

SCIENTIFIC OPINION

Scientific Opinion on the substantiation of health claims related to copper and protection of DNA, proteins and lipids from oxidative damage (ID 263, 1726), function of the immune system (ID 264), maintenance of connective tissues (ID 265, 271, 1722), energy-yielding metabolism (ID 266), function of the nervous system (ID 267), maintenance of skin and hair pigmentation (ID 268, 1724), iron transport (ID 269, 270, 1727), cholesterol metabolism (ID 369), and glucose metabolism (ID 369) 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 1924/2006. This opinion addresses the scientific substantiation of health claims in relation to copper and the following claimed effects: protection of DNA, proteins and lipids from oxidative damage, function of the immune system, maintenance of connective tissues, energy-yielding metabolism, function of the nervous system, maintenance of skin and hair pigmentation, iron transport, cholesterol metabolism, and glucose metabolism. 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 copper, which is a well recognised nutrient and is measurable in foods by established methods. The Panel considers that copper is sufficiently characterised.

The Panel concludes that a cause and effect relationship has been established between the dietary intake of copper and protection of DNA, proteins and lipids from oxidative damage, normal function of the immune system, maintenance of normal connective tissues, normal energy-yielding metabolism,

1 On request from the European Commission, Question No EFSA-Q-2008-1050, EFSA-Q-2008-1051, EFSA-Q-2008-1052, EFSA-Q-2008-1053, EFSA-Q-2008-1054, EFSA-Q-2008-1055, EFSA-Q-2008-1056, EFSA-Q-2008-1057, EFSA-Q-2008-1058, EFSA-Q-2008-1156, EFSA-Q-2008-2458, EFSA-Q-2008-2460, EFSA-Q-2008-2462, EFSA-Q-2008-2463, adopted on 2 July 2009.

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normal function of the nervous system, maintenance of normal skin and hair pigmentation, and normal iron transport.

The evidence provided does not establish that inadequate intake of copper leading to impaired functions 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 copper as per Annex to Regulation 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 copper and normal cholesterol metabolism and normal glucose metabolism.

KEY WORDS

Copper, oxidative damage, immune system, connective tissues, energy-yielding metabolism, nervous system, skin and hair pigmentation, iron transport, cholesterol metabolism, glucose metabolism, 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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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 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 claim is copper which is a well recognised nutrient and is measurable in foods by established methods.

Copper occurs naturally in foods and is authorised for addition to foods (Annex I of the Regulation (EC) No 1925/2006⁴ and Annex I of Directive 2002/46/EC⁵). This evaluation applies to copper 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, copper, which is the subject of the health claim, is sufficiently characterised.

2. Relevance of the claimed effect to human health

2.1. Protection of DNA, proteins and lipids from oxidative damage (ID 263, 1726)

The claimed effect is “protection of body tissues and cell from oxidative damage; antioxidant activity”. 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.

2.2. Function of the immune system (ID 264)

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

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

2.3. Maintenance of connective tissues (ID 265, 271, 1722)

The claimed effect is “connective tissues” and “hair, nail connective tissue formation”. The Panel assumes that the target population is the general population.

The connective tissue is a structural component of several body structures including bone, cartilage, gums, skin, hair follicles, nails, tendons and blood vessels.

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 maintenance of normal connective tissues is beneficial to human health.

2.4. Energy-yielding metabolism (ID 266)

The claimed effect is “energy production”. The Panel assumes that the target population is the general population.

The Panel considers that normal energy-yielding metabolism is beneficial to human health.

2.5. Function of the nervous system (ID 267)

The claimed effect is “neurological system structure and function”. The Panel assumes that the target population is the general population.

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

2.6. Maintenance of skin and hair pigmentation (ID 268, 1724)

The claimed effect is “skin and hair pigment”. The Panel assumes that the target population is the general population.

Skin and hair pigment (melanin) serves as a light filter for the protection of tissues against ultraviolet light damage.

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

2.7. Iron transport (ID 269, 270, 1727)

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

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

2.8. Cholesterol metabolism (ID 369)

The claimed effect is “cholesterol and glucose metabolism”. The Panel assumes that the target population is the general population.

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

2.9. Glucose metabolism (ID 369)

The claimed effect is “cholesterol and glucose metabolism”. The Panel assumes that the target population is the general population.

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

3. Scientific substantiation of the claimed effect

Copper is a component of some enzymes, cofactors, and proteins in the body. Among those copper metalloenzymes that have been identified in humans are: monoamine oxidase, diamine oxidase, lysyl oxidase, peptidylglycine- α -amidating monooxygenase, caeruloplasmin, ferrooxidase II, cytochrome c oxidase, dopamine β -hydroxylase, copper/zinc superoxide dismutase, and tyrosinase. The biochemical role of copper is primarily catalytic, with many copper metalloenzymes acting as oxidases to achieve the reduction of molecular oxygen (Biesalski et al., 1997; Garrow et al., 2000; EVM, 2002; Gibney et al., 2002; Mann and Truswell, 2001; Sadler et al., 1999; Wenzel, 1999).

3.1. Protection of DNA, proteins and lipids from oxidative damage (ID 263, ID 1726)

Copper functions as a component of a number of metalloenzymes acting as oxidases to achieve the reduction of molecular oxygen, such as cytochrome c oxidase, and copper/zinc superoxide dismutase (SOD) enzyme (IoM, 2001). This latter enzyme is localized in the cytosol of mammalian cells and provides a defence against oxidative damage from superoxide radicals that, if uncontrolled, can lead to the formation of other damaging reactive oxygen species (ROS). Its activity is related to copper intake (Turnlund, 1998), albeit other factors, such as the induction of oxidative stress, also affect superoxide dismutase (SOD) activity (Knasmuller et al., 2008). Caeruloplasmin is the predominant copper protein in plasma and may have antioxidant functions (IoM, 2001; Klotz et al., 2003).

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

3.2. Function of the immune system (ID 264)

Copper-related enzyme cytochrome c oxidase is needed for energy production of immune cells. Another cuproenzyme – superoxide dismutase - plays a role in the protection of immune cells against reactive oxygen species. Moderate and even marginal copper deficiency affects some activities of T-lymphocytes and phagocytic cells adversely (Kelley et al, 1995, Hopkins et al., 1999). Severe copper deficiency generally changes the phenotypic profiles of immune cells in blood, bone marrow, and lymphoid tissues. It also suppresses a number of activities of lymphocytes and phagocytic cells.

Cells of animals fed diets with marginally low copper had markedly impaired *in vitro* DNA synthesis and IL-2 secretion by mitogen-treated splenic T-lymphocytes and respiratory burst activity of neutrocytes (Hopkins, 1995).

Neutropenia is a hallmark of copper deficiency in humans (Heresi et al. 1985, Prohaska, 2006). However, clinical data confirming the importance of copper in the function of the immune system is sparse. Copper deficiency in humans results in thymus atrophy (Munoz et al., 2007). Hypocupraemic infants fed cow's milk formula containing copper showed normalization of copper and caeruloplasmin concentrations, and phagocytic index recovery to normal levels (Heresi et al, 1985). Infants with Menkes disease, a genetic disorder that results in severe copper deficiency in some tissues, suffer from frequent and severe infections (Percival, 1998; Failla and Hopkins, 1998).

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

3.3. Maintenance of connective tissues (ID 265, 271, 1722)

The evidence provided by consensus opinions/reports from authoritative bodies and reviews shows that there is good consensus on the role of copper in the formation of elastin and collagen, which constitute the structure of connective tissues.

Copper is a cofactor of lysyl oxidase (LO), which is an extracellular enzyme critical to the formation and function of connective tissue throughout the body. The reaction of oxidative deamination of specific lysine residues in the extracellular matrix initiates the formation of cross-links that stabilise newly formed elastin and collagen (Linder and Hazegh-Azam, 1996).

Symptoms of severe copper deficiency include lack of collagen maturation and defective sheathing of blood vessels, which can result in aneurysms (Rodriguez et al., 2008).

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

3.4. Energy-yielding metabolism (ID 266)

Copper participates as a cofactor for specific enzymes and electron transport proteins involved in many oxidative reactions that break down fats in fat tissue to produce energy in the form of ATP.

The copper-dependent enzyme cytochrome c oxidase plays a critical role in cellular energy production. Copper deficiency results in a decrease of cytochrome c oxidase activity and the respiratory capacity of mitochondria, particularly in liver, heart, and brain (Linder, 1991).

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

3.5. Function of the nervous system (ID 267)

Copper is required for the formation and maintenance of myelin. Myelin is composed primarily of phospholipids. Their synthesis depends on the activity of the cuproenzyme cytochrome c oxidase. In copper deficient animals, poor myelination, necrosis of nerve tissue, and neonatal ataxia are found (Desai and Kaler, 2008). Copper has also a function in catecholamine metabolism and therefore in normal neurotransmission (Prohaska and Bailey, 1994).

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

3.6. Maintenance of skin and hair pigmentation (ID 268, 1724)

The role of copper in the pigmentation of skin, hair, and eyes is related to the requirement of the cuproenzyme tyrosinase (monophenol oxidase) for melanin synthesis. Mutational loss of this catalytic function leads to albinism. Achromotrichia is observed in domestic and laboratory animals consuming diets low in copper (Arredondo and Nunez, 2005; Linder, 1991).

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

3.7. Iron transport (ID 269, 270, 1727)

Anaemia is a clinical sign of copper deficiency, and iron has been found to accumulate in the livers of copper deficient animals, indicating that copper (probably in the form of caeruloplasmin) is required for iron transport to the bone marrow for red blood cell formation (Turnlund, 1998). During severe copper deficiency, iron transport within the body is adversely affected, and iron tends to accumulate in many tissues. Copper deficiency is accompanied by a hypochromic microcytic anaemia similar to that produced by iron deficiency (Linder, 1991, Prohaska, 2006).

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

3.8. Cholesterol metabolism (ID 369)

A textbook and three consensus opinions/reports from authoritative bodies were cited to substantiate the claimed effect.

The role of copper on cholesterol metabolism is not well understood nor well established in humans (Turnlund, 2006). Blood cholesterol increases in animals fed copper-deficient diets, but the effects of

either copper deficiency or copper supplementation in humans are not consistent (Strain, 1994; Medeiros and Wildman, 1997, JHCI, 2003).

The Panel concludes that a cause and effect relationship has not been established between dietary intake of copper and normal cholesterol metabolism in humans.

3.9. Glucose metabolism (ID 369)

A textbook and three consensus opinions/reports from authoritative bodies were cited to substantiate the claimed effect.

The role of copper in the regulation of glucose metabolisms is not well understood nor well established in humans (Turnlund, 2006; JHCI, 2003)

The Panel concludes that a cause and effect relationship has not been established between dietary intake of copper and normal glucose metabolism in humans.

4. Panel's comments on the proposed wordings

4.1. Protection of DNA, proteins and lipids from oxidative damage (ID 263, 1726)

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

4.2. Function of the immune system (ID 264)

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

4.3. Maintenance of connective tissues (ID 265, 271, 1722)

The Panel considers that the following wording reflects the scientific evidence: "Copper contributes to maintenance of normal connective tissues".

4.4. Energy-yielding metabolism (ID 266)

The Panel considers that the following wording reflects the scientific evidence: "Copper contributes to normal energy yielding metabolism".

4.5. Function of the nervous system (ID 267)

The Panel considers that the following wording reflects the scientific evidence: "Copper contributes to normal function of the nervous system".

4.6. Maintenance of skin and hair pigmentation (ID 268, 1724)

The Panel considers that the following wording reflects the scientific evidence: "Copper contributes to normal skin and hair pigmentation".

4.7. Iron transport (ID 269, 270, 1727)

The Panel considers that the following wording reflects the scientific evidence: "Copper contributes to normal iron transport in the body".

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 copper as per Annex to Regulation (EC) 1924/2006. Such amounts can be easily consumed as part of a balanced diet. Tolerable Upper Intake Level (UL) has been established for copper as 5 mg/day in adults and

during pregnancy and lactation. For children and adolescents UL was established as 1 mg/day for 1-3 years, 2 mg/day for 4-6 years, 3 mg/day for 7-10 years, 4 mg/day for 11-17 years (SCF, 2003).

CONCLUSIONS

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

- The food constituent, copper, which is the subject of the health claim, is sufficiently characterised.

Protection of DNA, proteins and lipids from oxidative damage (ID 263, 1726)

- The claimed effect is “protection of body tissues and cell from oxidative damage; antioxidant activity”. The target population is assumed to be the general population. Protection of DNA, proteins and lipids from oxidative damage is beneficial to human health.
- The Panel considers that a cause and effect relationship has been established between the dietary intake of copper and the protection of DNA, proteins and lipids from oxidative damage.
- The evidence provided does not establish that inadequate intake of copper 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: “Copper contributes to the protection of cell constituents from oxidative damage”.

Function of the immune system (ID 264)

- 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 copper and normal function of the immune system.
- The evidence provided does not establish that inadequate intake of copper leading to impaired function of the immune system occurs in the general EU population
- The following wording reflects the scientific evidence: “Copper contributes to normal function of the immune system”.

Maintenance of connective tissues (ID 265, 271, 1722)

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

Energy-yielding metabolism (ID 266)

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

Function of the nervous system (ID 267)

- The claimed effect is “neurological system structure and function”. The target population is assumed to be the general population. Normal function of the nervous system is beneficial to human health.
- A cause and effect relationship has been established between the intake of copper and normal function of the nervous system.
- The evidence provided does not establish that inadequate intake of copper leading to impaired function of the nervous system occurs in the general EU population.
- The following wording reflects the scientific evidence: “Copper contributes to normal function of the nervous system”.

Maintenance of skin and hair pigmentation (ID 268, 1724)

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

Iron transport (ID 269, 270, 1727)

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

Cholesterol metabolism (ID 369)

- The claimed effect is “cholesterol and glucose metabolism”. The target population is assumed to be the general population. Normal cholesterol metabolism is beneficial to human health.
- A cause and effect relationship has not been established between the dietary intake of copper and normal cholesterol metabolism.

Glucose metabolism (ID 369)

- The claimed effect is “cholesterol and glucose metabolism”. The target population is assumed to be the general population. Normal glucose metabolism is beneficial to human health.
- A cause and effect relationship has not been established between the dietary intake of copper and normal glucose metabolism.

Conditions and possible restrictions of use

- In order to bear the claims a food should be at least a source of copper as per Annex to Regulation (CE) 1924/2006. 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-2008-1050, EFSA-Q-2008-1051, EFSA-Q-2008-1052, EFSA-Q-2008-1052, EFSA-Q-2008-1053, EFSA-Q-2008-1054, EFSA-Q-2008-1054, EFSA-Q-2008-1055, EFSA-Q-2008-1056, EFSA-Q-2008-1057, EFSA-Q-2008-1058, EFSA-Q-2008-1156, EFSA-Q-2008-2458, EFSA-Q-2008-2460, EFSA-Q-2008-2462, EFSA-Q-2008-2463). 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/panels/nda/claims/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.

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

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).

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

ID	Food or Food constituent	Health Relationship	Proposed wording
263	Copper	Protection of body tissues and cell from oxidative damage; Antioxidant activity	Copper contributes to cells protection from free radicals; Copper helps scavenging free radicals.
	Conditions of use <ul style="list-style-type: none"> - Erwachsene 1 mg - Tagesdosierungen zwischen 5 und 15 mg Zink und 0,5 - 1,5 mg Kupfer - Must at least be a source of mineral/s as per annex to Regulation 1924/2006. Applicable to both children and adults 		
264	Copper	Immune system	Copper is needed for the function of the immune system.
	Conditions of use <ul style="list-style-type: none"> - MINDESTENS 15 % RDA JE 100 G ODER 100 ML ODER JE PORTION GEMÄß 90/496/EWG - Must at least be a source of mineral/s as per annex to Regulation 1924/2006. Applicable to both children and adults 		
265	Copper	Connective tissues	Copper is needed / important for the structure of connective tissues.
	Conditions of use <ul style="list-style-type: none"> - Must at least be a source of mineral/s as per annex to Regulation 1924/2006. Applicable to both children and adults - Significant quantity (RDA 15 %) according to the directive 90/496/EEC on Nutrition labelling for foodstufs. ;;In case of food supplements significant quantity (RDA 15 %) must be in the daily portion of the product as recommended by the manufacturer; - 900 µg per day 		
266	Copper	Energy production	The body needs copper for energy production.
	Conditions of use <ul style="list-style-type: none"> - MINDESTENS 15 % RDA JE 100 G ODER 100 ML ODER JE PORTION GEMÄß 90/496/EWG - Erwachsene, 1 mg - Must at least be a source of mineral/s as per annex to Regulation 1924/2006. Applicable to both children and adults 		

ID	Food or Food constituent	Health Relationship	Proposed wording
267	Copper	Neurological system structure and function	Copper is needed for the nervous system to function.
	Conditions of use <ul style="list-style-type: none"> - MINDESTENS 15 % RDA JE 100 G ODER 100 ML ODER JE PORTION GEMÄß 90/496/EWG - Erwachsene, 1 mg - Must at least be a source of mineral/s as per annex to Regulation 1924/2006. Applicable to both children and adults 		
268	Copper	Skin and hair pigment	Copper is needed for colour (pigmentation) of skin and hair.
	Conditions of use <ul style="list-style-type: none"> - Must at least be a source of mineral/s as per annex to Regulation 1924/2006. Applicable to both children and adults 		
269	Copper	Transport and metabolism of iron	Copper helps the body use iron; Copper is needed for blood formation; Copper contributes to the transport and metabolism of iron in the body.
	Conditions of use <ul style="list-style-type: none"> - MINDESTENS 15 % RDA JE 100 G ODER 100 ML ODER JE PORTION GEMÄß 90/496/EWG - Must at least be a source of mineral/s as per annex to Regulation 1924/2006. Applicable to both children and adults 		
270	Copper	Iron metabolism	Component of enzymes in iron metabolism; Copper contributes to the normal transport and metabolism of iron in the body.
	Conditions of use <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. 		
271	Copper	Hair, Nail, connective tissue formation	Copper is essential for hair, nail and connective tissue formation.
	Conditions of use <ul style="list-style-type: none"> - MINDESTENS 15 % RDA JE 100 G ODER 100 ML ODER JE PORTION GEMÄß 90/496/EWG - Erwachsene, 1 mg - MINIMUM 15% RDA 		

ID	Food or Food constituent	Health Relationship	Proposed wording
369	Copper	Cholesterol and glucose metabolism	Copper contributes to the cholesterol and glucose
	Conditions of use - Erwachsene, 1 mg		
1722	Copper	Connective tissues	Copper helps build connective tissues.
	Conditions of use - 15% RDA/day = 135 µg Cu ; 270 mg of powder supports 30% RDA ; Daily Total Dose Cu = 5 mg/day		
1724	Copper	Skin and hair pigment	Copper is needed for colour (pigmentation) of skin and hair.
	Conditions of use - 15% RDA/day = 135 µg Cu ; 270 mg of powder supports 30% RDA ; Daily Total Dose Cu = 5 mg/day		
1726	Copper	Protection of body tissues and cells from oxidative damage	Copper contributes to cell protection from oxidation caused by free radicals.
	Conditions of use - 15% RDA/day = 135 µg Cu ; 270 mg of powder supports 30% RDA ; Daily Total Dose Cu = 5 mg/day		
1727	Copper	Transport and metabolism of iron	Copper helps the body use iron; Copper contributes to the transport and metabolism of iron to the body.
	Conditions of use - 15% RDA/day = 135 µg Cu ; 270 mg of powder supports 30% RDA ; Daily Total Dose Cu = 5 mg/day		