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SCIENTIFIC OPINION

Scientific Opinion on the substantiation of health claims related to polyphenols in olive and protection of LDL particles from oxidative damage (ID 1333, 1638, 1639, 1696, 2865), maintenance of normal blood HDL-cholesterol concentrations (ID 1639), maintenance of normal blood pressure (ID 3781), "anti-inflammatory properties" (ID 1882), "contributes to the upper respiratory tract health" (ID 3468), "can help to maintain a normal function of gastrointestinal tract" (3779), and "contributes to body defences against external agents" (ID 3467) pursuant to Article 13(1) of Regulation (EC) No 1924/2006[1]

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

European Food Safety Authority (EFSA), Parma, Italy

SUMMARY

Following a request from the European Commission, the Panel on Dietetic Products, Nutrition and Allergies was asked to provide a scientific opinion on a list of health claims pursuant to Article 13 of Regulation (EC) No 1924/2006. This opinion addresses the scientific substantiation of health claims in relation to polyphenols in olive and protection of LDL particles from oxidative damage, maintenance of normal blood HDL-cholesterol concentrations, maintenance of normal blood pressure, "anti-inflammatory properties", "contributes to the upper respiratory tract health", "can help to maintain a normal function of gastrointestinal tract", and "contributes to body defences against external agents". 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.

[1] On request from the European Commission, Question No EFSA-Q-2008-2070, EFSA-Q-2008-2374, EFSA-Q-2008-2375, EFSA-Q-2008-2432, EFSA-Q-2008-2615, EFSA-Q-2008-3598, EFSA-Q-2008-4195, EFSA-Q-2008-4196, EFSA-Q-2008-4498, EFSA-Q-2008-4500, adopted on 12 November 2010.

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[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.

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The food constituent, which is the subject of the health claims, is polyphenols (e.g. hydroxytyrosol and oleuropein complex) in olive (olive fruit, olive mill waste waters or olive oil, *Olea europaea* L. extract and leaf).

The Panel considers that polyphenols in olive (olive fruit, olive mill waste waters or olive oil, *Olea europaea* L. extract and leaf) standardised by their content of hydroxytyrosol and its derivatives (e.g. oleuropein complex) are sufficiently characterised in relation to the claimed effects.

Protection of LDL particles from oxidative damage

The claimed effects are "reduces oxidative stress", "antioxidant properties", "lipid metabolism", "antioxidant activity, they protect body cells and LDL from oxidative damages", and "antioxidant properties". 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 protection of low-density lipoproteins (LDL) particles from oxidative damage. The Panel considers that protection of LDL particles from oxidative damage may be a beneficial physiological effect.

In weighing the evidence, the Panel took into account that a well conducted and powered study, and two smaller-scale studies, showed a dose-dependent and significant effect of olive oil polyphenol consumption (for three weeks) on appropriate markers of LDL peroxidation (oxLDL), that these results were supported by one short-term and one acute study, and by supportive markers of LDL peroxidation (conjugated dienes, *ex vivo* resistance of LDL to oxidation) going in the same direction, and that evidence for a biologically plausible mechanism by which olive oil polyphenols could exert the claimed effect has been provided.

On the basis of the data presented, the Panel concludes that a cause and effect relationship has been established between the consumption of olive oil polyphenols (standardised by the content of hydroxytyrosol and its derivatives) and protection of LDL particles from oxidative damage.

The Panel considers that in order to bear the claim, 5 mg of hydroxytyrosol and its derivatives (e.g. oleuropein complex and tyrosol) in olive oil should be consumed daily. These amounts, if provided by moderate amounts of olive oil, can be easily consumed in the context of a balanced diet. The concentrations in some olive oils may be too low to allow the consumption of this amount of polyphenols in the context of a balanced diet. The target population is the general population.

Maintenance of normal blood HDL-cholesterol concentrations

The claimed effect is "lipid metabolism". 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 of normal blood HDL-cholesterol concentrations. The Panel considers that maintenance of normal blood HDL-cholesterol concentrations (without increasing LDL-cholesterol concentrations) is a beneficial physiological effect.

In weighing the evidence, the Panel took into account that the results from the studies provided are inconsistent, and that no evidence for a biologically plausible mechanism by which olive oil polyphenols could exert the claimed effect has been provided.

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 consumption olive oil polyphenols (standardised by the content of hydroxytyrosol and its derivatives) and maintenance of normal blood HDL-cholesterol concentrations.

Maintenance of normal blood pressure

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

No human studies 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 consumption of polyphenols in olive (olive fruit, olive mill waste waters or olive oil, *Olea europaea* L. extract and leaf) standardised by the content of hydroxytyrosol and its derivatives (e.g. oleuropein complex) and maintenance of normal blood pressure.

"Anti-inflammatory properties"

The claimed effect is "a potent source of olive biophenols with anti-inflammatory properties". The target population is assumed to be the general population. In the context of the proposed wordings, the Panel considers that the claim refers to diseases such as osteoarthritis or rheumatoid arthritis, in which a reduction of inflammation would be a therapeutic target for the treatment of the disease.

The Panel considers that the reduction of inflammation in the context of diseases such as osteoarthritis or rheumatoid arthritis is a therapeutic target for the treatment of the disease, and does not comply with the criteria laid down in Regulation (EC) No 1924/2006.

"Contributes to the upper respiratory tract health"

The claimed effect is "contributes to the upper respiratory tract health". The target population is assumed to be the general population.

The claimed effect is not sufficiently defined and no clarification has been provided by Member States. The Panel notes that different health outcomes were mentioned in the information provided, and that it was not possible to establish which specific effect is the target for the claim.

The Panel concludes 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.

"Can help to maintain a normal function of gastrointestinal tract"

The claimed effect is "can help to maintain a normal function of gastrointestinal tract". The target population is assumed to be the general population.

The claimed effect is not sufficiently defined and no clarification has been provided by Member States. The Panel notes that different health outcomes were mentioned in the information provided, and that it was not possible to establish which specific effect is the target for the claim.

The Panel concludes 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.

"Contributes to body defences against external agents"

The claimed effect is "contributes to body defences against external agents". The target population is assumed to be the general population.

The claimed effect is not sufficiently defined and no clarification has been provided by Member States. The Panel notes that different health outcomes were mentioned in the information provided, and that it was not possible to establish which specific effect is the target for the claim.

The Panel concludes 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.

KEY WORDS

Olive, polyphenols, LDL, HDL, cholesterol, oxidative damage, blood pressure, inflammation, upper respiratory tract, gastrointestinal tract, body defences, external agents, 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 polyphenols (e.g. hydroxytyrosol and oleuropein complex) in olive (olive fruit, olive mill waste waters or olive oil, *Olea europaea* L. extract and leaf).

The conditions of use specify 200 mg/day of polyphenols (ID 1638, 1882, 2865), 2-15 mg per day of hydroxytyrosyl or oleuropein complex (ID 1638, 1639, 1696), and 250-500 mg of an *Olea europaea* L. extract standardised to 4-23% oleuropein (ID 3467, 3468, 3779, 3781).

Polyphenols comprise a very wide group (several thousands of compounds) of plant secondary metabolites including flavonoids, isoflavonoids, phenolic acids, proanthocyanidins and other tannins, and lignans with different biological activities. The major polyphenols in olive oil are phenolic acids (e.g. hydroxytyrosol and tyrosol), secoiridoids (e.g. oleuropein) and lignans (e.g. pinoresinol). Table olives typically contain hydroxytyrosol, tyrosol, caffeoylquinic acid, verbacoside, luteolin and rutin. Hydroxytyrosol, a major polyphenol typically present in olives, is also present in olive mill waste water. In nature, hydroxytyrosol is found in olives in the form of its elenolic acid ester, oleuropein. These polyphenolic compounds can be measured in foods by established methods.

Total polyphenols are usually expressed as gallic acid equivalents (GAE), but other phenolic compounds such as catechin/epicatechin or caffeic acid have also been used for standardisation. This standardisation refers to the traditional spectrophotometrical measurement of total polyphenols using the Folin-Ciocalteau method (Singleton and Rossi, 1965), which is based on reducing capacity. The method is not specific for polyphenols because other reducing compounds such as ascorbic acid, sugars and proteins will also be included in the quantification, thus leading to an overestimation of the actual polyphenol content. The total polyphenol content assessed with this method is not suitable for characterisation of polyphenols in foods.

The Panel considers that polyphenols (e.g. hydroxytyrosol and oleuropein complex) in olive (olive fruit, olive mill waste waters or olive oil, *Olea europaea* L. extract and leaf) can be characterised by their content of hydroxytyrosol and its derivatives (e.g. oleuropein complex).

The Panel considers that the food constituent, polyphenols in olive (olive fruit, olive mill waste waters or olive oil, *Olea europaea* L. extract and leaf) standardised by their content of hydroxytyrosol and its derivatives (e.g. oleuropein complex), which is the subject of the health claims, is sufficiently characterised in relation to the claimed effects.

[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

2. Relevance of the claimed effect to human health

2.1. Protection of LDL particles from oxidative damage (ID 1333, 1638, 1639, 1696, 2865)

The claimed effects are "reduces oxidative stress", "antioxidant properties", "lipid metabolism", "antioxidant activity, they protect body cells and LDL from oxidative damages", and "antioxidant properties". 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 protection of low-density lipoprotein (LDL) particles from oxidative damage.

Reactive oxygen species (ROS) including several kinds of radicals are generated in biochemical processes (e.g. respiratory chain) and as a consequence of exposure to exogenous factors (e.g. radiation and pollutants). These reactive intermediates can 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 LDL particles from oxidative damage may be a beneficial physiological effect.

2.2. Maintenance of normal blood HDL-cholesterol concentrations (ID 1639)

The claimed effect is "lipid metabolism". 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 maintenance of normal blood HDL-cholesterol concentrations.

High-density lipoproteins (HDL) act as cholesterol scavengers and are involved in the reverse transport of cholesterol in the body (from peripheral tissues back to the liver). Conversely, low-density lipoproteins (LDL) carry cholesterol from the liver to peripheral tissues, including the arteries.

The Panel considers that maintenance of normal blood HDL-cholesterol concentrations (without increasing LDL-cholesterol concentrations) is a beneficial physiological effect.

2.3. Maintenance of normal blood pressure (ID 3781)

The claimed effect is "contributes to the maintenance of a normal blood pressure". The Panel assumes that the target population is the general population.

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 normal arterial and cardiac function.

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

2.4. "Anti-inflammatory properties" (ID 1882)

The claimed effect is "a potent source of olive biophenols with anti-inflammatory properties". The Panel assumes that the target population is the general population.

Inflammation is a non-specific physiological response to tissue damage that is mediated by the immune system. Adequate inflammatory responses are of primary importance for the defence against injury of any origin. Whether or not reduction of inflammatory markers is considered beneficial would depend on the context in which the claim is made. In the context of the proposed wordings, the Panel considers that the claim refers to diseases such as osteoarthritis or rheumatoid arthritis, in which a reduction of inflammation would be a therapeutic target for the treatment of the disease.

No clarification has been provided by Member States in relation to the scope of this claim.

The Panel considers that the reduction of inflammation in the context of diseases such as osteoarthritis or rheumatoid arthritis is a therapeutic target for the treatment of the disease, and does not comply with the criteria laid down in Regulation (EC) No 1924/2006.

2.5. "Contributes to the upper respiratory tract health" (ID 3468)

The claimed effect is "contributes to the upper respiratory tract health". The Panel assumes that the target population is the general population.

The claimed effect is not sufficiently defined and no clarifications have been provided by Member States. The Panel notes that different health outcomes were mentioned in the information provided, and that it was not possible to establish which specific effect is the target for the claim.

The Panel concludes 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.

2.6. "Can help to maintain a normal function of gastrointestinal tract" (ID 3779)

The claimed effect is "can help to maintain a normal function of gastrointestinal tract". The Panel assumes that the target population is the general population.

The claimed effect is not sufficiently defined and no clarifications have been provided by Member States. The Panel notes that different health outcomes were mentioned in the information provided, and that it was not possible to establish which specific effect is the target for the claim.

The Panel concludes 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.

2.7. "Contributes to body defences against external agents" (ID 3467)

The claimed effect is "contributes to body defences against external agents". The Panel assumes that the target population is the general population.

The claimed effect is not sufficiently defined and no clarifications have been provided by Member States. The Panel notes that different health outcomes were mentioned in the information provided, and that it was not possible to establish which specific effect is the target for the claim.

The Panel concludes 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.

3. Scientific substantiation of the claimed effect

3.1. Protection of LDL particles from oxidative damage (ID 1333, 1638, 1639, 1696, 2865)

The vast majority of the references provided for the scientific substantiation of this claim included narrative reviews, human intervention studies, animal studies and *in vitro* experiments on food/food constituents other than olive polyphenols, and/or on effects other than protection of lipids, including LDL particles, against oxidative damage. The latter include references on blood pressure, vasodilation, allergenicity, inflammation, immunotherapy, antimicrobial properties, renal disorders, gut disorders, postprandial absorption, carbohydrate and lipid metabolism, obesity, diabetes, and oxidative damage to molecules (e.g. DNA and proteins) other than LDL particles. The Panel considers that no conclusions can be drawn from these references for the scientific substantiation of the claimed effect.

In a randomised, single-blind, cross-over trial, 25 healthy male and female smokers consumed olive oil with low (3 mg/day) or high (21.6 mg/day) phenolic content for three weeks (Moschandreas et al.,

2002). Total plasma resistance to oxidation, and the ferric reducing ability of plasma, as markers of the antioxidant capacity of plasma, concentrations of protein carbonyl as a marker of protein oxidation, and malondialdehyde (MDA) and lipid hydroperoxides measured with a kit assay as markers of lipid peroxidation, were assessed. The Panel notes that no valid markers of lipid (or LDL) peroxidation were used in this study, and considers that no conclusions can be drawn from this study for the scientific substantiation of the claimed effect.

In a randomised, sequential cross-over acute study, 21 hypercholesterolaemic volunteers (16 female) received two breakfasts with olive oil (phenolic content 400 mg/kg olive oil, i.e. 14 mg/day or 80 mg/kg olive oil, i.e. 2.8 mg/day) (Ruano et al., 2005). Postprandial plasma concentrations of lipoperoxides (LPO, colorimetric assay) and 8-epi-prostaglandin-$F_{2\alpha}$ (immunoenzymatic assay) were obtained at baseline and 2 hours after consumption of the meal. The Panel notes that this was an acute study, that the phenolic composition of the olive oils used is not sufficiently characterised, that LPO measured by a colorimetric assay is not a reliable marker of lipid peroxidation, and that no markers of peroxidation of LDL particles were assessed. The Panel considers that no conclusions can be drawn from this study for the scientific substantiation of the claimed effect.

In a multicentre (six centres in Finland, Denmark, Germany, Italy and Spain), randomised, cross-over, controlled human intervention study, olive oils with high (366 mg/kg olive oil, i.e. 8.0 mg/day; hydroxytyrosol content 63.5 mg/L, tyrosol 24.4 mg/L, and oleuropein derivatives 327.2 mg/L as measured by HPLC) moderate (164 mg/kg olive oil, i.e. 3.6 mg/day, hydroxytyrosol content approx. 28.5 mg/L), and low (2.7 mg/kg olive oil, i.e. 0.1 mg/day, no hydroxytyrosol) phenolic content were consumed (25 mL/day) by 200 male subjects for three weeks (Covas et al., 2006b). The phenolic composition and content of the olive oils used in this study are reported by de la Torre-Carbot et al. (2010). Oxidative damage to lipids was assessed by measuring plasma-circulating oxidised LDL (oxLDL, immunoenzymatic assay), plasma total $F_{2\alpha}$-isoprostanes (HPLC, stable isotope-dilution and MS), plasma C18 hydroxy fatty acids (GC-MS) and serum LDL cholesterol un-induced conjugated dienes. Hydroxytyrosol and tyrosol excretion in urine were measured to assess compliance. A significant linear decrease in biomarkers of lipid peroxidation (conjugated dienes, hydroxy fatty acids and oxLDL) was observed in association with the increasing phenolic content of the olive oils. oxLDL significantly increased with the low phenolic-containing olive oil, and significantly decreased with the medium and high phenolic-containing olive oils ($p<0.014$). No consistent change was observed in plasma total $F_{2\alpha}$-isoprostanes. The Panel notes the large sample size of this multicentre study, the sufficient characterisation of polyphenols in the olive oils used, the use of valid biomarkers to assess lipid peroxidation, and in particular the peroxidation of LDL particles, and the dose-dependent response observed between the intake of polyphenols in olive oil and the decrease in LDL peroxidation.

A subsample from the study by Covas et al. (2006b) consisting of 36 males recruited from the six centres participating in the trial and consuming olive oils with high (366 mg/kg olive oil, i.e. 8.0 mg/day, hydroxytyrosol content 63.5 mg/L) or low (2.7 mg/kg olive oil, i.e. 0.1 mg/day, no hydroxytryrosol) phenolic content for three weeks (25 mL/day) were further investigated regarding the effect of specific metabolites in olive oil phenols on human LDL lipid composition and peroxidation (de la Torre-Carbot et al., 2010). The concentrations of hydroxytyrosol monosulfate and homovanillic acid sulphate (but not of tyrosol sulphate) in LDL particles significantly increased ($p<0.05$), whereas the concentration of circulating markers of lipid peroxidation, including LDL particles (oxLDL, conjugated dienes and hydroxy fatty acids), significantly decreased ($p<0.05$) after ingestion of olive oil with high phenolic content. The Panel notes the inverse relationship between the concentrations of phenolic metabolites in LDL particles and the degree of LDL peroxidation.

A controlled, double-blind, cross-over, randomised, clinical intervention using three olive oils (refined, common and virgin, 25 mL/day) with increasing phenolic concentrations (from 0 to 150 mg/kg, i.e. up to 3.3 mg/day of which 3 % tyrosol, 7 % hydroxytyrosol, 42 % oleuropein aglycones and 14 % ligstroside aglycones) was conducted in 30 healthy male volunteers for three weeks

(Marrugat et al., 2004). Urinary tyrosol and hydroxytyrosol were measured as markers of compliance. *In vivo* plasma oxLDL (measured by a sandwich ELISA procedure using the murine monoclonal antibody, mAb-4E6) significantly decreased (p=0.006 for linear trend), and *ex vivo* resistance of LDL to oxidation significantly increased (p=0.012 for linear trend) with the phenolic content of the olive oils administered. The Panel notes the use of a valid biomarker to assess LDL peroxidation (oxLDL), the inclusion of a supportive marker (*ex vivo* resistance of LDL to oxidation), the sufficient characterisation of polyphenols in the olive oils used, and the dose-dependent response observed between the intake of polyphenols in olive oil and the decrease in LDL peroxidation.

Twelve healthy men participated in a double-blind, randomised, cross-over study in which three olive oils with low (10 mg/kg, i.e. 0.2 mg/day), moderate (133 mg/kg, i.e. 2.9 mg/day), and high (486 mg/kg, i.e. 10.7 mg/day) phenolic content were consumed for four days (Weinbrenner et al., 2004). Percentages of individual phenolic compounds present in the olive oil were approximately 6.5 % hydroxytyrosol, 5.5 % tyrosol, 40 % oleuropein aglycones, 26 % ligstrosid aglycones, 12 % luteolin and 3 % apigenine as measured by HPLC. Consumption of olive oils significantly decreased plasma oxidised LDL (oxLDL measured by the ELISA method) and MDA in urine (HPLC-UV), and significantly increased glutathione peroxidase activity ($p<0.05$ for linear trend for all) in a dose-dependent manner in relation to the phenolic content of the olive oil administered, whereas plasma 8-oxo-prostaglandin $F_{2\alpha}$ (HPLC and stable isotope dilution MS) was not affected. The Panel notes the use of a valid biomarker to assess LDL peroxidation (oxLDL), the sufficient characterisation of the olive oil polyphenols, and the dose-dependent response observed between the intake of polyphenols in olive oil and the decrease in LDL peroxidation.

In an acute, cross-over study design, olive oils with high (366 mg/kg, i.e. 13.2 mg/day), moderate (164 mg/kg, i.e. 5.9 mg/day), and low (2.7 mg/kg, 0.2 mg/day) phenolic content were consumed (40 mL/day) by 12 male subjects (Covas et al., 2006a). Outcome variables were assessed in blood samples at 2, 4 and 6 hours after consumption of the olive oils. Total phenolic compounds in LDL increased at postprandial state in a direct relationship to the phenolic compounds content of the olive oil ingested ($p<0.05$). A significant decrease in plasma oxidised LDL (oxLDL, measured by a sandwich ELISA procedure using the murine monoclonal antibody mAb-4E6) was observed at 4 and 6 hours post-prandial, in a dose-dependent manner in relation to the phenolic content of the olive oils administered (p=0.43 and p=0.28 for linear trend, respectively). No dose-response relationships were observed between the phenolic content of the olive oils and linear trends for changes in total plasma 8-iso-prostaglandin $F_{2\alpha}$ (measured using HPLC-MS) at any time point. The Panel notes that this is an acute study which provides insufficient characterisation of the olive oil polyphenols. However, the Panel assumes that these oils were the same used in another study by the same authors published the same year, with exactly the same phenolic content (Covas et al., 2006b), and notes the dose-dependent response observed between the intake of polyphenols in olive oil and the decrease in LDL peroxidation.

A few studies addressed the bioavailability of polyphenolic compounds in olive showing that the absorption of olive oil phenolics is probably larger than 55-66 mol%, and that the absorption of hydroxytyrosol is dose-dependent, suggesting that olive oil phenolics are absorbed from the intestine, that tyrosol and hydroxytyrosol are incorporated in lipoprotein fractions, and that hydroxytyrosol is excreted in urine as glucuronide conjugate (Bonanome et al., 2000; de la Torre-Carbot et al., 2010; Edgecombe et al., 2000; Miro-Casas et al., 2003; Visioli et al., 2001; Vissers et al., 2002). The incorporation of phenolic compounds from olive oil in LDL particles has been proposed as the mechanism by which olive phenolics may protect LDL particles from peroxidation.

The Panel notes that most of the human intervention studies described have been conducted in males (aged 20-60 years) using a wide range of daily doses of polyphenols in olive oil (from 0.1 to 10.7 mg/day expressed as total polyphenolic content measured spectrophotometrically), and with a content of hydroxytyrosol and its derivatives measured by HPLC up to 10 mg/day. The Panel also notes that only studies on polyphenols present in (and consumed with) olive oil have been provided for

the substantiation of the claimed effect, and that no data are available for other food matrices (e.g. leaf tea or tea extract).

The Panel notes that polyphenols naturally occurring in olive oil were shown to significantly decrease the amount of circulating oxidised LDL particles *in vivo* in a dose-dependent manner in one large (n=200, Covas et al., 2006b) and three small scale (12 subjects, (Weinbrenner et al., 2004), 30 subjects, (Marrugat et al., 2004), and 36 subjects, (de la Torre-Carbot et al., 2010), respectively) human intervention studies, one of which was short-term (four days, Weinbrenner et al., 2004). A dose-dependent decrease in the amount of circulating oxidised LDL particles *in vivo* was also found in one small scale (n=12) acute post-prandial study (Covas et al., 2006a). The lowest daily dose of hydroxytyrosol and its derivatives (measured by HPLC) in olive oil which showed a significant effect on *in vivo* LDL peroxidation was 5 mg (Covas et al., 2006b). A significant decrease in relation to consumption of olive oil polyphenols was also reported for serum LDL un-induced conjugated dienes (Covas et al., 2006b; de la Torre-Carbot et al., 2010) and for *ex vivo* resistance of LDL to oxidation (Marrugat et al., 2004), which can be considered as supportive markers to assess peroxidation of LDL particles. The Panel also notes that a significant decrease in plasma C18 hydroxy fatty acids (Covas et al., 2006b; de la Torre-Carbot et al., 2010) and urinary MDA (Weinbrenner et al., 2004) was observed following consumption of olive oil polyphenols, but that olive oil polyphenols do not appear to have an effect on $F_{2\alpha}$-isoprostanes (Covas et al., 2006a; Covas et al., 2006b; Weinbrenner et al., 2004).

In weighing the evidence, the Panel took into account that a well conducted and powered study, and two smaller-scale studies, showed a dose-dependent and significant effect of olive oil polyphenol consumption (for three weeks) on appropriate markers of LDL peroxidation (oxLDL), that these results were supported by one short-term and one acute study, and by supportive markers of LDL peroxidation (conjugated dienes, *ex vivo* resistance of LDL to oxidation) going in the same direction, and that evidence for a biologically plausible mechanism by which olive oil polyphenols could exert the claimed effect has been provided.

The Panel concludes that a cause and effect relationship has been established between the consumption of olive oil polyphenols (standardised by their content of hydroxytyrosol and its derivatives) and protection of LDL particles from oxidative damage.

3.2. Maintenance of normal blood HDL-cholesterol concentrations (ID 1639)

In the multicentre, randomised, cross-over, controlled human intervention study in 200 healthy male volunteers over three weeks described in section 3.1 (Covas et al., 2006b), a significant linear dose-dependent increase in HDL-cholesterol concentrations was observed for low- (+0.025 mmol/L, 95 % CI=0.003 to 0.05 mmol/L), medium- (+0.032 mmol/L, 95 % CI=0.005 to 0.05 mmol/L), and high-polyphenol olive oil (p *per* trend 0.018). Total cholesterol to HDL cholesterol ratio decreased linearly with the phenolic content of the olive oils (p *per* trend 0.013).

Another randomised, controlled, double-blind, cross-over intervention using three olive oils (refined, common and virgin) with increasing phenolic concentration in 30 healthy volunteers over three weeks, described in section 3.1 (Marrugat et al., 2004), showed a significant increase in HDL-cholesterol concentrations after consumption of the extravirgin olive oil with the highest polyphenol content (p=0.029), whereas no significant effect was observed with the common or the refined olive oils. The Panel notes that between-group comparisons were not reported, and that no dose-response relationship was observed between the consumption of olive oil polyphenols and changes in HDL-cholesterol concentrations.

The Panel notes that no evidence for a biologically plausible mechanism by which olive oil polyphenols could exert the claimed effect has been provided. The Panel also notes that only studies on polyphenols present in (and consumed with) olive oil have been provided for the substantiation of the claimed effect, and that no data are available for other food matrices (e.g. leaf tea or tea extract).

In weighing the evidence, the Panel took into account that the results from the studies provided are inconsistent, and that no evidence for a biologically plausible mechanism by which olive oil polyphenols could exert the claimed effect has been provided.

The Panel concludes that the evidence provided is insufficient to establish a cause and effect relationship between the consumption of olive oil polyphenols (standardised by their content of hydroxytyrosol and its derivatives) and maintenance of normal blood HDL-cholesterol concentrations.

3.3. Maintenance of normal blood pressure (ID 3781)

The majority of the references provided for the scientific substantiation of the claim included monographs, narrative reviews, papers on extraction procedures, toxicity studies, human intervention studies, animal studies, and *in vitro* experiments on food(s)/food constituent(s) other than olive polyphenols, and/or on effects other than blood pressure. These included references on antioxidant activity, allergenicity, antimicrobial and antifungal properties, immunotherapy, gut disorders, liver function and diabetes. The Panel considers that no conclusions can be drawn from these references for the scientific substantiation of the claimed effect.

An internal report describing a human study on the effect on mild hypertension of the consumption of an olive leaf extract standardised to its oleuropein content (Moccetti et al., 2005) was submitted, in which the information provided regarding the study design, methodology and statistical analysis was insufficient for a complete scientific evaluation. The Panel considers that no conclusions can be drawn from this reference for the scientific substantiation of the claimed effect.

An animal study on the blood pressure lowering effect of an olive leaf extract in induced hypertension (Khayyal et al., 2002), and an animal study on the blood pressure lowering effect of an olive extract submitted intravenously (Gilani et al., 2005), were provided. The Panel considers that evidence provided in animal studies is not sufficient to predict the occurrence of an effect of consumption of olive polyphenols on blood pressure in humans. The Panel also considers that studies on intravenous administration cannot be used to substantiate a claim on a food/food constituent.

The Panel concludes that a cause and effect relationship has not been established between the consumption of polyphenols in olive (olive fruit, olive mill waste waters or olive oil, *Olea europaea* L. extract and leaf) standardised by their content of hydroxytyrosol and its derivatives (e.g. oleuropein complex) and maintenance of normal blood pressure.

4. Panel's comments on the proposed wording

4.1. Protection of LDL particles from oxidative damage (ID 1333, 1638, 1639, 1696, 2865)

The Panel considers that the following wording reflects the scientific evidence: "Consumption of olive oil polyphenols contributes to the protection of blood lipids from oxidative damage."

5. Conditions and possible restrictions of use

5.1. Protection of LDL particles from oxidative damage (ID 1333, 1638, 1639, 1696, 2865)

The Panel considers that in order to bear the claim, 5 mg of hydroxytyrosol and its derivatives (e.g. oleuropein complex and tyrosol) in olive oil should be consumed daily. These amounts, if provided by moderate amounts of olive oil, can be easily consumed in the context of a balanced diet. The concentrations in some olive oils may be too low to allow the consumption of this amount of polyphenols 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 constituent, polyphenols in olive (olive fruit, olive mill waste waters or olive oil, *Olea europaea* L. extract and leaf) standardised by their content of hydroxytyrosol and its derivatives (e.g. oleuropein complex), which is the subject of the health claims, is sufficiently characterised in relation to the claimed effects.

Protection of LDL particles from oxidative damage (ID 1333, 1638, 1639, 1696, 2865)

- The claimed effects are "reduces oxidative stress", "antioxidant properties", "lipid metabolism", "antioxidant activity, they protect body cells and LDL from oxidative damages", and "antioxidant properties". 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 protection of low-density lipoprotein (LDL) particles from oxidative damage. Protection of LDL particles from oxidative damage may be a beneficial physiological effect.
- A cause and effect relationship has been established between the consumption of olive oil polyphenols (standardised by the content of hydroxytyrosol and its derivatives) and protection of LDL particles from oxidative damage.
- The following wording reflects the scientific evidence: "Consumption of olive oil polyphenols contributes to the protection of blood lipids from oxidative damage."
- In order to bear the claim, 5 mg of hydroxytyrosol and its derivatives (e.g. oleuropein complex and tyrosol) in olive oil should be consumed daily. These amounts, if provided by moderate amounts of olive oil, can be easily consumed in the context of a balanced diet. The concentrations in some olive oils may be too low to allow the consumption of this amount of polyphenols in the context of a balanced diet. The target population is the general population.

Maintenance of normal blood HDL-cholesterol concentrations (ID 1639)

- The claimed effect is "lipid metabolism". 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 maintenance of normal blood HDL-cholesterol concentrations. Maintenance of normal blood HDL-cholesterol concentrations (without increasing LDL-cholesterol concentrations) is a beneficial physiological effect.
- The evidence provided is insufficient to establish a cause and effect relationship between the consumption of olive oil polyphenols (standardised by their content of hydroxytyrosol and its derivatives) and maintenance of normal blood HDL-cholesterol concentrations.

Maintenance of normal blood pressure (ID 3781)

- The claimed effect is "contributes to the maintenance of a normal blood pressure". The target population is assumed to be the general population. Maintenance of normal blood pressure is a beneficial physiological effect.
- A cause and effect relationship has not been established between the consumption of polyphenols in olive (olive fruit, olive mill waste waters or olive oil, *Olea europaea* L. extract and leaf) standardised by the content of hydroxytyrosol and its derivatives (e.g. oleuropein complex) and maintenance of normal blood pressure.

"Anti-inflammatory properties" (ID 1882)

- The claimed effect is "a potent source of olive biophenols with anti-inflammatory properties". The target population is assumed to be the general population. In the context of the proposed

wordings, the Panel considers that the claim refers to diseases such as osteoarthritis or rheumatoid arthritis, in which a reduction of inflammation would be a therapeutic target for the treatment of the disease.

- Reduction of inflammation in the context of diseases such as osteoarthritis or rheumatoid arthritis is a therapeutic target for the treatment of the disease, and does not comply with the criteria laid down in Regulation (EC) No 1924/2006.

"Contributes to the upper respiratory tract health" (ID 3468)

- The claimed effect is "contributes to the upper respiratory tract 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.

"Can help to maintain a normal function of gastrointestinal tract" (3779)

- The claimed effect is "can help to maintain a normal function of gastrointestinal tract". 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.

"Contributes to body defences against external agents" (ID 3467)

- The claimed effect is "contributes to body defences against external agents". 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.

DOCUMENTATION PROVIDED TO EFSA

Health claims pursuant to Article 13 of Regulation (EC) No 1924/2006 (No: EFSA-Q-2008-2070, EFSA-Q-2008-2374, EFSA-Q-2008-2375, EFSA-Q-2008-2432, EFSA-Q-2008-2615, EFSA-Q-2008-3598, EFSA-Q-2008-4195, EFSA-Q-2008-4196, EFSA-Q-2008-4498, EFSA-Q-2008-4500). 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.

REFERENCES

Bonanome A, Pagnan A, Caruso D, Toia A, Xamin A, Fedeli E, Berra B, Zamburlini A, Ursini F and Galli G, 2000. Evidence of postprandial absorption of olive oil phenols in humans. Nutrition, Metabolism and Cardiovascular Diseases, 10, 111-120.

Covas MI, de la Torre K, Farre-Albaladejo M, Kaikkonen J, Fito M, Lopez-Sabater C, Pujadas-Bastardes MA, Joglar J, Weinbrenner T, Lamuela-Raventos RM and de la Torre R, 2006a. Postprandial LDL phenolic content and LDL oxidation are modulated by olive oil phenolic compounds in humans. Free Radical Biology and Medicine, 40, 608-616.

Covas MI, Nyyssonen K, Poulsen HE, Kaikkonen J, Zunft HJ, Kiesewetter H, Gaddi A, de la Torre R, Mursu J, Baumler H, Nascetti S, Salonen JT, Fito M, Virtanen J, Marrugat J and Group ES, 2006b. The effect of polyphenols in olive oil on heart disease risk factors: a randomized trial. Annals of Internal Medicine, 145, 333-341.

de la Torre-Carbot K, Chavez-Servin JL, Jauregui O, Castellote AI, Lamuela-Raventos RM, Nurmi T, Poulsen HE, Gaddi AV, Kaikkonen J, Zunft HF, Kiesewetter H, Fito M, Covas MI and Lopez-

Sabater MC, 2010. Elevated circulating LDL phenol levels in men who consumed virgin rather than refined olive oil are associated with less oxidation of plasma LDL. Journal of Nutrition, 140, 501-508.

Edgecombe SC, Stretch GL and Hayball PJ, 2000. Oleuropein, an antioxidant polyphenol from olive oil, is poorly absorbed from isolated perfused rat intestine. Journal of Nutrition, 130, 2996-3002.

Gilani AH, Khan AU, Shah AJ, Connor J and Jabeen Q, 2005. Blood pressure lowering effect of olive is mediated through calcium channel blockade. International Journal of Food Sciences and Nutrition, 56, 613-620.

Khayyal MT, el-Ghazaly MA, Abdallah DM, Nassar NN, Okpanyi SN and Kreuter MH, 2002. Blood pressure lowering effect of an olive leaf extract (Olea europaea) in L-NAME induced hypertension in rats. Arzneimittel-Forschung, 52, 797-802.

Marrugat J, Covas MI, Fito M, Schroder H, Miro-Casas E, Gimeno E, Lopez-Sabater MC, de la Torre R and Farre M, 2004. Effects of differing phenolic content in dietary olive oils on lipids and LDL oxidation--a randomized controlled trial. European Journal of Nutrition, 43, 140-147.

Miro-Casas E, Covas MI, Farre M, Fito M, Ortuno J, Weinbrenner T, Roset P and de la Torre R, 2003. Hydroxytyrosol disposition in humans. Clinical Chemistry, 49, 945-952.

Moccetti T, Schmidlin CB, Aydogan C, Bradl B and Busjahn A, 2005. Effect of EFLA®943 in adult twins with mild hypertension. Internal Report.

Moschandreas J, Vissers MN, Wiseman S, van Putte KP and Kafatos A, 2002. Extra virgin olive oil phenols and markers of oxidation in Greek smokers: a randomized cross-over study. European Journal of Clinical Nutrition, 56, 1024-1029.

Ruano J, Lopez-Miranda J, Fuentes F, Moreno JA, Bellido C, Perez-Martinez P, Lozano A, Gomez P, Jimenez Y and Perez Jimenez F, 2005. Phenolic content of virgin olive oil improves ischemic reactive hyperemia in hypercholesterolemic patients. Journal of the American College of Cardiology, 46, 1864-1868.

Singleton VL and Rossi JA, Jr., 1965. Colorimetry of total phenolics with phosphomolybdic-phosphotungstic acid reagents. American Journal of Enology and Viticulture, 16, 144-158.

Visioli F, Caruso D, Plasmati E, Patelli R, Mulinacci N, Romani A, Galli G and Galli C, 2001. Hydroxytyrosol, as a component of olive mill waste water, is dose- dependently absorbed and increases the antioxidant capacity of rat plasma. Free Radical Research, 34, 301-305.

Vissers MN, Zock PL, Roodenburg AJ, Leenen R and Katan MB, 2002. Olive oil phenols are absorbed in humans. Journal of Nutrition, 132, 409-417.

Weinbrenner T, Fito M, de la Torre R, Saez GT, Rijken P, Tormos C, Coolen S, Albaladejo MF, Abanades S, Schroder H, Marrugat J and Covas MI, 2004. Olive oils high in phenolic compounds modulate oxidative/antioxidative status in men. Journal of Nutrition, 134, 2314-2321.

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[6] (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[7]

Foods are commonly involved in many different functions[8] of the body, and for one single food many health claims may therefore be scientifically true. Therefore, the relative importance of food e.g. nutrients in relation to other nutrients for the expressed beneficial effect should be considered: for functions affected by a large number of dietary factors it should be considered whether a reference to a single food is scientifically pertinent.

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

SUBSTANTIATION OF CLAIMS BY GENERALLY ACCEPTABLE SCIENTIFIC EVIDENCE

6 OJ L12, 18/01/2007
7 The term 'food' when used in this Terms of Reference refers to a food constituent, the food or the food category.
8 The term 'function' when used in this Terms of Reference refers to health claims in Article 13(1)(a), (b) and (c).

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

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

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

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

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

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

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

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

WORDING OF HEALTH CLAIMS

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

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

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

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

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

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

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

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

TERMS OF REFERENCE

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

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

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

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

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

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

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

APPENDIX B

EFSA DISCLAIMER

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

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

APPENDIX C

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

ID	Food or Food constituent	Health Relationship	Proposed wording
1333	Olive Oil.	Reduces oxidative stress.	Olive Oil has antioxidant effects.
	Conditions of use - Consumption of at least two soup-spoonfuls (23 g) of olive oil a day for at least three weeks, in the context of a diet low in saturated fatty acids.		
ID	**Food or Food constituent**	**Health Relationship**	**Proposed wording**
1638	Polyphenols from olive (olive fruit, olive mild waste waters or olive oil)	Antioxidant properties	Polyphenols from olive have an antioxidant activity that may help maintain healthy LDL cholesterol level and lipid oxidation / antioxidants
	Conditions of use - 20 g Olivenöl mit einem Polyphenolgehalt von 200 mg/kg / Mind 2 mg Hydroxytyrosol täglich - 20 g of an olive oil with a polyphenol content of 200 mg/kg / Min 2 mg per day of hydroxytyrosol - Frucht/–Tagesdosis > 10 mg Polyphenole		
ID	**Food or Food constituent**	**Health Relationship**	**Proposed wording**
1639	Polyphenols from olive (olive fruit, olive mild waste waters or olive oil)	Lipid metabolism	Polyphenols are absorbed from olive oil in the intestine and metabolized there or in the liver, and have been shown to be able to bind LDL in vivo. They have demonstrated scavenging properties in vitro that ensure olive oil stability and explain their ability to protect LDL against oxidation. Contributes to good HDL cholesterol level. Polyphenols from olive have an antioxidant activity that may help protect LDL cholesterol and lipid oxidation
	Conditions of use - Erwachsene. 300 Milligramm (mg). entspr. mind. 250 ml Rotwein - Erwachsene Männer. 300 Milligramm (mg) entspr. mind. 200 ml Grantapfelsaft - 20 g of an olive oil with a polyphenol content of 200 mg/kg / Min 2 mg per day of hydroxytyrosol		
ID	**Food or Food constituent**	**Health Relationship**	**Proposed wording**
1696	Hydroxytyrosol simple phenol; oleuropein complex polyphenol belonging to ai secoiridoids.	Antioxidant activity, they protect body cells and LDL from oxidative damages.	Phenolic compounds from extravergin olive oil are powerful antioxidants and protect LDL cholesterol from oxidative damage.

	Conditions of use - 2-15 mg per day		
ID	**Food or Food constituent**	**Health Relationship**	**Proposed wording**
1882	Name of Food product: Olive Biophenols Description of food in terms of food legislation categories: Food supplement Was food on Irish market before 1st July 2007: No	Health benefits of food: A potent source of olive biophenols with anti-inflammatory properties Do benefits relate to a disease risk factor: No Target group: All of the general population including children and adults	Exact wording of claim as it appears on product: A potent source of olive biophenols with anti-inflammatory properties Examples of any alternative wording that may be used in relation to claim: Olive biophenols can reduce inflammation related to Osteoarthritis and Rheumatoid arthritis Is claim a picture: No
	Conditions of use - Number of nutrients/other substances that are essential to claimed effect: 1. Names of nutrient/other substances and Quantity in Average daily serving: 100 miligrams Olive Biophenols. Weight of average daily food serving: 200 miligram(s). Daily amount to be consumed to produce claimed effect: 200 miligram(s). Number of food portions this equates to in everyday food portions: 1. Are there factors that could interfere with bioavailability: No. Length of time after consumption for claimed effect to become apparent: 1-2 weeks depending on the individual's state of health. Is there a limit to the amount of food which should be consumed in order to avoid adverse health effects: No. Where applicable outline nutritional composition (g per 100g) of food: Total Fat: .00, Saturated Fat: 1.24, Trans Fat: .08, Sugar: .00, Salt: .00, Sodium: .07		
	Comments from Member States Further references to support this claim were provided by the FBO - these are included in a separate document (identified by claim number - additional information).		
ID	**Food or Food constituent**	**Health Relationship**	**Proposed wording**
2865	Polyphenols (from Olea europaea extract).	Antioxidant properties.	Polyphenols contained in this product have an antioxidant effect/ polyphenols contained in this product ensure protective effect on the organism/ensure an antioxidant action/help prevent oxidative tissue damage. Help mop up free radicals in cells/helps guard against the damage caused by free radicals induced by pollution. Polyphenols from olive have an antioxidant activity that may help protect LDL cholesterol and lipid oxidation.
	Conditions of use - up to 200 mg/day		
ID	**Food or Food constituent**	**Health Relationship**	**Proposed wording**
3467	OLEA EUROPAEA L.	Contributes to body defences against external agents.	Increases the physiological resistance of the organism in case of severe ambiance conditions.

	Conditions of use - 250-500 mg (standardized extract), 1-3 times a day. Tea: 3-4 cups, 2 teaspoonfuls of herb per cup throughout the day (dietary supplement should be standardized to 4-23% oleuropein per dose)		
	No clarification provided by Member States		
ID	**Food or Food constituent**	**Health Relationship**	**Proposed wording**
3468	OLEA EUROPAEA L.	Contributes to the upper respiratory tract health.	Helps the upper respiratory tract.
	Conditions of use - 250-500 mg (standardized extract), 1-3 times a day. Tea: 3-4 cups, 2 teaspoonfuls of herb per cup throughout the day (dietary supplement should be standardized to 4-23% oleuropein per dose)		
	No clarification provided by Member States		
ID	**Food or Food constituent**	**Health Relationship**	**Proposed wording**
3779	OLEA EUROPAEA L.	Can help to maintain a normal function of gastrointestinal tract.	Contributes to the functions of the intestinal tract. Supports the function of intestinal tract.
	Conditions of use - 250-500 mg (standardized extract), 1-3 times a day. Tea: 3-4 cups, 2 teaspoonfuls of herb per cup throughout the day (dietary supplement should be standardized to 4-23% oleuropein per dose)		
	No clarification provided by Member States		
ID	**Food or Food constituent**	**Health Relationship**	**Proposed wording**
3781	OLEA EUROPAEA L.	Contributes to the maintenance of a normal blood pressure.	Traditionally known for helping the blood circulation and vascular pressure.
	Conditions of use - Leaf / 2 -2 g daily as infusion with water - 250-500 mg (standardized extract), 1-3 times a day. Tea: 3-4 cups, 2 teaspoonfuls of herb per cup throughout the day (dietary supplement should be standardized to 4-23% oleuropein per dose)		

GLOSSARY AND ABBREVIATIONS

CI	Confidence interval
DNA	Deoxyribonucleic acid
ELISA	Enzyme Linked ImmunoSorbent Assay
GAE	Gallic acid equivalents
GC-MS	Gas chromatography-mass spectrometry
HDL	High-density lipoproteins
HPLC	High performance liquid chromatography
HPLC-UV	High performance liquid chromatography with ultraviolet detection
LDL	Low-density lipoproteins
LPO	Lipoperoxides
MDA	Malondialdehyde
MS	Mass spectrometry
oxLDL	Oxidised low-density lipoproteins
ROS	Reactive oxygen species