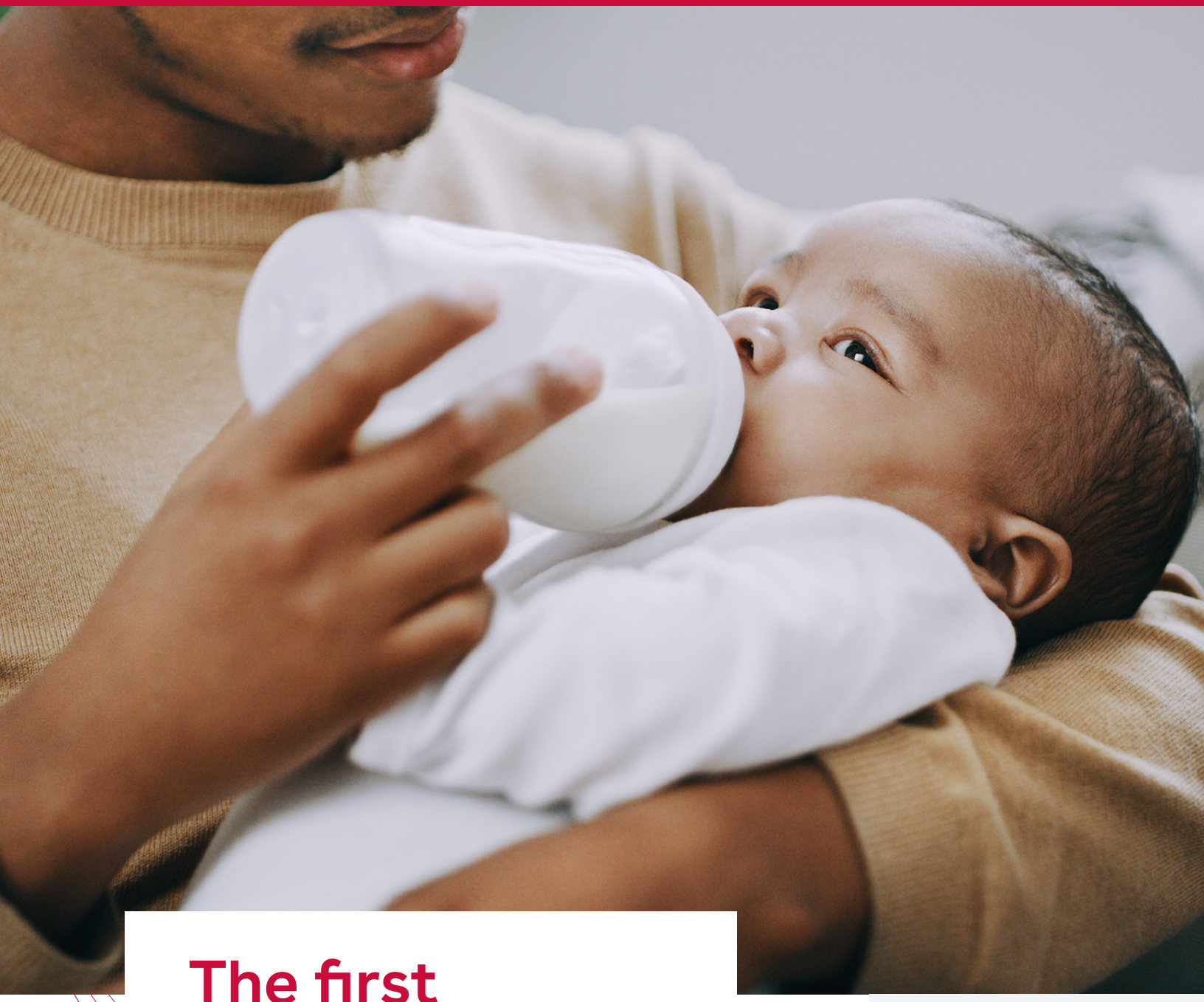


The first thousand days

We care about infants, right up to their very first steps.

Prinova
NAGASE Group

Contents

Health and nutrition solutions for the best start in life

Before we even take our first steps, much has been determined about our future. The thousand days spanning pregnancy and early infancy are a critical window - what happens then can have a dramatic impact on the rest of our lives.

Many physical and environmental factors play a part, but one of the most important is nutrition. How a baby and even the mum-to-be is nourished - before and during pregnancy and in the first two years of life - can affect IQ as well as affecting the risk of non-communicable diseases (NCDs) such as obesity in adult life.

Food and nutrition companies therefore have a huge responsibility to raise awareness of the importance of the first thousand days and to support parents across the world in giving their children the best possible start in life.

Wellness for everyone

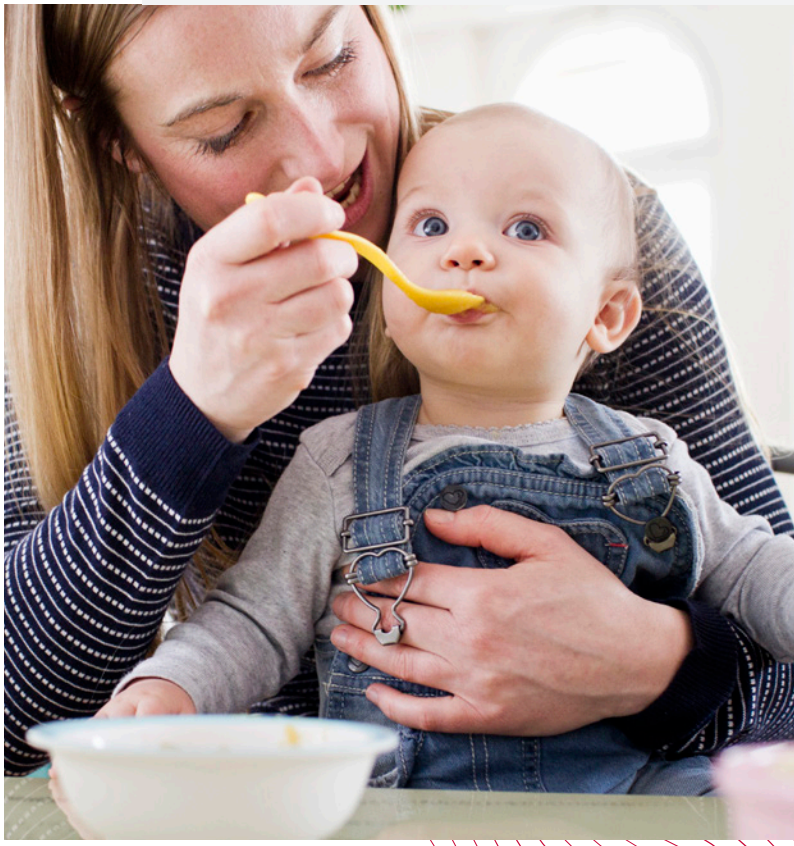
Prinova is committed to making wellness accessible at every stage of life and especially to meeting the needs of children and their parents. We therefore offer targeted health solutions to companies and brands worldwide.

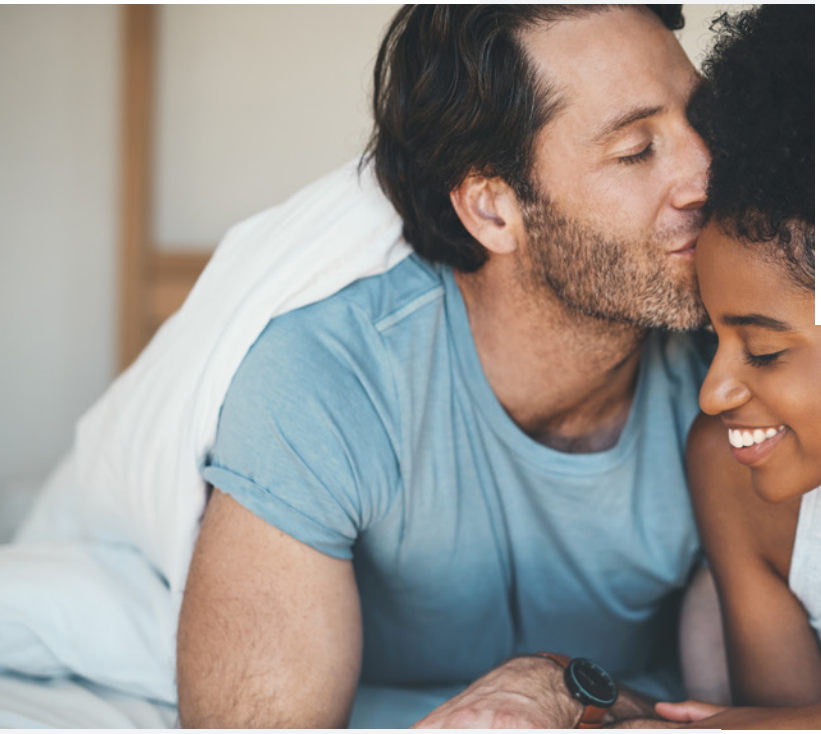
Our fortification and supplementation solutions can help at every step of the journey - from the point when a couple decides to start a family to the days when a child is uttering its first words. Our commitment is to deliver the right nutrients at every stage of early life for a brighter future. From pre-conception to the first days of life, every stage matters and has its specific consumption requirements. To fulfill those needs properly, adequate nutritional supplements may be necessary.

We believe in achieving synergies between ingredients in our nutritional blends to create added-value solutions for specific health conditions.

For example, calcium and vitamin D - which benefit skin, teeth and bone health and are hugely important in the early life stages - have been shown to function more effectively in combination.[1] The World Health Organization, meanwhile, recommends that folic acid and iron should be taken for a variety of reasons including tackling anemia.[2]

At every stage, Prinova is completely committed to helping manufacturers formulate responsibly, using scientifically proven ingredients to provide added-value products. Recognising the massive diversity in the needs of both consumers and manufacturers, a range of custom technical solutions are available, adhering to strict safety standards throughout.





Before the first thousand days - Fertility

The importance of good nutrition begins even before pregnancy. Food quality and fertility are strongly linked, and the chances of conceiving are greatly enhanced by a balanced diet. Moreover, the period before conception is the first opportunity to deliver the optimal ingredient supply to the expected baby.

Even the healthiest eaters can use extra help, so supplementation is widely recommended. Folic acid, for example, can boost the fertility of both men and women.[3] Women have further reason to supplement with folic acid prior to pregnancy as it can reduce the risk of neural tube defects such as spina bifida.[4] For men, zinc is important for optimal testosterone levels[5] and can work synergistically with folic acid to improve fertility[6], while vitamin C can improve sperm motility and viability[7] and vitamin E has been linked with improvements in sperm count and motility.[8, 9]

Research has found that iron supplements may decrease the risk of ovulatory infertility[10], while studies indicate that women should also supplement with zinc to improve the chances of conception.[11] Pre-conceptional folate and vitamin B12, meanwhile, have been linked to beneficial reproductive outcomes in clinical studies.[12]

In addition to nutritional needs related to fertility, many women of reproductive age have poor vitamin D status, so appropriate supplementation is recommended in many countries.

The important nutrients at this stage are:

- **Mother-to-be:** Fortified foods and / or supplements with folate or folic acid, vitamin D, iron, zinc and vitamin B12. Supplementation is especially important if a vegetarian or vegan diet is followed.
- **Father-to-be:** Supplements of folic acid, zinc, vitamin C and vitamin E.

Prinova offers supported vitamin, mineral and carotenoid functional ingredient solutions that are ideal for companies helping mothers and fathers meet these special health needs through supplementation.

Days 1 to 270 - Pregnancy

Pregnancy creates a range of nutritional demands, and diet is vital for both healthy fetal development and the mother's own wellbeing. Of course, nutrients are divided between mother and baby, and the gaps cannot easily be filled by a normal diet, particularly given that expectant mothers should avoid many nutrient-rich foods, such as fish and raw dairy.

Maternal nutritional deficiencies (and excesses) can harm the health of the unborn baby and are associated with poor maternal and fetal outcomes.[13] Fortunately, there is a wealth of evidence for the benefits of supplementation during pregnancy.

A 2017 meta-analysis concluded that multiple micronutrient supplementation during pregnancy contributes to lower risk of low birth weight.[14] A year earlier, a meta-analysis identified a decrease in risk for stillbirth among women receiving multivitamins plus iron and folic acid antenatally.[15] Another study showed that antenatal multi-micronutrient supplementation had a significant positive effect on the head circumference of children under the age of five.[16]

Studies have shown that the body needs increased levels of many specific micronutrients during pregnancy. Deficiencies in nutrients may occur when the needs of both the unborn child and mother are at their highest, particularly in the last trimester. During this period, the fetus stores 70% of its reserves of copper and zinc[17], also accumulating most of its iron, calcium, phosphorus and DHA for bone and brain growth respectively[18], effectively depleting the mother's reserves.

Research has also found that requirements for iron, iodine, calcium and folic acid increase during pregnancy.[19] Supplementation with vitamin D is recommended as well (even in countries with sunny climates), as is an increase in omega 3 fats (also known as DHA).[20]

In addition, supplementation with folic acid can help prevent neural tube birth defects during the first trimester of pregnancy as well as prior to conception.[21] While it is important to avoid excessive vitamin E intake, levels often drop during early pregnancy, and deficiency can lead to excessive free radicals, increasing the risk of aging the placenta, vascular endothelial injuries, and a higher number of hypertensive disorders in pregnancy.[22]

Magnesium can reduce the risk of fetal growth restriction and preeclampsia as well as increase birth weight[23] and vitamins A[24] (or beta carotene[25]), B12[26] and D[27] are also vital for fetal development. Supplementation with B12 is particularly important if the mother is vegan. Taking a vitamin B complex, meanwhile, can have a beneficial effect on birth weight, neonatal growth and risk of having a newborn that is small for its gestational age.[28]

In 2018, a systematic review and meta-analysis of vitamin K supplementation during pregnancy suggested it could offer numerous beneficial outcomes, including improved blood coagulation.[29] According to a 2019 study, alpha lipoic acid supplementation could have beneficial role on pregnancy as supported by preclinical observations indicating a protective effect against diabetic embryopathy, fetal losses, and ultrastructural alteration of diabetic placentas.[30]

A further consideration is the specific nutrient gaps that are apparent in different global regions. In many women in urban China, for example, intake of vitamins A and B6 plus calcium, magnesium and selenium has been found to be below recommended levels.[31]

In summary, the important nutrients for mums-to-be during pregnancy are:

- Fortified foods and/or supplements with iron, iodine, zinc, magnesium, calcium, folic acid, copper, phosphorus, vitamins A, D, K and B12, and DHA.
- Prinova offers a range of ways to support the health of both the mum-to-be and her baby. Our premix blends allow customers to fortify foods with folic acid, vitamins B12 and D and other nutrients.

Some vitamins from our range – such as E, D and K – are available without any nanoparticles. Engineered nanoparticles or nanomaterials are infinitesimally small ingredients that are commonly found in products including vitamin supplements. Research has raised concerns over their potential to harm human health.[32] According to an article published by the National Center for Biotechnology Information (NCBI), more than 20 of the most commonly used prenatal vitamin brands were detected to have toxic elements in their composition such as aluminum, nickel, titanium and thallium. Cumulative intake of toxic nanoparticles during this stage can cause toxicant exposure for the woman but the primary risk is to the child developing in-utero.[33]

The effect of maternal intake on the micronutrient content of breast milk:

MICRONUTRIENTS AFFECTED BY MATERNAL STATUS
Thiamin
Riboflavin
Vitamin B6
Vitamin B12
Vitamin D
Vitamin A
Iodine
Selenium

Low maternal intake or status of the above micronutrients decreases the amount secreted in milk, and low breast milk concentrations can adversely affect infant development.[34, 35]

The concentration in breast milk can be rapidly restored by increasing maternal intake.

MICRONUTRIENTS NOT AFFECTED BY MATERNAL STATUS
Zinc
Iron
Calcium

Maternal intake (and supplementation) and deficiency of the micronutrients above have relatively little effect on the amount secreted[36] but mothers can become vulnerable to depletion during lactation. These micronutrients are therefore more likely to benefit the mother than her infant.

Days 271 to 1,000 - The first two years

In the first two years of a child's life, physical growth is particularly fast. The brain develops rapidly – at birth, its weight is only 25% of that of an adult's brain. By the end of the second year, that figure is around 75%.[37]

During the first six months, breastfeeding is generally recommended as the best way to give a baby the best nutritional start. It can:

- Protect against infection[38]
- Support cognitive development[39]

Breast milk is rich in LC-PUFAs and iron, which are important for growth and brain development.[40] Furthermore, the oligosaccharides contained in human breast milk are known to affect the microbiome, supporting immunity in the long term.[41] To ensure the best start for her child, it is important that the mother receives the right nutrition during lactation. Low maternal intake of vitamins, minerals and carotenoids decreases the amount of some of the nutrients secreted in milk, with potential adverse effects for infant development.

Fortifying breast milk naturally through maternal nutrition and supplementation

With the right nutrition and supplementation, breast milk can be fortified naturally with specific nutrients needed by the child:

Composition (per 100ml) of mature human milk and compositional guidelines for infant formula.

COMPONENT	HUMAN MILK	INFANT FORMULA
Energy kJ (Kcal)	280 (67)	250-315 (60-75)
Protein g	1.3	1.2 - 1.95
Fat g	4.2	2.1 - 4.2
Carbohydrate g	7	4.6 - 9.1
Sodium mg	15	13 - 39
Chloride mg	43	32.5 -81
Calcium mg	35	59
Phosphorus mg	15	16.3 - 58.5
Iron mcg	76*	325 - 975*
Vitamin A mcg	60	39 - 117
Vitamin C mg	3.8	5.2
Vitamin E mcg	0.01	0.65 - 1.63

It is important that all breastfeeding women or infants have adequate vitamin D.[42] Alongside calcium, vitamin D is essential to bone health, which is key for children as they have a high rate of skeletal growth. Lactating women also need around 1,300 mcg of vitamin A daily – almost twice the amount required when pregnant.[43]

The carotenoid lutein has also been shown to be important during lactation. A 2014 study highlighted the connection between maternal intake, infant plasma concentrations and the importance of lutein as an antioxidant and in eye health, recommending that adequate levels are consumed either through diet or supplementation.[44]

For women who cannot breastfeed, it is important to provide the most complete nutrition possible through infant formula. Prinova provides manufacturers with the ingredients to ensure infant formula is dependably nutritious, with custom liquid or dry nutritional blends as well as water-soluble and fat-soluble vitamins.

Whether breastfeeding or using infant formula, vitamins free of nanoparticles are the best way to provide the correct nutrients for the baby. Silicon dioxide for instance, which is frequently found in baby formulas[45], is irritating to the skin and eyes on contact, while inhalation causes irritation in the respiratory tract.[46]

Complementing breast milk

WHO and UNICEF recommend that a child is exclusively breastfed for the first six months. After that (the remainder of the thousand days) they advise that breastfeeding continues alongside appropriate complementary foods. Other bodies advise that complementary foods should be added from four months. No sugar or salt should be added to complementary foods, while fruit juices and sugar-sweetened beverages should be avoided. For mothers who are unable to breastfeed, fortified infant formula is the best alternative.

Prinova offers a range of premixes for the fortification of baby foods and follow-on milks to ensure they deliver the right balance of nutrients.

Expert solutions at every step of the journey

With over two decades of experience in supplementation, Prinova offers a range of products to boost fertility and support the health of mother and baby during pregnancy and breastfeeding.

Meanwhile, we provide essential nutrients in premixes (both liquid and dry) to fortify infant formula, follow-on milks and baby foods. When Prinova works with you to develop premixes, we start by helping you decide what combination of nutrients is right for the specific needs of your customers. We then look at solubility issues with you to create blends that work. Finally, we custom-create the batch size required in the packaging you prefer, so it is exactly how you want it.

On each of the critical thousand days, and before, Prinova offers a solution to support the health of baby, mother, father, or all three.

Before conception

Nutrients such as folic acid, calcium and zinc can help boost fertility, and both men and women can benefit from dietary supplements and foods fortified with our custom premixes.

During pregnancy

Both mother-to-be and baby need folate, magnesium, DHA and other nutrients, Prinova's supplements and pre-mixes for fortified foods can play a vital role.

In early infancy

Our premixes for fortification of follow-on milks and baby foods can deliver all the vitamins and minerals a child needs in single or blended formats, while the breastfeeding mum can benefit from Prinova supplements and premix formulas.

In addition to offering customised premix solutions and unique ingredient concepts, we offer our industry partners flexible packaging options, co-branding opportunities, support with regulatory issues and marketing, and technical expertise.

WHO safe levels of vitamins & minerals

FAT SOLUBLE VITAMINS	0-3M	4-6M	7-9M	10-12M	1-3Y
Vitamin A	350RE	350RE	350RE	350RE	400RE
Vitamin D	10mcg	10mcg	10mcg	10mcg	10mcg
Vitamin E (Tocopherol)	0.15-2mg/kg BW	0.15-2mg/kg BW	0.15-2mg/kg BW	0.15-2mg/kg BW	0.15-2mg/kg BW
Vitamin C	20mg	20mg	20mg	20mg	20mg
Vitamin B1 (Thiamin)	0.3mg	0.3mg	0.3mg	0.3mg	0.5mg
Vitamin B2 (Riboflavin)	0.5mg	0.5mg	0.5mg	0.5mg	0.8mg
Vitamin B3 (Niacin)	5.4mg	5.4mg	5.4mg	5.4mg	9.0mg
Vitamin B12 (Cyanocobalamin)	0.1mcg	0.1mcg	0.1mcg	0.1mcg	0.5mcg
Folic Acid	16mcg*	24mcg	32mcg	32mcg	50mcg
Iron			8.5mg	8.5mg	5mg
Calcium	500mg	500mg	600mg	600mg	400mg
Zinc	5.3mg	3.1mg	5.6mg	5.6mg	5.5mg
Iodine	40mcg	40mcg	50mcg	50mcg	70-120mcg
Copper	0.33-0.55mg	0.37-0.62mg	0.6mg	0.6mg	0.56mg
Selenium	6mcg	9mcg	12mcg	12mcg	20mcg

Conclusion

Food and nutrition companies have a moral responsibility to meet the needs of children and parents across the world. The opportunity to have the greatest impact on lifelong wellbeing takes place in the narrow window of the first thousand days.

Prinova has the expertise, range of offerings and commitment to quality to help you give children the best possible start in life.

We provide custom dry and liquid premix blends for infant formulas, follow-on milks and other fortified foods to support mother and baby.

Our nutritional experts are on hand to formulate custom technical solutions based on your needs, including:

- Bespoke ingredients - spray dry for minerals
- Prinova's own vitamin and mineral range
- Vitamins E, D3, K1, B12 0.1%
- Stringently safe for infant nutrition
- Nanoparticle-free forms of vitamins E, D and K
- Flexible pack size from 0.1 kg to 25 kg

Nutritional portfolio for supplementation: Ingredients for dietary supplements

Carotenoids:

- Beta carotene
- Lutein
- Astaxanthin

Active ingredients for supplementation

Vitamins and minerals and other active ingredients including:

- Vitamins A, B1, B2, B3, B5, B6, B7, B9, D2, D3, E and K
- Chromium
- Iron
- Alpha lipoic acid

**Flexible formats are available for all the above.*

References

[1] Heaney, R.P. 'Vitamin D and calcium interactions: functional outcomes' The American Journal of Clinical Nutrition, Volume 88, Issue 2, August 2008

[2] World Health Organization, Daily iron and folic acid supplementation during pregnancy (Guidance summary)

[3] Gaskins A.J. & Chavarro J.E. 'Diet and fertility: a review' Am J Obstet Gynecol. 2018 Apr;218(4):379-389

[4] De-Regil LM, Peña-Rosas JP, Fernández-Gaxiola AC, Rayco-Solon P. Effects and safety of periconceptional oral folate supplementation for preventing birth defects. Cochrane Database of Systematic Reviews 2015, Issue 12. Art. No.: CD007950. DOI: 10.1002/14651858.CD007950.pub3.

[5] Prasad AS1, Mantzoros CS, Beck FW, Hess JW, Brewer GJ. Zinc status and serum testosterone levels of healthy adults Nutrition. 1996 May;12(5):344-8

[6] Buhling, K. 'Influence of oral vitamin and mineral supplementation on male infertility: a meta-analysis and systematic review' Reprod Biomed Online. 2019 Aug;39(2):269-279

[7] Akmal M1, Qadri JQ, Al-Waili NS, Thangal S, Haq A, Saloom KY Improvement in human semen quality after oral supplementation of vitamin C J Med Food. 2006 Fall;9(3):440-2

[8] Ener, K. et al. 'The impact of vitamin E supplementation on semen parameters and pregnancy rates after varicocelectomy: a randomised controlled study' Andrologia. 2016 Sep

[9] Moslemi M.K. & Tavanbakhsh S. 'Selenium-vitamin E supplementation in infertile men: effects on semen parameters and pregnancy rate' Int J Gen Med. 2011

[10] Chavarro, J.E. et al. 'Iron intake and risk of ovulatory infertility' Obstet Gynecol. 2006 Nov;108(5):1145-52.

[11] Chatzicharalampous, C. et al. 'Zinc: an essential metal for maintenance of female fertility' Fertility and Sterility 109(3):e19 March 2018

[12] Gaskins, A.J. et al. 'Association between serum folate and vitamin B-12 and outcomes of assisted reproductive technologies Am J Clin Nutr. 2015 Oct; 102(4): 943–950

[13] Purandare, C. N. 'Maternal Nutritional Deficiencies and Interventions' J Obstet Gynaecol India. 2012 Dec; 62(6): 621–623

[14] Haider B.A. & Bhutta Z.A. 'Multiple-micronutrient supplementation for women during pregnancy' Cochrane Database Syst Rev. 2017 Apr 13;4:CD004905. doi: 10.1002/14651858.CD004905.pub5.

[15] Rumbold, A. et al. 'Vitamin supplementation for preventing miscarriage (Review)' Cochrane Database Syst Rev. 2016 May 6;(5):CD004073

[16] Lu, W.-P., et al. 'Effects of multimicronutrient supplementation during pregnancy on postnatal growth of children under 5 years of age: a meta-analysis of randomized controlled trials' PLoS One 9, e88496 (2014)

[17] Airede, A.K. 'Copper, zinc and superoxide dismutase activities in premature infants: a review.' East Afr Med J. 1993 Jul;70(7):441-4

[18] C. S. Williamson 'Nutrition in pregnancy' British Nutrition Foundation (2006)

[19] Marangoni, F. 'Maternal Diet and Nutrient Requirements in Pregnancy and Breastfeeding. An Italian Consensus Document' Nutrients. 2016 Oct; 8(10): 629

[20] Società di Nutrizione Umana (SINU) LARN—Livelli di Assunzione di Riferimento di Nutrienti ed Energia per la Popolazione Italiana. SICS; Milano, Italy: 2014. pp. 1–655. IV Revisione

[21] De-Regil L.M. et al. 'Effects and safety of periconceptional oral folate supplementation for preventing birth defects' Cochrane Database of Systematic Reviews 2015, Issue 12. Art. No.: CD007950. DOI: 10.1002/14651858.CD007950.pub3.

[22] Han Chen et al. 'Role of serum vitamin A and E in pregnancy' Exp Ther Med. 2018

[23] Zarean, E. & Tarjan, A. 'Effect of Magnesium Supplement on Pregnancy Outcomes: A Randomized Control Trial' Adv Biomed Res. 2017; 6: 109

[24] Bastos Maia, S. et al. 'Vitamin A and Pregnancy: A Narrative Review' Nutrients. 2019 Mar; 11(3): 681

[25] Strobel M., Tinz J. & Biesalski HK. 'The importance of beta-carotene as a source of vitamin A with special regard to pregnant and breastfeeding women' Eur J Nutr. 2007 Jul;46 Suppl 1:I1-20

[26] Molloy et al. 'Maternal Vitamin B12 Status and Risk of Neural Tube Defects in a Population With High Neural Tube Defect Prevalence and No Folic Acid Fortification' Pediatrics March 2009, VOLUME 123 / ISSUE 3

[27] Hart, P.H. et al. 'Vitamin D in Fetal Development: Findings From a Birth Cohort Study' Pediatrics, September 2014

[28] Salcedo-Bellido, I. et al. 'Association between Vitamin Intake during Pregnancy and Risk of Small for Gestational Age' Nutrients. 2017 Dec; 9(12): 1277

[29] Shahrook, S. et al. 'Vitamin K supplementation during pregnancy for improving outcomes: a systematic review and meta-analysis' Sci Rep. 2018; 8: 11459

[30] Formoso, G. 'Inositol and antioxidant supplementation: Safety and efficacy in pregnancy' Diabetes Metab Res Rev. 2019 Jul; 35(5): e3154

[31] Liu F.L. et al. 'Nutrient Intakes of Pregnant Women and their Associated Factors in Eight Cities of China: A Cross-sectional Study' Chin Med J 2015;128:1778-86.

[32] Cornell Chronicle 'Nanoparticles in food, vitamins could harm human health' February 2012

[33] Nakashima, A. et al. 'Autophagy is a new protective mechanism against the cytotoxicity of platinum nanoparticles in human trophoblasts' Nature, April 2019

[34] Allen, L.H. 'B Vitamins in Breast Milk: Relative Importance of Maternal Status and Intake, and Effects on Infant Status and Function' Adv Nutr. 2012 May; 3(3): 362–369

[35] Dorea, J.G. 'Iodine nutrition and breast feeding' J Trace Elem Med Biol. 2002;16(4):207-20

[36] Yun Kyung Choi et al. 'Association of Maternal Diet With Zinc, Copper, and Iron Concentrations in Transitional Human Milk Produced by Korean Mothers' Clin Nutr Res. 2016 Jan; 5(1): 15–25

[37] Huelke et al. An Overview of Anatomical Considerations of Infants and Children in the Adult World of Automobile Safety Design Annu Proc Assoc Adv Automot Med. 1998; 42: 93–113

[38] Stuebe, A. 'The Risks of Not Breastfeeding for Mothers and Infants' Rev Obstet Gynecol. 2009 Fall; 2(4): 222–231

[39] Angelsena, N.K. et al. 'Breast feeding and cognitive development at age 1 and 5 years' Archives of Disease in Childhood October 2001; 85(3):183-8

[40] Kelishadi, R. et al. 'A study on lipid content and fatty acid of breast milk and its association with mother's diet composition' J Res Med Sci. 2012 Sep; 17(9): 824–82

[41] Le Doare, K. et al. 'Mother's Milk: A Purposeful Contribution to the Development of the Infant Microbiota and Immunity' Front Immunol. 2018; 9: 361

[42] The Scientific Advisory Committee on Nutrition (SACN) recommends pregnant and breastfeeding women take a vitamin D supplement of 10 micrograms daily

[43] Drugs and Lactation Database, National Library of Medicine (US)

[44] Sherry, C.L. et al. 'Lutein Supplementation Increases Breast Milk and Plasma Lutein Concentrations in Lactating Women and Infant Plasma Concentrations but Does Not Affect Other Carotenoids' The Journal of Nutrition, Volume 144, Issue 8, August 2014, Pages 1256–1263

[45] Friends of the Earth report 'Nano-Particles in Baby Formula' (2016)

[46] PubChem database