

SCIENTIFIC OPINION

Scientific Opinion on the substantiation of health claims related to vitamin A and cell differentiation (ID 14), function of the immune system (ID 14), maintenance of skin and mucous membranes (ID 15, 17), maintenance of vision (ID 16), maintenance of bone (ID 13, 17), maintenance of teeth (ID 13, 17), maintenance of hair (ID 17), maintenance of nails (ID 17), metabolism of iron (ID 206), and protection of DNA, proteins and lipids from oxidative damage (ID 209) pursuant to Article 13(1) of Regulation (EC) No 1924/2006¹

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 vitamin A and the following claimed effects: cell differentiation, function of the immune system, maintenance of skin and mucous membranes, maintenance of vision, maintenance of bone, maintenance of teeth, maintenance of hair, maintenance of nails, metabolism of iron, and protection of DNA, proteins and lipids from oxidative damage. 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 vitamin A, which is a well recognised nutrient and is measurable in foods by established methods. The Panel considers that vitamin A is sufficiently characterised.

The Panel concludes that a cause and effect relationship has been established between the dietary intake of vitamin A and normal cell differentiation, normal function of the immune system,

1 On request from the European Commission, Question No EFSA-Q-2008-800, EFSA-Q-2008-801, EFSA-Q-2008-802, EFSA-Q-2008-803, EFSA-Q-2008-804, EFSA-Q-2008-993, EFSA-Q-2008-996 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

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maintenance of normal skin and mucous membranes, maintenance of normal vision, and normal metabolism of iron.

The evidence provided does not establish that inadequate intake of vitamin A leading to impaired functions of the above-mentioned health relationships occur in the general EU population.

The Panel considers that, in order to bear the claims, a food should be at least a source of vitamin A 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 concludes that a cause and effect relationship has not been established between the dietary intake of vitamin A and maintenance of normal bone, maintenance of normal teeth, maintenance of normal hair, maintenance of normal nails, and protection of DNA, proteins and lipids from oxidative damage.

KEY WORDS

Vitamin A, cell differentiation, immune system, skin, vision, bone, teeth, hair, nails, iron, oxidative damage, health claims.

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BACKGROUND AS PROVIDED BY THE EUROPEAN COMMISSION

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TERMS OF REFERENCE AS PROVIDED BY THE EUROPEAN COMMISSION

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EFSA DISCLAIMER

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INFORMATION AS PROVIDED IN THE CONSOLIDATED LIST

The consolidated list of health claims pursuant to Article 13 of Regulation (EC) No 1924/2006³ 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 health claims is vitamin A which is a well recognised nutrient. It is measurable in foods by established methods.

The term vitamin A describes a group of lipid soluble compounds related metabolically to all-trans-retinol. In the diet, vitamin A is found in products of animal origin, as retinyl esters, mainly retinyl palmitate. Other esters (oleate, stearate, myristate), and retinol contribute to the dietary vitamin A intake. Some carotenoids (α - and β -carotenes, β -cryptoxanthine) can be cleaved into retinol, via an enzymatic process in the small intestine. Retinoic acids are considered as the molecular species responsible for all the functions attributed to vitamin A, with the exception of vision, where only retinal is able to exert an action (SCF, 2002).

Different forms of vitamin A are authorised for addition to foods and for use in food supplements (Annex II of the Regulation (EC) No 1925/2006⁴ and Annex II of Directive 2002/46/EC⁵). This evaluation applies to vitamin A naturally present in foods and those forms authorised for addition to foods and for use in food supplements (Annex II of the Regulation (EC) No 1925/2006 and Annex II of Directive 2002/46/EC).

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

2. Relevance of the claimed effect to human health

2.1. Cell differentiation (ID 14)

The claimed effect is “cell differentiation including immune system”. The Panel assumes that the target population is the general population.

The Panel considers that normal cell differentiation is beneficial to human health.

2.2. Function of the immune system (ID 14)

The claimed effect is “cell differentiation including immune system”. The Panel assumes that the target population is the general population.

³ 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. OJ L 404, 30.12.2006, p. 9–25.

⁴ 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. OJ L 404, 30.12.2006, p. 26–38.

⁵ Directive 2002/46/EC of the European Parliament and of the Council of 10 June 2002 on the approximation of the laws of the Member States relating to food supplements. OJ L 183, 12.7.2002, p. 51–57.

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

2.3. Maintenance of skin and mucous membranes (ID 15, 17)

The claimed effects are “structure and function of the skin and mucous membranes (such as in the lung, intestines, nose, eyes and female reproductive tract)” and “Bone/Teeth/Hair/Skin and Nail health”. The Panel assumes that the target population is the general population.

The Panel considers that maintenance of normal skin and mucous membranes is beneficial to human health.

2.4. Maintenance of vision (ID 16)

The claimed effect is “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.

2.5. Maintenance of bone (ID 13, 17)

The claimed effects are “bone/teeth/hair/skin and nail health” and “bone growth and development of teeth”. The Panel assumes that the target population is the general population.

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

2.6. Maintenance of teeth (ID 13, 17)

The claimed effects are “bone/teeth/hair/skin and nail health” and “bone growth and development of teeth”. The Panel assumes that the target population is the general population.

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

2.7. Maintenance of hair (ID 17)

The claimed effect is “bone/teeth/hair/skin and nail health”. The Panel assumes that the target population is the general population.

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

2.8. Maintenance of nails (ID 17)

The claimed effect is “bone/teeth/hair/skin and nail health”. The Panel assumes that the target population is the general population.

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

2.9. Metabolism of iron (ID 206)

The claimed effect is “metabolism of iron”. The Panel assumes that the target population is the general population.

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

2.10. Protection of DNA, proteins and lipids from oxidative damage (ID 209)

The claimed effect is “oxidative stress. Acts as antioxidant and helps protect the body tissues against the potentially damaging effects of free radicals”. 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 biologically relevant molecules such as DNA, proteins and lipids from oxidative damage is beneficial to human health.

3. Scientific substantiation of the claimed effect

It is recognised that vitamin A is important for normal vision, gene expression, reproduction, embryonic development, growth and immune function (IoM, 2001). Vitamin A deficiency signs include impaired dark adaptation, abnormal electroretinograms, follicular hyperkeratosis and lowered blood haemoglobin (SCF, 1992).

3.1. Cell differentiation (ID 14)

Vitamin A binds to nuclear retinoid receptors leading to either the activation or the inhibition of gene expression. Depending on the cell line and dosage, cell differentiation can be stimulated or inhibited. In animal models, it has been shown that vitamin A is involved in the differentiation of the epithelium, mainly in the respiratory tract (Biesalski et al., 1995). In rapidly dividing cells, retinoids efficiently inhibit progression through the cell cycle and induce cell differentiation. Although almost all studies of retinoid mechanisms have been conducted in isolated cells, good congruence exists between their action in cells and their effect in intact animals or humans (Ross, 2006).

The Panel notes that vitamin A is involved in the differentiation of many cells showing either an inhibiting or stimulating effect.

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

3.2. Function of the immune system (ID 14)

It has been reported that all-trans-retinoic acid stimulates the proliferation of T-lymphoid cells, while it inhibits the proliferation of B-cells and B-cell precursors. In particular, the lymphocyte response to mitogens is highly retinoid dependent. Retinoic acid also exerts an effect on the T-helper cell balance by suppressing Th1 development and enhancing Th2 development. In addition, it has been indicated that vitamin A deficiency enhances macrophage-mediated inflammation by increasing production of IL-12 and IFN- γ , but impairs the ability of macrophages to ingest and kill bacteria. Dendritic cells are also a target of retinoic acid. It regulates the survival and antigen presentation by immature dendritic cells, as well as the maturation of immature to mature dendritic cells. Other effects of vitamin A on the immune system are related to apoptotic effects on immune-competent cells during back regulation of immune reactions and during thymic selection and to the alteration of genes relevant to the immune response (Ruhl, 2007).

The efficacy of supplementing vitamin A on infection rates has been examined in several randomised, double-blind, placebo-controlled trials of malnourished children in various regions of the developing world. Antibody-mediated immunity has been shown to be severely impaired in children with vitamin A deficiency. Providing vitamin A supplements has been found to improve the antibody titer response to measles vaccines, maintain gut integrity, lower the incidence of respiratory tract infections, and reduce mortality associated with diarrhoea and measles but not pneumonia. There are clinical data suggesting that vitamin A deficiency in HIV-1-infected individuals contributes to mortality, disease progression, and maternal-infant disease transfer (Field et al., 2002).

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

3.3. Maintenance of skin and mucous membranes (ID 15, 17)

Vitamin A is required for the integrity of epithelial cells throughout the body. Retinoic acid, through the activation of retinoic acid and retinoid X receptors in the nucleus, regulates the expression of various genes that encode for structural proteins, enzymes, extracellular matrix proteins, and retinol binding proteins and receptors (IoM, 2001).

The systemic effects of vitamin A deficiency include dryness of the skin (follicular hyperkeratosis), loss of mucus-secreting goblet cells in the trachea and respiratory tract, and a generalised flattening of epithelia (squamous metaplasia, sometimes with keratinisation) throughout the body (Ross, 2005).

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

3.4. Maintenance of vision (ID 16)

11-cis-retinaldehyde (retinal) is required by the eye for the transduction of light into neural signals necessary for vision. In the rods 11-cis-retinal is bound to opsin, thus forming the visual pigment, rhodopsin. The absorption of light catalyses the photoisomerisation of 11-cis-retinal to all-trans-retinal, which triggers the signalling to neuronal cells associated with the brain's neuronal cortex. Without an adequate level of vitamin A in the retina the function of the rods in dim light situations becomes compromised, resulting in abnormal dark adaptation (night blindness) (IoM, 2001).

In a very different role, the cornea of the eye depends on vitamin A delivered in tear fluid to maintain cell differentiation and structural integrity. Vitamin A deficiency leads to a reduction in mucus production by the goblet cells of the conjunctival membranes and the cornea becomes dry (xerosis). Also Bitôt spots (cellular debris) may develop, usually at the outer quadrant of the eyes (Ross, 2006).

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

3.5. Maintenance of bone (ID 13, 17)

A total of 32 references were cited to substantiate the claimed effect. Some 13 of these were textbooks or opinions from scientific bodies in which the claimed effect was not stated. A further 19 references were related to vitamins other than vitamin A or minerals. The Panel notes that the references cited provided no 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 vitamin A and maintenance of normal bone.

3.6. Maintenance of teeth (ID 13, 17)

A total of 32 references were cited to substantiate the claimed effect. Some 13 were textbooks or opinions from scientific bodies in which the claimed effect was not stated. A further 19 references were related to vitamins other than vitamin A or minerals. The Panel notes that the references cited provided no 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 vitamin A and maintenance of normal teeth.

3.7. Maintenance of hair (ID 17)

A total of 17 references were cited to substantiate the claimed effect from which 7 were related to vitamins other than vitamin A, 5 were textbooks and 5 were opinions from scientific bodies in which the claimed effect was not stated. The Panel notes that the reference cited provided no 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 vitamin A and maintenance of normal hair.

3.8. Maintenance of nails (ID 17)

A total of 17 references were cited to substantiate the claimed effect from which 7 were related to vitamins other than vitamin A, 5 were textbooks and 5 were opinions from scientific bodies in which the claimed effect was not stated. The Panel notes that the reference cited provided no 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 vitamin A and maintenance of normal nails.

3.9. Metabolism of iron (ID 206)

A direct correlation between haemoglobin and serum retinol concentrations has been observed. Various studies suggest that vitamin A deficiency impairs iron mobilisation from stores and vitamin A supplementation improves haemoglobin concentration (IoM, 2001).

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

3.10. Protection of DNA, proteins and lipids from oxidative damage (ID 209)

One reference to a textbook on sports nutrition was cited to substantiate the claimed effect in which the claimed effect was not stated. The Panel notes that the reference cited provided no 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 pre-formed vitamin A and protection of DNA, proteins and lipids from oxidative damage.

4. Panel's comments on the proposed wording

4.1. Cell differentiation (ID 14)

The Panel considers that the following wording reflects the scientific evidence: "Vitamin A contributes to normal cell differentiation."

4.2. Function of the immune system (ID 14)

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

4.3. Maintenance of skin and mucous membranes (ID 15, 17)

The Panel considers that the following wording reflects the scientific evidence: "Vitamin A contributes to the maintenance of normal skin and mucous membranes."

4.4. Maintenance of vision (ID 16)

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

4.5. Metabolism of iron (ID 206)

The Panel considers that the following wording reflects the scientific evidence: "Vitamin A contributes to normal iron metabolism."

5. Conditions and possible restrictions of use

The Panel considers that in order to bear the claims a food should be at least a source of vitamin A 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. Tolerable Upper Intake Levels (UL) for pre-formed vitamin A have been established for children and adults. The Tolerable Upper Intake Level for adults has been set at 3000 µg RE/day (SCF, 2002).

CONCLUSIONS

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

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

Cell differentiation (ID 14)

- The claimed effect is “cell differentiation including immune system”. The target population is assumed to be the general population. Normal cell differentiation is beneficial to human health.
- A cause and effect relationship has been established between the dietary intake of vitamin A and normal cell differentiation.
- The evidence provided does not establish that inadequate intake of vitamin A leading to impaired cell differentiation occurs in the general EU population.
- The following wording reflects the scientific evidence: “Vitamin A contributes to normal cell differentiation”.

Function of the immune system (ID 14)

- The claimed effect is “cell differentiation including immune system”. The target population is assumed to be the general population. A normal function of the immune system is beneficial to human health.
- A cause and effect relationship has been established between the dietary intake of vitamin A and a normal function of the immune system.
- The evidence provided does not establish that inadequate intake of vitamin A leading to impaired function of the immune system occurs in the general EU population.
- The following wording reflects the scientific evidence: “Vitamin A contributes to a normal function of the immune system”.

Maintenance of skin and mucous membranes (ID 15, 17)

- The claimed effects are “structure and function of the skin and mucous membranes (such as in the lung, intestines, nose, eyes and female reproductive tract)” and “bone/teeth/hair/skin and nail health”. The target population is assumed to be the general population. Maintenance of normal skin and mucous membranes is beneficial to human health.
- A cause and effect relationship has been established between the dietary intake of vitamin A and maintenance of normal skin and mucous membranes.
- The evidence provided does not establish that intake of vitamin A inadequate for the maintenance of normal skin and mucous membranes occurs in the general EU population.
- The following wording reflects the scientific evidence: “Vitamin A contributes to the maintenance of normal skin and mucous membranes”.

Maintenance of vision (ID 16)

- The claimed effect is “vision”. The target population is assumed to be the general population. Maintenance of normal vision is beneficial to human health.
- A cause and effect relationship has been established between the dietary intake of vitamin A and maintenance of normal vision.
- The evidence provided does not establish that intake of vitamin A inadequate for the maintenance of normal vision occurs in the general EU population.
- The following wording reflects the scientific evidence: “Vitamin A contributes to the maintenance of normal vision”.

Maintenance of bone (ID 13, 17)

- The claimed effects are “bone/teeth/hair/skin and nail health” and “bone growth and development of teeth”. 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 not been established between the dietary intake of vitamin A and maintenance of normal bone.

Maintenance of teeth (ID 13, 17)

- The claimed effects are “bone/teeth/hair/skin and nail health” and “bone growth and development of teeth”. The target population is assumed to be the general population. Maintenance of normal teeth is beneficial to human health.
- A cause and effect relationship has not been established between the dietary intake of vitamin A and maintenance of normal teeth.

Maintenance of hair (ID 17)

- The claimed effect is “bone/teeth/hair/skin and nail health”. The target population is assumed to be the general population. Maintenance of normal hair is beneficial to human health.
- A cause and effect relationship has not been established between the dietary intake of vitamin A and maintenance of normal hair.

Maintenance of nails (ID 17)

- The claimed effect is “bone/teeth/hair/skin and nail health”. The target population is assumed to be the general population. Maintenance of normal nails is beneficial to human health.
- A cause and effect relationship has not been established between the dietary intake of vitamin A and maintenance of normal nails.

Metabolism of iron (ID 206)

- The claimed effect is “metabolism of iron” (ID 206). The target population is assumed to be the general population. Normal metabolism of iron is beneficial to human health.
- A cause and effect relationship has been established between the dietary intake of vitamin A and normal metabolism of iron.

- The evidence provided does not establish that inadequate intake of vitamin A leading to impaired metabolism of iron occurs in the general EU population.
- The following wordings reflect the scientific evidence: “Vitamin A contributes to normal iron metabolism”.

Protection of DNA, proteins and lipids from oxidative damage (ID 209)

- The claimed effect is “oxidative stress”. 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 not been established between the dietary intake of vitamin A and the protection of DNA, proteins and lipids from oxidative damage.

Conditions and restrictions of use

In order to bear the claims a food should be at least a source of vitamin A 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.

DOCUMENTATION PROVIDED TO EFSA

Health claims pursuant to Article 13 of Regulation (EC) No 1924/2006 (No: EFSA-Q-2008-800, EFSA-Q-2008-801, EFSA-Q-2008-802, EFSA-Q-2008-803, EFSA-Q-2008-804, EFSA-Q-2008-993, EFSA-Q-2008-996). 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 full list of supporting references as provided to EFSA is available on: http://www.efsa.europa.eu/EFSA/efsa_locale-1178620753812_article13.htm.

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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 foods⁶ (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 FOOD⁷

Foods are commonly involved in many different functions⁸ 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 DISCLAIMER

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 vitamin A, including conditions of use from similar claims, as proposed in the Consolidated List.

ID	Food or Food component	Health Relationship	Proposed wording
13	Vitamin A	Bone growth and development of teeth	Vitamin A aids healthy bone and teeth growth.
	<p>Conditions of use</p> <ul style="list-style-type: none"> - MUST AT LEAST BE A SOURCE OF MINERAL/S AS PER ANNEX TO REGULATION 1924/2006 Agency guidance for supplements is that products containing beta-carotene should carry the label advisory statement: "[Beta-carotene] should not be taken by heavy smokers" 15% RDA of vitamin A is equivalent to 720 micrograms beta-carotene . - Minimum 15% RDA (120 µg) - Number of nutrients/other substances that are essential to claimed effect: 5 Names of nutrient/other substances and Quantity in Average daily serving: 160 micorgrams Vitamin A, 12 miligrams Vitamin C, 1 microgram Vitamin D, 160 miligrams Calcium, 160 miligrams Phosphorus 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: Don't Know Length of time after consumption for claimed effect to become apparent: depends on the individual's nutritional status Is there a limit to the amount of food which should be consumed in order to avoid adverse health effects: Don't Know Other conditions for use: Product should be consumed in the context of a healthy diet and lifestyle. - Number of nutrients/other substances that are essential to claimed effect: 5 Names of nutrient/other substances and Quantity in Average daily serving: 1.44 micrograms Vitamin A, 10.80 miligrams Vitamin C, .90 micrograms Vitamin D, 144 milligrams Calcium, 144 miligrams Phosphorus Weight of average daily food serving: 90 gram(s) Daily amount to be consumed to produce claimed effect: 500 gram(s) Number of food portions this equates to in everyday food portions: 1 Are there factors that could interfere with bioavailability: Don't Know Length of time after consumption for claimed effect to become apparent: Dependent on the individual's nutritional status Is there a limit to the amount of food which should be consumed in order to avoid adverse health effects: Don't Know Other conditions for use: Product should be consumed in the context of a healthy diet and lifestyle 		
14	Vitamin A	Cell differentiation including immune system	Vitamin A helps the proper functioning of the immune system; - vitamin A contributes to the proper functioning of the cells.
	<p>Conditions of use</p> <ul style="list-style-type: none"> - Es werden nur die Nährstoffe beworben, die lt. Nährwertkennzeichnungs-verordnung (Anlage 1) mindestens 15 Prozent der empfohlenen Tagesdosis in 100 g oder 100 ml enthalten. - MINDESTENS 15 % RDA JE 100 G ODER 100 ML ODER JE PORTION GEMÄB 90/496/EWG - Presence of a nutrient or other substance Number of nutrients/other substances that are essential to claimed effect: 1 Names of nutrient/other substances and Quantity in Average 		

	<p>daily serving: 120 microgram(s) Vitamin A Daily amount to be consumed to produce claimed effect: 120 microgram(s) Are there factors that could interfere with bioavailability: Don't Know Length of time after consumption for claimed effect to become apparent: It is apparent after a period of regular use Is there a limit to the amount of food which should be consumed in order to avoid adverse health effects: Don't Know Other conditions for use: Must be at least a source of vitamin A as per annex to Regulation 1924/2006 present in the food.</p> <ul style="list-style-type: none"> - MUST AT LEAST BE A SOURCE OF VITAMINS/S AS PER ANNEX TO REGULATION 1924/2006 15% RDA of vitamin A is equivalent to 720 micrograms beta-carotene Beta-carotene can be converted to Vitamin A. Where beta-carotene is the main source the following statements could be preceded by:Beta- carotene can be converted to Vitamin A. Vitamin A is necessary for / contributes to Agency guidance for supplements is that products containing beta-carotene should carry the label advisory statement: '[Beta-carotene] should not be taken by heavy smokers' Applicable to both children and adults - 15% RDA of vitamin A is equivalent to 720 micrograms beta-carotin - Fruit drink with vitamin A content of 120 µg/100g, 300 µg/serving and 600 µg/daily serving - 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 Other conditions for use: The product should be consumed in the context of a healthy diet and lifestyle 		
	Food or Food component	Health Relationship	Proposed wording
15	Vitamin A	Structure and function of the skin and mucous membranes (such as in the lung, intestines, nose, eyes and female reproductive tract)	Vitamin A helps keep the skin and mucous membranes healthy.
	<p>Conditions of use</p> <ul style="list-style-type: none"> - Es werden nur die Nährstoffe beworben, die lt. Nährwertkennzeichnungs-verordnung (Anlage 1) mindestens 15 Prozent der empfohlenen Tagesdosis in 100 g oder 100 ml enthalten. - Tagesbedarf gemäß NwKVO 800 µg - Number of nutrients/other substances that are essential to claimed effect: 1 Names of nutrient/other substances and Quantity in Average daily serving: 120 microgram(s) Vitamin A Daily amount to be consumed to produce claimed effect: 120 microgram(s) Are there factors that could interfere with bioavailability: - MUST AT LEAST BE A SOURCE OF MINERAL/S AS PER ANNEX TO REGULATION 1924/2006 Agency guidance for supplements is that Products containing beta-carotene should carry the label advisory statement: '[Beta-carotene] should not be taken by heavy smokers" Beta-carotene can be converted to Vitamin A. Where beta-carotene is the main source the following statements could be preceded by: Beta- carotene can be converted to Vitamin A. Vitamin A is necessary for / contributes to 15% RDA of vitamin A is equivalent to 720 micrograms beta-carotene Applicable to both children and adults - 15% RDA Vitamin A entspricht 720 µg Betacarotin 		

	Food or Food component	Health Relationship	Proposed wording
16	Vitamin A	Vision	Vitamin A is needed/important for normal vision.
<p>Conditions of use</p> <ul style="list-style-type: none"> - 15% RDA Vitamin A entspricht 720 µg Betacarotin - MUST AT LEAST BE A SOURCE OF MINERAL/S AS PER ANNEX TO REGULATION 1924/2006 Agency guidance for supplements is that Products containing beta-carotene should carry the label advisory statement: "[Beta-carotene] should not be taken by heavy smokers" Beta-carotene can be converted to Vitamin A. Where beta-carotene is the main source the following statements could be preceded by: Beta- carotene can be converted to Vitamin A. Vitamin A is necessary for / contributes to 15% RDA of vitamin A is equivalent to 720 micrograms beta-carotene Applicable to both children and adults - Presence of a nutrient or other substance Number of nutrients/other substances that are essential to claimed effect: 1 Names of nutrient/other substances and Quantity in Average daily serving: 120 microgram(s) Vitamin A Daily amount to be consumed to produce claimed effect: 120 microgram(s) - Number of nutrients/other substances that are essential to claimed effect: 1 Names of nutrient/other substances and Quantity in Average daily serving: 360 micrograms vitamin A Weight of average daily food serving: 300 mililitre(s) Daily amount to be consumed to produce claimed effect: 300 mililitre(s) Number of food portions this equates to in everyday food portions: 1 Are there factors that could interfere with bioavailability: Don't Know Length of time after consumption for claimed effect to become apparent: depends on the individual's nutritional status Is there a limit to the amount of food which should be consumed in order to avoid adverse health effects: Don't Know Other conditions for use: 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: 800 micrograms vitamin A Weight of average daily food serving: 200 mililitre(s) Daily amount to be consumed to produce claimed effect: 200 mililitre(s) Number of food portions this equates to in everyday food portions: 1 Are there factors that could interfere with bioavailability: Don't Know Length of time after consumption for claimed effect to become apparent: depends on the individual's nutritional status Is there a limit to the amount of food which should be consumed in order to avoid adverse health effects: Don't Know Other conditions for use: Product should be consumed in the context of a healthy diet and lifestyle - >0,8mg / d—Erwachsene - Daily amount to be consumed to produce claimed effect: 700 microgram(s). Answer given is the recommended dietary allowance for Ireland 1999 for adult males. Are there factors that could interfere with bioavailability: No 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: Yes State the maximum limit in mg/kg body weight/day: 7.50. Maximum limit is expressed per day i.e. not per kg body weight per day as requested. Regular intake of retinol should not exceed 7500 micrograms of retinol equivalent per day for women and 9000 micrograms per day for men. Potential adverse health effects: Large amounts of retinol can cause liver and bone damage, hair loss, double vision, vomiting, headaches and other abnormalities. Retinol is teratogenic. Describe subgroups this limit applies to: Maximum limit given is for adults. Maximum limit is lower for children depending on age (ranges from 900 micrograms of retinol equivalent per day for infants to 6000 micrograms per day for adolescents). - MINDESTENS 15 % RDA JE 100 G ODER 100 ML ODER JE PORTION GEMÄß 			

	<p>90/496/EWG</p> <ul style="list-style-type: none"> - Es werden nur die Nährstoffe beworben, die lt. Nährwertkennzeichnungs-verordnung (Anlage 1) mindestens 15 Prozent der empfohlenen Tagesdosis in 100 g oder 100 ml enthalten. - Number of nutrients/other substances that are essential to claimed effect: 1 Names of nutrient/other substances and Quantity in Average daily serving: 160 micrograms vitamin A 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: Don't Know Length of time after consumption for claimed effect to become apparent: depends on the individual's nutritional status Is there a limit to the amount of food which should be consumed in order to avoid adverse health effects: Don't Know Other conditions for use: Product should be consumed in the context of a healthy diet and lifestyle 		
17	Food or Food component	Health Relationship	Proposed wording
	Vitamin A	Bone/Teeth/Hair/Skin and Nail health	Necessary for healthy teeth, bones, hair, skin and nails.
	<p>Conditions of use</p> <ul style="list-style-type: none"> - 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 beta-carotene should carry the label advisory statement "[Beta-carotene] should not be taken by heavy smokers." - Number of nutrients/other substances that are essential to claimed effect: 1 Names of nutrient/other substances and Quantity in Average daily serving: 360 Micrograms of Vitamin A Daily amount to be consumed to produce claimed effect: 667 ml - Daily amount to be consumed to produce claimed effect: 700 microgram(s). Answer given is the recommended dietary allowance for Ireland for adult males (FSAI 1999) 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: Yes State the maximum limit in mg/kg body weight/day: 7.50. Maximum limit is expressed per day i.e. not per kg body weight per day as requested. Regular intake of retinol should not exceed 7500 micrograms of retinol equivalent per day for women and 9000 micrograms per day for men. Potential adverse health effects: Large amounts of retinol can cause liver and bone damage, hair loss, double vision, vomiting, headaches and other abnormalities. Retinol is teratogenic. Describe subgroups this limit applies to: Maximum limit given is for adults. Maximum limit is lower for children depending on age (ranges form 900 micrograms of retinol equivalent per day for infants to 6000 micrograms per day for adolescents). 		
206	Food or Food component	Health Relationship	Proposed wording
	Vitamin A	Metabolism of iron	Vitamin A helps the body to maintain a normal iron level
	<p>Conditions of use</p> <ul style="list-style-type: none"> - 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 >7mg of Beta-carotene should carry the label advisory statement "[Beta-carotene]* should not be taken by heavy smokers.." 		
	Food or Food component	Health Relationship	Proposed wording

209	Vitamin A	OXIDATIVE STRESS. Acts as antioxidant and helps protect the body tissues against the potentially damaging effects of free radicals.	Vitamin A protects against free-radical-induced muscle damage.
<p>Conditions of use</p> <ul style="list-style-type: none"> - Claim to be only used for Foods for sports people under the Dir. 89/398/EEC For athletes who have inadequate food intakes in particular. Condition for use: 2000 IU (600 mcg RE) retinol daily. 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 >7mg of Beta-carotene should carry the label advisory statement "[Beta-carotene]* should not be taken by heavy smokers. 			

GLOSSARY AND ABBREVIATIONS

DNA Deoxyribonucleic acid

ROS Reactive oxygen species

UL Tolerable Upper Intake Levels