SCIENTIFIC OPINION

Scientific Opinion on the substantiation of health claims related to zinc and function of the immune system (ID 291, 1757), DNA synthesis and cell division (ID 292, 1759), protection of DNA, proteins and lipids from oxidative damage (ID 294, 1758), maintenance of bone (ID 295, 1756), cognitive function (ID 296), fertility and reproduction (ID 297, 300), reproductive development (ID 298), muscle function (ID 299), metabolism of fatty acids (ID 302), maintenance of joints (ID 305), function of the heart and blood vessels (ID 306), prostate function (ID 307), thyroid function (ID 308), acid-base metabolism (ID 360), vitamin A metabolism (ID 361) and maintenance of vision (ID 361) pursuant to Article 13(1) of Regulation (EC) No 1924/2006[1]

EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA)[2]

European Food Safety Authority (EFSA), Parma, Italy

SUMMARY

Following a request from the European Commission, the Panel on Dietetic Products, Nutrition and Allergies was asked to provide a scientific opinion on a list of health claims pursuant to Article 13 of Regulation (EC) No 1924/2006. This opinion addresses the scientific substantiation of health claims in relation to zinc and the following claimed effects: function of the immune system, DNA synthesis and cell division, protection of DNA, proteins and lipids from oxidative damage, maintenance of bone, cognitive function, fertility and reproduction, reproductive development, muscle function, metabolism of fatty acids, maintenance of joints, function of the heart and blood vessels, prostate function, thyroid function, acid-base metabolism, vitamin A metabolism and maintenance of vision.

1 On request from European Commission, Question No EFSA-Q-2008-1078, EFSA-Q-2008-1079, EFSA-Q-2008-1081, EFSA-Q-2008-1082, EFSA-Q-2008-1083, EFSA-Q-2008-1084, EFSA-Q-2008-1085, EFSA-Q-2008-1086, EFSA-Q-2008-1087, EFSA-Q-2008-1089, EFSA-Q-2008-1092, EFSA-Q-2008-1093, EFSA-Q-2008-1094, EFSA-Q-2008-1095, EFSA-Q-2008-1147, EFSA-Q-2008-1148, EFSA-Q-2008-2489, EFSA-Q-2008-2490, EFSA-Q-2008-2491, EFSA-Q-2008-2492, adopted on 02 July 2009.

2 Panel members: Jean-Louis Bresson, Albert Flynn, Marina Heinonen, Karin Hulshof, Hannu Korhonen, Pagona Lagiou, Martinus Løvik, Rosangela Marchelli, Ambroise Martin, Bevan Moseley, Hildegard Przyrembel, Seppo Salminen, Sean (J.J.) Strain, Stephan Strobel, Inge Tetens, Henk van den Berg, Hendrik van Loveren and Hans Verhagen.
Correspondence: nda@efsa.europa.eu.

For citation purposes: EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA); Scientific Opinion on the substantiation of health claims related to zinc and function of the immune system (ID 291, 1757), DNA synthesis and cell division (ID 292, 1759), protection of DNA, proteins and lipids from oxidative damage (ID 294, 1758), maintenance of bone (ID 295, 1756), cognitive function (ID 296), fertility and reproduction (ID 297, 300), reproductive development (ID 298), muscle function (ID 299), metabolism of fatty acids (ID 302), maintenance of joints (ID 305), function of the heart and blood vessels (ID 306), prostate function (ID 307), thyroid function (ID 308), acid-base metabolism (ID 360), vitamin A metabolism (ID 361) and maintenance of vision (ID 361) pursuant to Article 13 of Regulation (EC) No 1924/2006 on request from European Commission. EFSA Journal 2009; 7(9):1229. [34 pp.]. doi:10.2903/j.efsa.2009.1229 Available online: www.efsa.europa.eu

The scientific substantiation is based on the information provided by the Member States in the consolidated list of Article 13 health claims and references that EFSA has received from Member States or directly from stakeholders.

The food constituent that is the subject of the health claims is zinc, which is a well recognised nutrient and is measurable in foods by established methods. The Panel considers that zinc is sufficiently characterised.

The Panel concludes that a cause and effect relationship has been established between the dietary intake of zinc and normal function of the immune system, normal DNA synthesis and cell division, protection of DNA, proteins and lipids from oxidative damage, maintenance of normal bone, normal cognitive function, normal fertility and reproduction, normal metabolism of fatty acids, normal acid-base metabolism, normal vitamin A metabolism and maintenance of normal vision.

The evidence provided does not establish that inadequate intake of zinc leading to impaired function of the above-mentioned health relationships occurs in the general EU population.

The Panel considers that, in order to bear the claims, a food should be at least a source of zinc as per Annex to Regulation (EC) No 1924/2006. Such amounts can be easily consumed as part of a balanced diet. The target population is the general population.

The Panel notes, that reproductive development is related to children's development and health which is outside the scope of Article 13 of Regulation (EC) No 1924/2006.

The Panel concludes that a cause and effect relationship has not been established between the dietary intake of zinc and normal muscle function, maintenance of normal joints, normal function of the heart and blood vessels and normal prostate function.

The Panel concludes that the evidence provided is insufficient to establish a cause and effect relationship between the dietary intake of zinc and normal thyroid function.

KEY WORDS

Zinc, immune system, DNA synthesis, cell division, oxidative damage, bone, cognitive, fertility, reproduction, muscle, fatty acids, joints, heart, blood vessels, prostate, thyroid, acid-base metabolism, vitamin A , vision, health claims.

TABLE OF CONTENTS

BACKGROUND AS PROVIDED BY THE EUROPEAN COMMISSION

See Appendix A

TERMS OF REFERENCE AS PROVIDED BY THE EUROPEAN COMMISSION

See Appendix A

ACKNOWLEDGEMENTS

The European Food Safety Authority wishes to thank for the preparation of this opinion:

The members of the Working Group on Claims: Jean-Louis Bresson, Albert Flynn, Marina Heinonen, Hannu Korhonen, Martinus Løvik, Ambroise Martin, Hildegard Przyrembel, Seppo Salminen, Sean (J.J.) Strain, Inge Tetens, Henk van den Berg, Hendrik van Loveren and Hans Verhagen.

The members of the Claims Sub-Working Group on Bone/Teeth/Connective Tissue: Rikke Andersen, Olivier Bruyère, Albert Flynn, Ingegerd Johansson, Jukka Meurman and Hildegard Przyrembel.

The members of the Claims Sub-Working Group on Cardiovascular Health/Oxidative Stress: Antti Aro, Marianne Geleijnse, Marina Heinonen, Ambroise Martin, Wilhelm Stahl and Henk van den Berg.

INFORMATION AS PROVIDED IN THE CONSOLIDATED LIST

The consolidated list of health claims pursuant to Article 13 of Regulation (EC) No 1924/2006[3] submitted by Member States contains main entry claims with corresponding conditions of use and literature from similar health claims. The information provided in the consolidated list for the health claims subject to this opinion is tabulated in Appendix C.

ASSESSMENT

1. Characterisation of the food/constituent

The food constituent that is the subject of the claims is zinc, which is a well recognized nutrient and is measurable in foods by established methods. Zinc occurs naturally in foods and is authorised for addition to foods (Annex I of the Regulation (EC) No 1925/2006[4] and Annex I of Directive 2002/46/EC[5]). This evaluation applies to zinc naturally present in foods and those forms authorised for addition to foods (Annex II of the Regulation (EC) No 1925/2006 and Annex II of Directive 2002/46/EC).

The Panel considers that the food constituent, zinc, which is the subject of the health claims, is sufficiently characterised.

2. Relevance of the claimed effect to human health

2.1. Function of the immune system (ID 291, 1757)

The claimed effect is "immune system". The Panel assumes that the target population is the general population.

The Panel considers that the normal function of the immune system is beneficial to human health.

2.2. DNA synthesis and cell division (ID 292, 1759)

The claimed effect is "DNA synthesis / cell division". The Panel assumes that the target population is the general population.

The Panel notes that DNA synthesis and cell division are crucial processes for tissue growth and development and for tissue maintenance through cell turnover.

The Panel considers that normal DNA synthesis and cell division are beneficial to human health.

3 European Parliament and Council (2006). Regulation (EC) No 1924/2006 of the European Parliament and of the Council of 20 December 2006 on nutrition and health claims made on foods. Official Journal of the European Union OJ L 404, 30.12.2006. Corrigendum OJ L 12, 18.1.2007, p. 3–18.

4 European Parliament and of the Council (2006). Regulation (EC) No 1925/2006 of the European Parliament and of the Council of 20 December 2006 on the addition of vitamins and minerals and of certain other substances to foods. Official Journal of the European Union OJ L 404, 30.12.2006, p. 26-38.

5 European Parliament and of the Council (2002). Directive 2002/46/EC of the European Parliament and of the Council on the approximation of the laws of the Member States relating to food supplements Official Journal of the European Union OJ L 183, 12.7.2002, p. 51–57

2.3. Protection of DNA, proteins and lipids from oxidative damage (ID 294, 1758)

The claimed effects are "protection of body tissues and cells from oxidative damage; antioxidant activity; antioxidative properties" and "protection of body tissues and cells from oxidative damage". The Panel assumes that the target population is the general population.

Reactive oxygen species (ROS) including several kinds of radicals are generated in biochemical processes (e.g. respiratory chain) and as a consequence of exposure to exogenous factors (e.g. radiation, pollutants). These reactive intermediates damage biologically relevant molecules such as DNA, proteins and lipids if they are not intercepted by the antioxidant network which includes free radical scavengers like antioxidant nutrients.

The Panel considers that the protection of DNA, proteins and lipids from oxidative damage is beneficial to human health.

2.4. Maintenance of bone (ID 295, 1756)

The claimed effect is "bone formation". The Panel assumes that the target population is the general population.

The Panel considers that maintenance of normal bone is beneficial to human health.

2.5. Cognitive function (ID 296)

The claimed effect is "mental performance (where mental performance stands for those aspects of brain and nerve functions which determine aspects like concentration, learning, memory and reasoning, as well as resistance to stress)". The Panel assumes that the target population is the general population.

The Panel considers that normal cognitive function is beneficial to human health.

2.6. Fertility and reproduction (ID 297, 300)

The claimed effects are "normal fertility" and "reproduction in males". The Panel assumes that the target population is female and male population at the reproductive age.

The Panel considers that normal fertility and reproduction are beneficial to human health.

2.7. Reproductive development (ID 298)

The claimed effect is "reproductive development".

Reproductive development is related to children's development and health. The Panel notes that claims related to children's development and health are outside the scope of Article 13 of Regulation (EC) No 1924/2006.

2.8. Muscle function (ID 299)

The claimed effect is "required to maintain optimal muscle function". The Panel assumes that the target population is the general population.

The Panel considers that normal muscle function is beneficial to human health.

2.9. Metabolism of fatty acids (ID 302)

The claimed effect is "essential co-factor in fatty acid metabolism that impacts upon hormonal health". The Panel assumes that the target population is the general population.

The Panel notes that the claimed effect, hormonal health, has not been sufficiently defined in the evidence provided.

The Panel considers that normal metabolism of fatty acids is beneficial to human health.

2.10. Maintenance of joints (ID 305)

The claimed effect is "joint health". The Panel assumes that the target population is the general population.

The Panel notes that joint health relates to maintenance or improvement of joint function.

The Panel considers that maintenance of normal joints is beneficial to human health.

2.11. Function of the heart and blood vessels (ID 306)

The claimed effect is "cardiovascular health". The Panel assumes that the target population is the general population.

Cardiovascular health has not been defined in the list and is interpreted as function of the heart and blood vessels in order to allow a scientific evaluation.

The Panel considers that the normal function of the heart and blood vessels is beneficial to human health.

2.12. Prostate function (ID 307)

The claimed effect is "prostate health". The Panel assumes that the target population is the general male population.

The Panel considers that normal prostate function is beneficial to human health.

2.13. Thyroid function (ID 308)

The claim effect is "thyroid health". The Panel assumes that the target population is the general population.

The Panel considers that normal thyroid function is beneficial to human health.

2.14. Acid-base metabolism (ID 360)

The claimed effect is "acid-base metabolism". The Panel assumes that the target population is the general population.

The Panel considers that normal acid-base metabolism is beneficial to human health.

2.15. Vitamin A metabolism (ID 361)

The claimed effect is "involvement in vitamin A metabolism and process of vision". The Panel assumes that the target population is the general population.

The Panel considers that normal metabolism of vitamin A is beneficial to human health.

2.16. Maintenance of vision (ID 361)

The claimed effect is "involvement in vitamin A metabolism and process of vision". The Panel assumes that the target population is the general population.

The Panel considers that maintenance of normal vision is beneficial to human health.

3. Scientific substantiation of the claimed effect

Zinc is present in all tissues. It has essential structural, regulatory or catalytic roles in many enzymes. It maintains the configuration of a number of non-enzymatic proteins such as pre-secretory granules of insulin, some mammalian gene transcription proteins and thymulin. It facilitates hormone and receptor binding at membrane and nuclear levels, and it may maintain integrity of biomembranes. Consequently zinc participates in gene expression and in the mechanisms and control of major metabolic pathways involving proteins, carbohydrates, nucleic acids and lipids (SCF, 1993; DoH, 1991). Human zinc deficiency symptoms include retarded growth, depressed immune function, skin lesions, skeletal abnormalities, impaired reproductive ability and behavioural abnormalities such as changes in mood, loss of affect and emotional lability, anorexia, dysfunction of smell and taste, irritability and depression (SCF, 2003; EVM, 2002, Cousins, 2006).

3.1. Function of the immune system (ID 291, 1757)

Zinc deficiency is associated with a decline in most aspects of immune function. Lymphopaenia and thymic atrophy are observed. Cell mediated and antibody mediated responses are reduced. In addition to the generalized effects of zinc on DNA synthesis, zinc deficiency appears to induce apoptosis, resulting in a loss of B-cell and T-cell precursors within the bone marrow. Thymulin is a zinc-dependent enzyme that stimulates the development of T cells within the thymus. The production of cytokines by mononuclear cells is also reduced by zinc deficiency. Adequate zinc status is necessary for natural killers cell function. Zinc deficiency renders people more susceptible to infections, while zinc supplementation in humans has shown benefit in immune responses to bacterial and viral infections (Freake, 2006; King and Cousins, 2006; IoM, 2001). Infants with acrodermatitis enteropathica, a rare inborn error with a reduced ability to absorb dietary zinc, highlight the immune functions which are dependent on zinc. These patients show impaired lymphocyte proliferation and response to mitogens, decreased/inverted CD4/CD8 ratios, impaired NK activity and cytotoxicity.

The Panel concludes that a cause and effect relationship has been established between the dietary intake of zinc and the normal function of the immune system. However, the evidence provided does not establish that inadequate intake of zinc leading to impaired function of the immune system occurs in the general EU population.

3.2. DNA synthesis and cell division (ID 292, 1759)

Zinc has essential structural, regulatory or catalytic roles in many enzymes. Zinc plays a role in the stabilization of genetic material and is an essential component of some enzymes that participate in the synthesis of nucleic acids. About 1% of human genome codes for zinc finger proteins that play an important regulatory function in gene expression

Zinc inadequacy affects gene expression, DNA or RNA metabolism and impairs cell division (Freake, 2006; EVM, 2002; King and Cousins, 2006; IoM, 2001).

The Panel concludes that a cause and effect relationship has been established between the dietary intake of zinc and normal DNA synthesis and cell division. However, the evidence provided does not establish that inadequate intake of zinc leading to impaired DNA synthesis and cell division occurs in the general EU population.

3.3. Protection of DNA, proteins and lipids from oxidative damage (ID 294, 1758)

Zinc participates in the antioxidant defence system of the body. It can bind to thiol groups in proteins, making them less susceptible to oxidation. By displacing redox-reactive metals such as iron and copper from both proteins and lipids it can reduce the metal-induced formation of hydroxyl radicals and thus protect the macromolecules. Zinc induces the expression of metallothionein and increases the activity of catalase both of which can scavenge reactive oxygen species (ROS). Increased oxidative stress results in the release of zinc from metallothionein, presumably making it more available for other proteins. Zinc is a cofactor of the antioxidant enzyme copper/zinc-superoxide dismutase (Freake, 2006).

The Panel concludes that a cause and effect relationship has been established between the dietary intake of zinc and the protection of DNA, proteins and lipids from oxidative damage. However, the evidence provided does not establish that inadequate intake of zinc leading to impaired protection of DNA, proteins and lipids from oxidative damage occurs in the general EU population.

3.4. Maintenance of bone (ID 295, 1756)

Zinc is an essential cofactor for enzymes involved in synthesis of various bone matrix constituents and plays a particularly important role in the regulation of bone deposition and resorption. Zinc also plays a structural role in the bone matrix. Bone mineral is composed of hydroxyapatite crystals, which contain zinc complexed with fluoride. Zinc is required for osteoblastic activity, directly by activating aminoacyl-tRNA synthetase in osteoblastic cells and stimulating cellular protein synthesis. Zinc also promotes bone mineralization through its role as a cofactor of alkaline phosphatase (Lowe et al., 2002; Meunier et al., 2005).

Zinc deficiency results in impaired DNA synthesis and protein metabolism, which lead to negative effects on bone formation. In animals, zinc deficiency has been associated with abnormalities in bone growth, bone formation, and mineralization. Zinc concentration in bone is greatly reduced during zinc deficiency. Zinc intake has been reported to be associated with low bone mass in women. Furthermore, reduced serum or plasma zinc concentrations have also been reported in osteoporotic women (Ilich and Kerstetter, 2000; Lowe et al., 2002; Meunier, 2005).

A total of 54 references were cited for the substantiation of the claimed effect. Some studies show that serum zinc concentration could be reduced or that zinc excretion could be higher in bone disease (e.g. osteoporosis, osteopenia) (Herzberg et al., 1990; Holloway et al., 1996; Igarashi and Yamaguchi, 2001; Nishi, 1996; Sugiyama et al., 2000). Data from an observational study also suggest that low intake of zinc could be associated with an increased incidence of fracture (Elmstahl et al., 1998).

The Panel concludes that a cause and effect relationship has been established between the dietary intake of zinc and maintenance of normal bone. However, the evidence provided does not establish that intake of zinc inadequate for the maintenance of normal bone occurs in the general EU population.

3.5. Cognitive function (ID 296)

A total of 27 references were cited for the substantiation of the claimed effect. One of these, Maylor et al. (2006), studied the effects of zinc supplementation on cognitive function in healthy middle-aged and older adults. The study was a randomised double-blind placebo-controlled design (n=387) with healthy adults between 55 and 87 years. Zinc supplementation (0, 15 or 30 mg/day) were administered for 6 months. The Automated Neuropsychological Test Battery was performed at 0, 3 and 6 months. Younger adults (<70 years) performed significantly better on all tests than older adults (>70 years), and performance improved with practice on some measures. For two out of eight dependent variables, there were significant interactions indicating a beneficial effect (at 3 months only) of both 15 and 30 mg/day on one measure of spatial working memory and a detrimental effect of 15 mg/day on one measure of attention.

Evidence for improved cognitive function among school-aged children has been derived from studies of urban and rural children in China. In the rural population of children, the positive effect of zinc on cognitive function was dependent on the provision of other supplemental micronutrients, while in the urban group, supplemental zinc had a positive effect that was independent of the provision of other micronutrients (Hotz, 2006).

In the central nervous system zinc has a role as a neurosecretory product or cofactor, and is highly concentrated in the synaptic vesicles of specific neurons, called zinc containing neurons. Zinc-containing neurons are a subset of glutamatergic neurons (Frederickson, 2000).

The Panel concludes that a cause and effect relationship has been established between the dietary intake of zinc and normal cognitive function. However, the evidence provided does not establish that inadequate intake of zinc leading to impaired cognitive function occurs in the general EU population.

3.6. Fertility and reproduction (ID 297, 300)

Zinc plays a role in reproduction in males and females. Spermatogenesis is a zinc dependent process and seminal fluid is particularly rich in zinc. An important class of "zinc finger" transcription factors is the steroid/thyroid receptor superfamily, which is responsible for mediating the biological response to a wide range of hormonal and metabolic signals. Low dietary zinc status has been associated with low circulating concentrations of several hormones including testosterone. The original description of zinc deficiency in humans included lack of pubertal development (IoM, 2001; Freake, 2006).

The Panel concludes that a cause and effect relationship has been established between the dietary intake of zinc and normal fertility and reproduction. However, the evidence provided does not establish that inadequate intake of zinc leading to impaired fertility and reproduction occurs in the general EU population.

3.7. Muscle function (ID 299)

A total of six references were cited for the substantiation of the claimed effect. Four studies dealt with outcomes unrelated to the claimed effect such as serum testosterone levels and blood rheology during exercise and physical performance. The Panel notes, that these references did not provide any scientific data that could be used to substantiate the claimed effect.

In one double-blind cross over study with 16 women the effect of zinc on muscle strength and endurance, followed by zinc supplementation (135 mg/day for 14 days) was assessed using isometric and isokinetic tests of the knee extensor and flexor muscle groups . After zinc treatment, a significant increase in isometric endurance but not in dynamic endurance was observed (Krotkiewski et al., 1982). The Panel notes the small size of the study and the lack of information on the overall

nutritional status of intervention and control groups. The Panel also notes that the dose administered in this study is above the established upper intake level of 25 mg/day for zinc.

In a zinc repletion depletion study with eight men, the effect of zinc on isokinetic peak force and total work capacity was assessed. The peak force of the muscle groups tested was not affected by acute zinc depletion, but total work capacity for the knee extensor muscles and shoulder extensor and flexor muscles significantly declined (Van Loan et al., 1999).The Panel notes the small size of the study.

The Panel concludes that a cause and effect relationship has not been established between the dietary intake of zinc and normal muscle function.

3.8. Metabolism of fatty acids (ID 302)

Zinc is necessary for the conversion of linoleic acid to gamma-linolenic acid and the mobilization of dihomogammalinolenic acid for the synthesis of series-1 prostaglandins (IoM 2001, Freake HC, 2006).

The Panel concludes that a cause and effect relationship has been established between the dietary intake of zinc and normal metabolism of fatty acids. However, the evidence provided does not establish that inadequate intake of zinc leading to impaired fatty acid metabolism occurs in the general EU population.

3.9. Maintenance of joints (ID 305)

A total of 23 references were cited for the substantiation of the claimed effect, including three review and background papers, one national food consumption survey and 19 human studies. The Panel considers that the review and background papers, which were very general in nature, and the national food consumption survey, did not provide any scientific data that could be used to substantiate the claimed effect. A number of human studies dealt with zinc interaction with other nutrients, zinc metabolism and homeostasis and zinc status in different age populations. These studies dealt with outcomes unrelated to the claimed effects. The Panel notes, that these references did not provide any scientific data that could be used to substantiate the claimed effect.

The human studies in the diseased population (rheumatoid arthritis, juvenile arthritis or osteoarthritis patients) show that serum concentrations of zinc are reduced in some cases. As serum zinc can be influenced by inflammatory conditions this is not an unexpected result (Dore-Duffy et al., 1990; Grennan et al., 1980; Haugen et al., 1992; Helgeland et al., 2000; Helliwell et al., 1984; Honkanen et al., 1991; Naveh et al., 1997; Zoli et al., 1998; Niedermeier and Griggs, 1971). The Panel, moreover, considers that the evidence provided does not establish that patients with rheumatoid arthritis, juvenile arthritis or osteoarthritis are representative of the general population with regard to the functional condition of the joints.

The Panel concludes that a cause and effect relationship has not been established between the dietary intake of zinc and maintenance of normal joints.

3.10. Function of the heart and blood vessels (ID 306)

A total of 5 references were cited for the substantiation of the claimed effect, including three narrative reviews and two human studies. The Panel considers that the reviews, which were very general in nature, did not provide any scientific data that could be used to substantiate the claimed effect.

One human study dealt with erythrocyte carbonic anhydrase activity during exercise (Lukaski, 2005) which is unrelated to the claimed effect. In one cross sectional study Singh et al. (1998) reported an

association between a low dietary zinc intake, and low serum zinc concentrations, and an increased prevalence of coronary artery disease in a rural and urban Indian population. The Panel notes that limited conclusions can be drawn from this study on the claimed effect.

The Panel concludes that a cause and effect relationship has not been established between the dietary intake of zinc and normal function of the heart and blood vessels.

3.11. Prostate function (ID 307)

Prostate has high concentration of zinc. A total of 3 references were cited for the substantiation of the claimed effect. These studies dealt with outcomes such as the hypoxia-inducible-factor-1α, the anti-tumor effect of zinc in prostate cancer and the plasma zinc levels in prostate disorders, which are unrelated to the claimed effect. The Panel notes, that these references did not provide any scientific data that could be used to substantiate the claimed effect.

The Panel concludes that a cause and effect relationship has not been established between the dietary intake of zinc and normal prostate function.

3.12. Thyroid function (ID 308)

The major secretory product of the thyroid gland is thyroxine (T4), which is converted to the active thyroid hormone triiodo-L-thyronine (T3) within cells by deiodinases. T3 actions in its target tissues are initiated by binding of the hormone to specific thyroid hormone receptor proteins within the nucleus. T3 receptors are included among the nuclear zinc-binding proteins. Thus it appears that lack of zinc might impair thyroid hormone signalling by reducing the ability of the thyroid hormone receptor to bind to DNA and thereby influence target gene transcription (Freake, 2006; Freake et al., 2001).

A total of 7 references were cited for the substantiation of the claimed effect, including one opinion of a scientific body, one review paper, one human study and four *in vivo* studies.

In the review (Christianson, 1991) and the opinion of the scientific body (SCF 2003) the claimed effect was not stated. One *in vivo* study dealt with the effect of zinc deficiency on metabolic rate (Evans, 2004) which is unrelated to the claimed effect. The Panel notes that these references did not provide any scientific data that could be used to substantiate the claimed effect

In a 75 days metabolic study of low zinc intakes in six men, Wada and King (1986) reported that circulating TSH, total T4 and free T4 tended to decrease during the zinc depletion phase, returning to control concentrations after zinc repletion, but only the decrease in free T4 was considered to be significant. The Panel notes that limited conclusions can be drawn from this small study on the claimed effect.

In zinc deficient rats, reduced plasma T4 and T3 concentrations were observed (Lukaski et al., 1992; Freake et al., 2001). In zinc deficient guinea pigs, thyroid glands were smaller in size and showed histopathological changes of atrophy and degeneration in the follicles. They concluded that thyroid lesions were related to the depletion in serum T3 and T4 which was, in turn, owing to zinc deficiency (Gupta et al., 1997). The Panel considers that the evidence provided in animals does not predict an effect of zinc intake on thyroid function in humans.

The Panel concludes that the evidence provided is insufficient to establish a cause and effect relationship between the dietary intake of zinc and normal thyroid function.

3.13. Acid-base metabolism (ID 360)

Zinc has essential structural, regulatory or catalytic roles in many enzymes. Carbonic anhydrase, is a zinc metalloenzyme, where zinc is a direct participant in the catalytic function.

Blood and extracellular fluid pH are also tightly regulated by the presence of buffer systems which attenuate changes as a consequence of acid load mainly from cellular metabolism or the ingestion of acids in the diet. The principal buffer system is based on bicarbonate (HCO_3^-). In blood, the major product of oxidative metabolism, CO_2, reacts with water in the presence of carbonic anhydrase to form carbonic acid (H_2CO_3) which is relatively unstable and tends to dissociate and generate H^+ and HCO_3^-. *In vivo* studies have shown that dietary zinc deficiency significantly reduces red blood cell carbonic anhydrase activity (Freake, 2006; King and Cousins, 2006).

The Panel concludes that a cause and effect relationship has been established between the dietary intake of zinc and acid-base metabolism. However, the evidence provided does not establish that inadequate intake of zinc leading to impaired acid-base metabolism occurs in the general EU population.

3.14. Vitamin A metabolism (ID 361)

Zinc participates in the absorption, mobilization, transport and metabolism of micronutrients, including vitamin A, through its involvement in protein synthesis and cellular enzyme functions (IoM, 2001). In humans, cross-sectional studies and supplementation trials have failed to establish a consistent relationship between zinc and vitamin A status. However, a positive association may exist in malnourished populations in which deficiencies of both micronutrient often coexists (IoM, 2001; Christian and West, 1998). Because zinc is required for the synthesis of retinol binding protein (RBP), zinc deficiency influences the mobilization of vitamin A from the liver and its transport into the circulation (IoM, 2001).

The Panel concludes that a cause and effect relationship has been established between the dietary intake of zinc and normal metabolism of vitamin A. However, the evidence provided does not establish that inadequate intake of zinc leading to impaired vitamin A metabolism occurs in the general EU population.

3.15. Maintenance of vision (ID 361)

Zinc regulates the metabolic conversion of retinol to retinaldeyde (retinal) through the zinc-dependent enzyme retinol dehydrogenase. The conversion of retinol to retinal is a critical step in the visual cycle in the retina of the eye (Christian and West, 1998; Grahan, 2001). In retina and retinal pigment epithelium, there is evidence that zinc can modify photoreceptor plasma membranes, regulate the light-rhodopsin reaction, modulate synaptic transmission and serve as an antioxidant (Grahan et al., 2001; Ugarte and Osborne, 2001). A significant reduction in the synthesis of rhodopsin was reported in zinc deficient rats, which was postulated to be owing to impaired protein (opsin and alcohol dehydrogenase) synthesis (IoM, 2001). Zinc deficiency in humans has been shown to result in poor dark-adaptation, which improved after the provision of a therapeutic dose of 220 mg/day of zinc (Morrison, 1978).

The Panel concludes that a cause and effect relationship has been established between the dietary intake of zinc and maintenance of normal vision. However, the evidence provided does not establish that intake of zinc inadequate for the maintenance of normal vision occurs in the general EU population.

4. Panel's comments on the proposed wording

4.1. Function of the immune system (ID 291, 1757)

The Panel considers that the following wording reflects the scientific evidence: "Zinc contributes to a normal function of the immune system".

4.2. DNA synthesis and cell division (ID 292, 1759)

The Panel considers that the following wording reflects the scientific evidence: "Zinc contributes to normal DNA synthesis and cell division".

4.3. Protection of DNA, proteins and lipids from oxidative damage (ID 294, 1758)

The Panel considers that the following wording reflects the scientific evidence: "Zinc contributes to the protection of cell constituents from oxidative damage".

4.4. Maintenance of bone (ID 295, 1756)

The Panel considers that the following wording reflects the scientific evidence: "Zinc contributes to maintenance of normal bone".

4.5. Cognitive function (ID 296)

The Panel considers that the following wording reflects the scientific evidence: "Zinc contributes to normal cognitive function".

4.6. Fertility and reproduction (ID 297, 300)

The Panel considers that the following wording reflects the scientific evidence: "Zinc contributes to normal fertility and reproduction"

4.7. Metabolism of fatty acids (ID 302)

The Panel considers that the following wording reflects the scientific evidence: "Zinc contributes to normal metabolism of fatty acids".

4.8. Acid-base metabolism (ID 360)

The Panel considers that the following wording reflects the scientific evidence: "Zinc contributes to normal acid-base metabolism".

4.9. Vitamin A metabolism (ID 361)

The Panel considers that the following wording reflects the scientific evidence: "Zinc contributes to normal metabolism of vitamin A".

4.10. Maintenance of vision (ID 361)

The Panel considers that the following wording reflects the scientific evidence: "Zinc contributes to maintenance of normal vision".

5. Conditions and possible restrictions of use

The Panel considers that in order to bear the claim a food should be at least a source of zinc as per Annex to Regulation (EC) No 1924/2006. The target population is the general population. Such amounts can be easily consumed as part of a balanced diet. Tolerable Upper Intake Levels (UL) have been established for zinc as 25 mg/day in adults and to pregnant and lactating woman. For children and adolescents UL was established as 7 mg/day for 1-3 years, 10 mg/day for 4-6 years, 13 mg/day for 7-10 years, 18 mg/day for 11-14 years and 22 mg/day for 15-17 years (SCF 2003).

CONCLUSIONS

On the basis of the data presented, the Panel concludes that:

- The food constituent, zinc, which is the subject of the health claims is sufficiently characterised.

Function of the immune system (ID 291, 1757)

- The claimed effect is "immune system". The target population is assumed to be the general population. Normal function of the immune system is beneficial to human health.
- A cause and effect relationship has been established between the dietary intake of zinc and normal function of the immune system.
- However, the evidence provided does not establish that inadequate intake of zinc leading to impaired function of the immune system occurs in the general EU population.
- The following wording reflects the scientific evidence: "Zinc contributes to a normal function of the immune system".

DNA synthesis and cell division (ID 292, 1759)

- The claimed effect is "DNA synthesis / cell division". The target population is assumed to be the general population. Normal DNA synthesis and cell division are beneficial to human health.
- A cause and effect relationship has been established between the dietary intake of zinc and normal DNA synthesis and cell division.
- The evidence provided does not establish that inadequate intake of zinc leading to impaired DNA synthesis and cell division occurs in EU subpopulations.
- The following wording reflects the scientific evidence: "Zinc contributes to normal DNA synthesis and cell division".

Protection of DNA, proteins and lipids from oxidative damage (ID 294, 1758)

- The claimed effects are "protection of body tissues and cells from oxidative damage; antioxidant activity; antioxidative properties" and "protection of body tissues and cells from oxidative damage". The target population is assumed to be the general population. Protection of DNA, proteins and lipids from oxidative damage is beneficial to human health.
- A cause and effect relationship has been established between the dietary intake of zinc and the protection of DNA, proteins and lipids from oxidative damage.

- The evidence provided does not establish that inadequate intake of zinc leading to impaired protection of DNA, proteins and lipids from oxidative damage occurs in the general EU population.

- The following wording reflects the scientific evidence: "Zinc contributes to the protection of cell constituents from oxidative damage".

Maintenance of bone (ID 295, 1756)

- The claimed effect is "bone formation" The target population is assumed to be the general population. Maintenance of normal bone is beneficial to human health.

- A cause and effect relationship has been established between the dietary intake of zinc and maintenance of normal bone.

- The evidence provided does not establish that intake of zinc inadequate for the maintenance of normal bone occurs in the general EU population.

- The following wording reflects the scientific evidence: "Zinc contributes to maintenance of normal bone".

Cognitive function (ID 296)

- The claimed effect is "mental performance (where mental performance stands for those aspects of brain and nerve functions which determine aspects like concentration, learning, memory and reasoning, as well as resistance to stress)". The target population is assumed to be the general population. Normal cognitive function is beneficial to human health.

- A cause and effect relationship has been established between the dietary intake of zinc and normal cognitive function.

- The evidence provided does not establish that inadequate intake of zinc leading to impaired cognitive function occurs in the general EU population

- The following wording reflects the scientific evidence: "Zinc contributes to normal cognitive function".

Fertility and reproduction (ID 297, 300)

- The claimed effects are "normal fertility" and "reproduction in males". The target population is assumed to be female and male population at the reproductive age. Normal fertility and reproduction are beneficial to human health.

- A cause and effect relationship has been established between the dietary intake of zinc and normal fertility and reproduction.

- The evidence provided does not establish that inadequate intake of zinc leading to impaired fertility and reproduction occurs in the general EU population.

- The following wording reflects the scientific evidence: "Zinc contributes to normal fertility and reproduction".

Reproductive development (ID 298)

- The claimed effect is "reproductive development".

- Reproductive development is related to children's development and health which is outside the scope of Article 13 of Regulation (EC) No 1924/2006.

Muscle function (ID 299)

- The claimed effect is "required to maintain optimal muscle function". The target population is assumed to be the general population. Normal muscle function is beneficial to human health.

- A cause and effect relationship has not been established between the dietary intake of zinc and normal muscle function.

Metabolism of fatty acids (ID 302)

- The claimed effect is "essential co-factor in fatty acid metabolism that impacts upon hormonal health". The target population is assumed to be the general population. Normal metabolism of fatty acids is beneficial to human health.

- A cause and effect relationship has been established between the dietary intake of zinc and normal fatty acid metabolism.

- The evidence provided does not establish that inadequate intake of zinc leading to impaired fatty acid metabolism occurs in the general EU population.

- The following wording reflects the scientific evidence: "Zinc contributes to normal metabolism of fatty acids".

Maintenance of joints (ID 305)

- The claimed effect is "joint health". The target population is assumed to be the general population. Maintenance of normal joints is beneficial to human health.

- A cause and effect relationship has not been established between the dietary intake of zinc and maintenance of normal joints.

Function of the heart and blood vessels (ID 306)

- The claimed effect is "cardiovascular health". The target population is assumed to be the general population. Normal function of the heart and blood vessels is beneficial to human health.

- A cause and effect relationship has not been established between the dietary intake of zinc and normal function of the heart and blood vessels.

Prostate function (ID 307)

- The claimed effect is "prostate health". The Panel assumes that the target population is the general male population. Normal prostate function is beneficial to human health.

- A cause and effect relationship has not been established between the dietary intake of zinc and normal prostate function.

Thyroid function (ID 308)

- The claimed effect is "thyroid health". The target population is assumed to be the general population. Normal thyroid function is beneficial to human health.

- The evidence provided is insufficient to establish a cause and effect relationship between the dietary intake of zinc and normal thyroid function.

Acid-base metabolism (ID 360)

- The claimed effect is "acid-base metabolism". The target population is assumed to be the general population. Normal acid-base metabolism is beneficial to human health.
- A cause and effect relationship has been established between the dietary intake of zinc and acid-base metabolism.
- The evidence provided does not establish that inadequate intake of zinc leading to impaired acid-base metabolism occurs in the general EU population.
- The following wording reflects the scientific evidence: "Zinc contributes to normal acid-base metabolism".

Vitamin A metabolism (ID 361)

- The claimed effect is "involvement in vitamin A metabolism and process of vision". The target population is assumed to be the general population. Normal metabolism of vitamin A is beneficial to human health.
- A cause and effect relationship has been established between the dietary intake of zinc and normal metabolism of vitamin A.
- The evidence provided does not establish that inadequate intake of zinc leading to impaired vitamin A metabolism occurs in the general EU population.
- The following wording reflect the scientific evidence: "Zinc contributes to normal metabolism of vitamin A".

Maintenance of vision (ID 361)

- The claimed effect is "involvement in vitamin A metabolism and process of vision". The target population is assumed to be the general population. Normal vision is beneficial to human health.
- A cause and effect relationship has been established between the dietary intake of zinc and maintenance of normal vision.
- There evidence provided does not establish that intake of zinc inadequate for the maintenance of normal vision occurs in the general EU population.
- The following wording reflect the scientific evidence: "Zinc contributes to maintenance of normal vision".

Conditions and possible restrictions of use

- In order to bear the claim a food should be at least a source of zinc as per Annex to Regulation (EC) No 1924/2006. The target population is the general population. Such amounts can be easily consumed as part of a balanced diet.

DOCUMENTATION PROVIDED TO EFSA

Health claims pursuant to Article 13 of Regulation (EC) No 1924/2006 (No: EFSA-Q-2008-1078, EFSA-Q-2008-1079, EFSA-Q-2008-1081, EFSA-Q-2008-1082, EFSA-Q-2008-1083, EFSA-Q-2008-1084, EFSA-Q-2008-1085, EFSA-Q-2008-1086, EFSA-Q-2008-1087, EFSA-Q-2008-1089, EFSA-Q-2008-1092, EFSA-Q-2008-1093, EFSA-Q-2008-1094, EFSA-Q-2008-1095, EFSA-Q-2008-1147, EFSA-Q-2008-1148, EFSA-Q-2008-2489, EFSA-Q-2008-2490, EFSA-Q-2008-2491, EFSA-Q-2008-2492). The scientific substantiation is based on the information provided by the Members States in the consolidated list of Article 13 health claims and references that EFSA has received from Member States or directly from stakeholders.

The full list of supporting references as provided to EFSA is available on: http://www.efsa.europa.eu/panels/nda/claims/article13.htm.

REFERENCES

Christian P and West KP, Jr., 1998. Interactions between zinc and vitamin A: an update. Am J Clin Nutr, 68 Suppl 2, 435S-441S.

Christianson DW, 1991. Structural biology of zinc. Advances in Protein Chemistry, 42, 281-355

Cousins RJ 2006. Zinc. In Present Knowledge in Nutrition. Bowman BA and Russell RM (eds.). International Life Sciences Institute (ILSI), Washington, DC, 445-457.

DoH (Department of Health), 1991. Dietary Reference Values for Food Energy and Nutrients for the United Kingdom.

Dore-Duffy P, Peterson M, Catalanotto F, Marlow S, Ho SY, Ostrom M, Weinstein A, 1990. Zinc profiles in rheumatoid arthritis. Clin Exp Rheumatol, 8, 541-546.

Elmstahl S, Gullberg B, Janzon L, Johnell O, Elmstahl B, 1998. Increased incidence of fractures in middle-aged and elderly men with low intakes of phosphorus and zinc. Osteoporos Int, 8, 333-340.

Evans SA, Overton JM, Alshingiti A, Levenson CW, 2004. Regulation of metabolic rate and substrate utilization by zinc deficiency. Metabolism, 53, 727-732.

Expert Group on Vitamins and Minerals, 2002. Review of zinc. Revised Version.

Freake HC, 2006. Zinc: Physiology. In: Encyclopedia of Human Nutrition. Caballero B, Allen L, Prentice A (eds.). Academic Press, San Diego, 447-454.

Freake HC, Govoni KE, Guda K, Huang C, Zinn SA, 2001. Actions and interactions of thyroid hormone and zinc status in growing rats. J Nutr, 131, 1135-1141.

Frederickson CJ, Suh SW, Silva D, Thompson RB, 2000. Importance of zinc in the central nervous system: the zinc-containing neuron. J Nutr, 130, 1471S-1483S.

Grahn BH, Paterson PG, Gottschall-Pass KT, Zhang Z, 2001. Zinc and the eye. J Am Coll Nutr, 20 Suppl 2, 106-118.

Grennan DM, Knudson JM, Dunckley J, MacKinnon MJ, Myers DB, Palmer DG, 1980. Serum copper and zinc in rheumatoid arthritis and osteoarthritis. N Z Med J, 91, 47-50.

Gupta RP, Verma PC, Garg SL, 1997. Effect of experimental zinc deficiency on thyroid gland in guinea-pigs. Ann Nutr Metab, 41, 376-381.

Haugen MA, Hoyeraal HM, Larsen S, Gilboe IM, Trygg K, 1992. Nutrient intake and nutritional status in children with juvenile chronic arthritis. Scand J Rheumatol, 21, 165-170.

Helgeland M, Svendsen E, Forre O, Haugen M, 2000. Dietary intake and serum concentrations of antioxidants in children with juvenile arthritis. Clin Exp Rheumatol, 18, 637-641.

Helliwell M, Coombes EJ, Moody BJ, Batstone GF, Robertson JC, 1984. Nutritional status in patients with rheumatoid arthritis. Ann Rheum Dis, 43, 386-390.

Herzberg M, Foldes J, Steinberg R, Menczel J, 1990. Zinc excretion in osteoporotic women. J Bone Miner Res, 5, 251-257.

Holloway WR, Collier FM, Herbst RE, Hodge JM, Nicholson GC, 1996. Osteoblast-mediated effects of zinc on isolated rat osteoclasts: inhibition of bone resorption and enhancement of osteoclast number. Bone, 19, 137-142.

Hotz H, 2006. Zinc: Deficiency in developing countries, intervention studies. In: Encyclopedia of Human Nutrition. Caballero B, Allen L, Prentice A (eds.). Academic Press, San Diego, 454-462.

Honkanen V, Konttinen YT, Sorsa T, Hukkanen M, Kemppinen P, Santavirta S, Saari H, Westermarck T, 1991. Serum zinc, copper and selenium in rheumatoid arthritis. J Trace Elem Electrolytes Health Dis, 5, 261-263.

Igarashi A and Yamaguchi M, 2001. Increase in bone growth factors with healing rat fractures: the enhancing effect of zinc. Int J Mol Med, 8, 433-438.

Ilich JZ and Kerstetter JE, 2000. Nutrition in bone health revisited: a story beyond calcium. J Am Coll Nutr, 19, 715-737.

Institute of Medicine (IoM), 2001. Dietary Reference Intakes for Vitamin A, Vitamin K, Arsenic, Boron, Chromium, Copper, Iodine, Iron, Manganese, Molybdenum, Nickel, Silicon, Vanadium, and Zinc. National Academies Press. Washington DC.

King JC and Cousins RJ, 2006. Zinc. In: Modern Nutrition in Health and Disease. Shils M, Shike M, Ross C, Caballero B, Cousins R (eds.). Lippincott Williams & Wilkins, Baltimore, Philadephia, 271-285.

Krotkiewski M, Gudmundsson M, Backstrom P, Mandroukas K, 1982. Zinc and muscle strength and endurance. Acta Physiol Scand, 116, 309-311.

Lowe NM, Fraser WD, Jackson MJ, 2002. Is there a potential therapeutic value of copper and zinc for osteoporosis? Proc Nutr Soc, 61, 181-185.

Lukaski HC, 2005. Low dietary zinc decreases erythrocyte carbonic anhydrase activities and impairs cardiorespiratory function in men during exercise. American Journal of Clinical Nutrition, 81, 1045-1051.

Lukaski HC, Hall CB, Marchello MJ, 1992. Impaired thyroid hormone status and thermoregulation during cold exposure of zinc-deficient rats. Horm Metab Res, 24, 363-366.

Maylor EA, Simpson EE, Secker DL, Meunier N, Andriollo-Sanchez M, Polito A, Stewart-Knox B, McConville C, O'Connor JM, Coudray C, 2006. Effects of zinc supplementation on cognitive function in healthy middle-aged and older adults: the ZENITH study. British Journal of Nutrition, 96, 752-760.

Meunier N, O'Connor JM, Maiani G, Cashman KD, Secker DL, Ferry M, Roussel AM, Coudray C, 2005. Importance of zinc in the elderly: the ZENITH study. Eur J Clin Nutr, 59 Suppl 2, S1-4.

Morrison SA, Russell RM, Carney EA, Oaks EV, 1978. Zinc deficiency: a cause of abnormal dark adaptation in cirrhotics. Am J Clin Nutr, 31, 276-281.

Naveh Y, Schapira D, Ravel Y, Geller E, Scharf Y, 1997. Zinc metabolism in rheumatoid arthritis: plasma and urinary zinc and relationship to disease activity. J Rheumatol, 24, 643-646.

Niedermeier W and Griggs JH, 1971. Trace metal composition of synovial fluid and blood serum of patients with rheumatoid arthritis. J Chronic Dis, 23, 527-536.

Nishi Y, 1996. Zinc and growth. J Am Coll Nutr, 15, 340-344.

Singh RB, Niaz MA, Rastogi SS, Bajaj S, Gaoli Z, Shoumin Z, 1998. Current zinc intake and risk of diabetes and coronary artery disease and factors associated with insulin resistance in rural and urban populations of North India. J Am Coll Nutr, 17, 564-570.

SCF (Scientific Committee on Food), 2003. Opinion of the Scientific Committee on Food on the Tolerable Upper Intake Level of Zinc.

SCF (Scientific Committee on Food), 1993. Nutrient and energy intakes for the European Community. Reports of the Scientific Committee on Food (Thirty-first series). Luxembourg.

Sugiyama T, Tanaka H, Kawai S, 2000. Improvement of periarticular osteoporosis in postmenopausal women with rheumatoid arthritis by beta-alanyl-L-histidinato zinc: a pilot study. J Bone Miner Metab, 18, 335-338.

Van Loan MD, Sutherland B, Lowe NM, Turnlund JR, King JC, 1999. The effects of zinc depletion on peak force and total work of knee and shoulder extensor and flexor muscles. Int J Sport Nutr, 9, 125-135.

Ugarte M and Osborne NN, 2001. Zinc in the retina. Prog Neurobiol, 64, 219-249.

Wada L and King JC, 1986. Effect of low zinc intakes on basal metabolic rate, thyroid hormones and protein utilization in adult men. J Nutr, 116, 1045-1053.

Zoli A, Altomonte L, Caricchio R, Galossi A, Mirone L, Ruffini MP, Magaro M, 1998. Serum zinc and copper in active rheumatoid arthritis: correlation with interleukin 1 beta and tumour necrosis factor alpha. Clin Rheumatol, 17, 378-382.

APPENDICES

APPENDIX A

BACKGROUND AND TERMS OF REFERENCE AS PROVIDED BY THE EUROPEAN COMMISSION

The Regulation 1924/2006 on nutrition and health claims made on foods[6] (hereinafter "the Regulation") entered into force on 19th January 2007.

Article 13 of the Regulation foresees that the Commission shall adopt a Community list of permitted health claims other than those referring to the reduction of disease risk and to children's development and health. This Community list shall be adopted through the Regulatory Committee procedure and following consultation of the European Food Safety Authority (EFSA).

Health claims are defined as "any claim that states, suggests or implies that a relationship exists between a food category, a food or one of its constituents and health".

In accordance with Article 13 (1) health claims other than those referring to the reduction of disease risk and to children's development and health are health claims describing or referring to:

a) the role of a nutrient or other substance in growth, development and the functions of the body; or

b) psychological and behavioural functions; or

c) without prejudice to Directive 96/8/EC, slimming or weight-control or a reduction in the sense of hunger or an increase in the sense of satiety or to the reduction of the available energy from the diet.

To be included in the Community list of permitted health claims, the claims shall be:

(i) based on generally accepted scientific evidence; and

(ii) well understood by the average consumer.

Member States provided the Commission with lists of claims as referred to in Article 13 (1) by 31 January 2008 accompanied by the conditions applying to them and by references to the relevant scientific justification. These lists have been consolidated into the list which forms the basis for the EFSA consultation in accordance with Article 13 (3).

ISSUES THAT NEED TO BE CONSIDERED

IMPORTANCE AND PERTINENCE OF THE FOOD[7]

Foods are commonly involved in many different functions[8] of the body, and for one single food many health claims may therefore be scientifically true. Therefore, the relative importance of food e.g. nutrients in relation to other nutrients for the expressed beneficial effect should be considered: for functions affected by a large number of dietary factors it should be considered whether a reference to a single food is scientifically pertinent.

[6] OJ L12, 18/01/2007
[7] The term 'food' when used in this Terms of Reference refers to a food constituent, the food or the food category.
[8] The term 'function' when used in this Terms of Reference refers to health claims in Article 13(1)(a), (b) and (c).

It should also be considered if the information on the characteristics of the food contains aspects pertinent to the beneficial effect.

SUBSTANTIATION OF CLAIMS BY GENERALLY ACCEPTABLE SCIENTIFIC EVIDENCE

Scientific substantiation is the main aspect to be taken into account to authorise health claims. Claims should be scientifically substantiated by taking into account the totality of the available scientific data, and by weighing the evidence, and shall demonstrate the extent to which:

(a) the claimed effect of the food is beneficial for human health,

(b) a cause and effect relationship is established between consumption of the food and the claimed effect in humans (such as: the strength, consistency, specificity, dose-response, and biological plausibility of the relationship),

(c) the quantity of the food and pattern of consumption required to obtain the claimed effect could reasonably be achieved as part of a balanced diet,

(d) the specific study group(s) in which the evidence was obtained is representative of the target population for which the claim is intended.

EFSA has mentioned in its scientific and technical guidance for the preparation and presentation of the application for authorisation of health claims consistent criteria for the potential sources of scientific data. Such sources may not be available for all health claims. Nevertheless it will be relevant and important that EFSA comments on the availability and quality of such data in order to allow the regulator to judge and make a risk management decision about the acceptability of health claims included in the submitted list.

The scientific evidence about the role of a food on a nutritional or physiological function is not enough to justify the claim. The beneficial effect of the dietary intake has also to be demonstrated. Moreover, the beneficial effect should be significant i.e. satisfactorily demonstrate to beneficially affect identified functions in the body in a way which is relevant to health. Although an appreciation of the beneficial effect in relation to the nutritional status of the European population may be of interest, the presence or absence of the actual need for a nutrient or other substance with nutritional or physiological effect for that population should not, however, condition such considerations.

Different types of effects can be claimed. Claims referring to the maintenance of a function may be distinct from claims referring to the improvement of a function. EFSA may wish to comment whether such different claims comply with the criteria laid down in the Regulation.

WORDING OF HEALTH CLAIMS

Scientific substantiation of health claims is the main aspect on which EFSA's opinion is requested. However, the wording of health claims should also be commented by EFSA in its opinion.

There is potentially a plethora of expressions that may be used to convey the relationship between the food and the function. This may be due to commercial practices, consumer perception and linguistic or cultural differences across the EU. Nevertheless, the wording used to make health claims should be truthful, clear, reliable and useful to the consumer in choosing a healthy diet.

In addition to fulfilling the general principles and conditions of the Regulation laid down in Article 3 and 5, Article 13(1)(a) stipulates that health claims shall describe or refer to "the role of a nutrient or other substance in growth, development and the functions of the body". Therefore, the requirement to

describe or refer to the 'role' of a nutrient or substance in growth, development and the functions of the body should be carefully considered.

The specificity of the wording is very important. Health claims such as "Substance X supports the function of the joints" may not sufficiently do so, whereas a claim such as "Substance X helps maintain the flexibility of the joints" would. In the first example of a claim it is unclear which of the various functions of the joints is described or referred to contrary to the latter example which specifies this by using the word "flexibility".

The clarity of the wording is very important. The guiding principle should be that the description or reference to the role of the nutrient or other substance shall be clear and unambiguous and therefore be specified to the extent possible i.e. descriptive words/ terms which can have multiple meanings should be avoided. To this end, wordings like "strengthens your natural defences" or "contain antioxidants" should be considered as well as "may" or "might" as opposed to words like "contributes", "aids" or "helps".

In addition, for functions affected by a large number of dietary factors it should be considered whether wordings such as "indispensable", "necessary", "essential" and "important" reflects the strength of the scientific evidence.

Similar alternative wordings as mentioned above are used for claims relating to different relationships between the various foods and health. It is not the intention of the regulator to adopt a detailed and rigid list of claims where all possible wordings for the different claims are approved. Therefore, it is not required that EFSA comments on each individual wording for each claim unless the wording is strictly pertinent to a specific claim. It would be appreciated though that EFSA may consider and comment generally on such elements relating to wording to ensure the compliance with the criteria laid down in the Regulation.

In doing so the explanation provided for in recital 16 of the Regulation on the notion of the average consumer should be recalled. In addition, such assessment should take into account the particular perspective and/or knowledge in the target group of the claim, if such is indicated or implied.

TERMS OF REFERENCE

HEALTH CLAIMS OTHER THAN THOSE REFERRING TO THE REDUCTION OF DISEASE RISK AND TO CHILDREN'S DEVELOPMENT AND HEALTH

EFSA should in particular consider, and provide advice on the following aspects:

- Whether adequate information is provided on the characteristics of the food pertinent to the beneficial effect.

- Whether the beneficial effect of the food on the function is substantiated by generally accepted scientific evidence by taking into account the totality of the available scientific data, and by weighing the evidence. In this context EFSA is invited to comment on the nature and quality of the totality of the evidence provided according to consistent criteria.

- The specific importance of the food for the claimed effect. For functions affected by a large number of dietary factors whether a reference to a single food is scientifically pertinent.

In addition, EFSA should consider the claimed effect on the function, and provide advice on the extent to which:

- the claimed effect of the food in the identified function is beneficial.

- a cause and effect relationship has been established between consumption of the food and the claimed effect in humans and whether the magnitude of the effect is related to the quantity consumed.

- where appropriate, the effect on the function is significant in relation to the quantity of the food proposed to be consumed and if this quantity could reasonably be consumed as part of a balanced diet.

- the specific study group(s) in which the evidence was obtained is representative of the target population for which the claim is intended.

- the wordings used to express the claimed effect reflect the scientific evidence and complies with the criteria laid down in the Regulation.

When considering these elements EFSA should also provide advice, when appropriate:

- on the appropriate application of Article 10 (2) (c) and (d) in the Regulation, which provides for additional labelling requirements addressed to persons who should avoid using the food; and/or warnings for products that are likely to present a health risk if consumed to excess.

APPENDIX B

EFSA DISCAIMER

The present opinion does not constitute, and cannot be construed as, an authorisation to the marketing of the food/food constituent, a positive assessment of its safety, nor a decision on whether the food/food constituent is, or is not, classified as foodstuffs. It should be noted that such an assessment is not foreseen in the framework of Regulation (EC) No 1924/2006.

It should also be highlighted that the scope, the proposed wordings of the claims and the conditions of use as proposed in the Consolidated List may be subject to changes, pending the outcome of the authorisation procedure foreseen in Article 13(3) of Regulation (EC) No 1924/2006.

APPENDIX C

Table 1. Main entry health claims related to zinc, including conditions of use from similar claims, as proposed in the Consolidated List.

ID	Food or Food constituent	Health Relationship	Proposed wording
291	Zinc	Immune system	Zinc is necessary for the function of the immune system; Zinc helps to support a healthy immune system.
	Conditions of use - Person group: Erwachsene, Amount of consumption: 10 Milligramm (mg), Periood of consumption: Dauersupplementierung, Upper limit: 15 Milligramm (mg) - 15 mg/day - Mindestens 15 % RDA je 100 g oder 100 ml oder je portion gemäß 90/496/EWG - Daily amount to be consumed to produce claimed effect: 7 miligram(s). Are there factors that could interfere with bioavailability: Yes. Please give reason: The utilization of dietary zinc is highly dependent on diet composition. Length of time after consumption for claimed effect to become apparent: Habitual intake. Is there a limit to the amount of food which should be consumed in order to avoid adverse health effects: No - Number of nutrients/other substances that are essential to claimed effect: 5. Names of nutrient and Quantity in Average daily serving: 160 micrograms Vitamin A , 0.4 miligrams Vitamin B6, 1,000,000,000 CFUs LGG, 12 miligrams Vitamin C, 3 miligrams Zinc. Weight of average daily food serving: 100 gram(s). Daily amount to be consumed to produce claimed effect: 100 gram(s). Number of food portions this equates to in everyday food portions: 1. Are there factors that could interfere with bioavailability: No. Length of time after consumption for claimed effect to become apparent: it is dependent on the individual's vitamin status. The product should be consumed in the context of a healthy diet and lifestyle - Number of nutrients/other substances that are essential to claimed effect: 1. Names of nutrient/other substances and Quantity in Average daily serving: 15 miligrams zinc. Weight of average daily food serving: 30 gram(s). Daily amount to be consumed to produce claimed effect: 30 gram(s). Are there factors that could interfere with bioavailability: Yes. Please give reason: 1. Presence of Citric Acid inhibits the bio-availability of Zinc. 2. Presence of Vitamin C inhibits the bio-availability of Zinc. 3. Presence of Sorbitol, or Mannitol inhibits the bio-availability of Zinc. 4. It is recommended not to exceed the RDA (Recommended Daily Allowance). Length of time after consumption for claimed effect to become apparent: It is apparent immediately. State the maximum limit in mg/kg body weight/day: 150.00. Potential adverse health effects: 1. Excessive Zinc consumption has been associated with copper deficiency, altered iron function, reduced immune function. Other symptoms include nausea, vomiting, abdominal cramps. Where applicable outline nutritional composition (g per 100g) of food: Total Fat: .00, Saturated Fat: .00, Trans Fat: .00, Sugar: 98.60, Salt: .00, Sodium: .00. - Food supplement with 15mg of zinc in the daily dose - Must at least be a source of mineral/s as per annex to regulation 1924/2006. Agency guidance for supplements is that Products containing >25mg zinc should carry the label statement: 'Long term intake [of this amount of zinc] may lead to anaemia'. Applicable to both children and adults. Only for at least 0.5 g vitamin C, 10 mg zinc - Person group: Jugendliche, Erwachsene, Amount of consumption: 5 bis 15 Milligramm (mg), Upper limit: 15 Milligramm (mg)		

	Food or Food component	Health Relationship	Proposed wording
292	Zinc	DNA synthesis/cell division	Zinc is needed for cell division
	Conditions of use - Must at least be a source of mineral/s as per annex to Regulation 1924/2006. Agency guidance for supplements is that products containing >25mg zinc should carry the label statement: 'Long term intake [of this amount of zinc] may lead to anaemia. Applicable to both children and adults. - Person group: Jugendliche, Erwachsene. Amount of consumption: 5 bis 15 Milligramm (mg). Upper limit: 15 Milligramm (mg) - Person group: Erwachsene (adults). Amount of consumption: 10 Milligramm (mg). Period of consumption: Dauersupplementierung. Upper limit: 15 Milligramm (mg) - 500-1000 mg Calcium als Calciumcitrat, 10 µg Vitamin D, 8-16 mg Zink - 67% AJR enfants de 6 à 14 ans - 100% AJR : femmes enceintes		
294	**Food or Food component**	**Health Relationship**	**Proposed wording**
	Zinc	Protection of body tissues and cells from oxidative damage; Antioxidant activity, Antioxidative properties	Zinc is necessary for cells' protection; Zinc helps scavenging free radicals.
	Conditions of use - Person group: Jugendliche, Erwachsene. Amount of consumption: 5 bis 15 Milligramm (mg). Upper limit: 15 Milligramm (mg) - Food supplement with 15mg of zinc in the daily dose - Must at least be a source of Mineral/s as per annex to regulation 1924/2006. Agency guidance for supplements is that products containing >25mg zinc should carry the label statement: 'Long term intake [of this amount of zinc] may lead to anaemia - Amount of consumption: Tagesdosierungen zwischen 5 und 15 mg Zink und 0,5 - 1,5 mg Kupfer. - 10mg / d (Männer)–7mg / d (Frauen)—Erwachsene.		
295	**Food or Food component**	**Health Relationship**	**Proposed wording**
	Zinc	Bone formation	Zinc helps maintain strong bones. Zinc is needed for the structure of strong/healthy bones
	Conditions of use - Food supplement with 15mg of zinc in the daily dose - Must at least be a source of mineral/s as per annex to Regulation 1924/2006. Agency guidance for supplements is that products containing >25mg zinc should carry the label statement: 'Long term intake [of this amount of zinc] may lead to anaemia.' Applicable to both adults and children.		

	- Amount of consumption: Tagesdosierungen zwischen 5 und 15 mg Zink und 0,5 - 1,5 mg Kupfer. - 500-1000 mg Calcium als Calciumcitrat, 10 µg Vitamin D, 8-16 mg Zink - 67% AJR enfants de 6 à 14 ans. 100% AJR: femmes enceintes		
296	**Food or Food component**	**Health Relationship**	**Proposed wording**
	Zinc	Mental performance (where mental performance stands for those aspects of brain and nerve functions which determine aspects like concentration, learning, memory and reasoning, as well as resistance to stress)	Zinc is needed/important for mental function and performance
	Conditions of use - Minimum15% RDA (2,25 mg) dziennie - 15 % RDA. Agency guidance for supplements is that products containing >25 mg of zinc should carry the label advisory statement "Long term intake [of this amount of zinc] may lead to anaemia"		
297	**Food or Food component**	**Health Relationship**	**Proposed wording**
	Zinc	Normal fertility	Zinc is required for normal fertility
	Conditions of use - Must meet minimum requirements for use of the claim "source of [name of vitamin/s] and/or [name of mineral/s]" as per Annex to Regulation 1924/2006. Agency guidance for supplements is that products containing >25mg zinc should carry the label statement: 'Long term intake [of this amount of zinc] may lead to anaemia.'		
298	**Food or Food component**	**Health Relationship**	**Proposed wording**
	Zinc	Reproductive development	Zinc contributes to normal reproductive development. Zinc is needed for the development of the reproductive system.
	Conditions of use - Must at least be a source of mineral/s as per annex to Regulation 1924/2006. Agency guidance for supplements is that products containing >25mg zinc should carry the label statement: 'Long term intake [of this amount of zinc] may lead to anaemia.' Applicable to both children and adults.		
299	**Food or Food component**	**Health Relationship**	**Proposed wording**
	Zinc	Required to maintain optimal muscle function	Without enough zinc in your diet, muscular performance will be impaired
	Conditions of use - Minimum of 12 mg zinc per day. Must meet minimum requirements for use of the claim "source of [name of vitamin/s] and/or [name of mineral/s)" as per Annex to Regulation 1924/2006. Agency guidance for supplements is that products containing >25mg zinc should carry the label statement: 'Long term intake [of this amount of zinc] may lead to anaemia.'		

	Food or Food component	Health Relationship	Proposed wording
300	Zinc	Reproduction in males	To help maintain a healthy male reproductive system
	Conditions of use - The product must contain at least 15% of the RDA. Agency guidance for supplements is that products containing >25mg zinc should carry the label statement: 'Long term intake [of this amount of zinc] may lead to anaemia.' - Zinc gluconate: 7,5- 10 mg.		
302	**Food or Food component**	**Health Relationship**	**Proposed wording**
	Zinc	An essential co-factor in fatty acid metabolism that impacts upon hormonal health	Zinc contributes to the maintenance of hormonal health Zinc helps maintain hormonal health Zinc is an essential co-factor in fatty acid metabolism which impacts on hormonal health.
	Conditions of use - The product must contain no less than 15% RDA. Agency guidance for supplements is that products containing >25mg zinc should carry the label advisory statement "long term intake of this amount of zinc may lead to anaemia ". - Tagesbedarf gemäß NwKVO 15 mg pro Tag.		
305	**Food or Food component**	**Health Relationship**	**Proposed wording**
	Zinc	Joint health	Zinc promotes joint health Zinc helps support the function of the joints
	Conditions of use - 3-6 mg of zinc. Must meet minimum requirements for use of the claim "source of [name of vitamin/s] and/or [name of mineral/s]" as per Annex to Regulation 1924/2006. Agency guidance for supplements is that products containing >25 mg of Zinc should carry the label advisory statement "Long term intake may lead to anaemia".		
306	**Food or Food component**	**Health Relationship**	**Proposed wording**
	Zinc	Cardiovascular health	Zinc contributes to a healthy cardiovascular system
	Conditions of use - 3-6 mg of zinc. Must meet minimum requirements for use of the claim "source of [name of vitamin/s] and/or [name of mineral/s]" as per Annex to Regulation 1924/2006. Agency guidance for supplements is that products containing >25 mg of Zinc should carry the label advisory statement "Long term intake may lead to anemia".		
307	**Food or Food component**	**Health Relationship**	**Proposed wording**
	Zinc	Prostate Health	Zinc for a healthy prostate Zinc helps to maintain a healthy prostate

	Conditions of use - 3-6 mg of zinc. Must meet minimum requirements for use of the claim "source of [name of vitamin/s] and/or [name of mineral/s] " as per Annex to Regulation 1924/2006. Agency guidance for supplements is that products containing >25 mg of zinc should carry the label advisory statement 'Long term intake [of this amount of zinc]* may lead to anemia.'		
308	**Food or Food component**	**Health Relationship**	**Proposed wording**
	Zinc	Thyroid Health	Boron supports a healthy thyroid function Boron is beneficial for the thyroid function
	Conditions of use - 3-6 mg of zinc. Must meet minimum requirements for use of the claim "source of [name of vitamin/s] and/or [name of mineral/s]" as per Annex to Regulation 1924/2006. Agency guidance for supplements is that products containing >25 mg of Zinc should carry the label advisory statement "Long term intake may lead to anaemia "		
360	**Food or Food component**	**Health Relationship**	**Proposed wording**
	Zinc	Acid-base metabolism	Zinc is important for the regulation of the acid base balance
	Conditions of use - Must meet minimum requirements for use of the claim "source of [name of vitamin/s] and/or [name of mineral/s]" as per Annex to Regulation 1924/2006. Agency guidance for supplements is that products containing >25 mg of zinc should carry the label advisory statement "Long term intake [of this amount of zinc] may lead to anaemia"		
361	**Food or Food component**	**Health Relationship**	**Proposed wording**
	Zinc	Involvement in vitamin A metabolism and process of vision	Zinc is highly concentrated in the eye. Zinc is necessary for the transport of vitamin A in the body. Zinc is involved in the metabolism of vitamin A and vision. Zinc is necessary for dark adaptation. Zinc contributes to cell protection from damages caused by free radicals (e.g. as a constituent of superoxide dismutase)
	Conditions of use - Person group: Jugendliche, Erwachsene. Amount of consumption: 5 bis 15 Milligramm (mg). Upper limit: 15 Milligramm (mg) - Minimum 15% RDA per daily dosage as per 90/496/EC. Agency guidance for supplements is that products containing >25 mg of zinc should carry the label advisory statement "'Long term intake [of this amount of zinc]* may lead to anaemia."		

1756	**Food or Food component**	**Health Relationship**	**Proposed wording**
	Zinc and copper enriched Saccharomyces cerevisiae ATY-SC-109	Bone formation	Zinc helps maintain strong bones.
	Conditions of use - 15% RDA/day = 2,25 mg Zn ; 390 mg powder supports 15% RDA for Zn and 55% RDA for Cu ; Daily Total Dose Zn = 25 mg/day		
1757	**Food or Food component**	**Health Relationship**	**Proposed wording**
	Zinc and copper enriched Saccharomyces cerevisiae ATY-SC-109	Immune System	Zinc is necessary for the function of the immune system Zinc helps to support a healthy immune system.
	Conditions of use - 15% RDA/day = 2,25 mg Zn ; 390 mg powder supports 15% RDA for Zn and 55% RDA for Cu ; Daily Total Dose Zn = 25 mg/day		
1758	**Food or Food component**	**Health Relationship**	**Proposed wording**
	Zinc and copper enriched Saccharomyces cerevisiae ATY-SC-109	Protection of body tissues and cells from oxidative damage	-Zinc is necessary for cells protection from oxidation -Zinc helps scavenging free radicals.
	Conditions of use - 15% RDA/day = 2,25 mg Zn ; 390 mg powder supports 15% RDA for Zn and 55% RDA for Cu ; Daily Total Dose Zn = 25 mg/day		
1759	**Food or Food component**	**Health Relationship**	**Proposed wording**
	Zinc and copper enriched Saccharomyces cerevisiae ATY-SC-109	DNA synthesis / cell division	-Zinc is needed for cell division.
	Conditions of use - 15% RDA/day = 2,25 mg Zn ; 390 mg powder supports 15% RDA for Zn and 55% RDA for Cu ; Daily Total Dose Zn = 25 mg/day		

GLOSSARY / ABBREVIATIONS

DNA	Deoxyribonucleic acid
AMD	Age related macular degeneration
RBP	Retinol binding protein
UL	Tolerable Upper Intake Levels