

## SCIENTIFIC OPINION

### **Scientific Opinion on the substantiation of health claims related to walnuts and maintenance of normal blood LDL-cholesterol concentrations (ID 1156, 1158) and improvement of endothelium-dependent vasodilation (ID 1155, 1157) pursuant to Article 13(1) of Regulation (EC) No 1924/2006<sup>1</sup>**

**EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA)<sup>2, 3</sup>**

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 walnuts and maintenance of normal blood LDL-cholesterol concentrations and improvement of endothelium-dependent vasodilation. 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 that is the subject of the health claims is walnuts. The Panel considers that walnuts are sufficiently characterised in relation to the claimed effects.

#### **Maintenance of normal blood LDL-cholesterol concentrations**

The claimed effects are “heart health (cardiovascular health)” and “lipid metabolism/heart health”. The target population is assumed to be the general population. In the context of the proposed wordings and clarifications provided by Member States, it is assumed that the claimed effects refer to the maintenance of normal blood LDL-cholesterol concentrations. The Panel considers that maintenance of normal blood LDL-cholesterol concentrations is a beneficial physiological effect.

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<sup>1</sup> On request from the European Commission, Question No EFSA-Q-2008-1894, EFSA-Q-2008-1895, EFSA-Q-2008-1896, EFSA-Q-2008-1897, adopted on 28 January 2011.

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<sup>3</sup> 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.

In weighing the evidence, the Panel took into account that the evidence provided did not establish that consumption of walnuts had an effect on blood LDL-concentrations beyond what could be expected from their fatty acid composition, and that the LDL-cholesterol-lowering effect of walnuts could be attributed to their content of MUFAs and PUFAs.

On the basis of the data presented, the Panel concludes that a cause and effect relationship has not been established between the consumption of walnuts and maintenance of normal blood LDL-cholesterol concentrations beyond what could be expected from the fatty acid composition of walnuts.

A claim on the replacement of mixtures of SFAs with *cis*-MUFAs and/or *cis*-PUFAs in foods or diets and maintenance of normal blood LDL-cholesterol concentrations has already been assessed with a favourable outcome.

A claim on linoleic acid and maintenance of blood cholesterol concentrations and a claim on alpha-linolenic acid and maintenance of blood cholesterol concentrations have also already been assessed with favourable outcomes.

### **Improvement of endothelium-dependent vasodilation**

The claimed effects are “well-balanced ratio of n-3- to n-6-fatty acids: artery and heart health lipid metabolism”, and “artery health”. The target population is assumed to be the general population. In the context of the proposed wordings and clarifications provided by Member States, it is assumed that the claimed effects refer to the improvement of endothelium-dependent vasodilation. The Panel considers that a sustained improvement of endothelium-dependent vasodilation may be a beneficial physiological effect.

In weighing the evidence, the Panel took into account that one intervention study in healthy subjects, adequately powered and controlled, showed a sustained effect of the consumption of walnuts on endothelium-dependent vasodilation, that the results of one additional intervention study in type 2 diabetic subjects on blood pressure-lowering, cholesterol-lowering, and/or oral antidiabetic medication are consistent with these findings, and that an acute intervention study also showed a positive effect of the consumption of walnuts on endothelium-mediated vasodilation.

The Panel concludes that a cause and effect relationship has been established between the consumption of walnuts and improvement of endothelium-dependent vasodilation.

The Panel considers that in order to obtain the claimed effect, 30 g of walnuts should be consumed daily. These amounts can be consumed in the context of a balanced diet. The target population is the general population.

### **KEY WORDS**

Walnuts, fatty acids, cholesterol, vasodilation, health claims.

## TABLE OF CONTENTS

Summary .....	1
Table of contents .....	3
Background as provided by the European Commission .....	4
Terms of reference as provided by the European Commission .....	4
EFSA Disclaimer.....	4
Information as provided in the consolidated list .....	5
Assessment .....	5
1. Characterisation of the food/constituent .....	5
2. Relevance of the claimed effect to human health.....	5
2.1. Maintenance of normal blood LDL-cholesterol concentrations (ID 1156, 1158) .....	5
2.2. Improvement of endothelium-dependent vasodilation (ID 1155, 1157).....	6
3. Scientific substantiation of the claimed effect .....	6
3.1. Maintenance of normal blood LDL-cholesterol concentrations (ID 1156, 1158) .....	6
3.2. Improvement of endothelium-dependent vasodilation (ID 1155, 1157).....	7
4. Panel's comments on the proposed wording.....	9
4.1. Improvement of endothelium-dependent vasodilation (ID 1155, 1157).....	9
5. Conditions and possible restrictions of use .....	9
5.1. Improvement of endothelium-dependent vasodilation (ID 1155, 1157).....	9
Conclusions .....	9
Documentation provided to EFSA .....	10
References .....	10
Appendices .....	12
Glossary and Abbreviations .....	19

**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<sup>4</sup> 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<sup>5</sup>. 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 that is the subject of the health claims is walnuts.

Walnuts are seeds from the walnut tree (genus *Juglans*) of which about 20 different species are known in different parts of the world. Walnuts are drupes, rather than nuts. One of the most popular varieties of walnut is the Persian or English walnut, which has a large seed and a thinner shell, yielding more edible walnut meat by weight than other species. Black walnuts are another commonly sold walnut species, as are white walnuts, also called butternuts. The nut kernels contain about 57-65 % fat, of which about 3-6 % are saturated fatty acids (SFAs), 9-15 % are monounsaturated fatty acids (MUFAs), and 35-47 % are polyunsaturated fatty acids (PUFAs) (33-38 % linoleic acid (LA), and 2-9 % alpha-linolenic acid (ALA)). The nut kernels also contain about 5-7 % fibre, of which about 25 % is soluble fibre, 15-29 % protein, and small amounts of plant sterols and other phytochemicals. The Panel notes the variation in terms of macronutrient composition between different types of walnuts.

The Panel considers that the food, walnuts, which is the subject of the health claims, is sufficiently characterised in relation to the claimed effects.

### 2. Relevance of the claimed effect to human health

#### 2.1. Maintenance of normal blood LDL-cholesterol concentrations (ID 1156, 1158)

The claimed effects are “heart health (cardiovascular health)” and “lipid metabolism/heart health”. The Panel assumes that the target population is the general population.

In the context of the proposed wordings and clarifications provided by Member States, the Panel assumes that the claimed effects refer to the maintenance of normal blood LDL-cholesterol concentrations.

<sup>4</sup> 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.

<sup>5</sup> 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>

Low-density lipoproteins (LDL) carry cholesterol from the liver to peripheral tissues, including the arteries. Elevated LDL-cholesterol, by convention  $>160$  mg/dL ( $>4.1$  mmol/L), may compromise the normal structure and function of the arteries.

The Panel considers that maintenance of normal blood LDL-cholesterol concentrations is a beneficial physiological effect.

## **2.2. Improvement of endothelium-dependent vasodilation (ID 1155, 1157)**

The claimed effects are “well-balanced ratio of n-3- to n-6-fatty acids: artery and heart health lipid metabolism”, and “artery health”. The Panel assumes that the target population is the general population.

In the context of the proposed wordings and clarifications provided by Member States, the Panel assumes that the claimed effects refer to the improvement of endothelium-dependent vasodilation.

The Panel considers that a sustained improvement of endothelium-dependent vasodilation may be a beneficial physiological effect.

## **3. Scientific substantiation of the claimed effect**

### **3.1. Maintenance of normal blood LDL-cholesterol concentrations (ID 1156, 1158)**

Among the references provided for the scientific substantiation of the claim were consensus opinions or textbook chapters on the effects of different dietary fatty acids, as well as narrative reviews and human studies on the effect of diets with different fatty acid composition on cardiovascular risk factors. Some human studies addressed outcomes unrelated to the claimed effect, such as postprandial endothelial function or cardiovascular risk. The Panel considers that no conclusions can be drawn from these references for the scientific substantiation of the claimed effect.

All of the human intervention studies provided in the consolidated list on the effects of the consumption of walnuts on blood lipids were considered in the systematic review by Mukuddem-Petersen et al. (2005), which addressed the effects of nuts in general, including walnuts, on blood lipid profile. Nine of the studies selected used walnuts as the intervention (Abbey et al., 1994; Almario et al., 2001; Chisholm et al., 1998; Iwamoto et al., 2002; Morgan et al., 2002; Munoz et al., 2001; Ros et al., 2004; Sabate et al., 1993; Zambon et al., 2000). In two of these studies the intervention and control periods were in the same order for all subjects, with no wash-out period in between (Abbey et al., 1994; Almario et al., 2001); the Panel notes that these studies were not controlled for a temporal effect, and considers that no conclusions can be drawn from these studies for the scientific substantiation of the claimed effect.

Among the seven studies with randomised, controlled cross-over designs, three used a Mediterranean diet as control (Munoz et al., 2001; Ros et al., 2004; Zambon et al., 2000), two used a National Cholesterol Education Program (NCEP) step I diet (Morgan et al., 2002; Sabate et al., 1993), one used a low fat diet (Chisholm et al., 1998), and one used a Japanese diet (Iwamoto et al., 2002). The duration of the intervention was 4-6 weeks. Four of the studies, which included a total of 127 normo- and hypercholesterolaemic subjects with a daily walnut intake of 40-84 g, observed a significant decrease in total (from -4.3 to -12.4 %) and LDL-cholesterol (from -6.7 to -16.3 %) concentrations during the walnut diet compared to the “control” diet (Iwamoto et al., 2002; Ros et al., 2004; Sabate et al., 1993; Zambon et al., 2000), whereas in the remaining three studies differences between intervention and control groups were not significant ( $n=73$ ; walnut intake = 41-78 g/day). No significant differences between groups were observed in any of the studies with respect to HDL-cholesterol and triglyceride concentrations, with the exception of a significant decrease in HDL-

cholesterol (-4.9 %) in the study by Sabate et al. (1993), where walnuts primarily replaced MUFAs. The Panel notes that the data from these studies could not be pooled in a meta-analysis because of the heterogeneity of the designs, particularly with respect to the control diet and type of subjects included (normocholesterolaemic vs. hypercholesterolaemic). The Panel also notes that in these studies walnuts replaced various types of dietary fats in different amounts (SFAs, MUFAs), which had variable effects on the lipid profile (Mensink et al., 2003). None of these studies controlled for the fatty acid composition of the intervention diet, and therefore it could not be assessed whether the consumption of walnuts had an effect on blood lipids beyond what could be expected from their fatty acid profile (e.g. LA and ALA content). In the systematic review by Mukuddem-Petersen et al. (2005), the predictive equation by Mensink and Katan (1992) was used to compare the actual observed changes in total and LDL-cholesterol with the predicted changes in total and LDL-cholesterol concentrations, based on differences in the dietary fatty acid composition in the individual nut and control diets. However, all studies on nuts included in the review were pooled for this calculation, and no particular figure for walnuts only was provided.

One observational human study addressed the association between blood cholesterol and walnuts (oil and kernel) consumption. Lavedrine et al. (1999) carried out a cross-sectional survey on 793 subjects (426 males and 367 females) aged 18-65 years, from Dauphine, France, where walnuts and walnut oil are part of the usual diet. To assess the level of walnut consumption, a food frequency questionnaire (1-year recall) was used. Blood samples were taken to measure LDL and total cholesterol. No significant differences in blood LDL or total cholesterol concentrations were observed between non-consumers, intermediate consumers and frequent consumers of walnuts and walnut oil. The Panel notes that this cross-sectional study does not show an association between walnut or walnut oil consumption and blood LDL-cholesterol concentrations.

In weighing the evidence, the Panel took into account that the evidence provided did not establish that consumption of walnuts had an effect on blood LDL-concentrations beyond what could be expected from their fatty acid composition and that the LDL-cholesterol-lowering effect of walnuts could be attributed to their content of MUFAs and PUFAs.

The Panel concludes that a cause and effect relationship has not been established between the consumption of walnuts and maintenance of normal blood LDL-cholesterol concentrations beyond what could be expected from the fatty acid composition of walnuts.

A claim on the replacement of mixtures of SFAs with *cis*-MUFAs and/or *cis*-PUFAs in foods or diets and maintenance of normal blood LDL-cholesterol concentrations has already been assessed with a favourable outcome (EFSA Panel on Dietetic Products Nutrition and Allergies (NDA), 2011).

A claim on linoleic acid and maintenance of blood cholesterol concentrations (EFSA Panel on Dietetic Products Nutrition and Allergies (NDA), 2009a) and a claim on alpha-linolenic acid and maintenance of blood cholesterol concentrations (EFSA Panel on Dietetic Products Nutrition and Allergies (NDA), 2009b) have also already been assessed with favourable outcomes.

### **3.2. Improvement of endothelium-dependent vasodilation (ID 1155, 1157)**

The references provided for the scientific substantiation of the claim included narrative reviews, consensus opinions, and epidemiological and intervention studies on the effects of PUFAs, including ALA and LA, on health outcomes other than improvement of endothelium-dependent vasodilation (e.g. blood lipids, blood pressure and cardiovascular risk). In addition, some epidemiological studies which investigated the association between nut consumption, including walnuts, on health outcomes not related to the claimed effect (e.g. blood lipids, blood pressure and cardiovascular risk) were provided. The Panel considers that no conclusions can be drawn from these references for the scientific substantiation of the claimed effect.

In a randomised, controlled cross-over trial by Ros et al. (2004) 21 untreated hypercholesterolaemic men and women consumed a Mediterranean type diet low in saturated fatty acids (about 5 % energy) and a diet of similar energy and fat content (33 E%) in which 40-65 g/day of walnuts contributed to about 18 % total energy, and replaced approximately 32 % of the energy obtained from monounsaturated fat (olive oil, olives and avocados) in the control diet, for 4 weeks each without a wash-out period. There was a 4-week run-in period to allow for diet and weight stabilisation. The order of the diets was randomised. After each intervention, ultrasound measurements of brachial artery vasomotor function were taken. Endothelium-dependent vasodilation (EDV) was the primary outcome of the study. Endothelium-independent vasodilation (EIDV) was evaluated by administering 0.4 mg sublingual glyceryl trinitrate prior to the measurement, and was used as internal control. Reproducibility of measurements over one month was documented in 15 healthy volunteers. The repeatability coefficient was 5.16, and the mean $\pm$ SD difference between EDV values was 0.52 $\pm$ 2.66 %. It was calculated that 19 subjects were needed to detect a mean difference in EDV of 2 %, with a type I error of 5 % and a power  $\geq$ 90 %. A total of 20 subjects completed the study and suitable brachial artery ultrasound measurements were available for 18 subjects. Compared with the Mediterranean diet, the walnut diet significantly improved EDV (from 3.6 $\pm$ 3.3 % to 5.9 $\pm$ 3.3 %, a relative increase of 64 %), and significantly reduced concentrations of vascular cell adhesion molecule-1 (VCAM-1), which is a marker of endothelial activation. EIVD and concentrations of intercellular adhesion molecule-1 (ICAM-1) were not significantly different between diets. The walnut diet significantly decreased total cholesterol (-4.4 $\pm$ 7.4 %) and LDL-cholesterol (-6.4 $\pm$ 10.0 %) concentrations. Changes in EDV significantly correlated with changes in the total/HDL-cholesterol ratio. There was no evidence of carry-over effects between treatment periods. The Panel notes that this study provides evidence for a positive and sustainable effect of walnut consumption on endothelium-dependent vasodilation.

In a randomised, controlled cross-over trial by Ma et al. (2010), 24 type 2 diabetic subjects aged 30-75 years on stable medication use for at least three months (17 on blood pressure-lowering medication, 13 on cholesterol-lowering medication, 10 on oral antidiabetic medication) consumed a walnut-enriched *ad libitum* diet, and an *ad libitum* diet without walnuts, for 8 weeks each in a random order with an 8-week wash-out period in between, and after a 4-week run-in period to allow for diet and weight stabilisation. During the walnut period, subjects consumed 56 g English walnuts daily. EDV was the primary outcome of the study. A stimulus-adjusted response measure was used as internal control. The sample size was determined to allow for about 20 % attrition and non-compliance, and to provide  $\geq$ 80 % power to detect a minimal difference of 2.5 % in EDV between treatments, with a maximum allowable type I error of 5 %. A total of 96 % of subjects complied with the consumption of walnuts (defined as intake of  $\geq$ 80 % of the assigned dose). EDV improved significantly after consumption of the walnut-enriched diet as compared with the *ad libitum* diet without walnuts (2.2 $\pm$ 1.7 % vs. 1.2 $\pm$ 1.6 %,  $p=0.04$ ), whereas no significant changes between groups were observed in the stimulus-adjusted response measure. No significant differences were observed between diets with respect to changes in blood lipid profile, body weight, blood glucose control or insulin sensitivity, whereas a significant decrease in systolic and diastolic blood pressure was observed in the walnut diet compared to the control diet. The Panel notes that the results of this study are consistent with findings in human intervention studies in untreated subjects on the effect of walnut consumption on endothelium-dependent vasodilation.

In a randomised cross-over study, Cortes et al. (2006) investigated whether the addition of walnuts or olive oil to a fatty meal had different effects on post-prandial vasoactivity, lipoproteins, markers of oxidation and endothelial activation, and plasma asymmetric dimethylarginine (ADMA). Endothelium-dependent vasodilation was the primary outcome of the study. A total of 12 healthy subjects and 12 subjects with hypercholesterolaemia who received no pharmacological treatment were randomised to two high-fat meal sequences (separated by one week) to which 25 g olive oil or 40 g walnuts had been added. Both test meals contained 63 % of the energy as fat (80 g fat) and 35 E% saturated fatty acids. Ultrasound measurements of brachial artery endothelial function were performed

after fasting and 4 h after test meals. In both study groups, flow-mediated dilation (FMD) was lower after the olive oil meal than after the walnut meal ( $p=0.006$ ). Flow-independent dilation and plasma ADMA concentrations were unchanged, and concentrations of oxidised low-density lipoproteins decreased ( $p=0.051$ ) after both meals. The plasma concentrations of soluble inflammatory cytokines, and of adhesion molecules, decreased ( $p<0.01$ ) independently of meal type, except for E-selectin, which decreased significantly more after the walnut meal. E-selectin is an adhesion molecule involved in the early steps of monocyte recruitment to the endothelium. The Panel notes that this study is an acute study, and does not allow conclusions to be drawn on the sustainability of the effects of the consumption of walnuts on EDV.

In weighing the evidence, the Panel took into account that one intervention study in healthy subjects, adequately powered and controlled, showed a sustained effect of the consumption of walnuts on endothelium-dependent vasodilation, that the results of one additional intervention study in type 2 diabetic subjects on blood pressure-lowering, cholesterol-lowering, and/or oral antidiabetic medication are consistent with these findings, and that an acute intervention study also showed a positive effect of the consumption of walnuts on endothelium-mediated vasodilation.

The Panel concludes that a cause and effect relationship has been established between the consumption of walnuts and improvement of endothelium-dependent vasodilation.

#### **4. Panel's comments on the proposed wording**

##### **4.1. Improvement of endothelium-dependent vasodilation (ID 1155, 1157)**

The Panel considers that the following wording reflects the scientific evidence: "Walnuts contribute to the improvement of endothelium-dependent vasodilation".

#### **5. Conditions and possible restrictions of use**

##### **5.1. Improvement of endothelium-dependent vasodilation (ID 1155, 1157)**

The Panel considers that in order to obtain the claimed effect, 30 g of walnuts should be consumed daily. These amounts can be consumed in the context of a balanced diet. The target population is the general population.

## **CONCLUSIONS**

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

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

##### **Maintenance of normal blood LDL-cholesterol concentrations (ID 1156, 1158)**

- The claimed effects are "heart health (cardiovascular health)" and "lipid metabolism/heart health". The target population is assumed to be the general population. In the context of the proposed wordings and clarifications provided by Member States, it is assumed that maintenance of normal blood LDL-cholesterol concentrations is a beneficial physiological effect.
- A cause and effect relationship has not been established between the consumption of walnuts and maintenance of normal blood LDL-cholesterol concentrations beyond what could be expected from the fatty acid composition of walnuts.

- A claim on the replacement of mixtures of SFAs with *cis*-MUFAs and/or *cis*-PUFAs in foods or diets and maintenance of normal blood LDL-cholesterol concentrations has already been assessed with a favourable outcome.
- A claim on linoleic acid and maintenance of blood cholesterol concentrations and a claim on alpha-linolenic acid and maintenance of blood cholesterol concentrations have also already been assessed with favourable outcomes.

### **Improvement of endothelium-dependent vasodilation (ID 1155, 1157)**

- The claimed effects are “well-balanced ratio of n-3- to n-6-fatty acids: artery and heart health lipid metabolism”, and “artery health”. The target population is assumed to be the general population. In the context of the proposed wordings and clarifications provided by Member States, it is assumed that sustained improvement of endothelium-dependent vasodilation may be a beneficial physiological effect.
- A cause and effect relationship has been established between the consumption of walnuts and improvement of endothelium-dependent vasodilation.
- The following wording reflects the scientific evidence: “Walnuts contribute to the improvement of endothelium-dependent vasodilation”.
- In order to obtain the claimed effect, 30 g/day of walnuts should be consumed daily. These amounts can be consumed in the context 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-2008-1894, EFSA-Q-2008-1895, EFSA-Q-2008-1896, EFSA-Q-2008-1897). The scientific substantiation is based on the information provided by the Member States in the consolidated list of Article 13 health claims and references that EFSA has received from Member States or directly from stakeholders.

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

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## APPENDICES

### APPENDIX A

#### BACKGROUND AND TERMS OF REFERENCE AS PROVIDED BY THE EUROPEAN COMMISSION

The Regulation 1924/2006 on nutrition and health claims made on foods<sup>6</sup> (hereinafter "the Regulation") entered into force on 19<sup>th</sup> 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<sup>7</sup>

Foods are commonly involved in many different functions<sup>8</sup> 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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<sup>6</sup> OJ L12, 18/01/2007

<sup>7</sup> The term 'food' when used in this Terms of Reference refers to a food constituent, the food or the food category.

<sup>8</sup> 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 walnuts, including conditions of use from similar claims, as proposed in the Consolidated List.

ID	Food or Food constituent	Health Relationship	Proposed wording
1155	Walnuts	Well-balanced ratio of n-3- to n-6-fatty acids: Artery and Heart Health Lipid metabolism  <u>Clarification provided</u>  The consumption of walnuts improves endothelial function by increasing the endothelium dependent vasodilatation (in hypercholesterolemic subjects) (postprandial)	Walnuts in the daily diet support a healthy heart.
		<b>Conditions of use</b> - 30 g/day daily	
ID	Food or Food constituent	Health Relationship	Proposed wording
1156	Walnuts	Heart Health (Cardiovascular Health)  <u>Clarification provided</u>  Cardiovascular system: Consumption of walnuts helps to control cholesterol	Walnuts support cardiovascular health.
		<b>Conditions of use</b> - 30 g/day daily - Three to five walnuts per days or 2 spoons of walnuts oil in salads (Grenoble Walnuts)	
ID	Food or Food constituent	Health Relationship	Proposed wording
1157	Walnuts	Artery Health  <u>Clarification provided</u>  The consumption of walnuts improves endothelial function by increasing the endothelium dependent vasodilatation (in hypercholesterolemic subjects) (postprandial)	The consumption of walnuts supports the natural vascular functions /keeps the vessels healthy.
		<b>Conditions of use</b> - 30 g/day daily	

ID	Food or Food constituent	Health Relationship	Proposed wording
1158	Walnuts	Lipid Metabolism Heart Health <u>Clarification provided</u> Blood cholesterol: Consumption of walnuts helps to maintain healthy (favourable, normal) cholesterol level.	Walnuts contain a well-balanced ratio of unsaturated fatty acids which helps maintaining a healthy heart.
<b>Conditions of use</b> - 30 g/day daily			

## GLOSSARY AND ABBREVIATIONS

ADMA	Asymmetric dimethylarginine
ALA	Alpha-linolenic acid
EDV	Endothelium-dependent vasodilation
EIDV	Endothelium-independent vasodilation
FMD	Flow-mediated dilation
HDL	High-density lipoproteins
ICAM-1	Intercellular adhesion molecule-1
LA	Linoleic acid
LDL	Low-density lipoproteins
MUFA	Monounsaturated fatty acids
NCEP	National cholesterol education program
PUFA	Polyunsaturated fatty acids
SD	Standard deviation
SFA	Saturated fatty acids
VCAM-1	Vascular cell adhesion molecule-1