SCIENTIFIC OPINION

Scientific Opinion on the substantiation of health claims related to magnesium and "hormonal health" (ID 243), reduction of tiredness and fatigue (ID 244), contribution to normal psychological functions (ID 245, 246), maintenance of normal blood glucose concentrations (ID 342), maintenance of normal blood pressure (ID 344, 366, 379), protection of DNA, proteins and lipids from oxidative damage (ID 351), maintenance of the normal function of the immune system (ID 352), maintenance of normal blood pressure during pregnancy (ID 367), resistance to mental stress (ID 375, 381), reduction of gastric acid levels (ID 376), maintenance of normal fat metabolism (ID 378) and maintenance of normal muscle contraction (ID 380, ID 3083) 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

1 On request from the European Commission, Question No EFSA-Q-2008-1030, EFSA-Q-2008-1031, EFSA-Q-2008-1032, EFSA-Q-2008-1033, EFSA-Q-2008-1129, EFSA-Q-2008-1131, EFSA-Q-2008-1138, EFSA-Q-2008-1139, EFSA-Q-2008-1153, EFSA-Q-2008-1154, EFSA-Q-2008-1162, EFSA-Q-2008-1163, EFSA-Q-2008-1165, EFSA-Q-2008-1166, EFSA-Q-2008-1167, EFSA-Q-2008-1168, EFSA-Q-2008-3815, 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 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 Cardiovascular Health/Oxidative Stress: Antti Aro, Marianne Geleijnse, Marina Heinonen, Ambroise Martin, Wilhelm Stahl and Henk van den Berg. 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.

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in relation to magnesium and "hormonal health", reduction of tiredness and fatigue, contribution to normal psychological functions, maintenance of normal blood glucose concentrations, maintenance of normal blood pressure, protection of DNA, proteins and lipids from oxidative damage, maintenance of the normal function of the immune system, maintenance of normal blood pressure during pregnancy, resistance to mental stress, reduction of gastric acid levels, maintenance of normal fat metabolism and maintenance of normal muscle contraction. 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 magnesium. The Panel considers that magnesium is sufficiently characterised.

"Hormonal health"

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

The Panel considers that the claimed effect is general and non-specific and does not refer to any specific health claim as required by Regulation (EC) No 1924/2006.

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.

A decline in magnesium status is associated with various symptoms such as nausea, muscular weakness, fatigue or staggering.

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

Contribution to normal psychological functions

The claimed effects are "the role of vitamins and minerals in mental performance (where mental performance stands for those aspects of brain and nerve functions which determine aspects like concentration, learning, memory and reasoning)" and "brain function". 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.

A decline in magnesium status is associated with various symptoms such as depression, psychosis, irritability or confusion.

The Panel concludes that a cause and effect relationship has been established between the dietary intake of magnesium and contribution to normal psychological functions.

Maintenance of normal blood glucose concentrations

The claimed effect is "carbohydrate metabolism and insulin sensitivity". The target population is assumed to be the general population. In the context of the proposed wording, the Panel assumes that the claimed effect refers to the maintenance or achievement of normal blood glucose concentrations. The Panel considers that long-term maintenance of normal blood glucose concentrations is a beneficial physiological effect.

The Panel considers that no conclusions can be drawn for the scientific substantiation of the claim from the meta-analysis owing to the inclusion of studies that cannot be used for the substantiation of the claim, from the individual trials provided owing to inappropriate study groups or endpoints and from the observational studies provided owing to inadequate control of possible confounding factors

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 magnesium and maintenance of normal blood glucose concentrations.

Maintenance of normal blood pressure

The claimed effects are "cardiovascular system", "blood pressure" and "circulation". The target population is assumed to be the general population. In the context of the proposed wording, the Panel assumes that the claimed effects refer to the maintenance of normal blood pressure. The Panel considers that maintenance of normal blood pressure is a beneficial physiological effect.

In weighing the evidence, the Panel took into account that no conclusions could be drawn from the meta-analysis and the systematic review provided for the scientific substantiation of the claimed effect owing to the inclusion of studies that cannot be used for the substantiation of the claim, that in 16 RCTs in subjects with no pharmacological treatment for hypertension evidence for a blood-pressure lowering effect of magnesium was weak and inconsistent, and that in five epidemiological studies evidence for a relationship between magnesium intake and changes in blood pressure or prevention of hypertension was weak and inconsistent.

On the basis of the data presented, the Panel concludes that the evidence provided is insufficient to establish a cause and effect relationship between the dietary intake of magnesium and maintenance of normal blood pressure.

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.

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 magnesium and protection of DNA, proteins and lipids from oxidative damage.

Maintenance of the normal function of the immune system

The claimed effect is "immune system". The target population is assumed to be the general population. In the context of the proposed wording, the Panel assumes that the claimed effect refers to the normal function of the immune system. The Panel considers that maintenance of the normal function of the immune system 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 magnesium and maintenance of the normal function of the immune system.

Maintenance of normal blood pressure during pregnancy

The claimed effect is "pregnancy". The target population is assumed to be women of child-bearing age. In the context of the proposed wording, the clarifications provided by Member States and the references submitted, the Panel assumes that the claimed effect refers to the maintenance of normal blood pressure during pregnancy. The Panel considers that maintenance of normal blood pressure during pregnancy is a beneficial physiological 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 magnesium and maintenance of normal blood pressure during pregnancy.

Resistance to mental stress

The claimed effects are "système nerveux" and "magnésium et stress: magnesium is a mineral involved in stress and its reactions. On the one hand, stress tends to reduce the magnesium status and, on the other hand, an exogenous or endogenous deficit in magnesium increases the stress response. It matters to maintain a suitable magnesium status in order to better react against stress". The target population is assumed to be the general population. The Panel considers that resistance to mental stress might be 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 dietary intake of magnesium and resistance to mental stress.

Reduction of gastric acid levels

The claimed effect is "acid-base balance/gastric acidity". The target population is assumed to be the general population. In the context of the proposed wordings, the Panel assumes that the claimed effect refers to a reduction of gastric acid levels. The Panel considers that the evidence provided does not establish that reducing gastric acid levels is a beneficial physiological effect for the general population.

The Panel concludes that a cause and effect relationship has not been established between the dietary intake of magnesium and a beneficial physiological effect for the general population related to reduction of gastric acid levels.

Maintenance of normal fat metabolism

The claimed effect is "fat metabolism: acid base balance". The target population is assumed to be the general population. In the context of the proposed wording and the clarifications provided by Member States, the Panel assumes that the claimed effect refers to the maintenance of normal fat metabolism. The Panel considers that maintenance of normal fat metabolism 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 magnesium and maintenance of normal fat metabolism.

Maintenance of normal muscle contraction

The claimed effects are “fonctionnement musculaire” and “metabolism/muscle function”. The target population is assumed to be the general population.

In the context of the proposed wordings, the Panel assumes that the claimed effects refer to the maintenance of normal muscle contraction.

A claim on magnesium and muscle contraction has already been assessed with a favourable outcome.

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 magnesium 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

Magnesium, hormonal health, tiredness, fatigue, psychological functions, blood glucose, blood pressure, oxidative damage, immune system, pregnancy, mental stress, gastric acid, fat metabolism, muscle, health claims.

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INFORMATION AS PROVIDED IN THE CONSOLIDATED LIST

The consolidated list of health claims pursuant to Article 13 of Regulation (EC) No 1924/2006[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 magnesium, which is a well recognised nutrient and is measurable in foods by established methods.

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

2. Relevance of the claimed effect to human health

2.1. "Hormonal health" (ID 243)

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

"An essential co-factor in fatty acid metabolism that impacts upon hormonal health" is not sufficiently defined and no further details were provided in the proposed wording.

The Panel considers that the claimed effect is general and non-specific and does not refer to any specific health claim as required by Regulation (EC) No 1924/2006.

[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.

2.2. Reduction of tiredness and fatigue (ID 244)

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 reduction of tiredness and fatigue is a beneficial physiological effect.

2.3. Contribution to normal psychological functions (ID 245, 246)

The claimed effects are "the role of vitamins and minerals in mental performance (where mental performance stands for those aspects of brain and nerve functions which determine aspects like concentration, learning, memory and reasoning)" and "brain function". 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.

2.4. Maintenance of normal blood glucose concentrations (ID 342)

The claimed effect is "carbohydrate metabolism and insulin sensitivity". 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 refers to the maintenance or achievement of normal blood glucose concentrations.

The Panel considers that long-term maintenance of normal blood glucose concentrations is a beneficial physiological effect.

2.5. Maintenance of normal blood pressure (ID 344, 366, 379)

The claimed effects are "cardiovascular system", "blood pressure" and "circulation". 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 refer to the maintenance of normal blood pressure.

Blood pressure is the pressure (force per unit area) exerted by circulating blood on the walls of blood vessels. Elevated blood pressure, by convention above 140 mmHg (systolic) and/or 90 mmHg (diastolic), may compromise the normal arterial and cardiac function.

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

2.6. Protection of DNA, proteins and lipids from oxidative damage (ID 351)

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

Reactive oxygen species 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 molecules such as 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 protection of DNA, proteins and lipids from oxidative damage may be a beneficial physiological effect.

2.7. Maintenance of the normal function of the immune system (ID 352)

The claimed effect is "immune system". 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 refers to the normal function of the immune system.

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

2.8. Maintenance of normal blood pressure during pregnancy (ID 367)

The claimed effect is "pregnancy". The Panel assumes that the target population is women of child-bearing age.

In the context of the proposed wording, the clarifications provided by Member States and the references submitted, the Panel assumes that the claimed effect refers to the maintenance of normal blood pressure during pregnancy.

The Panel considers that maintenance of normal blood pressure during pregnancy is a beneficial physiological effect.

2.9. Resistance to mental stress (ID 375, 381)

The claimed effects are "système nerveux" and "magnésium et stress: magnesium is a mineral involved in stress and its reactions. On one hand, stress tends to reduce the magnesium status and, on the other hand, an exogenous or endogenous deficit in magnesium increases the stress response. It matters to maintain a suitable magnesium status in order to better react against stress". The Panel assumes that the target population is the general population.

In the context of the proposed wordings and from the references provided, the Panel assumes that the claimed effects refer to resistance to mental stress. Resistance to mental stress can be measured by established methods.

The Panel considers that resistance to mental stress might be a beneficial physiological effect.

2.10. Reduction of gastric acid levels (ID 376)

The claimed effect is "acid-base balance/gastric acidity". The Panel assumes that the target population is the general population.

In the context of the proposed wordings, the Panel assumes that the claimed effect refers to a reduction of gastric acid levels.

The Panel considers that the evidence provided does not establish that reducing gastric acid levels is a beneficial physiological effect for the general population.

The Panel concludes that a cause and effect relationship has not been established between the dietary intake of magnesium and a beneficial physiological effect for the general population related to the reduction of gastric acid levels.

2.11. Maintenance of normal fat metabolism (ID 378)

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

In the context of the proposed wording and the clarifications provided by Member States, the Panel assumes that the claimed effect refers to the maintenance of normal fat metabolism.

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

2.12. Maintenance of normal muscle contraction (ID 380, 3083)

The claimed effects are "fonctionnement musculaire" and "metabolism/muscle function". 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 refer to the maintenance of normal muscle contraction.

A claim on magnesium and muscle contraction has already been assessed with a favourable outcome (EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA), 2009).

3. Scientific substantiation of the claimed effect

Magnesium is an essential nutrient and serves as a cofactor for over 300 enzymes involved in biological processes. Magnesium is part of the Mg-ATPase complex and is essential for oxidative phosphorylation; it has roles in energy metabolism, mineral homeostasis, calcium metabolism, and neuromuscular and endocrine function (IoM, 1997; SCF, 2001; Volpe, 2006).

In the human body, 50 to 60 % of magnesium is located in the bone. Part of it is readily exchangeable with serum and therefore bone represents a magnesium store. The remaining magnesium is mainly intracellular; extracellular magnesium represents only 1 % of the total magnesium content of the body.

Because magnesium is mostly within cells or in bone, assessment of magnesium status is difficult (Rude and Shils, 2006).

Manifestations of magnesium deficiency include signs related to bone and mineral metabolism, neuromuscular and psychological manifestations (e.g. positive Chvostek and Trousseau signs, spontaneous carpal-pedal spasm, seizures, vertigo, ataxia, nystagmus, athetoid and choreiform movements, muscular weakness, tremor, fasciculation, wasting, depression, psychosis, hallucinations, confusion), symptoms related to potassium homeostasis, and cardiovascular manifestations (Rude and Shils, 2006; FAO/WHO, 2001; O'Brien, 1999). Most of the early symptoms of magnesium depletion are neurological or neuromuscular; thus, a decline in magnesium status produces loss of appetite, nausea, muscular weakness, vomiting, fatigue, lethargy, staggering and, if the deficit is prolonged, weight loss (FAO/WHO, 2001; Volpe, 2006). Progressively increasing with the severity and duration of deficiency are signs such as hyperirritability, hyperexcitability, muscular spasms and tetany, leading ultimately to convulsions (FAO/WHO, 2001).

3.1. Reduction of tiredness and fatigue (ID 244)

A decline in magnesium status is associated with various symptoms such as nausea, muscular weakness, fatigue or staggering (FAO/WHO, 2001; Rude and Shils, 2006; Volpe, 2006).

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

3.2. Contribution to normal psychological functions (ID 245, 246)

A decline in magnesium status is associated with various symptoms such as depression, psychosis, irritability or confusion (Rude and Shils, 2006; FAO/WHO, 2001; O'Brien, 1999).

The Panel concludes that a cause and effect relationship has been established between the dietary intake of magnesium and contribution to normal psychological functions.

3.3. Maintenance of normal blood glucose concentrations (ID 342)

The references provided for the substantiation of the claimed effect include textbooks, one reference unrelated to the food constituent, a general narrative review on magnesium metabolism, status and deficiency, and publications on health outcomes unrelated to the claimed effect: tension headaches and muscle tension, stress and neuropsychiatric disorders, cardiovascular disorders, sports, myocardial infarction. Also, a reference reporting on intracellular changes in magnesium before and after insulin stimulation in diabetic and obese children was provided. The Panel considers that no conclusions can be drawn from these references for the scientific substantiation of the claimed effect.

One meta-analysis of double-blind randomised controlled trials (RCTs) (Song et al., 2006) and four intervention studies in humans (Purvis et al., 1994; Rodriguez-Moran and Guerrero-Romero, 2003; Paolisso et al., 1989b; Guerrero-Romero et al., 2004) on the effects of oral magnesium supplementation on different outcomes were provided. Seven out of the nine trials considered in the meta-analysis (Gullestad et al., 1994; Purvis et al., 1994; Eibl et al., 1995; Erikson and Kohvakka, 1995; de Lourdes et al., 1998; de Valk et al., 1998; Rodriguez-Moran and Guerrero-Romero, 2003), including two of the intervention studies (Purvis et al., 1994; Rodriguez-Moran and Guerrero-Romero, 2003) provided, were performed in diabetic subjects under antidiabetic medications. The Panel considers that the evidence provided does not establish that interactions between magnesium and antidiabetic medication can be excluded. The two remaining trials in the meta-analysis (Paolissoet al., 1989a; 1994) and the two remaining intervention studies (Paolisso et al., 1989b; Guerrero-Romero et al., 2004), which were all performed in insulin resistant subjects or type-2 diabetic subjects under dietary treatment only, did not report on outcomes related to long-term blood glucose control but rather on insulin sensitivity using the euglycaemic-hyperinsulinaemic clamp technique (Paolisso et al., 1989a, 1994) or the surrogate HOMA index (Guerrero-Romero et al., 2004), or on the secretory capacity of the pancreas after stimulation with arginine or glucose (Paolisso et al., 1989b). The Panel considers that no conclusions can be drawn from these references for the scientific substantiation of the claimed effect.

Seven observational studies dealt with dietary intake, serum concentrations or urinary excretion of magnesium in very-low-birth-weight pre-term children in pre-school years (Bo et al. 2007), type 1-diabetic patients (Brown et al., 1999), obese children (Huerta et al., 2005), adults (Ma et al., 2006; Rumawas et al., 2006; Song et al., 2004) and nursing home residents (Worwag et al., 1999). Parameters such as fasting glucose or insulin, HOMA-IR, HbA1c, quantitative insulin sensitivity check index, intravenous glucose tolerance test, post-challenge plasma glucose and insulin, or risk or prevalence of diabetes were considered. The Panel notes that no conclusions can be drawn from these studies for the scientific substantiation of the claimed effect because residual confounding by other dietary and lifestyle factors inherent to the observational study design cannot be excluded.

The Panel considers that no conclusions can be drawn from the meta-analysis for the scientific substantiation of the claim owing to the inclusion of studies that cannot be used for the substantiation

of the claim, from the individual trials provided owing to inappropriate study groups or endpoints and from the observational studies provided owing to inadequate control of possible confounding factors.

The Panel concludes that a cause and effect relationship has not been established between the dietary intake of magnesium and maintenance of normal blood glucose concentrations.

3.4. Maintenance of normal blood pressure (ID 344, 366, 379)

The references provided for the substantiation of the claimed effect included textbooks, a website from a government body, a reference from an authoritative body on prevention, detection, evaluation and treatment of high blood pressure that did not mention magnesium, publications on magnesium-containing medicinal waters, narrative reviews and references that were either very general or did not address relevant endpoints, and one intervention study on the effects of dietary modifications on blood pressure. Endpoints addressed were ischaemic heart disease; clinical and analytical aspects related to magnesium; magnesium metabolism, deficiency and supplementation; sport; myocardial infarction; tension headaches and muscle tension; stress and neuropsychiatric disorders; and various cardiovascular aspects including atherogenesis. The Panel considers that no conclusions can be drawn from these references for the scientific substantiation of the claimed effect.

One meta-analysis of randomised controlled trials (RCTs) (Jee et al., 2002), a systematic review of epidemiological and intervention studies (Burgess et al., 1999), and three intervention studies on the effects of magnesium on blood pressure in humans were provided (Borello et al., 1996; Itoh et al., 1997; Kyriazis et al., 2004).

The Panel notes that the meta-analysis and the systematic review included trials that cannot be used for the substantiation of the claim (e.g. uncontrolled trials and trials with pharmacologically treated hypertensive subjects in which the evidence provided does not establish that interactions between magnesium intake and pharmacological treatment can be excluded), and that in one of the intervention studies magnesium was administered intravenously, which is not a route considered relevant for human nutrition (Kyriazis et al., 2004). The Panel considers that no conclusions can be drawn from these references (Jee et al., 2002; Burgess et al., 1999; Kyriazis et al., 2004) for the scientific substantiation of the claim.

Among the 20 RCTs which investigated the effects of magnesium supplementation on blood pressure considered in the meta-analysis by Jee et al. (2002), which were also included in the systematic review by Burgess et al. (1999), 15 (including Itoh et al., 1997) were performed in subjects with no pharmacological treatment for hypertension. The number of subjects ranged from 13 to 461, magnesium doses from 10.0 to 40 mmol/day, and intervention periods between 3 and 24 weeks. Seven trials were crossed over, eight had a parallel design, and all but one were double blind. One trial observed a significant decrease (Purvis et al., 1994) and one trial a significant increase (Nowson and Morgan, 1989) in systolic blood pressure in the magnesium group compared to controls, whereas two trials observed a significant decrease (Widman et al., 1993; Witteman et al., 1994) and two trials a significant increase (Nowson and Morgan, 1989; Patki et al., 1990) in diastolic blood pressure. The Panel notes that no significant differences between the magnesium and control groups were observed on either systolic or diastolic blood pressure in ten trials (Capuccio et al., 1985; Zemel et al., 1990; Lind et al., 1991; The TOHP (trials of hypertension prevention) Collaborative Research Group, 1992; Ferrara et al., 1992; Plum-Wirell et al., 1994; Sanjuliani et al., 1996; Itoh et al., 1997; Sacks et al., 1998; Doyle et al., 1989), including the two trials with the largest sample sizes (The TOHP (trials of hypertension prevention) Collaborative Research Group, 1992; Sacks et al., 1998, with n=461 and n=153, respectively). The Panel also notes that the third largest study (Witteman et al., 1994, n=91) observed a significant reduction in diastolic blood pressure only. The Panel considers that the evidence provided by these studies for a blood-pressure lowering effect of magnesium is weak and inconsistent.

The remaining trial, which was not included in the meta-analysis, was a double-blind RCT (Borello et al., 1996) which reported on the effects of magnesium supplementation (200 mg/day of magnesium oxide) in 83 mildly hypertensive patients without previous anti-hypertensive treatment (n=42 in the magnesium group, n=41 in the placebo (unspecified) group). All patients had periodic measurements of blood pressure and heart rate taken. In addition, a 24-hour ambulatory blood pressure monitoring was performed at the beginning and end of the study. A statistically significant reduction in systolic blood pressure was observed at the 12-week follow-up in the magnesium group compared to the placebo (148.5+/-7.1 mmHg *versus* 155.2+/-8.2 mmHg; $p<0.01$), whereas no significant difference was observed in diastolic blood pressure. The more robust 24-hour ambulatory monitoring of blood pressure showed no significant differences in systolic or diastolic blood pressure values between groups. The Panel considers that the findings of this study are not consistent regarding an effect of magnesium on blood pressure.

As regards epidemiological data, low dietary magnesium intakes have been reported to be inversely associated with blood pressure (Rude and Shils, 2006). The mechanism by which magnesium might affect blood pressure is not clear (Rude and Shils, 2006). In the systematic review by Burgess et al., 1999, five epidemiological studies were considered. Two were performed in women: one showed an association between a diet high in magnesium and a reduced risk of hypertension (based on self-reported blood pressure), the other, performed in the same population four years later after a modification in the food frequency questionnaire used to assess magnesium intakes, showed no association. Two studies performed in men did not show a clear association. The other study in both sexes showed a correlation between magnesium intake and measured blood pressure in women but not in men. The Panel considers that the epidemiological evidence for a relationship between magnesium intake and blood pressure or prevention of hypertension is weak and inconsistent.

In their joint Guidelines for the Management of Arterial Hypertension, the European Society of Hypertension (ESH) and the European Society of Cardiology (ESC), in line with other authoritative bodies, stated that the evidence for a blood pressure lowering effect of supplemental magnesium is inconsistent (Mancia et al., 2007). In their scientific statement on dietary approaches to prevent and treat hypertension (Appel et al., 2006), the American Heart Association considered data as insufficient to recommend supplemental magnesium as a means to lowering blood pressure.

In weighing the evidence, the Panel took into account that no conclusions could be drawn from the meta-analysis and the systematic review for the scientific substantiation of the claimed effect owing to the inclusion of studies that cannot be used for the substantiation of the claim, that in 16 RCTs in subjects with no pharmacological treatment for hypertension evidence for a blood-pressure lowering effect of magnesium was weak and inconsistent, and that in five epidemiological studies evidence for a relationship between magnesium intake and changes in blood pressure or prevention of hypertension was weak and inconsistent.

The Panel concludes that the evidence provided is insufficient to establish a cause and effect relationship between the dietary intake of magnesium and maintenance of normal blood pressure.

3.5. Protection of DNA, proteins and lipids from oxidative damage (ID 351)

Two references were cited for the scientific substantiation of the claimed effect.

In a RCT on patients (n=92) with acute myocardial ischaemia undergoing coronary artery bypass graft (Kurian et al., 2007), subjects received either magnesium supplementation (42 male, 10 female), or a placebo (30 male, 10 female). Serum concentrations of copper, zinc, iron, calcium, magnesium, sodium and potassium were measured as well as plasma TBARS and antioxidant enzyme (catalase, glutathione peroxidase, superoxide dismutase, caeruloplasmin) activities, and cardiac marker enzymes. The Panel considers that TBARS are not reliable markers of lipid peroxidation and notes

that induction of antioxidant enzymes provides an indication of response to oxidative stress, but it is non specific and does not reflect oxidative damage to cells or molecules.

The second study was an *in vitro* study which reported on the hydroxyl radical generating ability and scavenging activity of magnesium, manganese and zinc compounds. The Panel considers that evidence provided in *in vitro* studies is not sufficient to predict the occurrence of an effect of the dietary intake of magnesium on the protection of DNA, proteins and lipids from oxidative damage in humans.

The Panel concludes that a cause and effect relationship has not been established between the dietary intake of magnesium and protection of DNA, proteins and lipids from oxidative damage.

3.6. Maintenance of the normal function of the immune system (ID 352)

Three references, including a website from a government body, were cited for the scientific substantiation of the claimed effect. Another reference was a narrative review reporting on several outcomes: effects of dietary magnesium on inflammation, apoptosis and innate immune cell populations in animal models, apoptosis *in vitro*, and the importance of magnesium homeostasis in relation to asthma or in athletes and elderly people. The Panel considers that no conclusions can be drawn from these two references for the scientific substantiation of the claimed effect.

The remaining reference was an animal study reporting on effects of supplementation with manganese and magnesium on the immune function of rats. The Panel considers that while effects shown in animal studies may be used as supportive evidence, human studies are required for the substantiation of a claim and the evidence provided in animal studies alone is not sufficient to predict the occurrence of an effect of the dietary intake of magnesium on the normal function of the immune system in humans.

The Panel concludes that a cause and effect relationship has not been established between the dietary intake of magnesium and maintenance of the normal function of the immune system.

3.7. Maintenance of normal blood pressure during pregnancy (ID 367)

Five references were cited for the scientific substantiation of the claimed effect, including tables of dietary reference intakes set by the IoM (1997); a narrative review on the status of various micronutrients during pregnancy and outcomes for infants in developing countries; a narrative review on chronic gestational magnesium deficiency mainly focusing on pre-term birth and sudden infant death syndrome; a narrative review on magnesium and obstetrics (pre-eclampsia and eclampsia), cardiology and other clinical areas. The Panel considers that no conclusions can be drawn from these references for the scientific substantiation of the claimed effect.

The remaining reference (Villar et al., 2003) reported on systematic reviews and individual RCTs published before July 2002 on nutritional interventions during pregnancy for the prevention or treatment of maternal morbidity and pre-term delivery. The authors indicated that a Cochrane review (Makrides and Crowther, 2001), which included two trials for this outcome, showed no apparent effect of dietary magnesium supplementation on the prevention of pre-eclampsia (mean supplement dose of 365 mg and 500 mg/day).

The Panel concludes that a cause and effect relationship has not been established between the dietary intake of magnesium and maintenance of normal blood pressure during pregnancy.

3.8. Resistance to mental stress (ID 375, 381)

The references cited for the scientific substantiation of the claimed effect include textbooks or general publications, one consensus opinion from a national authoritative body (without any mention about mental stress) and one opinion of a European authoritative body. Many other provided references reported on outcomes not directly related to the claimed effect: physical exercise, extreme physical stress, alcohol and drug use by students before exams, delayed-type hypersensitivity and chronic fatigue syndrome, recommended dietary amounts, magnesium metabolism and deficiency, dietary intakes, sleep electroencephalogram and nocturnal hormonal secretion in the elderly, psychiatric disorders, depression, pregnancy-related outcomes, premenstrual symptoms, biorhythms, anxiety-depressive states in epilepsy, cardiovascular outcomes and atherosclerosis. The Panel considers that these endpoints are not relevant for the claimed effect and that no conclusions can be drawn from these references for the scientific substantiation of the claimed effect.

One reference, reporting on changes in the concentration of non-esterified fatty acids and magnesium in emotional stress, was in Russian, and the English translation was not available to the Panel. In addition, the provided narrative reviews on stress reactions and those specifically on noise-induced stress, did not provide any primary data for the scientific substantiation of the claimed effect.

One reference (Hanus et al., 2004) reported on the effects of a combination of two plant extracts and magnesium on mild-to-moderate anxiety disorders. The Panel considers that no conclusions can be drawn from a study using a fixed combination for the scientific substantiation of the claimed effect on magnesium alone. Another reference (James et al., 1989) reported on the inhibition by intravenous magnesium sulphate of catecholamine release associated with tracheal intubation. The Panel considers that the evidence provided does not establish that results obtained in studies on patients with tracheal intubation can be extrapolated to oral consumption and to the general population.

One reference (Cernak et al., 2000) reported on plasma magnesium and oxidative status in young volunteers exposed to chronic stress (political intolerance, awareness of potential military attacks, permanent stand-by duty and reduced holidays for more than 10 years) or sub-chronic stress consisting of everyday mortal danger in military actions lasting more than three months. Porta et al. (1994) reported on the differential regulation of free and bound plasma magnesium in healthy volunteers exposed to various forms of stress, and patients screened for thyroid disorder. Another reference (Grases et al., 2006) reported on alterations of calcium and magnesium excretion in urine in relation to stress and anxiety in university science students, in basal conditions and during exams, using stress and anxiety questionnaires. The reference of Mocci et al. (2001) reported on urinary catecholamine excretion and serum concentration and urinary excretion of magnesium and other related electrolytes in relation to a short-term exposure to loud noise, in healthy volunteers. Joachims et al. (1987) reported on the correlation between noise-induced hearing loss and serum magnesium concentration in air force pilots. Takase et al. (2004) reported on the effects of chronic stress on endothelial function and intracellular magnesium concentrations in humans. The Panel notes that in the absence of intervention studies with magnesium, changes in blood, intracellular and urinary magnesium in response to stress cannot be used for the scientific substantiation of the claimed effect.

Seven references were animal studies which reported on the effects of various magnesium salts and combinations thereof on the development of stress ulcers and cardiac necroses, antidepressant and anxiolytic-like activity, prevention of stress-induced damage and noise-induced hypertension. The Panel considers that evidence provided in animal studies is not sufficient to predict the occurrence of an effect of the dietary intake of magnesium on resistance to mental stress in humans.

The Panel notes that no human data were provided from which conclusions could be drawn for the scientific substantiation of the claimed effect.

The Panel concludes that a cause and effect relationship has not been established between dietary intake of magnesium and resistance to mental stress.

3.9. Maintenance of normal fat metabolism (ID 378)

Five references were cited for the scientific substantiation of the claimed effect, including one nutrition textbook and one review on the effects of magnesium deficiency on atherosclerosis. This reference was in Japanese and the English translation was not available to the Panel. Another narrative review on the role of magnesium and potassium in the pathogenesis of arteriosclerosis was also cited, but did not provide any primary data for the scientific substantiation of the claimed effect.

The other references reported on the effects of magnesium deficiency on various parameters, notably liver or plasma triglycerides, serum lipoproteins or the fatty acid pattern of total plasma lipids in animal models. The Panel considers that while effects shown in animal studies may be used as supportive evidence, human studies are required for the scientific substantiation of a claim, and that the evidence provided in animal studies alone is not sufficient to predict the occurrence of an effect of the dietary intake of magnesium on maintenance of normal fat metabolism.

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

4. Panel's comments on the proposed wording

4.1. Reduction of tiredness and fatigue (ID 244)

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

4.2. Contribution to normal psychological functions (ID 245, 246)

The Panel considers that the following wording reflects the scientific evidence: "Magnesium contributes to normal psychological functions".

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 magnesium 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. No Tolerable Upper Intake Level (UL) has been established for magnesium normally present in food and beverages. An UL for older children and adults has been established for readily dissociable magnesium salts and compounds like magnesium oxide in nutritional supplements, waters or added to food and beverages (SCF, 2001).

CONCLUSIONS

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

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

"Hormonal health" (ID 243)

- The claimed effect is "an essential co-factor in fatty acid metabolism that impacts upon hormonal health". The target population is assumed to be the general population.
- The claimed effect is general and non-specific and does not refer to any specific health claim as required by Regulation (EC) No 1924/2006.

Reduction of tiredness and fatigue (ID 244)

- 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 magnesium and a reduction of tiredness and fatigue.
- The following wording reflects the scientific evidence: "Magnesium can contribute to a reduction of tiredness and fatigue".

Contribution to normal psychological functions (ID 245, 246)

- The claimed effects are "the role of vitamins and minerals in mental performance (where mental performance stands for those aspects of brain and nerve functions which determine aspects like concentration, learning, memory and reasoning)" and "brain function". 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 been established between the dietary intake of magnesium and contribution to normal psychological functions.
- The following wording reflects the scientific evidence: "Magnesium contributes to normal psychological functions".

Maintenance of normal blood glucose concentrations (ID 342)

- The claimed effect is "carbohydrate metabolism and insulin sensitivity". The target population is assumed to be the general population. Long-term maintenance of normal blood glucose concentrations is a beneficial physiological effect.
- A cause and effect relationship has not been established between the dietary intake of magnesium and maintenance of normal blood glucose concentrations.

Maintenance of normal blood pressure (ID 344, 366, 379)

- The claimed effects are "cardiovascular system", "blood pressure" and "circulation". The target population is assumed to be the general population. Maintenance of normal blood pressure is a beneficial physiological effect.
- The evidence provided is insufficient to establish a cause and effect relationship between the dietary intake of magnesium and maintenance of normal blood pressure.

Protection of DNA, proteins and lipids from oxidative damage (ID 351)

- The claimed effect is "antioxidant properties". The Panel assumes that the target population is the general population. Protection of DNA, proteins and lipids from oxidative damage may be a beneficial physiological effect.
- A cause and effect relationship has not been established between the dietary intake of magnesium and protection of DNA, proteins and lipids from oxidative damage.

Maintenance of the normal function of the immune system (ID 352)

- The claimed effect is "immune system". The target population is assumed to be the general population. Maintenance of the normal function of the immune system is a beneficial physiological effect.
- A cause and effect relationship has not been established between the dietary intake of magnesium and maintenance of the normal function of the immune system.

Maintenance of normal blood pressure during pregnancy (ID 367)

- The claimed effect is "pregnancy". The target population is assumed to be women of child-bearing age. Maintenance of normal blood pressure during pregnancy is a beneficial physiological effect.
- A cause and effect relationship has not been established between the dietary intake of magnesium and maintenance of normal blood pressure during pregnancy.

Resistance to mental stress (ID 375, 381)

- The claimed effects are "système nerveux" and "magnésium et stress: magnesium is a mineral involved in stress and its reactions. On the one hand, stress tends to reduce the magnesium status and, on the other hand, an exogenous or endogenous deficit in magnesium increases the stress response. It matters to maintain a suitable magnesium status in order to better react against stress". The target population is assumed to be the general population. Resistance to mental stress might be a beneficial physiological effect.
- A cause and effect relationship has not been established between dietary intake of magnesium and resistance to mental stress.

Reduction of gastric acid levels (ID 376)

- The claimed effect is "acid-base balance/gastric acidity". The target population is assumed to be the general population. The evidence provided does not establish that reducing gastric acid levels is a beneficial physiological effect for the general population.
- A cause and effect relationship has not been established between the dietary intake of magnesium and a beneficial physiological effect for the general population related to reduction of gastric acid levels.

Maintenance of normal fat metabolism (ID 378)

- The claimed effect is "fat metabolism: acid base balance". The target population is assumed to be the general population. Maintenance of normal fat metabolism is a beneficial physiological effect.
- A cause and effect relationship has not been established between the dietary intake of magnesium and maintenance of normal fat metabolism.

Maintenance of normal muscle contraction (ID 380, 3083)

- The claimed effects are "fonctionnement musculaire" and "metabolism/muscle function". The target population is assumed to be the general population.
- A claim on magnesium and muscle contraction has already been assessed with a favourable outcome.

Conditions and possible restrictions of use

- In order to bear the claims a food should be at least a source of magnesium 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-2008-1030, EFSA-Q-2008-1031, EFSA-Q-2008-1032, EFSA-Q-2008-1033, EFSA-Q-2008-1129, EFSA-Q-2008-1131, EFSA-Q-2008-1138, EFSA-Q-2008-1139, EFSA-Q-2008-1153, EFSA-Q-2008-1154, EFSA-Q-2008-1162, EFSA-Q-2008-1163, EFSA-Q-2008-1165, EFSA-Q-2008-1166, EFSA-Q-2008-1167, EFSA-Q-2008-1168, EFSA-Q-2008-3815). 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.

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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 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.

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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).

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

SUBSTANTIATION OF CLAIMS BY GENERALLY ACCEPTABLE SCIENTIFIC EVIDENCE

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

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

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

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

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

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

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

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

WORDING OF HEALTH CLAIMS

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

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

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

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

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

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

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

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

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

TERMS OF REFERENCE

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

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

- Whether adequate information is provided on the characteristics of the food pertinent to the beneficial effect.
- Whether the beneficial effect of the food on the function is substantiated by generally accepted scientific evidence by taking into account the totality of the available scientific data, and by weighing the evidence. In this context EFSA is invited to comment on the nature and quality of the totality of the evidence provided according to consistent criteria.
- The specific importance of the food for the claimed effect. For functions affected by a large number of dietary factors whether a reference to a single food is scientifically pertinent.

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

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

consumed.

- where appropriate, the effect on the function is significant in relation to the quantity of the food proposed to be consumed and if this quantity could reasonably be consumed as part of a balanced diet.
- the specific study group(s) in which the evidence was obtained is representative of the target population for which the claim is intended.
- the wordings used to express the claimed effect reflect the scientific evidence and complies with the criteria laid down in the Regulation.

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

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

APPENDIX B

EFSA DISCLAIMER

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

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

APPENDIX C

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

ID	Food or Food constituent	Health Relationship	Proposed wording
243	Magnesium	An essential co-factor in fatty acid metabolism, that impacts upon hormonal health	Magnesium contributes to the maintenance of hormonal health Magnesium helps to maintain hormonal health. Magnesium is an essential co-factor in fatty acid metabolism which impacts on hormonal health.
	Conditions of use **-** The product must contain no less than 15 % RDA. Agency guidance for supplements is that products containing > 400 mg magnesium should carry the label advisory statement "this amount of magnesium may cause mild stomach upset in sensitive individuals". - ab 50 mg/l Magnesium (siehe EG-Mineralwasser-Richtlinie)		
ID	**Food or Food constituent**	**Health Relationship**	**Proposed wording**
244	Magnesium	Vitamin/mineral supplementation to reduce fatigue and tirednes in situations of inadequate micronutrient status Clarification provided The role of magnesium for optimal circulating levels of oxygen and energy use by the body Reduce fatigue and tiredness, particularly in situations of inadequate micronutrient status	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 - 60 mg of magnesium, as magnesium oxide per day - 300 mg of magnesium as glycerol-phosphate per day - 45 à 150 mg/jour		
ID	**Food or Food constituent**	**Health Relationship**	**Proposed wording**
245	Magnesium	The role of vitamins and minerals in mental performance (where mental performance stands for those aspects of brain and nerve	Water-soluble vitamins, calcium, magnesium and zinc are essential for mental function and performance In situations of inadequate

		functions which determine aspects like concentration, learning, memory and reasoning)	micronutrient status, supplementation with water-soluble vitamins, minerals and zinc can sustain mental performance (e.g. concentration, learning, memory, reasoning)
	Conditions of use - 15 % RDA of vitamins. Agency guidance for supplements is that products containing > 400 mg of Magnesium should carry the label advisory statement " [This amount of Magnesium] may cause mild stomach upset in sensitive individuals" - Magnesium. At least 45 mg/day		
ID	**Food or Food constituent**	**Health Relationship**	**Proposed wording**
246	Magnesium	Brain function	Magnesium may protect the brain function/brain activity
	Conditions of use - Must meet minimum requirements for use of the claim "source of [name of vitamin/s] and/or [name of mineral/s]" as per Annex to Regulation 1924/2006. Agency guidance for supplements is that products containing > 400 mg of Magnesium should carry the label advisory statement "[This amount of Magnesium] may cause mild stomach upset in sensitive individuals" - 15 %AJR		
ID	**Food or Food constituent**	**Health Relationship**	**Proposed wording**
342	Magnesium	Carbohydrate metabolism and insulin sensitivity	Regulates sugar balance.
	Conditions of use **-** Food supplement with 100 – 350 mg of magnesium in the daily dose		
ID	**Food or Food constituent**	**Health Relationship**	**Proposed wording**
344	Magnesium	Cardiovascular system.	Regulates blood pressure.
	Conditions of use - Food supplement with 100 – 350 mg of magnesium in the daily dose - 152 – 470 mg		
ID	**Food or Food constituent**	**Health Relationship**	**Proposed wording**
351	Magnesium	Antioxidant properties	Magnesium has antioxidative properties It prolongs the ageing process
	Conditions of use **-**153 – 470 mg		
ID	**Food or Food constituent**	**Health Relationship**	**Proposed wording**
352	Magnesium	Immune system	Magnesium maintains healthy immune system
	Conditions of use		

	- 154 – 470 mg - 300 mg of magnesium as glycerol-phosphate per day		
ID	**Food or Food constituent**	**Health Relationship**	**Proposed wording**
366	Magnesium	Blood pressure	An adequate magnesium intake can support to maintain normal blood pressure.
	Conditions of use - ab 50 mg/l Magnesium (siehe EG-Mineralwasser-Richtlinie) - See abovet		
ID	**Food or Food constituent**	**Health Relationship**	**Proposed wording**
367	Magnesium	Pregnancy Clarification provided Pregnancy; Adequate normal magnesium status in pregnancy could help the normal course of pregnancy and delivery. There is an increased requirement for magnesium during this periode.	Magnesium contributes to meeting the increased requirement for magnesium in pregnant women, so it could help the normal course of pregnancy and delivery and birth of a healthy baby.
	Conditions of use **-** Lásd fent		
ID	**Food or Food constituent**	**Health Relationship**	**Proposed wording**
375	Aliments contenant du Magnésium	Magnésium et stress : Magnesium is a mineral involved in stress and its reactions. On one hand, stress tends to reduce the magnesium status and, on the other hand, an exogenous or endogenous deficit in magnesium increases the stress response. It matters to maintain a suitable magnesium status in order to better react against stress.	Le Magnésium vous aide à lutter contre les petits stress quotidiens
	Conditions of use - A serving should provide at least 15% RDA - Magnesium. At least 45 mg/day - 45 à 300 mg / jour - 45 à 300 mg / jour. cible: femmes enceintes		
	No clarification provided by Member States		
ID	**Food or Food constituent**	**Health Relationship**	**Proposed wording**
376	Magnesium hydroxide	Acide-base balance / Gastric acidity	Helps to maintain acid-base balance.

			Helps to decrease dietary acid load. Helps in case of occasional gastric acidity. Contributes to decrease gastric acidity.
	Conditions of use **-** Magnesium hydroxide corresponding to 300 mg of magnesium per day		
ID	**Food or Food constituent**	**Health Relationship**	**Proposed wording**
378	Magnesium	Métabolisme lipidique Clarification provided Fat metabolism: acid base balance;	Le magnésium est essentiel au métabolisme des lipides.
	Conditions of use - Jugendliche, Erwachsene. Amount of consumption: 100 – 350 Milligramm (mg). Upper limit: 350 Milligramm (mg) - 12mg/j		
ID	**Food or Food constituent**	**Health Relationship**	**Proposed wording**
379	Magnesium	Circulation	Essentiel à la régulation de la pression artérielle
	Conditions of use **-** 12mg/j		
	No clarification provided by Member States		
ID	**Food or Food constituent**	**Health Relationship**	**Proposed wording**
380	Magnesium	Fonctionnement musculaire	Rôle important dans le soulagement des crampes
	Conditions of use - 12mg/j - 130mg/j		
	No clarification provided by Member States		
ID	**Food or Food constituent**	**Health Relationship**	**Proposed wording**
381	Magnesium	Système nerveux	Permet à l'organisme de s'adapter au stress
	Conditions of use **-** 120mg/j		
	No clarification provided by Member States		
ID	**Food or Food constituent**	**Health Relationship**	**Proposed wording**
3083	Natural mineral water: Magnesium	Metabolism/ muscle function Clarification provided	Plays an important role in metabolism. Magnesium is important for good muscle

		Metabolism/ muscle function/ Enzymes activation / neuromuscular stimulation	function.
	Conditions of use - 15% RDA per 100 ml		
	Comments from Member States MS clarification to example of wording: 'Magnesium is important for the organism, since it activates many enzymes (especially oxidative phosphorylation). Magnesium contributes to the regulation of cellular permeability and consequently neuromuscular stimulation.		

GLOSSARY AND ABBREVIATIONS

ATP	Adenosine Triphosphate
DNA	Deoxyribonucleic Acid
CI	Confidence Interval
ESC	European Society of Cardiology
ESH	European Society of Hypertension
FAO	Food and Agricultural Organization of the United Nations
HbA1	Haemoglobin, alpha 1
HbA1c	Glycated Haemoglobin
HDL	High-density Lipoprotein
HOMA	Homeostasis Model Analysis
IoM	Institute of Medicine
LDL	Low-density Lipoprotein
RCT	Randomised Controlled Trial
SCF	Scientific Committee on Food
TBARS	Thiobarbituric Acid Reactive Substances
TOHP	Trials of Hypertension Prevention
UL	Tolerable Upper Intake Levels
WHO	World Health Organization