SCIENTIFIC OPINION

Scientific Opinion on the substantiation of health claims related to riboflavin (vitamin B2) and contribution to normal energy-yielding metabolism (ID 29, 35, 36, 42), contribution to normal metabolism of iron (ID 30, 37), maintenance of normal skin and mucous membranes (ID 31, 33), contribution to normal psychological functions (ID 32), maintenance of normal bone (ID 33), maintenance of normal teeth (ID 33), maintenance of normal hair (ID 33), maintenance of normal nails (ID 33), maintenance of normal vision (ID 39), maintenance of normal red blood cells (ID 40), reduction of tiredness and fatigue (ID 41), protection of DNA, proteins and lipids from oxidative damage (ID 207), and maintenance of the normal function of the nervous system (ID 213) pursuant to Article 13(1) of Regulation (EC) No 1924/2006[1]

EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA)[2, 3]

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 riboflavin (vitamin B2) and contribution to normal energy-yielding metabolism, contribution to normal metabolism of iron, maintenance of normal skin and mucous membranes, contribution to normal psychological functions, maintenance of normal bone, maintenance of normal

[1] On request from the European Commission, Question No EFSA-Q-2008-816, EFSA-Q-2008-817, EFSA-Q-2008-818, EFSA-Q-2008-819, EFSA-Q-2008-820, EFSA-Q-2008-822, EFSA-Q-2008-823, EFSA-Q-2008-824, EFSA-Q-2008-826, EFSA-Q-2008-827, EFSA-Q-2008-829, EFSA-Q-2008-994, adopted on 11 February 2010 and Question No EFSA-Q-2008-828, EFSA-Q-2008-1000, adopted on 10 September 2010.

[2] Panel members: Carlo Agostoni, Jean-Louis Bresson, Susan Fairweather-Tait, Albert Flynn, Ines Golly, Hannu Korhonen, Pagona Lagiou, Martinus Løvik, Rosangela Marchelli, Ambroise Martin, Bevan Moseley, Monika Neuhäuser-Berthold, Hildegard Przyrembel, Seppo Salminen, Yolanda Sanz, Sean (J.J.) Strain, Stephan Strobel, Inge Tetens, Daniel Tomé, Hendrik van Loveren and Hans Verhagen. Correspondence: nda@efsa.europa.eu

[3] Acknowledgement: The Panel wishes to thank for the preparatory work on of this scientific opinion: The members of the Working Group on Claims: Carlo Agostoni, Jean-Louis Bresson, Susan Fairweather-Tait, Albert Flynn, Ines Golly, Marina Heinonen, Hannu Korhonen, Martinus Løvik, Ambroise Martin, Hildegard Przyrembel, Seppo Salminen, Yolanda Sanz, Sean (J.J.) Strain, Inge Tetens, Hendrik van Loveren and Hans Verhagen. The members of the Claims Sub-Working Group on Mental/Nervous System: Jacques Rigo, Astrid Schloerscheidt, Barbara Stewart-Knox, Sean (J.J.) Strain, and Peter Willatts.

Suggested citation: EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA); Scientific Opinion on the substantiation of health claims related to riboflavin (vitamin B2) and contribution to normal energy-yielding metabolism (ID 29, 35, 36, 42), contribution to normal metabolism of iron (ID 30, 37), maintenance of normal skin and mucous membranes (ID 31,33), contribution to normal psychological functions (ID 32), maintenance of normal bone (ID 33), maintenance of normal teeth (ID 33), maintenance of normal hair (ID 33), maintenance of normal nails (ID 33), maintenance of normal vision (ID 39), maintenance of normal red blood cells (ID 40), reduction of tiredness and fatigue (ID 41), protection of DNA, proteins and lipids from oxidative damage (ID 207), and maintenance of the normal function of the nervous system (ID 213) pursuant to Article 13(1) of Regulation (EC) No 1924/2006. EFSA Journal 2010;8(10):1814. [28 pp.]. doi:10.2903/j.efsa.2010.1814. Available online: www.efsa.europa.eu/efsajournal.htm

teeth, maintenance of normal hair, maintenance of normal nails, maintenance of normal vision, maintenance of normal red blood cells, reduction of tiredness and fatigue, protection of DNA, proteins and lipids from oxidative damage, and maintenance of the normal function of the nervous system. 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 riboflavin. The Panel considers that riboflavin is sufficiently characterised.

Contribution to normal energy-yielding metabolism

The claimed effects are "energy metabolism", "riboflavin participates in oxidation-reduction reactions in numerous metabolic pathways and in energy production via respiratory chain", "macronutrient metabolism" and "release of energy from food". The target population is assumed to be the general population. The Panel considers that contribution to normal energy-yielding metabolism is a beneficial physiological effect.

Riboflavin has an important role as a coenzyme in energy-yielding metabolism acting as an electron carrier in a wide variety of oxidation and reduction reactions that are central to many metabolic processes.

The Panel concludes that a cause and effect relationship has been established between the dietary intake of riboflavin and contribution to normal energy-yielding metabolism.

Contribution to normal metabolism of iron

The claimed effects are "transport and metabolism of iron" and "healthy iron status". The target population is assumed to be the general population. The Panel considers that contribution to normal metabolism of iron is a beneficial physiological effect.

Iron metabolism is impaired in riboflavin deficiency. The utilisation of iron reserves from the intracellular protein, ferritin, requires riboflavin. Riboflavin is required for haemoglobin synthesis.

The Panel concludes that a cause and effect relationship has been established between the dietary intake of riboflavin and contribution to normal metabolism of iron.

Maintenance of normal skin and mucous membranes

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 nails health". The target population is assumed to be the general population. The Panel considers that maintenance of normal skin and mucous membranes is a beneficial physiological effect.

Mucocutaneous lesions are present in both acute and chronic riboflavin deficiency. Mucosal and skin symptoms disappear after administration of riboflavin in adequate doses.

The Panel concludes that a cause and effect relationship has been established between the dietary intake of riboflavin and maintenance of normal skin and mucous membranes.

Contribution to normal psychological functions

The claimed effect is "mental performance (where mental performance stands for those aspects of brain and nerve functions which determine aspects like concentration, learning, memory and reasoning, as well as resistance to stress)". The target population is assumed to be the general population. The Panel considers that contribution to normal psychological functions, which encompass cognitive and affective domains, is a beneficial physiological effect.

None of the references provided addressed the relationship between the dietary intake of riboflavin and contribution to normal psychological functions.

On the basis of the data presented, the Panel concludes that a cause and effect relationship has not been established between the dietary intake of riboflavin and contribution to normal psychological functions.

Maintenance of normal bone

The claimed effect is "bone/teeth/hair/skin and nails health". The target population is assumed to be the general population. The Panel considers that maintenance of normal bone is a beneficial physiological effect.

No references were provided from which conclusions could be drawn for the scientific substantiation of the claimed effect.

On the basis of the data presented, the Panel concludes that a cause and effect relationship has not been established between the dietary intake of riboflavin and maintenance of normal bone.

Maintenance of normal teeth

The claimed effect is "bone/teeth/hair/skin and nails health". The target population is assumed to be the general population. The Panel considers that maintenance of normal teeth is a beneficial physiological effect.

No references were provided from which conclusions could be drawn for the scientific substantiation of the claimed effect.

On the basis of the data presented, the Panel concludes that a cause and effect relationship has not been established between the dietary intake of riboflavin and maintenance of normal teeth.

Maintenance of normal hair

The claimed effect is "bone/teeth/hair/skin and nails health". The target population is assumed to be the general population. The Panel considers that maintenance of normal hair is a beneficial physiological effect.

No references were provided from which conclusions could be drawn for the scientific substantiation of the claimed effect.

On the basis of the data presented, the Panel concludes that a cause and effect relationship has not been established between the dietary intake of riboflavin and maintenance of normal hair.

Maintenance of normal nails

The claimed effect is "bone/teeth/hair/skin and nails health". The target population is assumed to be the general population. The Panel considers that maintenance of normal nails is a beneficial physiological effect.

No references were provided from which conclusions could be drawn for the scientific substantiation of the claimed effect.

On the basis of the data presented, the Panel concludes that a cause and effect relationship has not been established between the dietary intake of riboflavin and maintenance of normal nails.

Maintenance of normal vision

The claimed effect is "eyes". The Panel target population is assumed to be the general population. The Panel considers that maintenance of normal vision is a beneficial physiological effect.

Riboflavin deficiency can cause conjunctivitis with vascularisation of the cornea and opacity of the lens. Glutathione is important in maintaining the normal clarity of crystallins in the lens and glutathione reductase is a flavoprotein that is particularly sensitive to riboflavin depletion.

The Panel concludes that a cause and effect relationship has been established between the dietary intake of riboflavin and maintenance of normal vision.

Maintenance of normal red blood cells

The claimed effect is "red blood cells". The target population is assumed to be the general population. The Panel considers that maintenance of normal red blood cells is a beneficial physiological effect.

Riboflavin deficiency induces normocytic and normochromic anaemia characterised by an increase in the number of reticulocytes that are immature precursors of red blood cells which are virtually absent from normal blood.

The Panel concludes that a cause and effect relationship has been established between the dietary intake of riboflavin and maintenance of normal red blood cells.

Protection of DNA, proteins and lipids from oxidative damage

The claimed effect is "antioxidant properties". The target population is assumed to be the general population. The Panel considers that protection of DNA, proteins and lipids from oxidative damage may be a beneficial physiological effect.

It is well established that riboflavin participates in a diversity of redox reactions through the cofactors flavin mononucleotide (FMN) and flavin-adenine dinucleotide (FAD), which act as electron carriers.

The Panel concludes that a cause and effect relationship has been established between the dietary intake of riboflavin and protection of DNA, proteins and lipids from oxidative damage.

Reduction of tiredness and fatigue

The claimed effect is "vitamin/mineral supplementation to reduce fatigue and tiredness in situations of inadequate micronutrient status". The target population is assumed to be the general population. The Panel considers that reduction of tiredness and fatigue is a beneficial physiological effect.

Symptoms of riboflavin deficiency include weakness and fatigue.

The Panel concludes that a cause and effect relationship has been established between the dietary intake of riboflavin and a reduction of tiredness and fatigue.

Maintenance of the normal function of the nervous system

The claimed effect is "nervous system". The target population is assumed to be the general population. The Panel considers that maintenance of the normal function of the nervous system is a beneficial physiological effect.

Riboflavin deficiency causes degenerative changes in peripheral nerves found in experimental conditions in several species of animals which are characterised by demyelination with hypertrophy of Schwann cells, marked lipid accumulation, paranodal tomacula and fibroblastic onion bulbs. Some

case reports are available in humans showing the presence of peripheral polyneuropathy in riboflavin depleted subjects.

The Panel concludes that a cause and effect relationship has been established between the dietary intake of riboflavin and maintenance of the normal function of the nervous system.

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 riboflavin 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.

KEY WORDS

Vitamin B2, riboflavin, energy-yielding metabolism, iron metabolism, skin, psychological functions, bone, teeth, hair, nails, vision, red blood cells, oxidative damage, fatigue, tiredness, nervous system, health claims.

TABLE OF CONTENTS

BACKGROUND AS PROVIDED BY THE EUROPEAN COMMISSION

See Appendix A

TERMS OF REFERENCE AS PROVIDED BY THE EUROPEAN COMMISSION

See Appendix A

EFSA DISCLAIMER

See Appendix B

INFORMATION AS PROVIDED IN THE CONSOLIDATED LIST

The consolidated list of health claims pursuant to Article 13 of Regulation (EC) No 1924/2006[4] submitted by Member States contains main entry claims with corresponding conditions of use and literature for similar health claims. EFSA has screened all health claims contained in the original consolidated list of Article 13 health claims which was received by EFSA in 2008 using six criteria established by the NDA Panel to identify claims for which EFSA considered sufficient information had been provided for evaluation and those for which more information or clarification was needed before evaluation could be carried out[5]. The clarifications which were received by EFSA through the screening process have been included in the consolidated list. This additional information will serve as clarification to the originally provided information. The information provided in the consolidated list for the health claims which are the subject of 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 riboflavin (vitamin B2), which is a well recognised nutrient and is measurable in foods by established methods.

Riboflavin occurs naturally in foods and is authorised for addition to foods (Annex I of the Regulation (EC) No 1925/2006[6] and Annex I of Directive 2002/46/EC[7]). This evaluation applies to riboflavin 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, riboflavin, which is the subject of the health claims, is sufficiently characterised.

2. Relevance of the claimed effect to human health

2.1. Contribution to normal energy-yielding metabolism (ID 29, 35, 36, 42)

The claimed effects are "energy metabolism", "riboflavin participates in oxidation-reduction reactions in numerous metabolic pathways and in energy production via respiratory chain", "macronutrient metabolism" and "release of energy from food". The Panel assumes that the target population is the general population.

In the context of the proposed wordings, the Panel assumes that the claimed effects relate to energy-yielding metabolism.

The Panel considers that contribution to normal energy-yielding metabolism is a beneficial physiological effect.

2.2. Contribution to normal metabolism of iron (ID 30, 37)

The claimed effects are "transport and metabolism of iron" and "healthy iron status". The Panel assumes that the target population is the general population.

The Panel considers that contribution to normal metabolism of iron is a beneficial physiological effect.

[4] 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.
[5] Briefing document for stakeholders on the evaluation of Article 13.1, 13.5 and 14 health claims: http://www.efsa.europa.eu/en/ndameetings/docs/nda100601-ax01.pdf
[6] 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.
[7] 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.

2.3. Maintenance of normal skin and mucous membranes (ID 31, 33)

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 nails health". The Panel assumes that the target population is the general population.

The Panel considers that maintenance of normal skin and mucous membranes is a beneficial physiological effect.

2.4. Contribution to normal psychological functions (ID 32)

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

The Panel considers that contribution to normal psychological functions, which encompass cognitive and affective domains, is a beneficial physiological effect.

2.5. Maintenance of normal bone (ID 33)

The claimed effect is "bone/teeth/hair/skin and nails health". The Panel assumes that the target population is the general population.

The Panel considers that maintenance of normal bone is a beneficial physiological effect.

2.6. Maintenance of normal teeth (ID 33)

The claimed effect is "bone/teeth/hair/skin and nails health". The Panel assumes that the target population is the general population.

The Panel considers that maintenance of normal teeth is a beneficial physiological effect.

2.7. Maintenance of normal hair (ID 33)

The claimed effect is "bone/teeth/hair/skin and nails health". The Panel assumes that the target population is the general population.

The Panel considers that maintenance of normal hair is a beneficial physiological effect.

2.8. Maintenance of normal nails (ID 33)

The claimed effect is "bone/teeth/hair/skin and nails health". The Panel assumes that the target population is the general population.

The Panel considers that maintenance of normal nails is a beneficial physiological effect.

2.9. Maintenance of normal vision (ID 39)

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

The Panel considers that maintenance of normal vision is a beneficial physiological effect.

2.10. Maintenance of normal red blood cells (ID 40)

The claimed effect is "red blood cells". The Panel assumes that the target population is the general population.

In the context of the proposed wording, the Panel assumes that the claimed effect relates to the maintenance of normal red blood cells.

The Panel considers that maintenance of normal red blood cells is a beneficial physiological effect.

2.11. Protection of DNA, proteins and lipids from oxidative damage (ID 207)

The claimed effect is "antioxidant properties". 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 DNA, proteins and lipids if they are not intercepted by the antioxidant network which includes free radical scavengers such as antioxidant nutrients.

The Panel considers that the protection of DNA, proteins and lipids from oxidative damage may be a beneficial physiological effect.

2.12. Reduction of tiredness and fatigue (ID 41)

The claimed effect is "vitamin/mineral supplementation to reduce fatigue and tiredness in situations of inadequate micronutrient status". The Panel assumes that the target population is the general population.

The Panel considers that the reduction of tiredness and fatigue is a beneficial physiological effect.

2.13. Maintenance of the normal function of the nervous system (ID 213)

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

The Panel considers that maintenance of the normal function of the nervous system is a beneficial physiological effect.

3. Scientific substantiation of the claimed effect

Riboflavin (vitamin B2) is a water-soluble, yellow, fluorescent compound, chemically specified as a 7,8-dimethyl-10-(1'-D-ribityl)-isoalloxazine. The vitamin is a precursor of certain essential coenzymes such as flavin mononucleotide (FMN) and flavin-adenine dinucleotide (FAD). In these coenzyme forms riboflavin functions as a catalyst for oxidation and reduction reactions and electron transport. Riboflavin is thus involved in a wide variety of metabolic pathways, including the biosynthesis and catabolism of amino acids, fatty acids and carbohydrates (IoM, 1998; SCF, 2000; Powers, 2003).

Riboflavin deficiency usually occurs in conjunction with other nutritional deficiencies. Early signs of riboflavin deficiency are soreness and burning of the lips, mouth, and tongue; burning and itching of the eyes; photophobia; and a loss of visual acuity. The most common signs are pallor and maceration of the mucosa at the angles of the mouth (angular stomatitis) and vermilion surfaces of the lips (cheilosis), eventually replaced by superficial linear fissures. The fissures can become infected with *Candida albicans*, causing grayish white lesions (perlèche). The tongue may appear magenta. Seborrheic dermatitis develops, usually affecting the nasolabial folds, ears, eyelids, and scrotum or labia majora. These areas become red, scaly, and greasy. Rarely, neovascularisation and keratitis of the cornea can also occur, causing lacrimation and photophobia (Bates, 2005; Bender, 2002). Deficiency symptoms also include normochromic, normocytic anaemia associated with pure erythrocyte cytoplasia of the bone marrow (IoM, 1998).

3.1. Contribution to normal energy-yielding metabolism (ID 29, 35, 36, 42)

The evidence provided by consensus opinions/reports from authoritative bodies and reviews shows that there is consensus on the role of riboflavin in energy-yielding metabolism (JHCI, 2003; Bates, 2005; SCF, 2000; IoM, 1998; EVM, 2002).

Riboflavin has an important role as a coenzyme in energy-yielding metabolism acting as an electron carrier in a wide variety of oxidation and reduction reactions that are central to many metabolic processes, including the mitochondrial electron transport chain, fatty acid and amino acid oxidation, and the citric acid cycle (Bender, 2002; Rivlin, 2006).

The Panel concludes that a cause and effect relationship has been established between the dietary intake of riboflavin and the contribution to normal energy-yielding metabolism.

3.2. Contribution to normal metabolism of iron (ID 30, 37)

The evidence provided by consensus opinions/reports from authoritative bodies and reviews shows that there is consensus on the role of riboflavin in the metabolism of iron (JHCI, 2003; Bates, 2005; SCF, 2000; IoM, 1998; Bender, 2002).

Iron metabolism is impaired in riboflavin deficiency. The utilisation of iron reserves from the intracellular protein, ferritin, requires riboflavin. Animal studies show that riboflavin deficiency increases the rate of gastrointestinal iron loss (Powers, 2003). Riboflavin is required for haemoglobin synthesis (Bates, 2005).

The Panel concludes that a cause and effect relationship has been established between the dietary intake of riboflavin and contribution to normal metabolism of iron.

3.3. Maintenance of normal skin and mucous membranes (ID 31, 33)

The evidence provided by consensus opinions/reports from authoritative bodies and reviews shows that there is consensus on the role of riboflavin in the structure and function of skin and mucous membranes (JHCI, 2003; Bates, 2005; EVM, 2002; IoM, 1998).

This evidence comes mainly from the observation of symptoms of riboflavin deficiency. Mucocutaneous lesions are present in both acute and chronic riboflavin deficiency. The distribution of the lesions varies with the age and sex of the patient. Lesions of acute riboflavin deficiency are similar to those observed in protein-energy malnutrition of the kwashiorkor type. In chronic riboflavin deficiency the cutaneous lesions resemble monilial intertrigo and the mucous membrane lesions include a characteristic glossitis. Mucosal and skin symptoms disappear after administration of riboflavin in adequate doses (Roe, 1991).

The Panel concludes that a cause and effect relationship has been established between the dietary intake of riboflavin and maintenance of normal skin and mucous membranes.

3.4. Contribution to normal psychological functions (ID 32)

A total of 22 references, 14 of which were textbooks, were provided for the substantiation of the claimed effect.

Four studies were randomised clinical trials of the effects of multivitamin supplementation in normal healthy adults (Benton et al, 1995a; Carroll et al., 2000; Heseker et al., 1995). The Panel considers that no conclusions can be drawn from studies on fixed combinations for the substantiation of the claim on riboflavin alone.

One article was a review of the nutritional effects of oral contraceptive use in women (Webb, 1980), another was a short report from a meeting on malnutrition (Buzina et al, 1989), and a third was on dietary reference intakes. The Panel considers that no conclusions can be drawn from these references for the scientific substantiation of the claimed effect.

Two articles were narrative reviews of the influence of micronutrients and vitamins on cognitive function and performance (Huskisson et al, 2007a) and the role of vitamins and minerals in energy metabolism and well-being (Huskisson et al, 2007b). The Panel notes that neither focused on the

specific role of riboflavin, but rather considered the benefits of multivitamin and micronutrient supplementation in vitamin and micronutrient deficiencies.

One observational study found an association between severe riboflavin deficiency and clinical signs of behavioural disturbance in psychiatric patients (Carney et al., 1982), and suggested that affective changes are characteristic of riboflavin and pyridoxine deficiencies. This study did not investigate relevant endpoints of cognitive outcomes. The Panel notes that no evidence was presented to indicate that findings from an observational study on affective changes in psychiatric patients could be extrapolated to the general population and, moreover, no conclusions on a causal relationship between the dietary intake of riboflavin and contribution to normal psychological function can be drawn from this study because residual confounding by other dietary and lifestyle factors inherent to the observational study design cannot be excluded.

The Panel notes that none of the references provided addressed the relationship between the intake of riboflavin and psychological functions.

The Panel concludes that a cause and effect relationship has not been established between the dietary intake of riboflavin and contribution to normal psychological functions.

3.5. Maintenance of normal bone (ID 33)

Four consensus references were provided for the substantiation of the claimed effect (SCF, 1993; IoM, 1998; SCF, 2000; EVM, 2003). None mentioned a specific relationship between riboflavin intake and the maintenance of normal bone. The Panel considers that no conclusions can be drawn from these references for the scientific substantiation of the claimed effect.

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

3.6. Maintenance of normal teeth (ID 33)

Four consensus references were provided for the substantiation of the claimed effect (SCF, 1993; IoM, 1998; SCF, 2000; EVM, 2003). None mentioned a specific relationship between riboflavin intake and maintenance of normal teeth. The Panel considers that no conclusions can be drawn from these references for the scientific substantiation of the claimed effect.

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

3.7. Maintenance of normal hair (ID 33)

Four consensus references were provided for the substantiation of the claimed effect (SCF, 1993; IoM, 1998; SCF, 2000; EVM, 2003). None mentioned a specific relationship between riboflavin intake and maintenance of normal hair. The Panel considers that no conclusions can be drawn from these references for the scientific substantiation of the claimed effect.

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

3.8. Maintenance of normal nails (ID 33)

Four consensus references were provided for the substantiation of the claimed effect (SCF, 1993; IoM, 1998; SCF, 2000; EVM, 2003). None mentioned a specific relationship between riboflavin intake and maintenance of normal nails. The Panel considers that no conclusions can be drawn from these references for the scientific substantiation of the claimed effect.

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

3.9. Maintenance of normal vision (ID 39)

Riboflavin deficiency can cause conjunctivitis with vascularisation of the cornea and opacity of the lens – the only lesion of araboflavinosis for which the biochemical basis is known. Glutathione is important in maintaining the normal clarity of crystallins in the lens and glutathione reductase is a flavoprotein that is particularly sensitive to riboflavin depletion (Gibney et al., 2002).

The Panel concludes that a cause and effect relationship has been established between the dietary intake of riboflavin and maintenance of normal vision.

3.10. Maintenance of normal red blood cells (ID 40)

Riboflavin deficiency induces normocytic and normochromic anaemia characterised by an increase in the number of reticulocytes, immature precursors of red blood cells, which are virtually absent from normal blood. Symptoms are corrected by treatment with riboflavin. (Bates, 2005; Powers, 2003).

The Panel considers that a cause and effect relationship has been established between the dietary intake of riboflavin and maintenance of normal red blood cells.

3.11. Protection of DNA, proteins and lipids from oxidative damage (ID 207)

It is well established that riboflavin participates in a diversity of redox reactions, through the cofactors FMN and FAD, which act as electron carriers (Powers, 2003; Rivlin, 2007). A protective role of riboflavin against lipid peroxidation is provided mainly by the glutathione redox cycle (Sadler et al., 1999). Glutathione peroxidase requires reduced glutathione, which in turn is generated by glutathione reductase. The glutathione reductase enzyme requires the riboflavin co-enzyme FAD and this enzyme is particularly sensitive to riboflavin deficiency making glutathione reductase enzyme measures most suitable for assessing riboflavin status (Hoey et al, 2009). Riboflavin deficiency is associated with increased lipid peroxidation, a process that can be inhibited by riboflavin (Bates, 2005; Dutta et al., 1995; Miyazawa et al., 1983; Taniguchi et al., 1983).

The Panel concludes that a cause and effect relationship has been established between the dietary intake of riboflavin and protection of DNA, proteins and lipids from oxidative damage.

3.12. Reduction of tiredness and fatigue (ID 41)

The evidence provided by consensus opinions/reports from authoritative bodies and reviews shows that there is consensus that the symptoms of riboflavin deficiency include weakness and fatigue (Rivlin, 2006).

The Panel concludes that a cause and effect relationship has been established between the dietary intake of riboflavin and a reduction of tiredness and fatigue.

3.13. Maintenance of the normal function of the nervous system (ID 213)

The evidence provided by consensus opinions/reports from authoritative bodies and reviews shows that there is consensus on the role of riboflavin in maintaining normal function of the nervous system (Powers, 2003).

Riboflavin deficiency causes degenerative changes in peripheral nerves found in experimental conditions in several species of animals, which are characterised by demyelination with hypertrophy of Schwann cells, marked lipid accumulation, paranodal tomacula and fibroblastic onion bulbs. The presence of lipid depositions in Schwann cells and the formation of paranodal redundant loops of normal myelin suggest a disturbance of lipid metabolism and control of myelin membrane formation in the myelinating Schwann cell. Spinal cord and brain are unaffected (Cai et al., 2009). Some case reports are available in humans showing the presence of peripheral polyneuropathy in riboflavin depleted subjects (Powers, 2003; Bates, 2005).

The Panel concludes that a cause and effect relationship has been established between the dietary intake of riboflavin and maintenance of the normal function of the nervous system.

4. Panel's comments on the proposed wordings

4.1. Contribution to normal energy-yielding metabolism (ID 29, 35, 36, 42)

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

4.2. Contribution to normal metabolism of iron (ID 30, 37)

The Panel considers that the following wording reflects the scientific evidence: "Riboflavin contributes to the normal metabolism of iron in the body".

4.3. Maintenance of normal skin and mucous membranes (ID 31, 33)

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

4.4. Maintenance of normal red blood cells (ID 40)

The Panel considers that the following wording reflects the scientific evidence: "Riboflavin contributes to the maintenance of normal red blood cells".

4.5. Maintenance of normal vision (ID 39)

The following wording reflects the scientific evidence: "Riboflavin contributes to the maintenance of normal vision".

4.6. Protection of DNA, protein and lipids from oxidative damage (ID 207)

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

4.7. Reduction of tiredness and fatigue (ID 41)

The Panel considers that the following wording reflects the scientific evidence: "Riboflavin can contribute to the reduction of tiredness and fatigue".

4.8. Maintenance of the normal function of the nervous system (ID 213)

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

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 riboflavin as per Annex to Regulation (EC) No 1924/2006. Such amounts can be easily consumed as part of a balanced diet. Tolerable Upper Intake Levels (UL) have not been established for riboflavin in children, adolescents and adults (SCF, 2000).

CONCLUSIONS

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

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

Contribution to normal energy-yielding metabolism (ID 29, 35, 36, 42)

- The claimed effects are "energy metabolism", "riboflavin participates in oxidation-reduction reactions in numerous metabolic pathways and in energy production via respiratory chain", "macronutrient metabolism" and "release of energy from food". The target population is assumed to be the general population. Contribution to normal energy-yielding metabolism is a beneficial physiological effect.
- A cause and effect relationship has been established between the dietary intake of riboflavin and contribution to normal energy-yielding metabolism.
- The following wording reflects the scientific evidence: "Riboflavin contributes to normal energy-yielding metabolism".

Contribution to normal metabolism of iron (ID 30, 37)

- The claimed effects are "transport and metabolism of iron", and "healthy iron status". The target population is assumed to be the general population. Contribution to normal metabolism of iron is a beneficial physiological effect.
- A cause and effect relationship has been established between the dietary intake of riboflavin and contribution to normal metabolism of iron.
- The following wording reflects the scientific evidence: "Riboflavin contributes to normal metabolism of iron in the body".

Maintenance of normal skin and mucous membranes (ID 31, 33)

- 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 nails health". The target population is assumed to be the general population. Maintenance of normal skin and mucous membranes is a beneficial physiological effect.
- A cause and effect relationship has been established between the dietary intake of riboflavin and maintenance of normal skin and mucous membranes.
- The following wording reflects the scientific evidence: "Riboflavin contributes to the maintenance of normal skin and mucous membranes".

Contribution to normal psychological functions (ID 32)

- The claimed effect is "mental performance (where mental performance stands for those aspects of brain and nerve functions which determine aspects like concentration, learning, memory and reasoning, as well as resistance to stress)". The target population is assumed to be the general population. Contribution to normal psychological functions, which encompass cognitive and affective domains, is a beneficial physiological effect.
- A cause and effect relationship has not been established between the dietary intake of riboflavin and contribution to normal psychological functions.

Maintenance of normal bone (ID 33)

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

Maintenance of normal teeth (ID 33)

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

Maintenance of normal hair (ID 33)

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

Maintenance of normal nails (ID 33)

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

Maintenance of normal vision (ID 39)

- The claimed effect is "eyes". The Panel target population is assumed to be the general population. Maintenance of normal vision is a beneficial physiological effect.
- A cause and effect relationship has been established between the dietary intake of riboflavin and maintenance of normal vision.
- The following wording reflects the scientific evidence: "Riboflavin contributes to the maintenance of normal vision".

Maintenance of normal red blood cells (ID 40)

- The claimed effect is "red blood cells". The target population is assumed to be the general population. Maintenance of normal red blood cells is a beneficial physiological effect.
- A cause and effect relationship has been established between the dietary intake of riboflavin and maintenance of normal red blood cells.
- The following wording reflects the scientific evidence: "Riboflavin contributes to the maintenance of normal red blood cells".

Protection of DNA, proteins and lipids from oxidative damage (ID 207)

- The claimed effect is "antioxidant properties". The target population is assumed to be the general population. Protection of DNA, proteins and lipids from oxidative damage may be a beneficial physiological effect.
- A cause and effect relationship has been established between the dietary intake of riboflavin and protection of DNA, proteins and lipids from oxidative damage.

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

Reduction of tiredness and fatigue (ID 41)

- The claimed effect is "vitamin/mineral supplementation to reduce fatigue and tiredness in situations of inadequate micronutrient status". The target population is assumed to be the general population. Reduction of tiredness and fatigue is a beneficial physiological effect.
- A cause and effect relationship has been established between the dietary intake of riboflavin and a reduction of tiredness and fatigue.
- The following wording reflects the scientific evidence "Riboflavin can contribute to the reduction of tiredness and fatigue".

Maintenance of the normal function of the nervous system (ID 213)

- The claimed effect is "nervous system". The target population is assumed to be the general population. Maintenance of the normal function of the nervous system is a beneficial physiological effect.
- A cause and effect relationship has been established between the dietary intake of riboflavin and maintenance of the normal function of the nervous system.
- The following wording reflects the scientific evidence "Riboflavin contributes to the maintenance of the normal function of the nervous system".

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 riboflavin 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-2008-816, EFSA-Q-2008-817, EFSA-Q-2008-818, EFSA-Q-2008-819, EFSA-Q-2008-820, EFSA-Q-2008-822, EFSA-Q-2008-823, EFSA-Q-2008-824, EFSA-Q-2008-826, EFSA-Q-2008-827, EFSA-Q-2008-828, EFSA-Q-2008-829, EFSA-Q-2008-994, EFSA-Q-2008-1000). The scientific substantiation is based on the information provided by the Members States in the consolidated list of Article 13 health claims and references that EFSA has received from Member States or directly from stakeholders.

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

REFERENCES

Bates, CJ, 2005. Riboflavin. In: Encyclopaedia of Human Nutrition. Eds Sadler, MJ, Strain, JJ and Caballero, B. Academic Press, San Diego, 100-108.

Bender DA, 2003. Nutritional Biochemistry of the Vitamins. Cambridge University Press, Cambridge.

Benton D, Fordy J and Haller J, 1995a. The impact of long-term vitamin supplementation on cognitive functioning. Psychopharmacology (Berl), 117, 298-305.

Benton D, Haller J and Fordy J, 1995b. Vitamin supplementation for 1 year improves mood. Neuropsychobiology, 32, 98-105.

Buzina, 1989. Workshop on Functional Significance of Mild-to-Moderate Malnutrition. American Journal of Clinical Nutrition 50, 172-176.

Cai Z, Blumbergs PC, Finnie JW, Manavis J and Thompson PD, 2009. Selective vulnerability of peripheral nerves in avian riboflavin deficiency demyelinating polyneuropathy. Veterinary Pathology, 46, 88-96.

Carney MW, Ravindran A, Rinsler MG and Williams DG, 1982. Thiamine, riboflavin and pyridoxine deficiency in psychiatric in-patients. British Journal of Psychiatry, 141, 271-272.

Carroll D, Ring C, Suter M and Willemsen G, 2000. The effects of an oral multivitamin combination with calcium, magnesium, and zinc on psychological well-being in healthy young male volunteers: a double-blind placebo-controlled trial. Psychopharmacology (Berl), 150, 220-225.

Dutta P, Seirafi J, Halpin D, Pinto J and Rivlin R, 1995. Acute ethanol exposure alters hepatic glutathione metabolism in riboflavin deficiency. Alcohol, 12, 43 – 47.

EVM (Expert Group on Vitamins and Minerals), 2003. Safe Upper Levels for Vitamins and Minerals. Food Standards Agency, London.

Gibney MJ, Vorster HH and Kok FJ, 2002. Introduction to Human Nutrition. The Nutrition Society. Blackwell Science, Oxford.

Heseker H, Kubler W, Pudel V and Westenhofer J, 1995. Interaction of vitamins with mental performance. Bibliotheca Nutritio et Dieta, 52, 43-55.

Hoey L, McNulty H and Strain JJ, 2009. Studies of biomarker responses to intervention with riboflavin: a systematic review. American Journal of Clinical Nutrition, 89, 1960S-1980S

Huskisson E, Maggini S and Ruf M, 2007a. The influence of micronutrients on cognitive function and performance. Journal of International Medical Research, 35, 1-19.

Huskisson E, Maggini S and Ruf M, 2007b. The role of vitamins and minerals in energy metabolism and well-being. Journal of International Medical Research, 35, 277-289.

IoM (Institute of Medicine), 1998. Dietary reference intakes for thiamin, riboflavin, niacin, vitamin B6, folate, vitamin B12, pantothenic acid, biotin and choline. National Academy Press, Washington D.C.

JHCI (Joint Health Claims Initiative), 2003. A list of well established nutrient function statements. A Report by the Joint Health Claims Initiative to the Food Standard Agency.

Miyazawa T, Sato C and Kaneda T, 1983. Antioxidative effects of α-tocopherol and riboflavin-butyrate in rats dosed with methyl linoleate hydroperoxide. Agricultural and Biological Chemistry, 47, 1577 – 1582.

Powers HJ, 2003. Riboflavin (vitamin B-2) and health. American Journal of Clinical Nutrition, 77, 1352-1360.

Rivlin RS, 2007. Riboflavin (vitamin B2). In: Handbook of Vitamins. Eds Rucker R, Zempleni J, Suttie, JW and McCormick DB. CRC Press, Boca Raton, 241 – 242.

Rivlin RS, 2006. Riboflavin. In: Present Knowledge in Nutrition. Eds Bowman BA and Russell RM, ILSI Press, Washington D.C., 250–258.

Roe DA, 1991. Riboflavin deficiency: mucocutaneous sign of acute and chronic deficiency. Seminars in Dermatology, 10, 293–295.

Sadler MJ, Strain JJ and Caballero B, 1999. Encyclopedia of Human Nutrition, Academic Press, San Diego, 100-108.

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

SCF (Scientific Committee on Food), 2000. Opinion of the Scientific Committee on Food on the Tolerable Upper Intake Level of vitamin B2.

Taniguchi M and Hara T, 1983. Effects of riboflavin and selenium deficiencies on glutathione and related enzyme activities with respect to lipid peroxide content of rat livers. Journal of Nutritional Science and Vitaminology, 29, 283-292.

Webb JL, 1980. Nutritional effects of oral contraceptive use: a review. The Journal of Reproductive Medicine, 25, 150-156.

APPENDICES

APPENDIX A

BACKGROUND AND TERMS OF REFERENCE AS PROVIDED BY THE EUROPEAN COMMISSION

The Regulation 1924/2006 on nutrition and health claims made on foods[8] (hereinafter "the Regulation") entered into force on 19th January 2007.

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

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

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

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

b) psychological and behavioural functions; or

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

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

(i) based on generally accepted scientific evidence; and

(ii) well understood by the average consumer.

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

ISSUES THAT NEED TO BE CONSIDERED

IMPORTANCE AND PERTINENCE OF THE FOOD[9]

Foods are commonly involved in many different functions[10] 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

[8] OJ L12, 18/01/2007

[9] The term 'food' when used in this Terms of Reference refers to a food constituent, the food or the food category.

[10] 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 DISCAIMER

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

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

APPENDIX C

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

ID	Food or Food component	Health Relationship	Proposed wording
29	Vitamin B2(Riboflavin)	Energy metabolism	Riboflavin contributes to the normal release of energy from foods.
	Conditions of use – Milks, buttermilks and milk drinks with riboflavin content of 0.2mg/100g, 0.4mg/serving – 0.85mg/day (equal to 50% of ADI (Acceptable Daily Intake)) – Tagesbedarf gemäß NwKVO 1,6 mg pro Tag – Minimum 15% RDA (0.24mg) per daily dosage as per 90/496/EC – Must at least be a source of vitamin/s as per annex to regulation 1924/2006 – Applicable to both children and adults		
ID	**Food or Food component**	**Health Relationship**	**Proposed wording**
30	Vitamin B2	Transport and metabolism of iron	Vitamin B2 (Riboflavin) helps the body to maintain a normal iron level.
	Conditions of use – Must at least be a source of vitamin/s as per annex to regulation 1924/2006 – Minimum 15% RDA per 100g or 100ml or per single servings as per 90/496/EEC – Applicable to both children and adults – All adults aged 18 years and over		
ID	**Food or Food component**	**Health Relationship**	**Proposed wording**
31	Vitamin B2	Required for the normal structure of mucous membranes (such as the surface of the tongue, the mouth, eyes and intestines).	Vitamin B2 (Riboflavin) helps keep your skin and mucous membranes
	Conditions of use – 0.24 miligrams Vitamin B2 (Riboflavin) per day – Must at least be a source of vitamin/s as per annex to regulation 1924/2006 – MINDESTENS 15 % RDA JE 100 G ODER 100 ML ODER JE PORTION GEMÄß 90/496/EWG – Applicable to both children and adults – All adults aged 18 years and over		
ID	**Food or Food component**	**Health Relationship**	**Proposed wording**
32	Vitamin B2	Mental performance (where mental performance stands for those aspects of brain and nerve functions which determine aspects like concentration, learning, memory and reasoning, as well as resistance to stress)	- Riboflavin is needed/important for mental function and performance

	Conditions of use: – 0,6mg pro 4,2 MJ (1000 kcal) bzw. 1mg (Frauen) / 1,2mg (Männer) – Erwachsene – Only for products with at least 100 % RDA of vitamins – Minimum15% RDA (0,24 mg) dziennie		
ID	**Food or Food component**	**Health Relationship**	**Proposed wording**
33	**Vitamin B2**	Bone/Teeth/ Hair / Skin and Nail health	Necessary for healthy teeth, bones, hair, skin and nails.
	Conditions of use – Must meet minimum requirements for use of the claim "source of riboflavin" as per Annex to Regulation 1924/2006.		
ID	**Food or Food component**	**Health Relationship**	**Proposed wording**
35	Riboflavin	Riboflavin participates in oxidation-reduction reactions in numerous metabolic pathways and in energy production via respiratory chain	Riboflavin is a component in the formation of energy
	Conditions of use – 0.85mg/day (equal to 50% of ADI (Acceptable Daily Intake)) – Must meet minimum requirements for use of the claim "source of riboflavin" as per Annex to Regulation 1924/2006.		
ID	**Food or Food component**	**Health Relationship**	**Proposed wording**
36	Riboflavin (vitamin B2)	Macronutrient metabolism	- Riboflavin/vitamin B2 helps many enzymatic reactions in the body.
	Conditions of use – Source of 15% of RDA per 100g		
ID	**Food or Food component**	**Health Relationship**	**Proposed wording**
37	Riboflavin (vitamin B2)	Healthy iron status	- Riboflavin/vitamin B2 is important for normal iron status in the blood.
	Conditions of use – Source of 15% of RDA per 100g		
ID	**Food or Food component**	**Health Relationship**	**Proposed wording**
39	Riboflavin (vitamin B2)	Eyes	- Riboflavin (Vitamin B2) contributes to the normal structure of eyes
	Conditions of use – Minimum 15% RDA per 100g or 100ml or per single servings as per 90/496/EEC		
ID	**Food or Food component**	**Health Relationship**	**Proposed wording**
40	Riboflavin (vitamin B2)	Red blood cells	- Riboflavin (Vitamin B2) contributes to the normal structure of red blood cells
	Conditions of use – Minimum 15% RDA per 100g or 100ml or per single servings as per 90/496/EEC		

ID	Food or Food component	Health Relationship	Proposed wording
41	Vitamin B2(Riboflavin)	Vitamin/mineral supplementation to reduce fatigue and tiredness in situations of inadequate micronutrient status **Clarification from MS**: Reduce fatigue and tiredness, particularly in situations of inadequate micronutrient status, due to role in macronutrient metabolism	Supplementation with B-vitamins, iron, magnesium as well as vitamin C can reduce fatigue and tiredness in situations of inadequate micro-nutrient status **Clarification from MS**: Supplementation with B-vitamins, iron, magnesium as well as vitamin C can reduce fatigue and tiredness in situations of inadequate micro-nutrient status
	Conditions of use – Must meet minimum requirements for use of the claim "source of [name of vitamin/s] and/or [name of mineral/s]," as per Annex to Regulation 1924/2006.		
ID	**Food or Food component**	**Health Relationship**	**Proposed wording**
42	Riboflavin (vitamin B2)	Release of energy from food	- Riboflavin contributes to the normal release of energy from food.
	Conditions of use – 0.24mg Vitamin B2 per day – Minimum 15% RDA per 100g or 100ml or per single servings as per 90/496/EEC – Applicable to both adults and children		
ID	**Food or Food component**	**Health Relationship**	**Proposed wording**
207	Riboflavin (vitamin B2)	Antioxidant properties	- Riboflavin protects the body's cells - can protect from radicals which cause cell damage - can protect cells and tissues from oxidative damage - can contribute to the total antioxidant capacity of the body.
	Conditions of use – Must meet minimum requirements for use of the claim "source of riboflavin" as per Annex to Regulation 1924/2006.		
ID	**Food or Food component**	**Health Relationship**	**Proposed wording**
213	Vitamin B2(Riboflavin)	Nervensystem **Clarification from MS**: nervous system: formation of the myelin sheath	[In german :] Wichtig für den Erhalt der Nervenummantelung **Clarification from MS**: significantly supports myelin sheath of nerve fibres
	Conditions of use – Must at least be a source of vitamin/s as per annex to regulation 1924/2006		

GLOSSARY AND ABBREVIATIONS

FAD	Flavin-adenine dinucleotide
FMN	Flavin mononucleotide