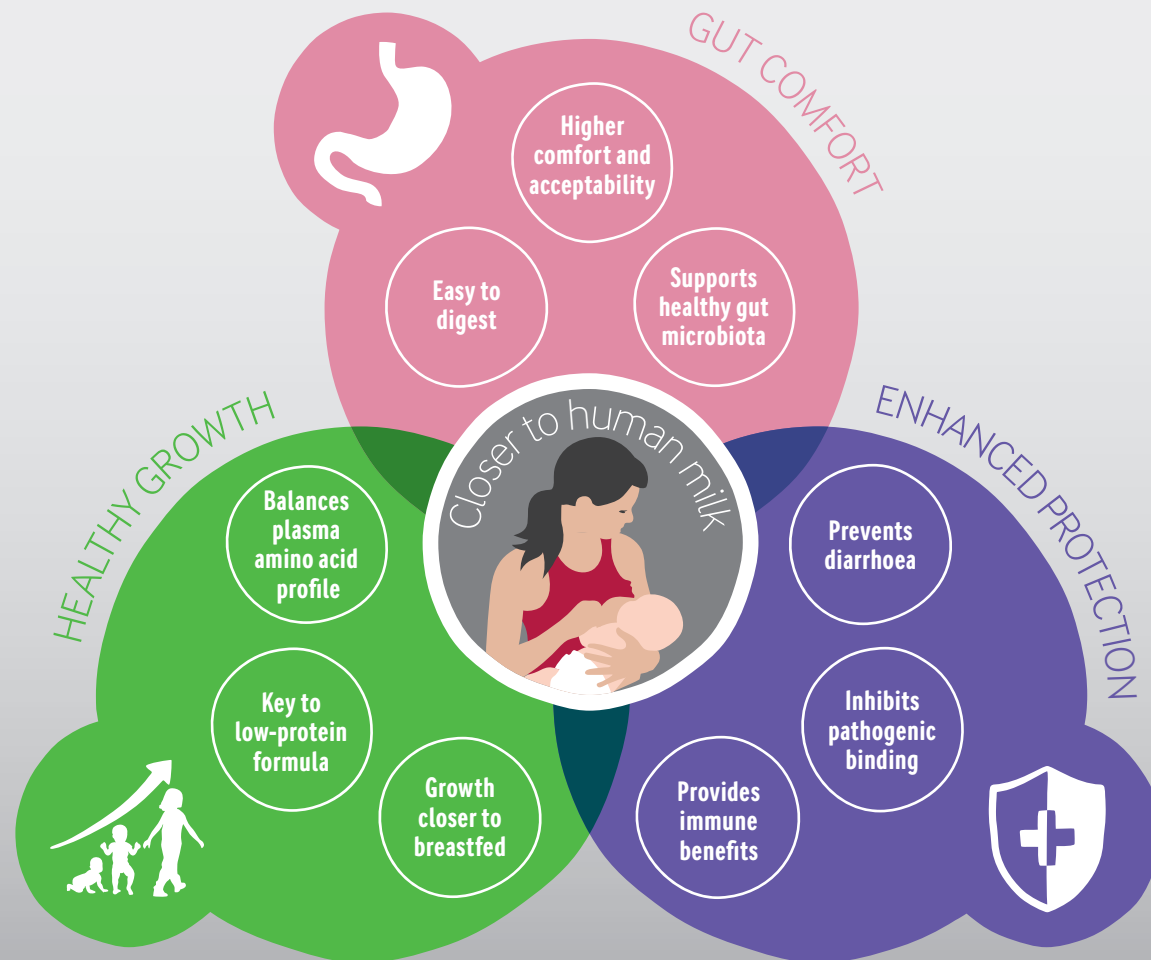
Human milk is designed to provide the building blocks for the growth and development of infants' immature organs and systems. When breastfeeding is not possible, providing the closest substitute to human milk is essential to ensure a healthy development and start in life.

ALPHA-lactalbumin (α) is the most abundant protein in human milk^{1,2}. The high concentration and functionalities of this protein makes it a key ingredient for mimicking the composition and benefits of human milk. Infant formulas (IF) enriched with ALPHA-lactalbumin are **closer to human milk** and promote a **healthy gut, enhanced protection** and **healthy growth** in early life nutrition.

Arla Foods Ingredients is proud to be the world's largest manufacturer of ALPHA-lactalbumin and we continuously invest in documenting the benefits of this gold standard protein in infant nutrition.



ALPHA-lactalbumin health benefits for infant nutrition



Closer to human milk

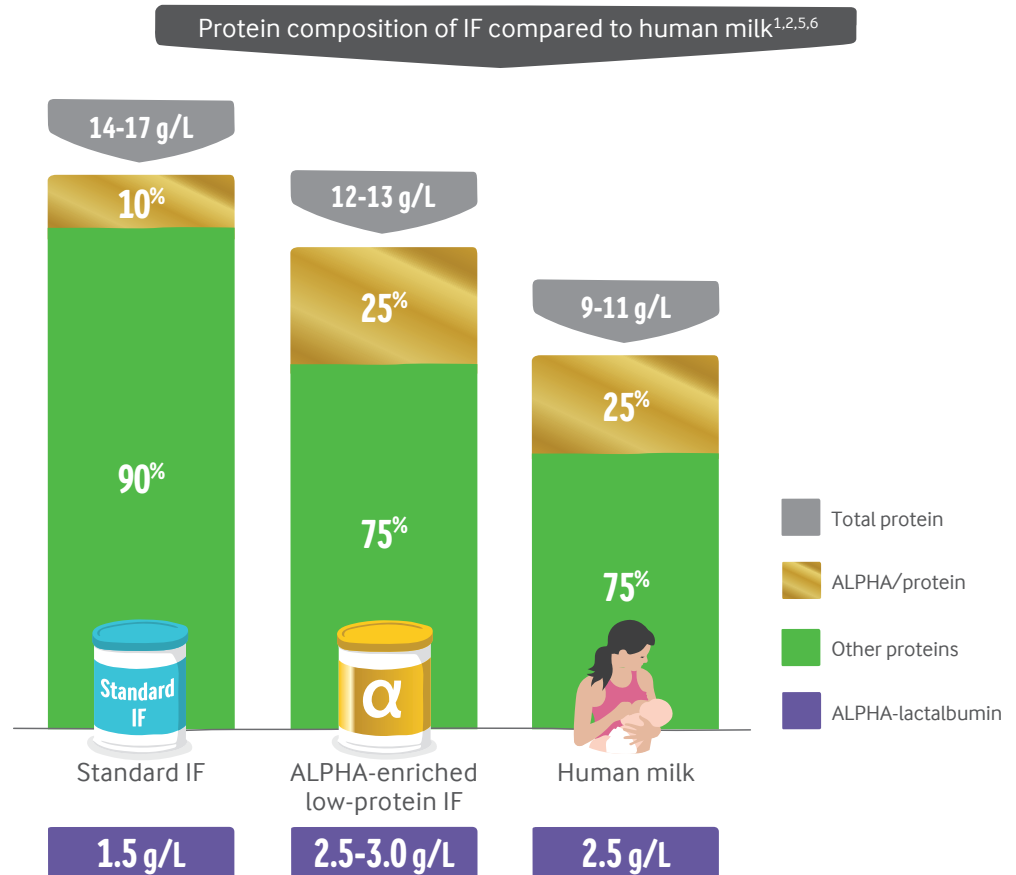


The high level of ALPHA-lactalbumin in human milk is likely to be of great nutritional importance for the infant³, yet standard IF has significantly lower ALPHA-lactalbumin levels compared to human milk.

Early human milk has high levels of ALPHA-lactalbumin (> 3 g/L) and remains high at 2.3-2.8 g/L during the 2 to 8 months of lactation^{3,4}.

The amino acid sequence of human and bovine ALPHA-lactalbumin is very similar¹, which makes bovine ALPHA-lactalbumin an excellent substitute for the human source. ALPHA-lactalbumin-enriched IF enables optimisations that closely match the protein composition and content of human milk.

- Protein composition of human milk can be mimicked by increasing the amount of ALPHA-lactalbumin in the IF.
- Due to the high proportion of essential amino acids (63%) in ALPHA-lactalbumin¹, it is possible to lower the total protein content of IF when ALPHA-lactalbumin is added to the formulation.



Easy to digest with higher comfort and acceptability

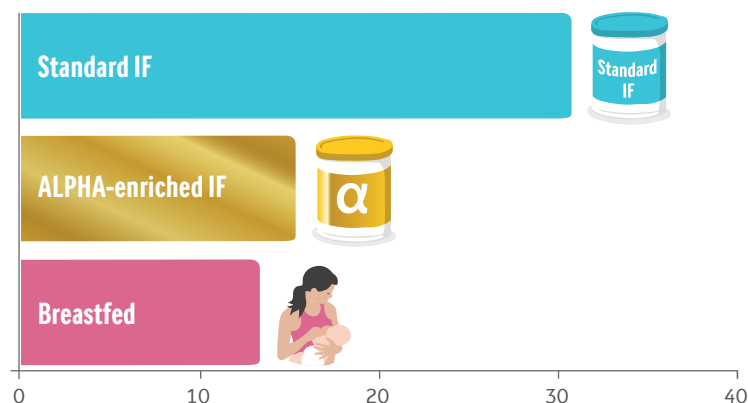


Formula-fed infants often experience gastrointestinal (GI) discomfort such as colic and constipation leading to general discomfort, poor sleep and long crying intervals. Gut comfort is generally regarded of high importance for the infant's well-being and sleep.

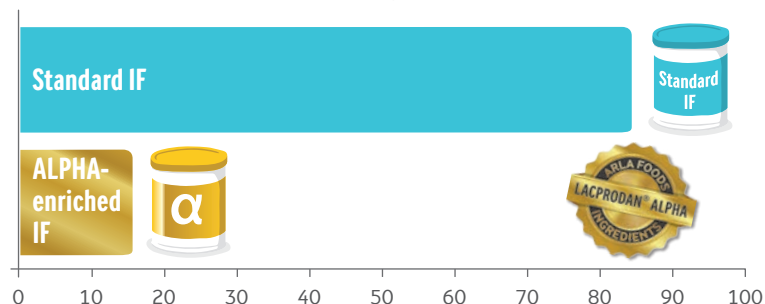
ALPHA-lactalbumin is an easily digestible protein⁷, which provides IF-fed a similar GI tolerance to breastfed⁸. IF supplemented with ALPHA-lactalbumin reduces feeding-related GI incidents, such as abdominal pain, constipation, vomiting and regurgitation⁸, and increases general formula acceptability and tolerance².

IF enriched with ALPHA-lactalbumin and pre- and probiotics have also been shown to temporally reduce crying and agitation, and result in quieter behaviour compared to infants fed with standard IF⁹. IF with ALPHA-lactalbumin and probiotics correspondingly decreases feeding-related GI incidents in infants with colic¹⁰. Ingestion of IF enriched with ALPHA-lactalbumin and LC-PUFA also reduces the rate of adverse events, where 10% were related to GI incidents. Hence, the impact of the IF was more similar to the outcome with human milk compared to a standard IF¹¹.

% Feeding-related GI incidents in infants⁸



% Feeding-related GI incidents in infants with colic¹⁰



Supports a healthy microbiota

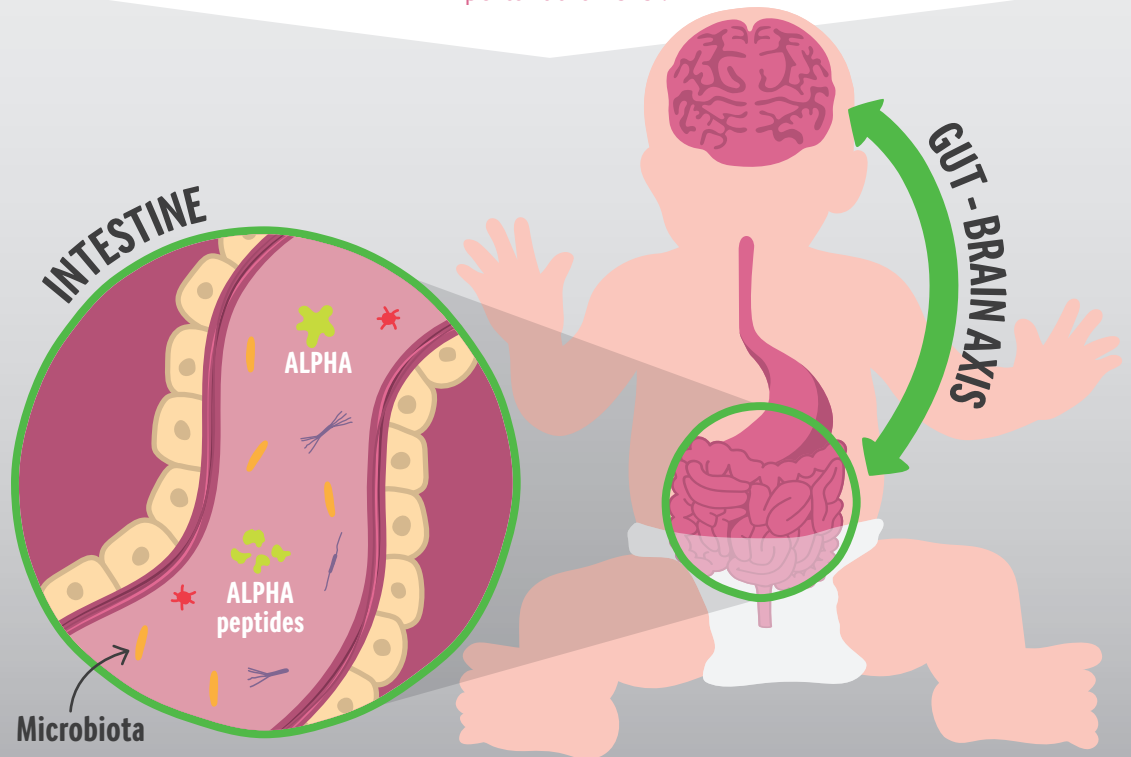


It is recognised that gut microbiota plays an important role in early development, yet breastfed and standard formula-fed infants have different composition of their microbiota¹². Bifidobacteria represents one of the most common group of species in the gut of breastfed infants up to age 3 to 6 months, and the colonisation of different bifidobacteria species is used as an indicator of the infant's gut health.

ALPHA-lactalbumin-enriched IF is found to increase faecal bifidobacteria concentrations similar to human milk, thus supporting a healthy development of the infant's gut microbiota¹³. The increase in bifidobacteria concentrations is found to be more pronounced in infants with lower starting concentrations^{13,14}.

Infant monkeys fed with ALPHA-lactalbumin-enriched IF are also shown to develop a microbiota more similar to that of a breastfed group compared to a standard IF group¹⁵.

Accumulating research suggests a functional connection between the gut and brain (the gut-brain axis) and describes a bidirectional communication from brain to gut-microbiota and vice versa, highlighting the importance of the gut microbiota in influencing these interactions¹⁶. As the gut microbiota is likely to have more widespread impact on our well-being than previously thought, the composition of the microbiota seems more important than ever.



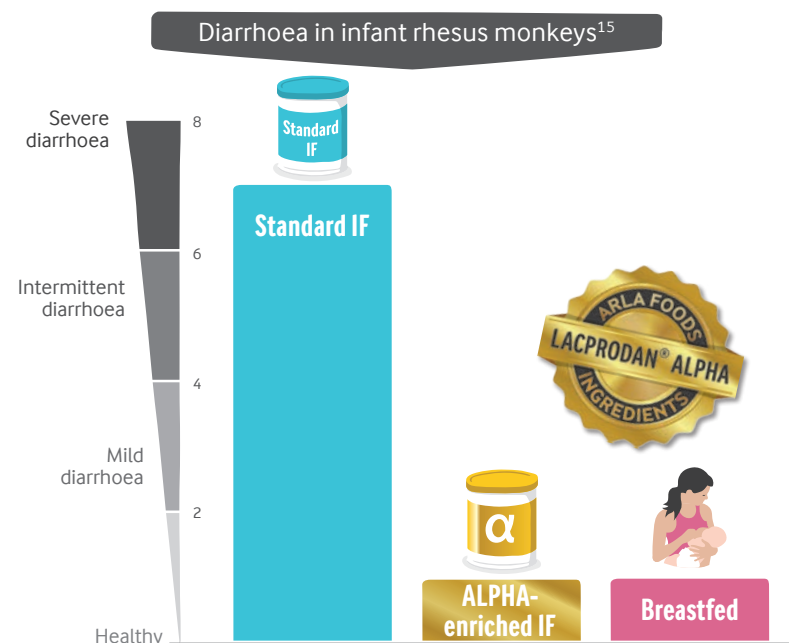
Prevents diarrhoea, binds pathogens and provides immune benefits



ALPHA-lactalbumin provides an enhanced protection against intestinal infections which may be linked to its pathogenic binding capability or bioactive peptides released during digestion. Intact and digested ALPHA-lactalbumin is shown to reduce attachment of the pathogens *E. coli*, *Salmonella* and *Shigella* to Caco-2 cells¹⁷. An inhibitory effect of ALPHA-lactalbumin comparable to human milk is also observed on *Bacteroides*, *Clostridia*, *E. coli*^{18,19} and *Salmonella*¹⁹ using faecal material of infants.

ALPHA-lactalbumin's enhanced gut protection may also be attributed to its bioactive peptides released during digestion. An example is the tripeptide [GLY-LEU-PHE (GLF)], which has been shown to have immunostimulatory effects in animal and *in vitro* studies^{20,21}. Furthermore, prebiotic and antibacterial peptides have been shown to be formed during *in vitro* digestion of ALPHA-lactalbumin²¹. Although these observations have been made *in vitro*, it is possible that these peptides exert their activities in the lower gut, which may explain the inhibitory effect of ALPHA-lactalbumin on *E. coli*-induced diarrhoea observed in infant rhesus monkeys^{15,21}.

Pathogenic bacteria such as *E. coli* and *Salmonella* are major diarrhoea-causing bacteria in infants. ALPHA-lactalbumin-enriched IF has been shown to exhibit an inhibitory effect on *E. coli*-induced diarrhoea in infant rhesus monkeys. This group also had a similar number of immune cells as the breastfed group which were higher than for the standard IF-fed monkeys¹⁵.



Growth closer to breastfed and balanced plasma amino acid profile

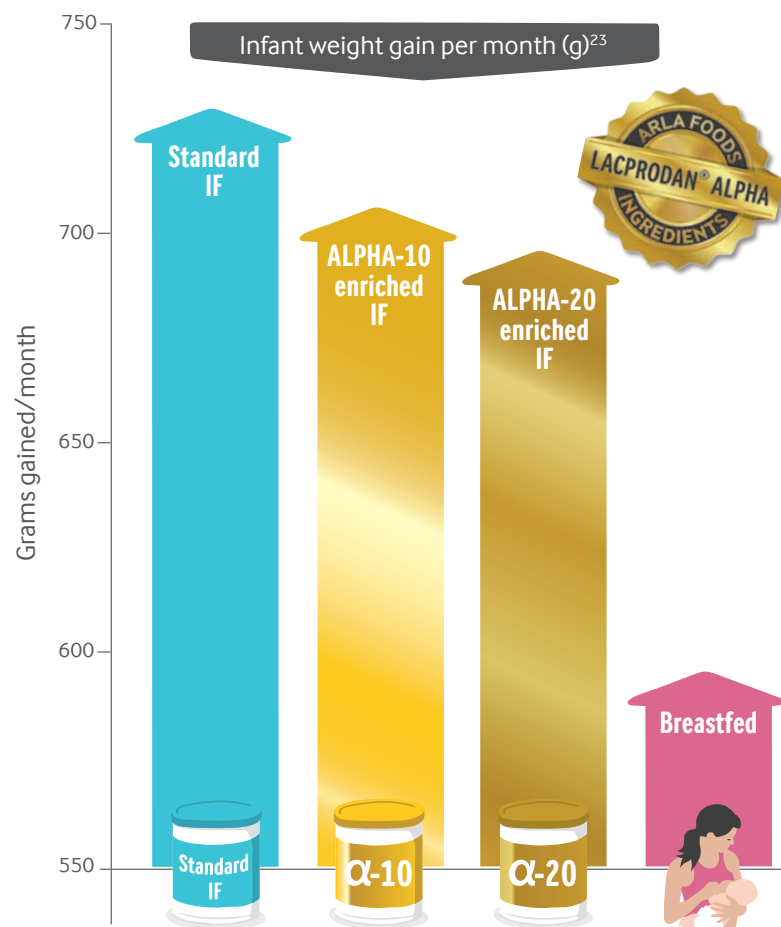


ALPHA-enriched IF, often with reduced protein level, is clinically documented to support age-appropriate growth^{2,8,11,22,23} with the observation that in some studies weight gain is closer to breastfed infants compared to standard formula-fed infants^{22,23}.

The favourable effect of ALPHA-lactalbumin supplementation may partly be attributed to a temporarily reduced level of branched-chain amino acids, which may influence weight gain^{22,23}.

IF enriched with ALPHA-lactalbumin and reduced protein level promotes a plasma amino acid profile closer to breastfed compared to infants receiving standard IF^{11,22}. The plasma amino acid profile of infant rhesus monkeys receiving IF with ALPHA-lactalbumin without protein reduction has also been shown to be closer to that of breastmilk²⁴.

ALPHA-lactalbumin is rich in tryptophan, a precursor of serotonin which is involved in the regulation of functions like sleep and appetite^{11,25}. IF enriched with ALPHA-lactalbumin is shown to increase the plasma level of tryptophan^{8,23}, which may support the healthy development of the infant.



Key to low-protein formula that reduces risk of later obesity



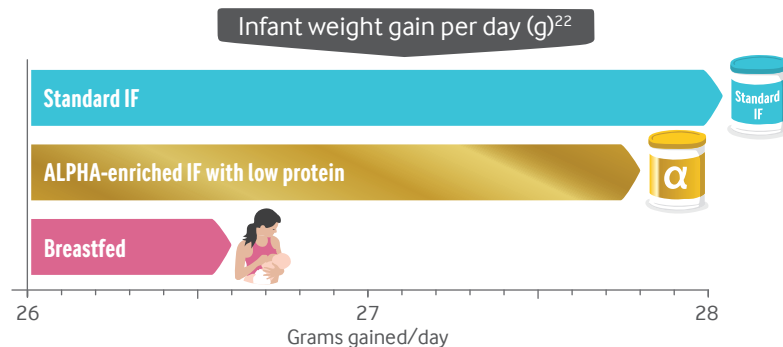
The primary limiting factor in low-protein formulations is the need to ensure its nutritional value with the required level of amino acids. Lowering the total protein content places higher demands on the quality of the protein ingredients in the formulation. ALPHA-lactalbumin is the major protein in human milk¹ and bovine ALPHA-lactalbumin has an exceptionally high content of essential amino acids¹, making it a key ingredient in low-protein formulations.

Studies have indicated that differences in macronutrient levels and quality, including different protein and amino acid constituents may affect the energy utilisation^{11,23,25}. Even though the total energy content of IF and human milk is similar, formula-fed infants consume more energy and have a higher protein intake compared to breastfed. This means that energetic efficiency (i.e. growth - weight gain or length gain per 100 kcal of energy intake) is higher for breastfed infants²⁵.

A recent clinical trial of low-protein IF and ALPHA-lactalbumin found that energetic efficiency was enhanced when protein dosage – and thus the protein-energy ratio – was lowered, while the protein composition was modified to have a higher proportion of ALPHA-lactalbumin¹¹. A beneficial effect could therefore be achieved by consuming smaller amount of high-quality ALPHA-lactalbumin-enriched low-protein IF, which supports adequate infant development and growth while avoiding the increased obesity risk caused by high protein intake. The prevailing hypothesis indicates that the growth of infants, expressed in terms of energy utilisation, may be impacted by the whey to casein ratio, level of tryptophan and ALPHA-lactalbumin^{11,25}.

Infants grow as a function of milk intake, and thus energy intake and utilisation. IFs are designed to have a total energy content of 60-70 kcal/100 ml, matching that of human milk. As such, the content of the three major energy sources – protein, lipid, and carbohydrate – may vary within defined limits²⁶⁻²⁸. The protein dosage in IF, expressed as protein per energy level (i.e. the protein:energy ratio), may vary from 1.8 g/100 kcal and up to 2.5-3 g/100 kcal. At higher protein dosage, intake of protein becomes higher per amount of formula consumed, with a potential impact on metabolism and growth.

According to the “early protein hypothesis”, high early protein intake causes rapid early weight gain, which has been associated with an increased risk of obesity and associated disorders in later life. This was shown in a European study (the CHOP study) comparing the impact of IF and follow-on formula with low or high protein contents in the first year²⁹⁻³². While more documentation is still needed to confirm the long-term effect, lowering the protein concentration in IF seems promising for reducing the risk of overweight and obesity in children^{33,34}.



Formulation strategies to bring infant formula closer to human milk

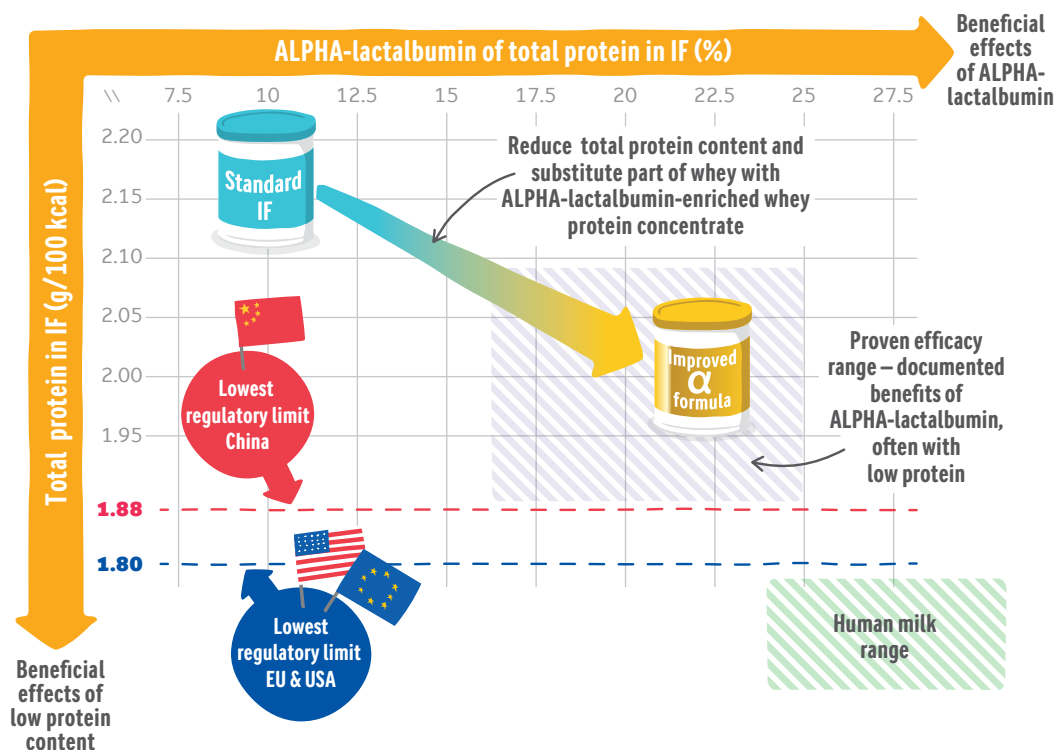


Many clinical trials have shown benefits from increasing the ALPHA-lactalbumin content in combination with lowering the overall protein dosage^{2,8,10,11,22,23}, resulting in an IF composition and biological efficacy that is truly closer to human milk.

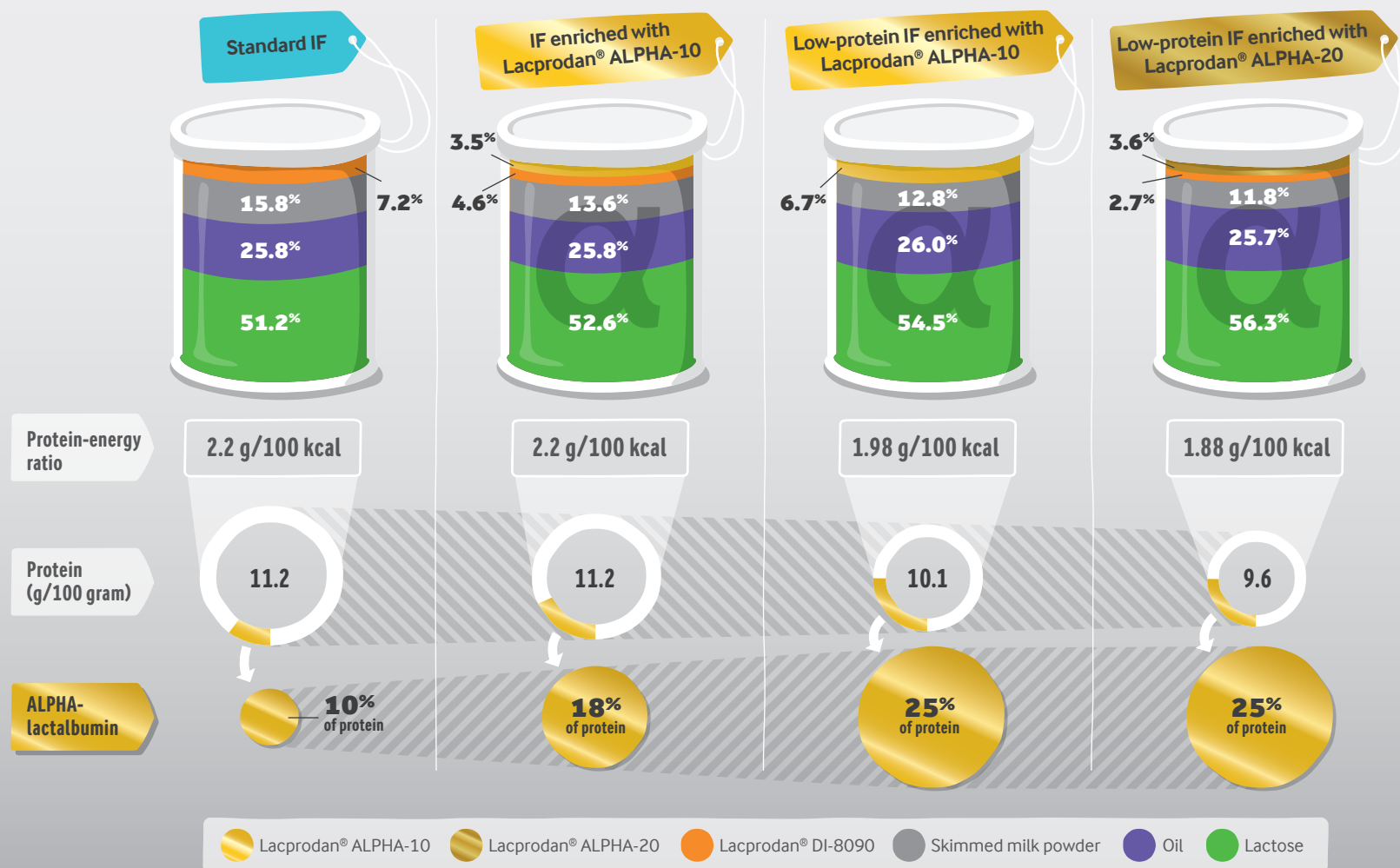
A standard stage 1 IF typically contains 2.1-2.3 g protein/100 kcal and approx. 10% of total protein as ALPHA-lactalbumin (~1.5 g ALPHA-lactalbumin/litre)⁶.

An improved ALPHA-lactalbumin-enriched formula typically has 1.8-2.05 g protein/100 kcal and 15-25% of total protein as ALPHA-lactalbumin (~2-3 g ALPHA-lactalbumin/litre). Mature human milk has around 1.6 g protein/100 kcal³⁵ and 25% of total protein as ALPHA-lactalbumin^{1,2}. The proven efficacy range from a number of published clinical trials^{2,8,10,11,22,23} showing benefits of low protein content and high ALPHA-lactalbumin dosage are highlighted in the plot.

Formulation strategies to improve protein content & composition of IF



Our suggestions for formulations with Lacprodan® ALPHA-lactalbumin



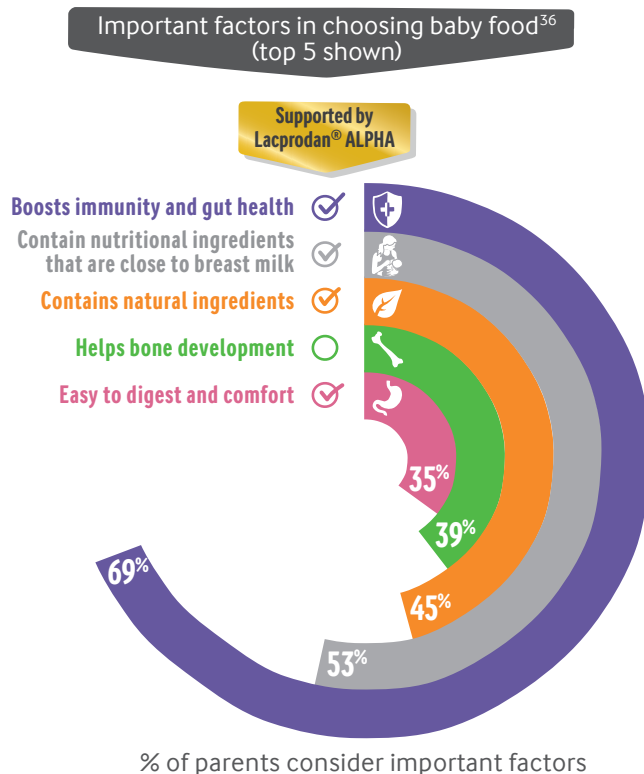
All formulas have similar energy content of 510 kcal/100 gram powder. The standard formulation has a whey:casein ratio of 60:40, whereas the three formulas enriched with ALPHA-lactalbumin have a whey:casein ratio of 65:35.

Address key consumer and market needs with ALPHA-lactalbumin



Tap into major consumer needs with documented benefits of ALPHA-lactalbumin:

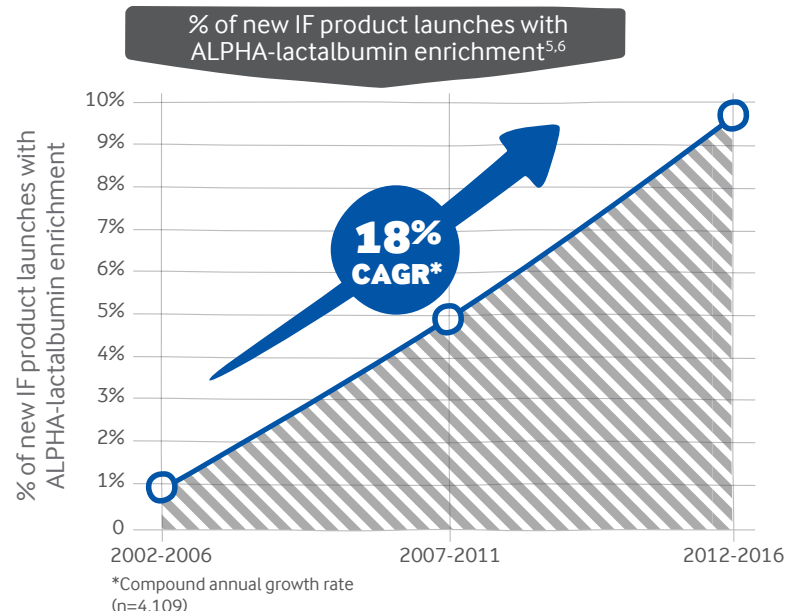
4 out of the top 5 most important functional benefits that parents consider important when choosing IF products.



Follow global trend of improving IF by adding ALPHA-lactalbumin:

The growth of the IF market with ALPHA-lactalbumin enrichment is driven by:

- Growing clinical evidence on the benefits of ALPHA-lactalbumin in infant nutrition.
- Development of the low-protein formula category.
- Focus on improving IF protein composition and quality.

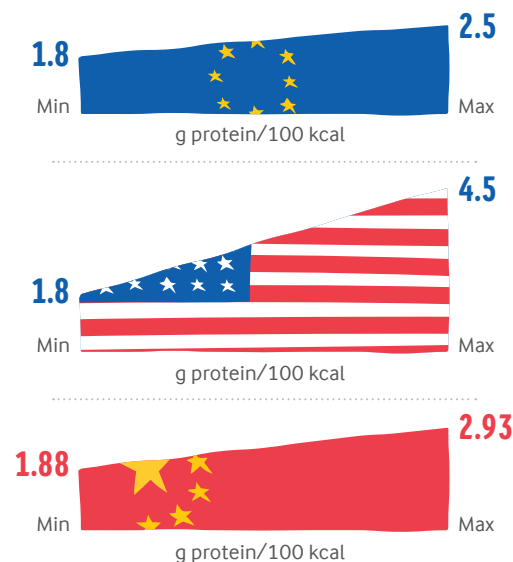


Meet the demand for protein-reduced infant formula with ALPHA-lactalbumin



In recent years, the protein content in IF has been reduced, going hand-in-hand with the enrichment of ALPHA-lactalbumin.

The regulation of protein content in stage 1 IF is centred on the amount of protein out of the total energy content²⁶⁻²⁸. In most countries, legislation on IF allows for protein content down to 1.8 g protein per 100 kcal.



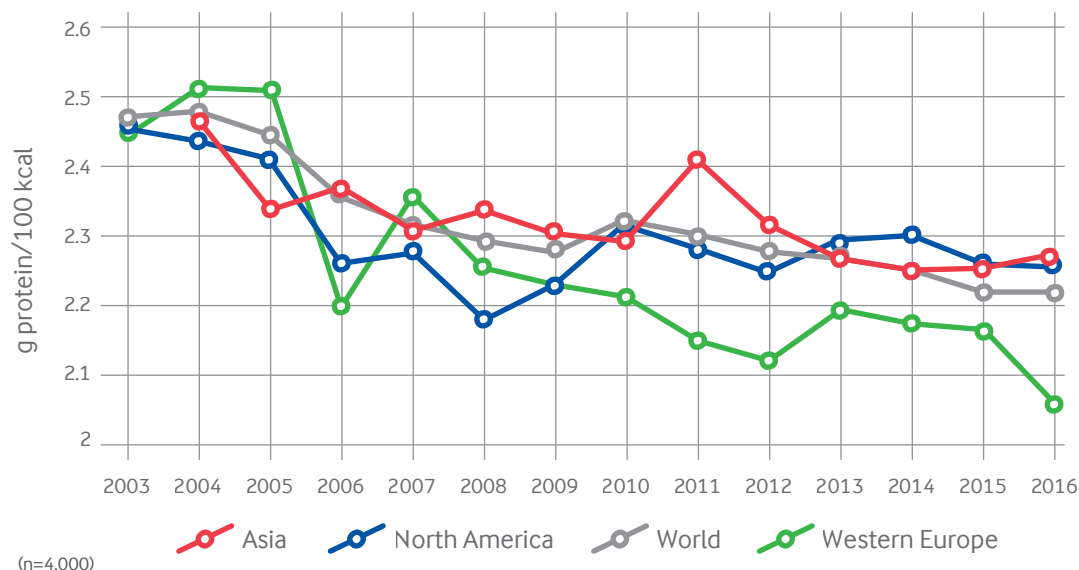
IF protein content has been reduced globally in the past 15 years, driven by clinical trials showing the benefits of low-protein formula, often enriched with ALPHA-lactalbumin.

However, today stage 1 formula protein content still remains on average relatively high in the USA and Asia, while Europe has made reductions.

Many IF are improved through enrichment with ALPHA-lactalbumin combined with reduced total protein content. It truly brings both formula composition and biological efficacy closer to that of human milk.

Global historical trends for protein content in IF^{5,6}

Development of average stage 1 IF protein content globally and in three key regions:

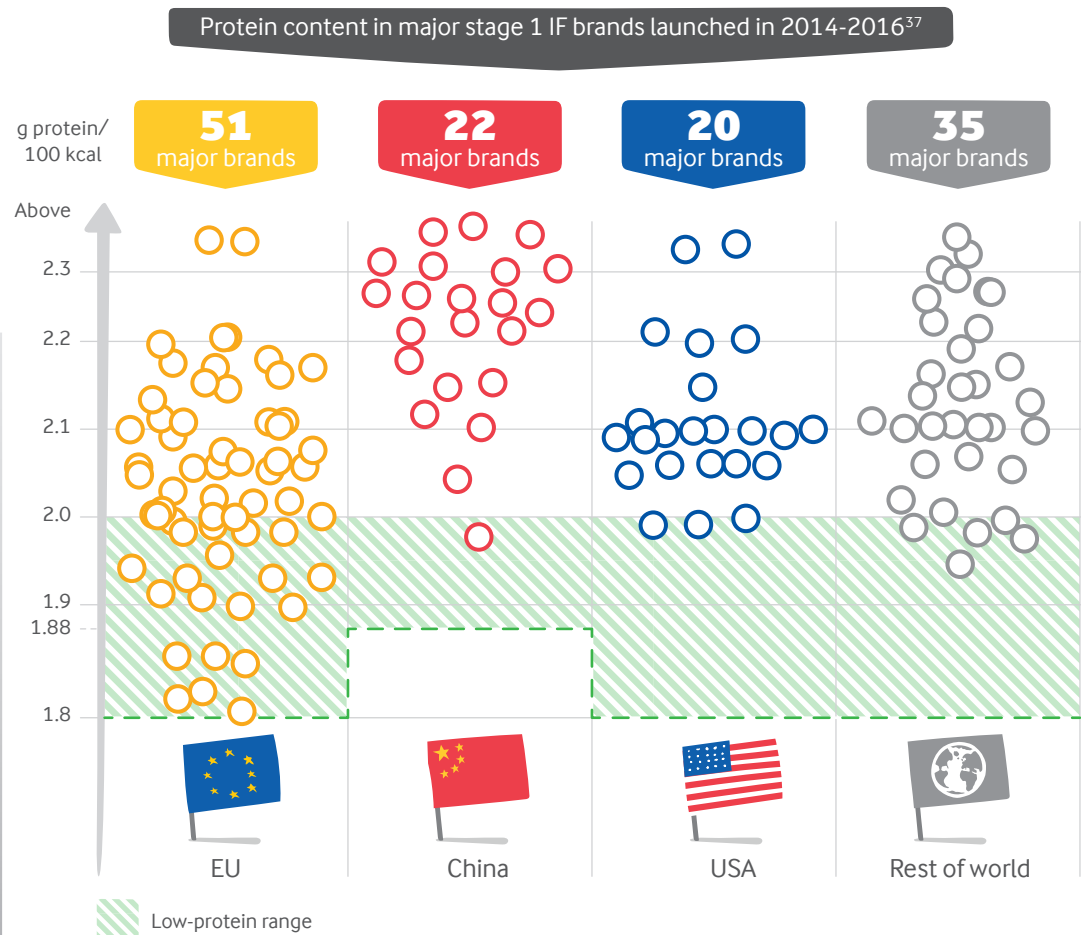


*New 2016 EU regulation endorses low-protein IF by removing the clinical trial requirement for IF with less than 2.0 g/100 kcal protein and by reducing the maximum limit for total protein content.

Global map of infant formula protein content



There are many opportunities for IF manufacturers in Europe, Asia, China, the Americas, and rest of the world to lower total protein content while improving formula protein composition and efficacy by increasing ALPHA-lactalbumin content. In many regions, it could even have a first-mover market effect to follow the European low-protein trend.



Our ALPHA-lactalbumin



Product range

We produce two clinically documented ALPHA-lactalbumin ingredients: Lacprodan® ALPHA-10 and ALPHA-20.

Quality

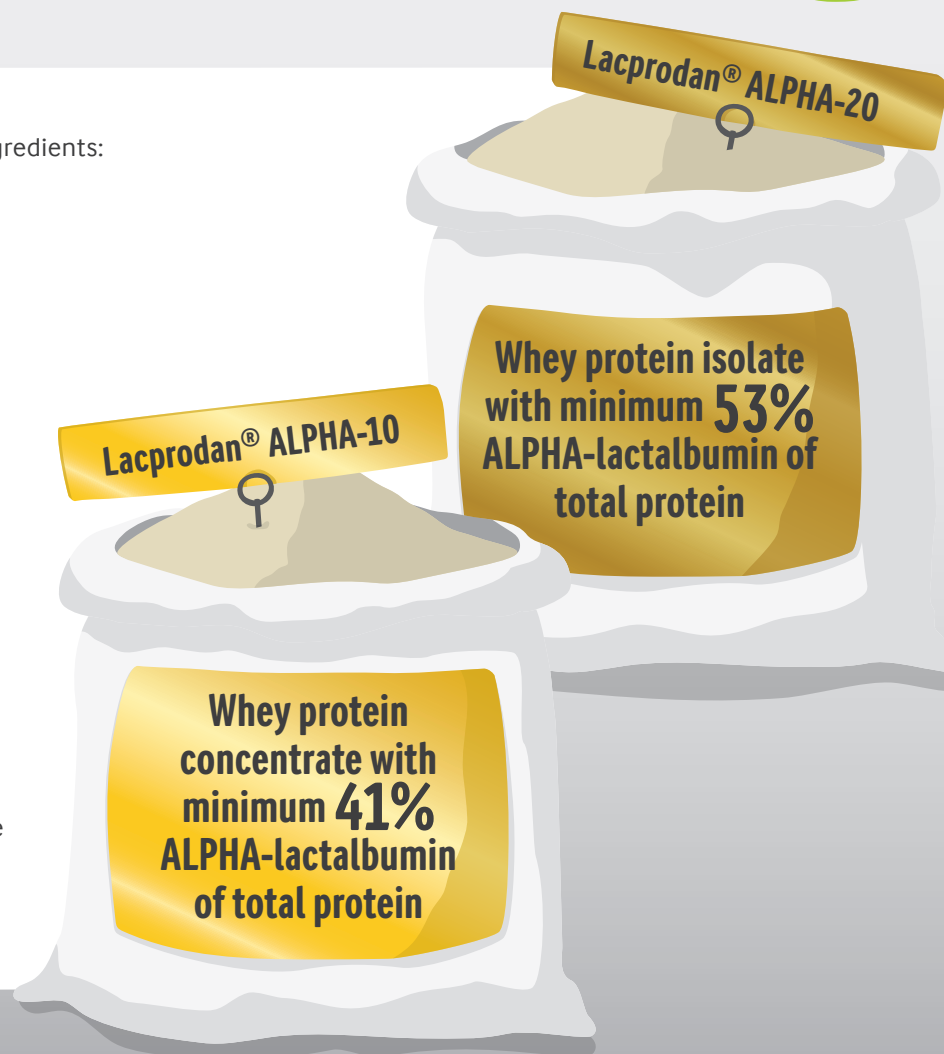
In 1996, Arla Foods Ingredients became one of the world's first commercial producers of ALPHA-lactalbumin. We produce the ingredient at our Danmark Protein facility in Denmark, which adheres to the strictest quality and safety standards in the IF industry today. Our raw material originates from high quality milk and with state-of-the-art equipment, advanced processes and leading product and application experts, we are proud to deliver a uniform, best in class ALPHA-lactalbumin to our customers. Our ingredients are Kosher and Halal certified, and free of annatto.

Analysis

ALPHA-lactalbumin levels are analysed in both ingredients and IF by means of size-exclusion high-performance liquid chromatography (SEC HPLC).

Arla Foods Ingredients collaborates with laboratories in Europe and China to offer IF analysis of ALPHA-lactalbumin.

Our ALPHA-lactalbumin ingredient range is also suitable for maternal nutrition and toddler nutrition.



Why choose Arla Foods Ingredients?

A world leader in natural whey solutions

- World's largest commercial manufacturer of ALPHA-lactalbumin
- Among the world's top 5 producers of whey protein concentrate, whey protein isolate, whey protein hydrolysate, whey protein fractions and lactose
- Producing whey proteins since 1980

R&D in our DNA

- +15% of our employees in Denmark work in R&D
- Collaboration with top universities worldwide
- Clinical and scientific documentation
- Application centres on two continents

Superior quality by design

- Premium quality ingredients
- Kosher and Halal certification
- Our factories adhere to the strictest quality and safety standards
- Free of annatto

Your trusted business partner

- Application support
- Business development support
- In-depth nutrition research and formulation support

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Discovering the wonders of whey