

(19) World Intellectual Property Organization  
International Bureau



(43) International Publication Date  
9 December 2010 (09.12.2010)

PCT

(10) International Publication Number  
**WO 2010/139703 A2**

(51) International Patent Classification:  
*A23L 1/29* (2006.01) *A23L 1/30* (2006.01)

(21) International Application Number:  
PCT/EP2010/057663

(22) International Filing Date:  
1 June 2010 (01.06.2010)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:  
09161669.8 2 June 2009 (02.06.2009) EP

(71) Applicant (for all designated States except US):  
NESTEC S.A. [CH/CH]; Avenue Nestlé 55, CH-1800  
Vevey (CH).

(72) Inventors; and

(75) Inventors/Applicants (for US only): STEENHOUT,  
Philippe [CH/CH]; Route de Blonay 156, CH-1814 La  
Tour-de-peilz (CH). VOSS, Theresa [CH/CH]; Av.  
Reller 22, CH-1800 Vevey (CH).

(74) Agent: CHAUTARD, Cécile; Avenue Nestlé 55,  
CH-1800 Vevey (CH).

(81) Designated States (unless otherwise indicated, for every  
kind of national protection available): AE, AG, AL, AM,  
AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ,  
CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO,

DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT,  
HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP,  
KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD,  
ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI,  
NO, NZ, OM, PE, PG, PH, PL, PT, RO, RS, RU, SC, SD,  
SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR,  
TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every  
kind of regional protection available): ARIPO (BW, GH,  
GM, KE, LR, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG,  
ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ,  
TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK,  
EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU,  
LV, MC, MK, MT, NL, NO, PL, PT, RO, SE, SI, SK,  
SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ,  
GW, ML, MR, NE, SN, TD, TG).

**Declarations under Rule 4.17:**

- as to applicant's entitlement to apply for and be granted  
a patent (Rule 4.17(ii))
- as to the applicant's entitlement to claim the priority of  
the earlier application (Rule 4.17(iii))

**Published:**

- without international search report and to be republished  
upon receipt of that report (Rule 48.2(g))



WO 2010/139703 A2

(54) Title: NUTRITIONAL COMPOSITION FOR SUPPORTING BRAIN DEVELOPMENT AND FUNCTION OF TODDLERS

(57) Abstract: The present invention relates to a nutritional composition, in particular directed to toddlers and/or a weaning child, said nutritional composition comprising a protein source, a source of available carbohydrates, a lipid source, at least one probiotic microorganism, and prebiotics, wherein said lipid source comprises DHA (docosahexaenoic acid). The nutritional composition improves cognitive performance, in particular learning and memory of the child. Preferably, the composition comprises sphingomyelin, sialic acid, choline, essential fatty acids and taurine.

## **Nutritional Composition for Supporting Brain Development and Function of Toddlers**

### **Technical Field**

5 The present invention relates to a nutritional composition. More particularly, the present invention relates to a nutritional composition for improving the cognitive performance of children, in particular children of an age of 1 to 6, preferably 1 to 3 years.

### **Prior Art and the Problem Underlying the Invention**

10

Human breast milk is the ideal form of nutrition for infant and offers medical and psychological benefits not available from human milk substitutes. WHO recommends that all babies should be breastfed exclusively for the first six months of life. Thereafter, the babies should received appropriate complementary feeding with continued breastfeeding up to two  
15 years or beyond (WHO Infant and young child feeding, 2009). In some situations, however, breast milk is not longer available or not possible or not the preferred option of providing nutrition to an infant. Infant formulas, generally based on cow's milk, can provide a satisfactory alternative to breast milk as a sole source of nutrient to young infants. In the period starting from the age of about 6 to 18 months, a child is generally weaning and starts to  
20 take up solid food. Instead of milk-based infant formula, pure milk will continue to make a major contribution of energy and important nutrient requirements to the children at this age.

Infants should not be given unmodified cow's milk as a drink before at least the age of 9 months, because cow's milk alone is not suitable to meet the increased needs of some  
25 nutrients, such as iron, for example. Follow-up formulae are designed to complement the changing diet of the older infant and provide a more balanced and complete food, better adapted to the child's nutritional needs at this age than normal milk. Growing-up milks (GUMs) can be considered a subgroup of follow-up formulas, adapted more particularly to the nutritional needs of children of one year or older, for example 1-6 years. Accordingly, the  
30 objective of follow-up formulae and growing-up milks has generally been to provide nutrients that are important for supporting the healthy growth of a child. Generally, GUMs are adapted specifically to the nutritional needs of children of a specific age. For example, there are GUMs for children of 1-3 years, 3-5 years and above 5 years old.

35 More recently, it has also become an objective to strengthen a child's immune defences. For example, in US2007/0031537, a formula comprising LC-PUFA (long-chain poly unsaturated fatty acids) and a probiotic is disclosed. However, the formula disclosed in this document is directed to infants, not to children above 1 year.

Brain development and growth exceeds that of any other organ or body tissue, reaching its peak at 26 weeks of gestation and continuing at a rapid rate throughout the first two to three years of life. The energy demands (kcal/g/min) of brain and other neuronal tissue are extremely high: approximately 16 times that of skeletal muscle. Brain energy demands in the foetus and newborn are >80% of resting energy expenditure (adult 20-25%). The large allocation of our energy budget to brain metabolism has important implications for our dietary need. Sub-optimal nutrition during this phase has well recognised, irreversible consequences for cognitive function. Also during this critical period, the molecular, biochemical, physiological, and psychological development are established, which influences events all the way into adulthood.

In addition to strengthening a child's immune defences and improving a child's health, physical well-being and tonus, the present invention addresses the problem of providing further benefits to children of the age of about 1 to 6, preferably 1 to 3 years.

In addition, the present invention has to objective to provide a nutritional composition for children of the indicated age, said nutritional composition supports normal brain and/or mental development of the child and the associated mental and/or cognitive aspects.

Furthermore, the present invention has the objective to provide a nutritional composition that contributes to a good performance of a child in school, to an adaptive behaviour, to cognitive function, to language skills, to motor skills and to socio-emotional skills.

For example, the present invention addresses the problem of providing nutritional composition that contributes to or even improves the normal mental performance, cognition, visual function, language abilities and intellectual development of a child.

The present invention also addresses the problem of providing a nutritional composition comprising nutrients and precursors that are important building blocks for newly laid down tissues during brain maturation. In other words the invention provides a nutritional composition providing the right or necessary nutrition for the developing brain of a child. This implies nutrients that the child's body needs for building up the brain ("structural building blocks"), nutrients that are necessary for the processes, such as metabolic processes, taking place in the brain, and nutrients that provide an adequate availability of energy that the brain needs for proper functioning.

More specifically, the present invention addresses the problem of providing nutritional composition that contributes to or even improves mental capacities and properties such as short and long term memory, learning capacity, alertness, attentiveness and concentration capacity of a child.

5

It is important to note that the present invention addresses the above problems while at the same time providing a balanced nutrition, providing important macro- and micronutrients, such as proteins, carbohydrates and fats, and vitamins and minerals, respectively.

10 The present invention addresses the problems depicted above, which problems thus are integral part of this invention.

### **Summary of Invention**

15 The present invention provides a nutritional composition comprising a protein source, a source of available carbohydrates, a lipid source, wherein said lipid source comprises DHA (docosahexaenoic acid).

In another aspect, the present invention provides a nutritional composition comprising:

20

- one or more protein source,
- one or more source of available carbohydrates,
- one or more lipid source,
- one or more probiotic microorganism, and,
- prebiotics,

25 wherein at least one of said one or more lipid source comprises DHA (docosahexaenoic acid).

According to an aspect, DHA is provided in the form of triglycerides comprising DHA.

30 According to an aspect, the present invention provides the use of a protein source, a source of available carbohydrates, a lipid source and other ingredients as disclosed in this specification for preparing a nutritional composition.

Remarkably, the nutritional composition as defined by the present invention and its preferred embodiments, if used as nutritional complement in children of 1 to 6, preferably 1 to 3 years,  
35 provides nutrients useful to contribute to the body's build-up of the brain and to its proper functioning.

Furthermore, the nutritional composition is useful as a growing up milk, contributes to or even improves the normal mental, behavioural, emotional, language and intellectual development of a child.

- 5 Accordingly, the present invention provides, in an aspect, the use of the nutritional composition as disclosed herein for supporting and/or improving cognitive performance, in particular the verbal, perceptual, quantitative abilities, as well as memory and motor development in a child of 1 to 6, preferably 1 to 3 years of age.
- 10 In a similar aspect, the present invention provides, in another aspect, the use of the nutritional composition as disclosed herein for supporting and/or improving behavioural, cognitive, communicational, such as language, expressive and receptive communication, motor and social-emotional skills in a child of 1 to 6, preferably 1 to 3 years of age.
- 15 In another aspect, the present invention provides a method for supporting and/improving cognitive performance in a child of 1 to 6 years, said method comprising the step of administrating a nutritional composition comprising:
- one or more protein source,
  - one or more source of available carbohydrates,
  - 20 - one or more lipid source,
  - one or more probiotic microorganism, and,
  - prebiotics,
- wherein at least one of said one or more lipid source comprises DHA (docosahexaenoic acid).
- 25 In another aspect, the present invention provides a method of providing nutrition, the method comprising the step of administering to a child of 1 to 6 years a nutritional composition comprising:
- one or more protein source,
  - one or more source of available carbohydrates,
  - 30 - one or more lipid source,
  - one or more probiotic microorganism, and,
  - prebiotics,
- wherein said lipid source comprises DHA (docosahexaenoic acid).
- 35 In another aspect, the present invention provides a method for preparing a nutritional composition, said method comprising mixing:
- one or more protein source,
  - one or more source of available carbohydrates,

- one or more lipid source,
- one or more probiotic microorganism, and,
- prebiotics,

5 wherein said lipid source comprises DHA (docosahexaenoic acid), and thereby obtaining the nutritional composition of the invention.

Further, aspects and preferred embodiments of the present invention are provided in the description below as well as in the appended claims.

## 10 **Detailed Description of the Preferred Embodiments**

The nutritional composition preferably comprises a protein source, a source of available carbohydrates, and a lipid source. Preferably, the composition comprises at least one probiotic microorganism. Preferably, the nutritional composition comprises soluble fiber, in particular  
15 at least one prebiotic. The term "comprises", for the purpose of the present invention means "includes, amongst other" and is not intended to mean "consists only of".

In the present specification, the term "nutrient" is repeatedly used. The term "nutrient" refers to typical macro-and micronutrients, such as proteins, lipids, carbohydrates, vitamins and  
20 trace elements, for example. However, for the purpose of the present specification, the term nutrient may also be used with respect to ingredients that are added for the purpose of exerting any kind of beneficial purpose on the child, for example, non-essential but beneficial components such as, for example, probiotics, fiber, in particular prebiotics, DHA (docosahexaenoic acid) and other functional ingredients.

25 For the purpose of the present specification, a child of 1 year refers to a child of the age of at least 1 year and up to 2 years, but not yet complete 2 years elapsed. Accordingly, an age range of 1-2, for example, refers to a spent life span of at least 1 year and up to 3 years, but not yet 3 completely elapsed years. A child having an age of 1 year, 11 months and 29 days is  
30 encompassed in the age group of 1-2 years.

According to an embodiment of the nutritional composition of the invention, said protein source provides about 12 to about 21%, preferably about 14-18%, more preferably 15.5-17.5% of the total energy. Said source of available carbohydrates provides from about 40 to  
35 about 55%, preferably about 43-52%, more preferably about 45-50% of the total energy. Said lipid source preferably provides from about 31 to about 42%, more preferably about 33-40%, and most preferably about 35-38% of the total energy of the composition.

The protein source may be of vegetal or animal origin, for example. Examples of protein sources soy protein, rice protein, wheat protein, milk protein and egg protein. Preferably, the nutritional composition comprises milk protein. Preferably, the composition comprises whey protein, casein, or both. More preferably, the composition comprises whey protein and casein.

5 Whey is preferably sweet whey. The protein source may be provided in the form of intact protein, partial and total protein hydrolysates, di-, tri-, oligo- and polypeptides, free amino acids, and mixtures of the afore-mentioned, for example.

Milk, for the purpose of the present invention, is generally obtained from domesticated  
10 animals, such as cow, buffalo, goat, sheep, camel, dromedary, buffalo, and so forth. Preferably, milk is cow's or goat's milk. Accordingly, milk protein may be, for example, cow's milk protein. Milk contains several nutrients that are implied in the build-up and the functioning of the brain, thereby supporting cognitive development of a child. Without wishing to be bound by theory, the present inventors believe that by combining the  
15 ingredients naturally contained and delivered by milk, if combined with further nutrient in a nutritional composition, mutually interact and together synergistically affect brain build-up and functions as defined in greater detail further below.

The expression "available carbohydrates" refers to carbohydrates that break down during  
20 digestion, in particular in the upper digestive tract during the cephalic and intestinal phase, under the action of digestive enzymes produced by the human body, but also to carbohydrates that are directly absorbed, such as glucose. In particular, the available carbohydrates refers to a source of glucose, since glucose is the main source of energy used by the brain under normal physiological conditions.

25 Preferably, available carbohydrates are provided in the form of at least one selected from lactose, sugars, and maltodextrin, and preferably a combination of at least two or of all three of the latter. The term sugar, for the purpose of the present invention, includes mono- and di-saccharides. Preferably, maltodextrin provides at least 40%, more preferably at least 50% by  
30 dry weight of all available carbohydrates. Preferably, lactose provides less than 50%, more preferably less than 45% by dry weight of all available carbohydrates. Preferably, sugars include one or more selected from fructose, glucose and saccharose. Preferably, sugars provide less than 15%, more preferably less than 10% by dry weight of all available carbohydrates. Saccharose preferably provides less than 2%, more preferably less than 1%,  
35 and most preferably 0.5% or less by dry weight of all available carbohydrates. According to an embodiment, the composition of the invention comprises available carbohydrates, of which 50-60wt.% are maltodextrin, 35-45wt% are lactose and 1-15% are sugars.

Cereals are a preferred source of carbohydrates. According to an embodiment, the nutritional composition is free of modified starch.

5 The lipid source includes lipids useful form human nutrition of any origin, such as vegetal and animal oils or fat, for example. Animal oils include fish oil. Lipid sources include lipids obtained from milk, fish, eggs, seeds, nuts, fungi, microorganisms such as yeast and bacteria, for example. Lipid sources include sources containing phospholipids, mono- di-, triglycerides, fatty acids, sterol-related compounds such as cholesterol, sphingosines, ceramides, glycosphingolipids, gangliosides and the like. Preferred sources of lipids are milk, vegetal oils  
10 and fish oil.

Among the lipids, there are important elements that the human body uses in order to build up the brain, especially during infancy and childhood. Nervous tissue has the second highest concentration of fatty acids after adipose tissue. Fatty acids constitute slightly more than 50%  
15 of the dry weight of the brain. Levels of long chain polyunsaturated fatty acids are particularly high in the cerebral cortex and the retina. Brain phospholipids contain a high proportion of arachidonic acid (ARA, 20:4  $\omega$ -6). Brain is also unusually rich in  $\omega$ -3 fatty acids, in particular docosahexaenoic acid (DHA, 22:6  $\omega$ -3, also referred to as cervonic acid). DHA can account for up to 50% of phospholipid fatty acid in the cerebral cortex and the retina, being  
20 particularly abundant in the rod photoreceptors and in gray matter. This suggests that DHA is heavily involved in neuronal and visual functions. In the brain, DHA and ARA can be synthesised from essential fatty acids, such as linoleic acid (LA: 18:2  $\omega$ -6) and  $\alpha$ -linolenic acid (ALA: 18:3  $\omega$ -3). In summary, DHA is a key component of cell membranes in the brain and the retina, where it accumulates during development.

25 The brain accumulates DHA during childhood, so that by the age of 5-6 years, most of the brain growth is completed. It is thus important to provide lipids in a way that supports the brain development during this period.

30 According to an embodiment, the nutritional composition of the present invention comprises DHA. Preferably, the nutritional composition comprises at least 10 mg (milligram) DHA per 100 g of the dry weight of the nutritional composition. According to an embodiment, the nutritional composition comprises 15-40, more preferably 17-30, and most preferably 20-26 mg DHA per 100 g of the dry weight of the nutritional composition.

35 "Dry weight", for the purpose of the present specification, refers to the dry matter of the nutritional composition from which all water has been removed.

Expressed per 100 kcal of nutritional formula, the nutritional composition comprises at least about 2 mg DHA per 100 kcal of the nutritional composition. According to an embodiment, the nutritional composition comprises 3-8, preferably 3.5-7.5, even more preferably 4-7, and most preferably 4.5-6 mg DHA per 100 kcal of the nutritional composition.

5

According to an embodiment, DHA is provided in the form of triglycerides comprising DHA. Oils comprising DHA and generally other polyunsaturated fatty acids (PUFAs), in particular EPA (eicosapentaenoic acid), may be of various origin. Preferably, the DHA is provided in the form of a fish oil comprising DHA. Fish oils generally comprise 5wt.% or more, preferably 10wt.% or more of DHA. Oils comprising substantial amounts of DHA obtained from algae or microorganisms in general are also available. For example, oils harvested from algae comprising 10wt.% or more, for example 20wt.% or more of DHA may be used.

10

Particularly refined oils may comprise 30wt.% or more of DHA.

15

According to an embodiment, the nutritional composition of the invention comprises an ingredient, which comprises triglycerides comprising DHA. Preferably, the ingredient comprises fish oil containing DHA. Preferably, the ingredient comprises 5-40wt.% of DHA.

20

The nutritional composition preferably comprises ARA. ARA may be added independently from DHA and at quantities independent from the quantity of DHA added. According to an embodiment, however, the nutritional composition comprises about the same amounts of DHA and ARA. For example, the weight ratio of DHA:ARA is in the range of 2:1 to 1:2, preferably example 1.5:1 to 1:1.5, in particular 1.1:1 to 1:1.1.

25

Preferably, the nutritional composition comprises at least 10 mg (milligram) ARA per 100 g of the dry weight of the nutritional composition. According to an embodiment, the nutritional composition comprises 15-40, more preferably 17-30, and most preferably 20-26 mg ARA per 100 g of the dry weight of the nutritional composition.

30

The nutritional composition of the present invention preferably comprises linoleic acid (LA: 18:2  $\omega$ -6),  $\alpha$ -linolenic acid (ALA: 18:3  $\omega$ -3) or both. LA and ALA are both essential long chain polyunsaturated fatty acids (LC-PUFAs). As mentioned above, these fatty acids may be transformed to DHA by the body.

35

Accordingly, the nutritional composition preferably comprises at least 1 g linoleic acid per 100 g of the dry weight of the nutritional composition. Preferably, the nutritional composition

comprises from 2-8g, more preferably 3-7, and most preferably 3.5-5 g of linoleic acid per 100 g of the dry weight of the nutritional composition.

5 According to an embodiment, the nutritional composition preferably comprises at least 100 mg  $\alpha$ -linolenic acid per 100 g of the dry weight of the nutritional composition. Preferably, the nutritional composition comprises 200-700 mg, more preferably 300-600 mg, and most preferably 400-550 mg of  $\alpha$ -linolenic acid per 100 g of the dry weight of the nutritional composition.

10 Preferably, the ratio of linoleic acid to  $\alpha$ -linolenic acid in the nutritional composition of the invention is in the range (including endpoints) of 5:1 to 12:1, preferably 7:1 to 11:1, more preferably 8:1 to 10:1.

15 According to an embodiment, the ratio of  $\omega$ -6 to  $\omega$ -3 fatty acids in the nutritional composition of the present invention is 3:1 and 12:1, more preferably between 4:1 and 11:1, even more preferably 5:1 and 10:1. Preferably the ratio of  $\omega$ -6 to  $\omega$ -3 fatty acids is at least 4.5, more preferably at least 5. The human body cannot convert fatty acids from  $\omega$ -6 to  $\omega$ -3 and *vice versa*. Furthermore, linoleic acid and  $\alpha$ -linolenic acid compete for the same enzymes of the metabolism, and they both inhibit each other's desaturation and elongation. Therefore, it is  
20 important to provide a balanced ratio of these essential fatty acids in the diet to ensure optimal growth and development.

According to an embodiment, the nutritional composition comprises sphingomyelin. Sphingomyelins are a subgroup of sphingophospholipids, which in turn are part of the larger  
25 group of sphingolipids in general. Sphingomyelins consist of a ceramide moiety (for example sphingosine) and a phosphacholine as a polar head group. Sphingomyelin is a structural component of cellular membranes and is found in the membranes of neurons and glia cells, and also in axons. Sphingomyelin facilitates the efficient and rapid propagation of nerve electrical signals. In particular, sphingomyelin is a component of the myelin sheath  
30 surrounding the nerve cell axons. In the present nutritional composition, sphingomyelin is mainly naturally provided as a natural component of milk, in particular cow's milk, or milk fat globule membrane.

The term "naturally delivered", for the purpose of the present specification, indicates that a  
35 respective nutrient is comprised in the nutritional composition by way of the ingredients that are used to prepare the nutritional composition. It generally indicates that a respective nutrient is not specifically added in an isolated or highly concentrated form.

The nutritional composition of the invention preferably comprises at least 10 mg sphingomyelin per 100 g of the dry weight of the nutritional composition. According to an embodiment, the nutritional composition comprises 10-200, preferably 20-150, more preferably 25-100 mg sphingomyelin per 100 g of the dry weight of the nutritional composition.

According to an embodiment, the nutritional composition comprises sialic acid. Sialic acids are a family of over 50 members of 9-carbon sugars, all of which are derivatives of neuraminic acid. The predominant sialic acid family found in humans is from the N-acetylneuraminic acid sub-family. Sialic acids are contained in milk, such as cow's and goat's milk, for example. In mammals, neuronal cell membranes have the highest concentration of sialic acid compared to the other body cell membranes. The majority of sialic acid is present in gangliosides. Gangliosides are cell membrane components consisting of a lipid portion and a carbohydrate portion containing at least one or more sialic acid residues. Sialic acid plays an essential role in the transmission and storage of information in the brain. In the present nutritional composition, sialic acid may be added separately, but is preferably provided in sufficient amounts by way of milk components used as ingredients of the nutritional composition (naturally provided). Preferably, the nutritional composition comprises at least 40 mg of sialic acid per 100 g of dry weight of the nutritional composition. According to an embodiment, the nutritional composition comprises 40-250, preferably 50-180, more preferably 60-120 mg sialic acid per 100 g of the dry weight of the nutritional composition.

According to an embodiment, the nutritional composition comprises choline. The human brain is rich in choline containing compounds. Choline is present in gray matter (10% of dry weight), white matter (8% of dry weight) and is a component of myelin (12% of dry weight). In the nutritional composition of the invention, choline is preferably not specifically added but is contained and therefore naturally provided by other ingredients, such as milk components and/or from ingredient comprising phospholipids rich in DHA mentioned above, for example.

The nutritional composition of the invention preferably comprises at least 20 mg of choline per 100 g of the dry weight of the nutritional composition. According to an embodiment, the nutritional composition comprises 20-300, preferably 30-200, more preferably 40-110 mg choline per 100 g of the dry weight of the nutritional composition.

According to an embodiment, the nutritional composition comprises thiamine. Thiamin, also known as vitamin B<sub>1</sub>, is a water soluble vitamin of the B vitamin family. Thiamin functions as part of a coenzyme in energy-yielding systems, especially those involved in the metabolism of carbohydrates and to the breakdown of glucose to energy. Thiamin also plays a role in the

conduction of nerve impulses. Studies showed that deficiencies in thiamine may lead to decrease of short term memory, confusion and irritability (behavioral problems), besides negative effects on muscles and the cardiovascular system. The composition preferably comprises at least 0.2 mg thiamin per 100 g of dry weight of the nutritional composition.

5 According to an embodiment, the composition comprises 0.4-1.5, preferably 0.6-1.3, more preferably 0.8-1.1 mg thiamin per 100 g of dry weight of the nutritional composition.

According to an embodiment, the nutritional composition comprises folic acid. Folic acid, also known as vitamin B<sub>9</sub>, is required for cell division and maintenance, formation of DNA  
10 and RNA, and the synthesis and breakdown of amino acids. Folic acid acts as a coenzyme in the transfer of one-carbon units. In infants and children, folate deficiency can slow overall growth. It is assumed, for the purpose of the present specification, that folate up-take is associated with cognitive performance, such as memory performance. The composition preferably comprises at least 50 µg folate per 100 g of dry weight of the nutritional  
15 composition. According to an embodiment, the composition comprises 60-200, preferably 90-190, more preferably 100-170, most preferably 120-160 µg folic acid per 100 g of dry weight of the nutritional composition.

According to an embodiment, the nutritional composition comprises taurine. The composition  
20 preferably comprises at least 10 mg taurine per 100 g of dry weight of the nutritional composition. According to an embodiment, the composition comprises 15-140, preferably 20-90, more preferably 25-70, most preferably 30-50 mg taurine per 100 g of dry weight of the nutritional composition.

25 According to an embodiment, the nutritional composition comprises vitamin D. There is biological evidence to suggest an important role for vitamin D in brain development and function. The composition preferably comprises at least 1.5 µg vitamin D per 100 g of dry weight of the nutritional composition. According to an embodiment, the composition comprises 2-10, preferably 3.5-9, more preferably 5-8 µg vitamin D per 100 g of dry weight  
30 of the nutritional composition.

According to an embodiment, the nutritional composition comprises iron. Generally, iron is an essential component of several cellular functions such as the transport of oxygen, mitochondrial electron transport and DNA synthesis. Brain tissue is overall rich in iron. Iron  
35 is also involved in the production of myelin, in the synthesis of neurotransmitters and their breakdown. For example, iron is essential for the synthesis of dopamine, an important neurotransmitter for attention, executive functioning and motivation. Iron has been implicated in the organization of axonal growth and synaptogenesis. Today, iron deficiency is the most

common single nutrient deficiency in the world. Associations between iron deficiency anaemia and deficit in cognitive or behavioural performance in children have been observed. Iron is thus important for brain development.

5 Iron, if added as a nutritional supplement to a nutritional composition, is not always easily absorbed in the digestive tract. There are forms of iron that have low bioavailability. Therefore, according to an embodiment, iron is added in a form having high bioavailability. Preferably, iron is provided in the form of a salt comprising ferrous iron (iron with the oxidation state II+). For example, iron is provided in the form of added ferrous sulphate,  
10 including hydrates of ferrous sulfate.

According to an embodiment, the nutritional composition of the present invention comprises at least 2 mg iron per 100 g of dry weight of the nutritional composition. According to an embodiment, the composition comprises 2-10, preferably 3-8, more preferably 5-7 mg of iron  
15 per 100 g of dry weight of the nutritional composition.

According to an embodiment, the nutritional composition comprises iodine. Iodine is a trace element that is necessary for normal production of thyroid hormones, normal growth and normal brain development. Studies show that iodine deficiency may lead to mental  
20 impairment such as manifested by poor school performance reduced intellectual ability and impaired work capacity. In certain geographical areas, soil and water is naturally low in iodine, raising the risk of deficiencies in the population living in these areas. According to an embodiment, the present nutritional composition comprises at least 40 µg (microgram) of iodine per 100 g of dry weight of the nutritional composition. According to an embodiment,  
25 the composition comprises 40-300, preferably 60-250, more preferably 80-200, and most preferably 90-150 µg of iodine per 100 g of dry weight of the nutritional composition.

According to an embodiment, the nutritional composition of the present invention comprises zinc. Zinc (Zn) is an essential trace mineral that needs to be provided by the diet. Zinc is  
30 required for the biological function of more than 300 enzymes and stabilizes the tertiary structure of some proteins. In the central nervous system, zinc is concentrated in the synaptic vesicles of specific glutaminergic neurons, which are found primarily in the forebrain and connect with other cerebral structures. Furthermore, in the synapse, zinc appears to be involved in neurotransmission.

35 According to an embodiment, the nutritional composition of the present invention comprises at least 2 mg of zinc per 100 g of dry weight of the nutritional composition. According to an

embodiment, the composition comprises 2-10, preferably 3.5-9, more preferably 5-8 mg of zinc per 100 g of dry weight of the nutritional composition.

According to an embodiment, the nutritional composition comprises at least one probiotic. Probiotics are living microorganisms which, when administered in adequate amounts confer a health benefit on the host. According to an embodiment, the nutritional composition comprises at least two different probiotic microorganisms. Preferably, each of said microorganisms is provided at about  $1 \times 10^5$  to  $1 \times 10^{12}$  CFU per g of dry matter of the composition, preferably at least  $5 \times 10^5$  to  $1 \times 10^9$ , more preferably at least  $1 \times 10^6$ . The "x" means "times" and thus refers to a multiplication of the respective numbers. Preferably, a combination of two or more different probiotic microorganisms is selected that provides a health benefit, in particular when administered to children of one year and older, in particular children of the age classes as defined for the nutritional composition herein. Preferably, the two different probiotic microorganisms are selected from different species, more preferably from of different genus. According to an embodiment, the nutritional composition comprises the two probiotic microorganisms, one of which of the genus *Bifidobacterium* and the other of the genus *Lactobacillus*. Preferably, the composition comprises *Bifidobacterium longum* and a *Lactobacillus rhamnosus* strain. According to a preferred embodiment, the nutritional composition comprises the *Bifidobacterium longum* deposited as ATCC BAA-999, and the *Lactobacillus rhamnosus* strain deposited as ATCC 53103.

According to an embodiment, the nutritional composition comprises dietary fiber. Preferably, the composition comprises soluble fiber. According to an embodiment, the composition of the present invention comprises at least one prebiotic. Preferably, the nutritional comprises one or more selected from inulin, fructooligosaccharides (FOS), or a mixture of inulin and fructooligosaccharides. Preferably, the nutritional composition comprises at least 1, more preferably at least 2 and even more preferably at least 3 g soluble fiber per 100 g of dry weight of the nutritional composition. According to an embodiment, the nutritional composition comprises 1 to 10 g, preferably 2 to 7 g, more preferably 3 to 4 g of soluble fiber. Preferably, the soluble fiber is a mixture of inulin and FOS, said mixture comprising at least 50%, more preferably at least 60% by weight of dry matter of FOS.

According to an embodiment, the nutritional composition of the present invention comprises at least one or more selected from essential fatty acids (preferably ALA and LA), DHA, ARA, sphingomyelin, sialic acid, and choline. It is believed, without wishing to be bound by theory, that ingredients providing this combination of nutrients provide the advantages on brain development, functioning, mental performance and/or other brain-associated advantages as reported herein.

5 In addition, taurine is believed, without wishing to be bound by theory, if administered in combination with sialic acid, sphingomyelin, choline, essential fatty acids (preferably ALA, LA), DHA, and ARA, to provide the brain-associated advantages reported in this specification.

10 In addition, folic acid and thiamine are believed, without wishing to be bound by theory, if administered in combination with sialic acid, sphingomyelin, choline, essential fatty acids (preferably ALA, LA), DHA, and ARA, and, optionally, taurine, to provide the brain-associated advantages reported in this specification.

15 In addition, iron, iodine and zinc are believed, without wishing to be bound by theory, if administered in combination with sialic acid, sphingomyelin, choline, essential fatty acids (preferably ALA, LA), DHA, and ARA, and, optionally, one, two or all three selected from of taurine, folic acid and thiamine, to provide the brain-associated advantages reported in this specification. Iron and zinc are also believed, without wishing to be bound by theory, to play an important protective role, strengthening the child's immune system, increasing the child's ability to fight pathogens or diseases in general, and/or the physical health in general.

20 Also the probiotics, antioxidants (in particular vitamin C and A) are believed, without wishing to be bound by theory, to play an important protective role, strengthening the child's immune system and/or the physical health in general.

25 According to a preferred embodiment, the composition of the present invention comprises one, a combination of several or all nutrients selected from the group of LA, ALA, DHA, ARA, sphingomyelin, sialic acid, and choline.

30 According to a more preferred embodiment, the composition further comprises iron, zinc, and iodine.

According to a still further preferred embodiment, the nutritional composition further comprises vitamin D, taurine, thiamine and folic acid.

35 In the combinations of preferred nutrients indicated above, quantities are preferably for each ingredient individually as provided within this specification.

Without wishing to be bound by theory, it is believed that key nutrients as specified herein synergetically interact if present in the combinations as specified herein and thereby achieve the advantages and benefits on mental performance as disclosed in this specification.

5 According to an embodiment, the nutritional composition of the invention comprises macronutrients and soluble fiber in the quantities indicated in Table 1 below.

It is noted that in the tables and claims herein, quantities are indicated as percent per 100 g of a powdered (substantially dry), reconstitutable formula of the nutritional composition.

10 Basically, these quantities correspond to the quantity per 100 g of complete dry matter, taking into account that a powdered formula generally has a residual moisture content of about 1.8 g to 2.2 g per 100 g of powder.

**Table 1:** Preferred amounts of macronutrients and soluble fiber in the nutritional composition of the invention

Nutrient		Unity	Weight per 100g
<b>Fat</b>		g	16.3-19.3
	LA	g	2-8
	ALA	mg	200-700
	DHA	mg	15-40
	ARA	mg	15-40
<b>Protein</b>		g	14.5-17.5
<b>Available carbohydrates</b>		g	54-59
<b>Soluble fiber</b>		g	at least 3

According to a preferred embodiment, the nutritional composition of the invention comprises macronutrients and soluble fiber in the quantities (percent per 100 g dry matter) indicated in Table 2 below:

20

**Table 2:** More preferred amounts of macronutrients and soluble fiber in the nutritional composition of the invention

Nutrient		Unity	Weight per 100g
<b>Fat</b>		g	16.3-19.3
	LA	g	3-7
	ALA	mg	300-600

	DHA	mg	17-30
	ARA	mg	17-30
<b>Protein</b>		g	14.5-17.5
<b>Available carbohydrates</b>		g	54-59
<b>Soluble fiber</b>		g	at least 3

According to a most preferred embodiment, the nutritional composition of the invention comprises macronutrients and soluble fiber in the quantities (percent per 100 g dry matter) indicated in Table 3 below:

5

**Table 3:** Most preferred amounts of macronutrients and soluble fiber in the nutritional composition of the invention

Nutrient		Unity	Weight per 100g
<b>Fat</b>		g	16.3-19.3
	LA	g	3.5-5
	ALA	mg	400-450
	DHA	mg	20-26
	ARA	mg	20-26
<b>Protein</b>		g	14.5-17.5
<b>Available carbohydrates</b>		g	54-59
<b>Soluble fiber</b>		g	at least 3

10 With respect to the micronutrients, in particular vitamins and minerals, the preferred, more preferred and most preferred quantities of key micro-nutrients for the purpose of the present invention are set out in Tables 4-6 below.

**Table 4:** Preferred amounts of some key micronutrients in the nutritional composition of the invention

Minerals and vitamins		Unity	Weight per 100g
	sphingomyelin	mg	10-200
	sialic acid	mg	40-250
	choline	mg	20-300
	thiamine	mg	0.4-1.5
	folic acid	μg	60-200
	taurine	mg	15-140

	vitamin D	µg	2-10
--	-----------	----	------

**Table 5:** More preferred amounts of some key micronutrients in the nutritional composition of the invention

Minerals and vitamins		Unity	Weight per 100g
	sphingomyelin	mg	20-150
	sialic acid	mg	50-180
	choline	mg	30-200
	thiamine	mg	0.6-1.3
	folic acid	µg	90-190
	taurine	mg	20-90
	vitamin D	µg	3.5-9

5

**Table 6:** Most preferred amounts of some key micronutrients in the nutritional composition of the invention

Minerals and vitamins		Unity	Weight per 100g
	sphingomyelin	mg	25-100
	sialic acid	mg	60-120
	choline	mg	40-110
	thiamine	mg	0.8-1.1
	folic acid	µg	100-170
	taurine	mg	30-50
	vitamin D	µg	5-8

The Tables 1-3 and 4-6 concerning macro- and micronutrients, respectively may be combined in any way in accordance with the nutritional composition of the present invention. Accordingly, a nutritional composition of the invention may be defined by combining Table 1 with micronutrients as defined in Table 4, Table 5 or Table 6; Table 2 may be combined with micronutrients as defined in Table 4, with Table 5 or with Table 6; Table 3 may be combined with micronutrients as defined in Table 4, with Table 5 or with Table 6, thereby providing the nutritional composition of the present invention.

According to an embodiment, the nutritional compositions as defined by Tables 1-6 and combinations thereof further comprise one, two or all three selected from iron, iodine and zinc, preferably in the amounts indicated above.

In any event, the nutritional compositions of the invention as described in the tables above preferably comprise probiotics and prebiotics as defined further above.

- 5 According to an embodiment, the present invention provides a nutritional composition comprising the nutrients as defined in Table 7 below:

**Table 7** Embodiment of a nutritional composition according to the present invention:

<b>Nutrient</b>	Unity	Weight per 100g	
<b>Fat</b>	g	<b>16.61</b>	<b>21.23</b>
Comprised in the oil and fat ingredients:			
Lecithin	g	0.29	0.37
Linoleic acid	g	3.44	6.02
Linolenic acid	mg	384.00	672.00
Arachidonic acid	mg	19.20	33.60
DHA	mg	18.40	32.20
<b>Protein</b>	g	<b>17.17</b>	<b>21.94</b>
<b>Available carbohydrates</b>	g	<b>49.64</b>	<b>63.42</b>
Lactose	g	24.97	35.26
Maltodextrin	g	17.52	24.73
Other	g	1.00	8.00
<b>Dietary fiber</b>	g	<b>2.51</b>	<b>5.37</b>
Inulin & oligosaccharides	g	2.51	5.37
<b>Minerals (ash)</b>	g	<b>1.86</b>	<b>5.57</b>
Sodium	mg	140.00	420.00
Potassium	mg	445.00	1335.00
Chloride	mg	325.00	975.00
Calcium	mg	360.00	1080.00
Phosphorus	mg	275.00	825.00
Magnesium	mg	30.00	90.00
Manganese	µg	20.00	60.00
Selenium	µg	4.50	13.50
<b>Micronutrients (other)<sup>1</sup></b>	mg	159.00	604.20
Sphingomyelin <sup>2</sup>	mg	15.00	150.00
Choline <sup>2</sup>	mg	28.00	144.00
Sialic acid <sup>2</sup>	mg	44.00	220.00
Vitamin A (retinol)	µg RE <sup>3</sup>	378.00	702.00
Vitamin D	µg	4.76	10.20
Vitamin E	mg	3.78	8.10
Vitamin K	µg	14.00	30.00
Vitamin B <sub>2</sub>	mg	0.77	1.65

Vitamin C	mg	37.80	81.00
Thiamin (B <sub>1</sub> )	mg	0.66	1.41
Niacin (vit B <sub>3</sub> )	mg	8.40	15.60
Pyridoxin (vit B <sub>6</sub> )	mg	0.98	2.10
Biotin (B <sub>8</sub> )	µg	18.90	35.10
Folic acid (vit B <sub>9</sub> )	µg	70.00	210.00
Pantothenic acid	mg	2.80	6.00
Cobalamin (vit B <sub>12</sub> )	µg	0.63	1.35
Taurine	mg	25.20	54.00
Iodine <sup>2</sup>	µg	28.20	282.00
Iron	mg	2.70	9.18
Zinc	mg	3.40	11.56
Total solids	g	<b>100</b>	

1) These micronutrients are also part of the ash

2) Naturally provided, in particular milk ingredients

3) RE=Retinol Equivalents

- 5 According to a preferred embodiment, the present invention provides a nutritional composition comprising the nutrients as defined in Table 8 below:

**Table 8** Preferred embodiment of a nutritional composition according to the present invention:

Nutrient	Unity	Weight per 100g	
<b>Fat</b>	<b>g</b>	<b>16.98</b>	<b>20.31</b>
Milk fat	g	3.20	4.09
Non-milk Fat	g	13.08	16.71
Lecithin	g	0.27	0.45
Comprised in the above fats and oils:			
Linoleic acid	g	3.66	5.59
Linolenic acid	mg	408.00	624.00
Arachidonic acid	mg	20.40	31.20
DHA	mg	19.55	29.90
<b>Protein</b>	<b>g</b>	<b>17.55</b>	<b>20.99</b>
Casein	g	13.17	16.82
Whey protein	g	3.94	5.04
<b>Available carbohydrates</b>	<b>g</b>	<b>50.74</b>	<b>60.67</b>
Lactose	g	26.44	33.79
Maltodextrin	g	18.55	23.70
Other (mainly sugars such as fructose, glucose, saccharose)	g	4.64	5.93
<b>Dietary fiber</b>	<b>g</b>	<b>2.86</b>	<b>4.65</b>
Inulin & oligosaccharides	g	2.86	4.65

<b>Minerals (ash)</b>	g	<b>2.23</b>	<b>5.19</b>
Sodium	mg	182.00	378.00
Potassium	mg	578.50	1201.50
Chloride	mg	422.50	877.50
Calcium	mg	468.00	972.00
Phosphorus	mg	357.50	742.50
Magnesium	mg	39.00	81.00
Manganese	µg	26.00	54.00
Selenium	µg	5.85	12.15
<b>Micronutrients (other)<sup>1</sup></b>	mg	190.80	556.50
Sphingomyelin <sup>2</sup>	mg	21.00	120.00
Choline <sup>2</sup>	mg	50.40	126.00
Sialic acid <sup>2</sup>	mg	61.60	167.20
Vitamin A (retinol)	µg RE <sup>3</sup>	432.00	648.00
Vitamin D	µg	5.44	8.16
Vitamin E	mg	4.32	7.02
Vitamin K	µg	16.00	24.00
Vitamin B <sub>2</sub>	mg	0.88	1.32
Vitamin C	mg	43.20	64.80
Thiamin (B <sub>1</sub> )	mg	0.75	1.22
Niacin (vit B <sub>3</sub> )	mg	9.60	14.40
Pyridoxin (vit B <sub>6</sub> )	mg	1.12	1.68
Biotin (B <sub>8</sub> )	µg	21.60	32.40
Folic acid (vit B <sub>9</sub> )	µg	98.00	182.00
Pantothenic acid	mg	3.20	4.80
Cobalamin (vit B <sub>12</sub> )	µg	0.72	1.08
Taurine	mg	28.80	43.20
Iodine <sup>2</sup>	µg	47.00	235.00
Iron	mg	3.78	8.10
Zinc	mg	4.76	10.20
Total solids	g	<b>100</b>	

The reference numbers 1-3 have the same meaning as with Table 7.

According to a still more preferred embodiment, the present invention provides a nutritional composition comprising the nutrients as defined in Table 9 below:

5

**Table 9** More preferred embodiment of a nutritional composition according to the present invention:

Nutrient	Unity	Weight per 100g	
<b>Fat</b>	g	<b>17.54</b>	<b>19.94</b>

Milk fat	g	3.28	3.92
Non-milk Fat	g	13.37	15.98
Lecithin	g	0.29	0.42
Comprised in the above fats and oils:			
Linoleic acid	g	3.87	5.16
Linolenic acid	mg	432.00	576.00
Arachidonic acid	mg	21.60	28.80
DHA	mg	20.70	27.60
<b>Protein</b>	<b>g</b>	<b>18.13</b>	<b>20.61</b>
Casein	g	13.46	16.09
Whey protein	g	4.03	4.82
<b>Available carbohydrates</b>	<b>g</b>	<b>52.39</b>	<b>59.56</b>
Lactose	g	27.03	32.91
Maltodextrin	g	18.96	23.08
Sugars (fructose, glucose, saccharose)	g	4.75	5.78
<b>Dietary fiber</b>	<b>g</b>	<b>3.47</b>	<b>3.76</b>
Inulin & oligosaccharides	g	3.22	4.30
<b>Minerals (ash)</b>	<b>g</b>	<b>2.60</b>	<b>4.82</b>
Sodium	mg	210.00	350.00
Potassium	mg	667.50	1112.50
Chloride	mg	487.50	812.50
Calcium	mg	540.00	900.00
Phosphorus	mg	412.50	687.50
Magnesium	mg	45.00	75.00
Manganese	µg	30.00	50.00
Selenium	µg	6.75	11.25
<b>Micronutrients (other)<sup>1</sup></b>	<b>mg</b>	<b>222.60</b>	<b>540.60</b>
Sphingomyelin <sup>2</sup>	mg	24.00	60.00
Choline <sup>2</sup>	mg	54.00	108.00
Sialic acid <sup>2</sup>	mg	70.40	132.00
Vitamin A (retinol)	µg RE <sup>3</sup>	486.00	594.00
Vitamin D	µg	6.12	7.48
Vitamin E	mg	4.86	5.94
Vitamin K	µg	18.00	22.00
Vitamin B <sub>2</sub>	mg	0.99	1.21
Vitamin C	mg	43.20	64.80
Thiamin (B <sub>1</sub> )	mg	0.80	1.18
Niacin (vit B <sub>3</sub> )	mg	10.80	13.20
Pyridoxin (vit B <sub>6</sub> )	mg	1.26	1.54
Biotin (B <sub>8</sub> )	µg	24.30	29.70
Folic acid (vit B <sub>9</sub> )	µg	105.00	175.00
Pantothenic acid	mg	3.60	4.40

	Cobalamin (vit B <sub>12</sub> )	µg	0.81	0.99
	Taurine	mg	30.60	41.40
	Iodine <sup>2</sup>	µg	65.80	178.60
	Iron	mg	4.32	7.29
	Zinc	mg	5.44	9.18
	Total solids	g	<b>100</b>	

The nutritional composition of the present invention preferably provides 400-500 kcal, more preferably 420-480 kcal per 100 g of dry weight of the composition. According to an embodiment, per dl of the reconstituted formula, the composition provides preferably 40-80, more preferably 45-75, most preferably 50-70 kcal. The caloric content of the nutritional composition per volume (for example 100 ml) may generally also be determined on the basis of the caloric content per 100 g and considering reconstitution quantities as indicated above.

According to an embodiment, the nutritional composition of the present invention is adapted to children of an age of 1-6, preferably 1-5, more preferably 1-4, even more preferably 1-3 and most preferably 1-2 years.

Preferably, the nutrients provided in the nutritional composition are adapted to the needs and nutritional recommendations of children of a specific age. Accordingly, the values of nutrients as discussed above in particular correspond to the needs of children of 1-3, preferably 1-2 years, and are thus particularly valid for nutritional compositions adapted to children of 1-3, preferably 1-2 years.

For children that have an age of 3 years or older, for example 3-6, preferably 3-5 and most preferably 3-4 years, the amounts of some nutrients in the nutritional composition are preferably adapted, while other nutrients are the same as discussed above.

With respect to the macronutrients, it is noted that children of 3 years and older generally have higher requirements in proteinogenic matter (protein source) and lower requirements in carbohydrates and slightly higher requirements in than children of more than 1 and up to three years. According to an embodiment of a nutritional composition for children of 3 or more years, for example 3-4 years, said protein source provides about 13 to about 23, preferably 16-20 percent of the total energy, said source of available carbohydrates provides from about 33 to about 50, preferably 40-46 percent of the total energy, and said lipid source provides from about 38 to about 48, preferably 37-44 percent of the total energy of the composition.

The nutritional composition of the present invention may be provided as a ready-to-drink liquid form or in the form of a dry powder to be reconstituted with water, or another water

containing liquid (less preferred). Preferably, the nutritional composition is provided in powdered form, and reconstituted by addition of water by the consumer shortly (for example 1 minute to 2 hours) before consumption. As is usual, the water has to be clean, that is preferably bottled water or has been boiled and filtered and cooled to 60°C or lower before addition to the nutritional composition.

If the nutritional composition is provided in the form of a powder, it is preferably reconstituted by mixing 12-20 g powder in 1 dl water, preferably 14-20 g powder, more preferably about 16-18 g powder in 1 dl (0.1 liter) water.

The typical serving size is about 200 ml, that is, in two times the quantity defined above (for example, 32 g) is added to 200 ml water. Per day, ideally 2 to 3 serving sizes are consumed per child of 1 to 3 years.

According to a preferred embodiment, the nutritional composition is a growing up milk, also referred to as a GUM.

The nutritional composition provides several benefits associated with the healthy mental, behavioural and intellectual development of the child.

In an aspect the nutritional composition supports and/or improves overall cognitive performance, for example cognitive capacities and/or abilities in a child.

In an aspect, the nutritional composition is used to provide nutrients that have at least one of the following purposes: nutrients that (1) the body of a child can use to structurally build up the brain, (2) are needed for the biochemical processes taking place in the brain, and/or (3) that provide the energy necessary for the functioning of the brain. Preferably, the nutritional composition provides nutrients for (1), for (1) and (2), for (1) and (3), for (2) and (3) or for (1), (2) and (3) above.

According to an aspect, the nutritional composition provides nutrients or a combination of nutrients that is bioavailable. Preferably, the nutrients have increased bioavailability if compared to nutrients provided in a different, for example conventional form, or in a different combination of nutrients. Preferably, the nutrients are provided in a form that is actually absorbed in the digestive tract and used by the body to build up the brain.

In an aspect, the nutritional composition supports the healthy, normal or improved behavioural, cognitive, communicational, such as language, expressive and receptive communication, psychomotor and social-emotional development of a child.

5 In an aspect, the nutritional composition supports and/or improves cognitive development of a child. In particular, the nutritional composition supports one or more selected from sensorimotor development, exploration and manipulation, object relatedness, concept formation, memory, habituation, visual acuity, visual preference, object recognition, visual attention, or other aspects of cognitive processing. In dependence of the age, the nutritional composition supports and/or improves cognitive development and/or capacities in one or  
10 more of the areas selected from counting (with one-to-one correspondence and cardinality), visual and tactile exploration, object assembly, puzzle board completion, matching colors, comparing masses, representational and/or pretend play, discriminating patterns.

With respect to language skills, the nutritional composition of the present invention supports and/or improves the development and/or abilities of expressive communication, preverbal  
15 communications such as babbling, gesturing, joint referencing, turn taking, vocabulary development such as naming objects, pictures, using words to make needs or wants known, and actions, morpho-syntactic development such as use of two-word utterances and use of plurals and verb tense, receptive communication, preverbal behaviors and vocabulary development such as the ability to identify objects and pictures that are referenced,  
20 vocabulary related to morphological development such as pronouns and prepositions, understanding of morphological markers such as plurals and tense markings.

In an aspect, the nutritional composition supports and/or improves social-emotional development and/or abilities. Depending on the specific age of an infant or a child, the nutritional composition supports and/or improves the child's self-regulation, interest in the  
25 world, engagement in relationships, use of emotions in an interactive, purposeful manner, use of interactive, emotional signals or gestures to communicate, use of interactive, emotional signals or gestures to solve problems, use of ideas to convey feelings, wishes, or intentions, the creation of logical bridges between emotions and ideas

The above examples of cognitive, language and social-emotional skills may be assessed, for  
30 example, using statistical tests designed for infants and children, such as the Bayley Scales of Infant and Toddler Development®, Third Edition (Bayley-III®), of Nancy Bayley, Ph.D.. The modified Bayley II can also be used. These tests can be used to assess infants and children of 1 to 42 months of age, with subtests directed to specific age ranges, for example 2 to 2.5 years of age.

Another suitable test for assessing performance, such as cognitive and the like are the McCarthy Scales (*McCarthy Scales of Children's Abilities*. New York, NY: Psychological Corp; 1972 of Dorothea McCarthy). This test is useful to assess abilities of children of the age of 2.5 to 8.5 years.

- 5 In an aspect, the nutritional composition of the invention supports and/or improves memory, in particular short term memory, working memory and/or long term memory, preferably at least short term memory and/or working memory. Short term memory and working memory can be more readily tested in typical experimental settings.

10 "Memory" is an organism's mental ability to store, retain and recall information. For the purpose of the present specification, memory is an organism's mental ability selected from one, two (for example, (a) and (c)) or all three of (a) to store, (b) retain and (c) recall information. Memory phenomena that can be examined for the purpose of the present specification include: (1) knowledge (what is remembered?); (2) comprehension (what does it mean?); (3) context/function (why remember?); and (4) strategy (how to remember?).

15 Memory is complex psychological process that is not independent of a single memory domain process. Memory is related to several other cognition domains including, sensory memory, audio memory and visual memory. The terms of "memory" include:

20 "Short-term memory": a system for temporarily, for example up to 60 (= 1 minute), up to 30, up to 20 or up to 15 seconds, storing and managing information required to carry out cognitive tasks such as learning, reasoning, and comprehension, for example.

"Working memory": refers to short-term memory and requires the simultaneous storage and processing of information.

25

"Long-term memory" is memory that can last beyond a few, for example beyond 2-3, minutes to a few decades. Items of information stored as long-term memory may be available for a lifetime.

30 Memory is generally understood to be a process by which what is learned persists across time. In this sense, learning and memory are inextricably connected. Accordingly, the composition of the present invention supports and/or improves a child's learning and/or memory capacities.

35 For example, the nutritional composition of the present invention supports and/or increases a child's capacity recall words, numbers, pictures, symbols, letters, and/or tonal sequences within the short-term.

According to an aspect, the nutritional composition supports and/or improves at least one selected from learning capacity, alertness, attentiveness, and concentration capacity of a child.

5 According to an aspect, the composition of the present invention supports and/or improves a child's skills and/or abilities in one or more of (1) the comprehension and use of language, (2) mathematical abilities, (3) the conceptualization and reasoning without words.

### Examples

10 The following examples are illustrative of some of the products and methods of making the same falling within the scope of the present invention. They are not to be considered in any way limitative of the invention. Changes and modifications can be made with respect to the invention. That is, the skilled person will recognize many variations in these examples to cover a wide area of formulas, ingredients, processing and mixtures to rationally adjust the  
15 nutrients and other elements of the invention for a variety of applications.

#### Example 1: Nutritional composition for children of 1-3 years according to the invention

A powdered milk for toddlers of 1 to 3 years is produced by preparing a slurry of ingredients,  
20 in particular skimmed milk, whole milk, maltodextrin, honey, vegetable oil, flavouring ingredients, an emulsifier, a vitamin mix and phospholipids rich in DHA. The slurry is subjected to heating for evaporation and then transformed to a powder by spray-drying.

The final composition of the nutrients of the growing up milk per 100 grams of dry matter  
25 (residual moisture not shown) is provided in Table 10 below.

The composition of Table 10 contains about 470 kcal per 100 g dry matter.

30 Thereafter, two different probiotic microorganisms, *Bifidobacterium longum* (ATCC BAA-999) and *Lactobacillus rhamnosus* (ATCC 53103) in powdered form are added so as to each provide at least  $1 \times 10^6$  CFU per 1 g of dry weight of the composition.

**Table 10:** Nutrients of the nutritional composition for children of 1-3 years

Nutrient		Unity	Weight per 100g
<b>Fat</b>		g	<b>18.46</b>
	Milk fat	g	3.56
	Non-milk Fat	g	14.53
	Lecithin	g	0.32
Comprised in the fats and oils			

	Linoleic acid	g	4.3
	Linolenic acid	mg	480
	Arachidonic acid	mg	24
	DHA	mg	23
<b>Protein</b>		g	<b>19.08</b>
	Casein	g	14.63
	Whey protein	g	4.38
<b>Available carbohydrates</b>		g	<b>55.15</b>
	Lactose	g	29.38
	Maltodextrin	g	20.61
	Other (mainly sugars: fructose, glucose, saccharose)	g	5.16
<b>Dietary fiber</b>		g	<b>3.58</b>
	Inulin & oligosaccharides	g	3.58
<b>Minerals (ash)</b>		g	<b>3.71</b>
	Sodium	mg	280
	Potassium	mg	890
	Chloride	mg	650
	Calcium	mg	720
	Phosphorus	mg	550
	Magnesium	mg	60
	Manganese	µg	40
	Selenium	µg	9
<b>Micronutrients (other)<sup>1</sup></b>		mg	318
	Sphingomyelin <sup>2</sup>	mg	30
	Choline <sup>2</sup>	mg	72
	Sialic acid <sup>2</sup>	mg	88
	Vitamin A (retinol)	µg RE <sup>3</sup>	540
	Vitamin D	µg	6.8
	Vitamin E	mg	5.4
	Vitamin K	µg	20
	Vitamin B <sub>2</sub>	mg	1.1
	Vitamin C	mg	54
	Thiamin (B <sub>1</sub> )	mg	0.94
	Niacin (vit B <sub>3</sub> )	mg	12
	Pyridoxin (vit B <sub>6</sub> )	mg	1.4
	Biotin (B <sub>8</sub> )	µg	27
	Folic acid (vit B <sub>9</sub> )	µg	140
	Pantothenic acid	mg	4
	Cobalamin (vit B <sub>12</sub> )	µg	0.9
	Taurine	mg	36
	Iodine <sup>2</sup>	µg	94

	Iron	mg	5.4
	Zinc	mg	6.8
Total solids		g	<b>100</b>

- 1) These micronutrients are also part of the ash
- 2) Naturally provided, in particular milk ingredients
- 3) RE=Retinol Equivalents

5 Example 2: Clinical Studies For Assessing Mental and Cognitive Performance of Children of 1.5 to about 2.5 years of age

In a clinical study, the cognitive, language, motor, adaptive behaviour and social-emotional skills of children are to be assessed.

10

For the study, a randomized, controlled, double blind, multi centre design with two parallel groups is used. A total of 400 healthy children of the age of 12 months of both sexes are recruited. The toddlers are split in two groups. One group receives the growing up milk as detailed in Example 1, the other group is the control group and receives milk powder. The treatment takes place until the child is 16 months old (for four months). Both groups take up food, in particular food as usual. The children receiving the nutritional composition of the invention receive 2 serving sizes per day. One serving size is obtained by mixing 32 g of powder with 200 ml water. The children of the control group receive an equivalent amount of the control powder.

20

Growth assessments include body weight, body height and head circumference.

Assessment of motor, cognitive and behavior development was done according to the Bayley Scales of Infant and Toddler Development, Third Edition (Bayley-III®), of Nancy Bayley, Ph.D., which is commercially available at:

25

(<http://pearsonassess.com/HAIWEB/Cultures/en-us/Productdetail.htm?Pid=015-8027-23X&Mode=summary>).

The Bayley - III consists of three administered scales: the Cognitive Scale, the Language Scale (including the Receptive communication and Expressive Communication subtests), and the Motor Scale (including the Fine Motor and Gross Motor subtests). The Bayley-III scale is completed by two additional questionnaires: The Social-Emotional Scale and Adaptive Behavior Scale. Questionnaires were filled in by parents and evaluated by trained psychologists at month 12 and month 24.

35

The test is adapted to the child's culture and language. According to the protocol of this test, each child's capacity is assessed separately.

5 At the end, the test group turned out to be better in most aspects measured by the test, in particular in the cognitive and language sub-tests. This suggests that the nutritional composition of the invention supports or improves cognitive and/or language skills.

10 In the area of cognitive performance, it is, for example, shown that the children receiving the nutritional composition of the present invention have better results in the areas of memory, in particular short term memory, alertness, learning capacity, attention capacity, concentration capacity and language ability.

15 These results show that the nutritional composition of the invention is a growing up milk that supports and/or improves the cognitive performance, in particular the learning and memory capacities in children of the age of 1 to 3 years.

**Claims**

1. The use of a nutritional composition for improving cognitive performance in a child of 1 to 3 years, said nutritional composition comprising:
- 5           - one or more protein source,  
          - one or more source of available carbohydrates,  
          - one or more lipid source,  
          - one or more probiotic microorganism, and,  
          - prebiotics,
- 10 wherein at least one of said one or more lipid source comprises DHA (docosahexaenoic acid).
2. The use of claim 1, wherein the child is a child of 1-2 years.
3. The use of claim 1 or 2, wherein cognitive performance refers to any one selected  
15 from short term memory, long term memory, learning capacity, alertness, attention, and concentration capacity.
4. The use of any one of the preceding claims, wherein said nutritional formula comprises at least 10 mg DHA.
- 20
5. The use of any one of the preceding claims, wherein said nutritional formula comprises at least 10 mg ARA.
5. The use of any one of the preceding claims, wherein said nutritional composition  
25 comprises at least 1 g linoleic acid and at least 100 mg  $\alpha$ -linolenic acid per 100 g of the dry weight of the nutritional composition.
6. The use of any one of the preceding claims, wherein said nutritional composition comprises, per 100 gram of dry matter, at least 10 mg (milligram) sphingomyelin.
- 30
7. The use of any one of the preceding claims, wherein said nutritional composition comprises, per 100 gram of dry matter, at least 40 mg sialic acid.
8. The use of any one of the preceding claims, wherein said nutritional composition  
35 comprises, per 100 gram of dry matter, at least 20 mg choline.

9. The use of any one of the preceding claims, wherein said nutritional composition comprises a combination of nutrients, said combination comprising LA, ALA, DHA, ARA, sphingomyelin, sialic acid, choline, folic acid, and taurine.
- 5 10. The use of any one of the preceding claims, wherein said nutritional composition comprises thiamine, folic acid and vitamin D.
11. The use of claim 9, wherein the nutritional composition further comprises iron, iodine and zinc.
- 10 12. The use of any one of the preceding claims, wherein said protein source provides about 12 to about 21 percent of the total energy, said source of available carbohydrates provides from about 40 to about 55 percent of the total energy, and said lipid source provides from about 31 to about 42 percent of the total energy of the composition.
- 15 13. The use of any one of the preceding claims, wherein said nutritional composition comprises at least two different probiotic microorganisms, each of said microorganisms being provided at about  $1 \times 10^5$  to  $1 \times 10^9$  CFU per g of dry matter of the composition.
- 20 14. The use of any one of the preceding claims, wherein said prebiotic comprises one or more selected from inulin, fructooligosaccharides, or a mixture of inulin and fructooligosaccharides.
- 25 15. The use of any one of the preceding claims, wherein said nutritional composition is a growing-up milk, which is provided in powdered form.
16. The use of any one of the preceding claims, wherein said nutritional composition comprises the nutrients as detailed in the Tables 1 + 4
- 30 17. A method for supporting and/improving cognitive performance in a child of 1 to 6 years, said method comprising the step of administrating a nutritional composition comprising:
- one or more protein source,
  - one or more source of available carbohydrates,
  - 35 - one or more lipid source,
  - one or more probiotic microorganism, and,
  - prebiotics,
- wherein at least one of said one or more lipid source comprises DHA (docosahexaenoic acid).

18. A method of providing nutrition, the method comprising the step of administering to a child of 1 to 6 years a nutritional composition comprising:

- one or more protein source,
- 5 - one or more source of available carbohydrates,
- one or more lipid source,
- one or more probiotic microorganism, and,
- prebiotics,

wherein said lipid source comprises DHA (docosahexaenoic acid).

10

19. A method for preparing a nutritional composition, said method comprising mixing:

- one or more protein source,
- one or more source of available carbohydrates,
- one or more lipid source,
- 15 - one or more probiotic microorganism, and,
- prebiotics,

wherein said lipid source comprises DHA (docosahexaenoic acid), and thereby obtaining the nutritional composition of the invention.

20 20. The uses and methods according to the preceding claims, wherein said nutritional composition is a growing up milk.

21. The uses and methods according to the preceding claims, wherein said nutritional composition is provided in powdered, reconstitutable form.

25