

## SCIENTIFIC OPINION

### **Scientific Opinion on the substantiation of health claims related to coenzyme Q<sub>10</sub> and contribution to normal energy-yielding metabolism (ID 1508, 1512, 1720, 1912, 4668), maintenance of normal blood pressure (ID 1509, 1721, 1911), protection of DNA, proteins and lipids from oxidative damage (ID 1510), contribution to normal cognitive function (ID 1511), maintenance of normal blood cholesterol concentrations (ID 1721) and increase in endurance capacity and/or endurance performance (ID 1913) 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

This scientific output, published on 9 December 2010, replaces the earlier version published on 19 October 2010<sup>4</sup>.

#### 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

<sup>1</sup> On request from the European Commission, Question No EFSA-Q-2008-2246, EFSA-Q-2008-2247, EFSA-Q-2008-2457, EFSA-Q-2008-2644, EFSA-Q-2008-2646, adopted on 30 April 2010 and Question No EFSA-Q-2008-2245, EFSA-Q-2008-2248, EFSA-Q-2008-2249, EFSA-Q-2008-2456, EFSA-Q-2008-2645, EFSA-Q-2010-00621, adopted on 10 September 2010.

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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. The members of the Claims Sub-Working Group on Mental/Nervous System: Jacques Rigo, Astrid Schloerscheidt, Barbara Stewart-Knox, Sean (J.J.) Strain and Peter Willatts. The members of the Claims Sub-Working Group on Weight Management/Satiety/Glucose and Insulin Control/Physical Performance: Kees de Graaf, Joanne Harrold, Mette Hansen, Mette Kristensen, Anders Sjödin and Inge Tetens.

<sup>4</sup> After publication of this opinion, the following changes have been made on page 1 of the opinion: In the acknowledgment section the members of the Claims Sub-Working Group on Weight Management/Satiety/Glucose and Insulin Control/Physical Performance have been added.

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in relation to coenzyme Q<sub>10</sub> and contribution to normal energy-yielding metabolism, maintenance of normal blood pressure, protection of DNA, proteins and lipids from oxidative damage, contribution to normal cognitive function, maintenance of normal blood cholesterol concentrations and increase in endurance capacity and/or endurance performance. The scientific substantiation is based on the information provided by the Member States in the consolidated list of Article 13 health claims and references that EFSA has received from Member States or directly from stakeholders.

The food constituent, which is the subject of the health claims, is coenzyme Q<sub>10</sub> (ubiquinone). The Panel considers that coenzyme Q<sub>10</sub> (ubiquinone) is sufficiently characterised.

### **Contribution to normal energy-yielding metabolism**

The claimed effects are “energy metabolism”, “ubiquinone takes part in electron-transferring in the respiratory chain”, “for physiological energy”, “energy production, muscle function” and “energising by stimulating the obtainance of adenosine triphosphate from the cellular energetic processes”. The target population is assumed to be the general population. In the context of the proposed wordings and clarifications provided by Member States, the Panel assumes that the claimed effects relate to energy-yielding metabolism. The Panel considers that contribution to normal energy-yielding metabolism is a beneficial physiological effect.

The Panel notes that no data have been provided supporting an effect of coenzyme Q<sub>10</sub> consumption on energy-yielding metabolism under the proposed conditions of use in the target population.

On the basis of the data presented, the Panel concludes that a cause and effect relationship has not been established between the consumption of coenzyme Q<sub>10</sub> (ubiquinone) and contribution to normal energy-yielding metabolism.

### **Maintenance of normal blood pressure**

The claimed effects are “blood pressure”, “heart health” and “maintenance and promotion of heart health”. The target population is assumed to be the general population. The Panel considers that maintenance of normal blood pressure is a beneficial physiological effect.

In weighing the evidence, the Panel took into account that most of the studies presented have been conducted in hypertensive patients on pharmacological treatment for hypertension, that the evidence provided does not establish that interactions between coenzyme Q<sub>10</sub> and antihypertensive treatment can be excluded, and that only one intervention study, which had considerable weaknesses, reported a significant effect of coenzyme Q<sub>10</sub> supplementation on blood pressure.

On the basis of the data presented, the Panel concludes that a cause and effect relationship has not been established between the consumption of coenzyme Q<sub>10</sub> (ubiquinone) and the maintenance of normal blood pressure.

### **Protection of DNA, proteins and lipids from oxidative damage**

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

In weighing the evidence, the Panel took into account that the markers and methods used were inadequate to assess oxidative damage to molecules, and that evidence provided in animal and *in vitro* studies does not predict an effect on the protection of DNA from oxidative damage in humans.

On the basis of the data presented, the Panel concludes that a cause and effect relationship has not been established between the consumption of coenzyme Q<sub>10</sub> (ubiquinone) and the protection of DNA, proteins or lipids from oxidative damage.

### **Contribution to normal cognitive function**

The claimed effect is “protection of healthy neurological system”. The target population is assumed to be the general population. In the context of the clarifications provided by Member States, the Panel assumes that the claimed effect refers to normal cognitive function. The Panel considers that contribution to normal cognitive function is a beneficial physiological effect.

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

On the basis of the data presented, the Panel concludes that a cause and effect relationship has not been established between the consumption of coenzyme Q<sub>10</sub> (ubiquinone) and contribution to normal cognitive function.

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

The claimed effect is “maintenance and promotion of heart health”. The target population is assumed to be the general population. In the context of the proposed wordings, the Panel assumes that the claimed effect relates to the maintenance of normal blood cholesterol concentrations. The Panel considers that the maintenance of normal blood cholesterol concentrations is a beneficial physiological effect.

No references were provided from which scientific conclusions could be drawn for the 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 coenzyme Q<sub>10</sub> (ubiquinone) and the maintenance of normal blood cholesterol concentrations.

### **Increase in endurance capacity and/or endurance performance (ID 1913)**

The claimed effect is “physical activity”. The target population is assumed to be active individuals in the general population. The Panel considers that an increase in endurance capacity and/or endurance performance is a beneficial physiological effect.

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

On the basis of the data presented, the Panel concludes that a cause and effect relationship has not been established between the consumption of coenzyme Q<sub>10</sub> (ubiquinone) and an increase in endurance capacity and/or endurance performance.

### **KEY WORDS**

Coenzyme Q<sub>10</sub>, energy-yielding metabolism, blood pressure, oxidative damage, cognitive function, cholesterol, endurance, health claims.

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**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>5</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>6</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 constituent that is the subject of the health claim is coenzyme Q<sub>10</sub> (ubiquinone).

Coenzyme Q<sub>10</sub> (CoQ<sub>10</sub>) is part of the ubiquinone family of compounds, all containing 1,4 benzoquinone as the functional group with a side chain of isoprenyl units, which is 10 units in the case of coenzyme Q<sub>10</sub>. Coenzyme Q<sub>10</sub> can exist in three oxidation states: the fully reduced ubiquinol form (CoQ<sub>10</sub>H<sub>2</sub>), the radical semiquinone intermediate (CoQ<sub>10</sub>H) and the fully oxidised ubiquinone form (CoQ<sub>10</sub>). Coenzyme Q<sub>10</sub> can be synthesised in most human tissues and occurs widely in nature, including foods, mainly in meat, poultry and fish. Coenzyme Q<sub>10</sub> is measurable in foods by established methods.

The Panel considers that the food constituent, coenzyme Q<sub>10</sub> (ubiquinone), which is the subject of the health claims, is sufficiently characterised.

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

#### 2.1. Contribution to normal energy-yielding metabolism (ID 1508, 1512, 1720, 1912, 4668)

The claimed effects are “energy metabolism”, “ubiquinone takes part in electron-transferring in the respiratory chain”, “for physiological energy”, “energy production, muscle function” and “energising by stimulating the obtainance of adenosine triphosphate from the cellular energetic processes”. 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 relate to energy-yielding metabolism.

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

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<sup>5</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>6</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>

## **2.2. Maintenance of normal blood pressure (ID 1509, 1721, 1911)**

The claimed effects are “blood pressure”, “heart health” and “maintenance and promotion of heart health”. The Panel assumes that the target population is the general population.

In the context of the proposed wordings, the Panel notes that the claimed effect relates to the maintenance of normal blood pressure.

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

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

## **2.3. Protection of DNA, proteins and lipids from oxidative damage (ID 1510)**

The claimed effects are “antioxidant activity” and “normal 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 relate to the protection of cells and molecules from oxidative damage caused by free radicals.

Reactive oxygen species (ROS) including several kinds of radicals are generated in biochemical processes (e.g. respiratory chain) and as a consequence of exposure to exogenous factors (e.g. radiation, pollutants). These reactive intermediates damage biologically relevant molecules such as DNA, proteins and lipids if they are not intercepted by the antioxidant network, which includes free radical scavengers such as antioxidant nutrients.

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

## **2.4. Contribution to normal cognitive function (ID 1511)**

The claimed effect is “protection of healthy neurological system”. The Panel assumes that the target population is the general population.

In the context of the clarifications provided, the Panel assumes that the claimed effect refers to normal cognitive function. Cognitive function includes memory, attention (concentration), learning, intelligence and problem solving, which are well defined constructs and can be measured by validated psychometric cognitive tests.

The Panel considers that contribution to normal cognitive function is a beneficial physiological effect.

## **2.5. Maintenance of normal blood cholesterol concentrations (ID 1721)**

The claimed effect is “maintenance and promotion of heart health”. The Panel assumes that the target population is the general population.

In the context of the proposed wordings, the Panel assumes that the claimed effect relates to the maintenance of normal blood cholesterol concentrations.

Low-density lipoproteins (LDL) carry cholesterol from the liver to peripheral tissues, including the arteries. Elevated LDL-cholesterol, by convention  $>160$  mg/dL ( $>4.14$  mmol/L), may compromise the normal structure and function of the arteries. 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).

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

## **2.6. Increase in endurance capacity and/or endurance performance (ID 1913)**

The claimed effect is “physical activity”. The Panel assumes that the target population is active individuals in the general population.

In the context of the proposed wordings, it is unclear whether the claim refers to endurance capacity or to endurance performance. It should be noted that in the literature these terms are often used as synonyms. Endurance capacity refers to the exercise time to volitional fatigue when exercising at a constant workload or speed. Endurance performance relates to completing a certain task (running a certain distance) as fast as possible. This claim will be evaluated in relation to both of these definitions.

The Panel considers that an increase in endurance capacity and/or endurance performance is a beneficial physiological effect.

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

Coenzyme Q<sub>10</sub> (ubiquinone) is found in high concentrations in the mitochondria, it is involved in the mitochondrial electron transport chain as an electron acceptor/donor, and is known to play a role in oxidative mitochondrial phosphorylation (ATP production). Coenzyme Q<sub>10</sub> can be synthesised by the body and there is no need for coenzyme Q<sub>10</sub> in human diets (SCF, 1993).

### **3.1. Contribution to normal energy-yielding metabolism (ID 1508, 1512, 1720, 1912, 4668)**

A total of 86 references were provided in the consolidated list in relation to this claim. Most of the references were narrative reviews from textbooks and scientific journals in relation to the biochemical function, metabolism, kinetics and antioxidant capacity of coenzyme Q<sub>10</sub>, and to the potential therapeutic applications of high supplemental doses (>100 mg/day) in patients with heart failure, diabetes and/or hypertension. Some of the references provided reported on outcomes in relation to physical performance, blood pressure, oxidative damage and antioxidant function, whereas others reported on *in vitro/ex vivo* studies on the saturation kinetics of coenzyme Q<sub>10</sub> in relation to different enzymes in animal muscle biopsies, such as in beef heart mitochondria (Lenaz et al., 1994; 1997). The Panel considers that no conclusions can be drawn from these references for the scientific substantiation of the claimed effect.

One uncontrolled intervention study was provided on the effect of coenzyme Q<sub>10</sub> supplementation (100 mg/day) for six months in middle aged post-polio subjects (n=3) and healthy volunteers (n=4). Muscle energy metabolism during exercise and recovery was measured using <sup>31</sup>P-NMR spectroscopy (Mizuno et al., 1997). The Panel considers that no conclusions can be drawn from this small and uncontrolled study for the scientific substantiation of the claimed effect.

In another randomised, double-blind, placebo controlled intervention study the effect of coenzyme Q<sub>10</sub> supplementation (300 mg/day), for four weeks in elderly subjects prior to hip replacement, on muscle fibre type composition and induced changes in gene and protein expression, was measured in muscle biopsies (Linnane et al., 2002). Results on gene expression were presented for five subjects (treatment/placebo: 3/2), and on fibre type composition in 14 subjects (treatment/placebo: 7/7). A

significant effect was observed on both gene expression and induced protein synthesis, as well as on fibre type (higher proportion of type IIb 'fast twitch' fibre) in the intervention compared to the control group. The Panel notes the small number of subjects included in the study and that, although the changes observed in relation to coenzyme Q<sub>10</sub> supplementation might affect muscle energy metabolism, the relevance of these results to the claimed effect are unclear.

The Panel notes that no data have been provided supporting an effect of coenzyme Q<sub>10</sub> consumption on energy-yielding metabolism under the proposed conditions of use in the target population.

The Panel concludes that a cause and effect relationship has not been established between the consumption of coenzyme Q<sub>10</sub> (ubiquinone) and contribution to normal energy-yielding metabolism.

### **3.2. Maintenance of normal blood pressure (ID 1509, 1721, 1911)**

A total of 54 references were presented in the consolidated list in relation to this claim. One meta-analysis focused on coenzyme Q<sub>10</sub> supplementation as a therapy in patients with heart failure. In three non-controlled intervention studies and seven randomised controlled trials in humans, oral coenzyme Q<sub>10</sub> intake was studied in patients with clinical heart disease, mainly heart failure. Subjects in these studies cannot be considered representative of the general population in relation to the claimed effect. There were 21 review papers and eight textbook chapters that discussed the role of coenzyme Q<sub>10</sub> in heart disease, coenzyme Q<sub>10</sub> status in relation to statin treatment, and/or the role of coenzyme Q<sub>10</sub> in human health from a mechanistic or physiological viewpoint. These papers and textbook chapters did not contain original data on the health effects of oral coenzyme Q<sub>10</sub> intake in non-clinical populations. Furthermore, there was one conference abstract on the effect of coenzyme Q<sub>10</sub> in heart failure patients, one animal study (in mice) on the relation between age and mitochondrial coenzyme Q<sub>10</sub> concentrations and one biopsy study assessing coenzyme Q<sub>10</sub> concentrations in the heart tissue of patients with cardiomyopathy. The Panel considers that no conclusions can be drawn from these references for the scientific substantiation of the claimed effect.

The US Institute of Medicine (IoM, 2005) report on dietary reference intakes for vitamins and minerals was cited in the consolidated list, but no information on coenzyme Q<sub>10</sub> in relation to blood pressure could be retrieved.

Two systematic reviews and one meta-analysis on the health effects of coenzyme Q<sub>10</sub>, including blood pressure, were presented. Tran et al. (2001) performed a systematic review on the safety and efficacy of oral coenzyme Q<sub>10</sub> as co-adjuvant in the pharmacological treatment of different clinical conditions, including hypertension. The Panel considers that no scientific conclusions can be drawn from this systematic review for the scientific substantiation of the claim. A systematic review (Rosenfeldt et al., 2003) on the effects of coenzyme Q<sub>10</sub> in the treatment of hypertension and a meta-analysis (Rosenfeldt, 2007) of clinical trials on coenzyme Q<sub>10</sub> consumption in the treatment of hypertension were provided. The meta-analysis included a number of human intervention studies on the effects of coenzyme Q<sub>10</sub> on blood pressure, of which four had a randomised controlled design (Yamamagi et al., 1986; Burke et al., 2001; Digiesi et al., 1990; Singh et al., 1999) and are described below. Three of these have also been cited individually in the consolidated list (Yamamagi et al., 1986; Burke et al., 2001; Digiesi et al., 1990).

Six intervention studies in humans were provided on the effects of coenzyme Q<sub>10</sub> intake on blood pressure. One was a one arm, uncontrolled human study on the effects of coenzyme Q<sub>10</sub> supplementation (100 mg/day) for 10 weeks on blood pressure in 26 subjects with essential hypertension (Diegisi et al., 1994), from which no conclusions could be drawn for the scientific substantiation of the claimed effect owing to the uncontrolled nature of the study.

Two randomised controlled trials (Singh et al., 1999; Yamagami et al., 1986) on the effect of coenzyme Q<sub>10</sub> consumption on blood pressure included subjects who were on conventional (pharmacological) antihypertensive treatment before and during the studies. The Panel considers that no conclusions can be drawn from these studies for the substantiation of the claim as the evidence provided does not establish that interactions between coenzyme Q10 and antihypertensive treatment can be excluded.

A placebo-controlled cross-over study was conducted by Digiesi et al. (1990) including 18 Italian patients (four women, mean age 56 years) with baseline blood pressure of 167/103 mmHg on antihypertensive pharmacological treatment, which was suspended two weeks prior to enrolment. Patients were not selected for low coenzyme Q<sub>10</sub> status. Coenzyme Q<sub>10</sub> (100 mg/day) and placebo were administered for 10 weeks with a 2-week washout period in between. Blood pressure values were recorded weekly. The Panel notes the small size of the study, that differences in blood pressure changes between interventions were not reported, that intermediate blood pressure measurements were not reported nor considered in the statistical analysis, and that carry-over effects were not assessed. The Panel considers that no conclusions can be drawn from this study for the scientific substantiation of the claimed effect.

In a placebo-controlled, parallel intervention, 76 older patients (35 women, mean age 68 years) with isolated systolic hypertension (ISH), who were asked to discontinue antihypertensive medications 10 days before enrolment, were randomised to consume 120 mg/day coenzyme Q<sub>10</sub> or placebo for 12 weeks (Burke, 2001). Nine normotensive subjects were also recruited and all received coenzyme Q<sub>10</sub> (120 mg/day) for 12 weeks. The Panel notes that differences in blood pressure changes between treatment and placebo ISH groups were not reported. The Panel considers that no conclusions can be drawn from this study for the scientific substantiation of the claim.

In a 12-week placebo-controlled intervention, 80 subjects (mean age 53 years) with type 2 diabetes, dyslipidaemia and blood pressure <160/90 mmHg who were not on antihypertensive medication were randomised to consume coenzyme Q<sub>10</sub> (200 mg/day) and fenofibrate (200 mg/day), coenzyme Q<sub>10</sub> and fenofibrate placebo, coenzyme Q<sub>10</sub> placebo and fenofibrate, or double placebo (Hodgson et al., 2002). The primary outcome of the study was endothelial dysfunction. Secondary outcomes were blood lipids, blood pressure, glycaemic control and markers of oxidative stress. A total of 74 subjects completed the study and entered data analysis. A significant reduction in systolic (-6.1±2.6 mmHg, p=0.021) and diastolic (-2.9±1.4 mmHg, p=0.048) blood pressure was observed in subjects consuming 200 mg/day coenzyme Q<sub>10</sub> with or without fenofibrate (n = 36) compared to subjects not consuming coenzyme Q<sub>10</sub> (n = 38). No interaction between coenzyme Q<sub>10</sub> and fenofibrate was observed for any of the variables studied. The Panel notes that change in blood pressure was not the primary outcome of the study, that no statistical adjustment for multiple outcomes was considered, that data analysis was only provided for completers, that a direct comparison between the double placebo group and the CoQ<sub>10</sub> and fenofibrate placebo groups was not reported, and that in a more recent publication the same research group found an interaction between CoQ<sub>10</sub> and fenofibrate for blood pressure (Chew et al., 2008). The Panel considers that these weaknesses greatly limit the conclusions that can be drawn from this study with respect to an independent effect of CoQ<sub>10</sub> on blood pressure.

No evidence for a mechanism by which CoQ<sub>10</sub> could exert the claimed effect has been provided.

In weighing the evidence, the Panel took into account that most of the studies presented have been conducted in hypertensive patients on pharmacological treatment for hypertension, that the evidence provided does not establish that interactions between coenzyme Q10 and antihypertensive treatment can be excluded, and that only one intervention study with considerable weaknesses reported a significant effect of coenzyme Q<sub>10</sub> supplementation on blood pressure.

The Panel concludes that a cause and effect relationship has not been established between the consumption of coenzyme Q<sub>10</sub> (ubiquinone) and the maintenance of normal blood pressure.

### 3.3. Protection of DNA, proteins and lipids from oxidative damage (ID 1510)

Most of the references provided were narrative reviews on the (biochemical) functions of coenzyme Q<sub>10</sub> and its potential role in disease prevention and treatment, especially cardiovascular disease. The Panel considers that no conclusions can be drawn from these references for the scientific substantiation of the claimed effect. Also, a number of human studies on the effects of coenzyme Q<sub>10</sub> supplementation on the antioxidant capacity of plasma (e.g. assessed by the TRAP method) were cited. The Panel notes that this measure is a marker of antioxidant status and does not assess oxidative damage to molecules.

Six human intervention studies on effects of coenzyme Q<sub>10</sub> supplementation on lipid peroxidation were cited (Alleva, 1995; Stocker et al., 1991, revised by Kaikkonen et al., 2002; Mohr et al., 1992; Singh et al., 2005; Weber et al., 1994; Kontush et al., 1994).

Three human intervention studies were presented on the effects of coenzyme Q<sub>10</sub> supplementation (from 30 to 100 mg/day) on LDL resistance to oxidation *ex vivo* (lag time) assessed by different methods (Alleva, 1995; Stocker et al., 1991, revised by Kaikkonen et al., 2002; Mohr et al., 1992). Also, a cross-sectional study on the association between the rate of (induced) oxidative modification of LDL and its ubiquinol-10 content in healthy blood donors (Kontush et al., 1994) was provided. The Panel notes that LDL resistance to oxidation *ex vivo* is not a reliable marker of lipid peroxidation (Griffiths et al., 2002).

Three human intervention studies were presented on the effects of coenzyme Q<sub>10</sub> supplementation (from 90 to 200 mg/day) on plasma concentrations of malondialdehyde (MDA) and/or thiobarbituric acid reactive substances (TBARS) and/or lipid hydroperoxides (Stocker et al., 1991, revised by Kaikkonen et al., 2002; Singh et al., 2005; Weber et al., 1994). The Panel notes that measuring TBARS is not an accepted method to assess lipid peroxidation (non specific) and that MDA and lipid hydroperoxides measured by HPLC are not reliable markers of lipid peroxidation when used alone (Griffiths et al., 2002; Lykkesfeldt, 2007; Knasmüller et al., 2008).

Two rat studies on the effect of supplementation with coenzyme Q10 on DNA strand breaks were presented (Quiles et al., 2004; 2005), as well as one *in vitro* study with human lymphocytes (Tomasetti et al., 1999). The Panel considers that the evidence provided in animal and *in vitro* studies does not predict an effect of coenzyme Q<sub>10</sub> consumption on the protection of DNA from oxidative damage in humans, and that no scientific conclusions can be drawn from these studies for the substantiation of the claimed effect.

In weighing the evidence, the Panel took into account that LDL resistance to oxidation *ex vivo* is not a reliable marker of lipid peroxidation, that measuring TBARS is not an accepted method to assess lipid peroxidation, that MDA and lipid hydroperoxides measured by HPLC are not reliable markers of lipid peroxidation when used alone, and that evidence provided in animal and *in vitro* studies does not predict an effect on the protection of DNA from oxidative damage in humans.

The Panel concludes that a cause and effect relationship has not been established between the intake of coenzyme Q<sub>10</sub> (ubiquinone) and protection of DNA, proteins or lipids from oxidative damage.

### 3.4. Contribution to normal cognitive function (ID 1511)

Four references were provided to substantiate the claimed effect, including one narrative review, two human studies and one animal study.

One human study evaluated the efficacy of idebenone versus tacrine in patients suffering from dementia of the Alzheimer type (Gutzmann et al., 2002). The Panel considers that no conclusions can be drawn for the scientific substantiation of the claimed effect from a study using a synthetic analogue

of coenzyme Q<sub>10</sub>, and furthermore that the study did not evaluate endpoints of relevance for the claimed effect in those patients who were suffering from dementia.

The narrative review was related to the treatment of neurodegenerative diseases with coenzyme Q<sub>10</sub> (Young et al., 2007), and one human study investigated the effect of coenzyme Q<sub>10</sub> in subjects with Parkinson's disease (Shults et al., 2002). The evidence provided does not establish that results obtained in patients with neurodegenerative diseases can be extrapolated to the general population with regard to normal cognitive function.

The animal study examined whether supplemental intake of coenzyme Q<sub>10</sub> (ubiquinone-10) or alpha-tocopherol, either alone or in combination, could improve cognitive and psychomotor performance of aged mice (McDonald et al., 2005). The Panel considers that evidence provided in animal studies is not sufficient to predict the occurrence of an effect of coenzyme Q<sub>10</sub> consumption on cognitive function in humans.

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

The Panel concludes that a cause and effect relationship has not been established between the consumption of coenzyme Q<sub>10</sub> (ubiquinone) and contribution to normal cognitive function.

### **3.5. Maintenance of normal blood cholesterol concentrations (ID 1721)**

Only one reference was provided in relation to this claim on the use of coenzyme Q<sub>10</sub> as a therapeutic adjuvant in patients with congestive heart failure. The Panel considers that no conclusions can be drawn from this reference for the scientific substantiation of the claimed effect.

The Panel concludes that a cause and effect relationship has not been established between the consumption of coenzyme Q<sub>10</sub> (ubiquinone) and the maintenance of normal blood cholesterol concentrations.

### **3.6. Increase in endurance capacity and/or endurance performance (ID 1913)**

Three references were provided in the consolidated list for the scientific substantiation of the claimed effect (Cerioli et al., 1991; Yamabe and Fukuzaki., 1991; Zeppilli et al., 1991). These references were published in a book and details given in the description of the studies are limited.

In the first one arm, uncontrolled intervention (Cerioli et al., 1991) 12 healthy untrained male subjects were studied before and after 30 days of supplementation with 100 mg/day of coenzyme Q<sub>10</sub>. In a second one arm, uncontrolled intervention (Yamabi and Fukuzaki, 1991), nine female patients complaining of "easy fatigability and decreased work ability" were given 90 mg/day of coenzyme Q<sub>10</sub> for six months. The study by Zeppilli et al. (1991) described the effects of coenzyme Q<sub>10</sub> supplementation (100 mg/day for 30 days) on work capacity in both athletes (n=9) and sedentary subjects (n=10), as well as in a group of patients with "mitochondrial disease" (n=8). Athletes and sedentary volunteers received coenzyme Q<sub>10</sub> for 30 days and placebo for an additional 30 days with a 21-day washout period in between. However, it is unclear from the paper whether treatment and placebo were administered in a random order or in the sample order to all subjects. Statistical methods used for data analysis were not reported and direct comparisons between coenzyme Q<sub>10</sub> and placebo were not made for any of the groups. The Panel considers that no conclusions can be drawn from these small, uncontrolled studies for the scientific substantiation of the claimed effect.

The Panel concludes that a cause and effect relationship has not been established between the consumption of coenzyme Q<sub>10</sub> (ubiquinone) and an increase in endurance capacity and/or endurance performance.

## CONCLUSIONS

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

- The food constituent, coenzyme Q<sub>10</sub> (ubiquinone), which is the subject of the health claims, is sufficiently characterised.

### **Contribution to normal energy-yielding metabolism (ID 1508, 1512, 1720, 1912, 4668)**

- The claimed effects are “energy metabolism”, “ubiquinone takes part in electron-transferring in the respiratory chain”, “for physiological energy”, “energy production, muscle function” and “energising by stimulating the obtainance of adenosine triphosphate from the cellular energetic processes”. The target population is assumed to be the general population. Contribution to normal energy-yielding metabolism is a beneficial physiological effect.
- A cause and effect relationship has not been established between the consumption of coenzyme Q<sub>10</sub> (ubiquinone) and contribution to normal energy-yielding metabolism.

### **Maintenance of normal blood pressure (ID 1509, 1721, 1911)**

- The claimed effects are “blood pressure”, “heart health” and “maintenance and promotion of heart health”. 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 coenzyme Q<sub>10</sub> (ubiquinone) and the maintenance of normal blood pressure.

### **Protection of DNA, proteins and lipids from oxidative damage (ID 1510)**

- The claimed effects are “antioxidant activity” and “normal antioxidant properties”. The target population is assumed to be the general population. Protection of DNA, proteins and lipids from oxidative damage may be a beneficial physiological effect.
- A cause and effect relationship has not been established between the consumption of coenzyme Q<sub>10</sub> (ubiquinone) and the protection of DNA, proteins or lipids from oxidative damage.

### **Contribution to normal cognitive function (ID 1511)**

- The claimed effect is “protection of healthy neurological system”. The target population is assumed to be the general population. Contribution to normal cognitive function is a beneficial physiological effect.
- A cause and effect relationship has not been established between the consumption of coenzyme Q<sub>10</sub> (ubiquinone) and contribution to normal cognitive function.

### **Maintenance of normal blood cholesterol concentrations (ID 1721)**

- The claimed effect is “maintenance and promotion of heart health”. The target population is assumed to be the general population. Maintenance of normal blood cholesterol concentrations is a beneficial physiological effect.
- A cause and effect relationship has not been established between the consumption of coenzyme Q<sub>10</sub> (ubiquinone) and the maintenance of normal blood cholesterol concentrations.

### **Increase in endurance capacity and/or endurance performance (ID 1913)**

- The claimed effect is “physical activity”. The target population is assumed to be active individuals in the general population. An increase in endurance capacity and/or endurance performance is a beneficial physiological effect.
- A cause and effect relationship has not been established between the consumption of coenzyme Q<sub>10</sub> (ubiquinone) and an increase in endurance capacity and/or endurance performance.

### **DOCUMENTATION PROVIDED TO EFSA**

Health claims pursuant to Article 13 of Regulation (EC) No 1924/2006 (No: EFSA-Q-2008-2245, EFSA-Q-2008-2246, EFSA-Q-2008-2247, EFSA-Q-2008-2248, EFSA-Q-2008-2249, EFSA-Q-2008-2456, EFSA-Q-2008-2457, EFSA-Q-2008-2644, EFSA-Q-2008-2645, EFSA-Q-2008-2646, EFSA-Q-2010-00621). 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>7</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>8</sup>

Foods are commonly involved in many different functions<sup>9</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>7</sup> OJ L12, 18/01/2007

<sup>8</sup> The term 'food' when used in this Terms of Reference refers to a food constituent, the food or the food category.

<sup>9</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 coenzyme Q10, including conditions of use from similar claims, as proposed in the Consolidated List.

ID	Food or Food constituent	Health Relationship	Proposed wording
1508	Coenzyme Q10 (Ubiquinone);	<p>Energy metabolism</p> <p><u>Clarification provided</u></p> <p>Energy metabolism.</p> <p>CoQ10 has a unique function since it transfers electrons from the primary substrates to the oxidase system at the same time that it transfers protons to the outside of the mitochondrial membrane. This transfer results in a proton gradient across the membrane. As the protons return to the interior through the enzymatic machinery for making ATP, they drive the formation of ATP.</p> <p>Promotes energy production</p> <ul style="list-style-type: none"> <li>- is needed/important for energy production in the cell</li> <li>- is needed/important for the energy metabolism and the transformation of food into physiological energy</li> </ul>	<p>Supports energy production</p> <ul style="list-style-type: none"> <li>-is needed/important for energy production in the cell</li> <li>-plays an important role in the ATP production to maintain healthy condition</li> <li>-is needed/important for the energy metabolism and the transformation of food into physiological</li> </ul>
<p><b>Conditions of use</b></p> <ul style="list-style-type: none"> <li>- Amount of consumption: 30 mg/Tag. Upper limit: 200 Milligramm (mg)</li> <li>- 3-5 mg. The condition is based on amount in typical diet which is reported to be 3 to 5 mg.</li> <li>- Amount of consumption: 30 Milligramm (mg). Other condition: 30 mg,was aber 5 Fach besser resorbiert wird</li> <li>- Amount of consumption: 30 Milligramm (mg). Upper limit: 60 Milligramm (mg).</li> <li>- Food supplement with 30-60mg of ubiquinone acid in the daily dose.</li> <li>- 30-200 mg per day. Regular consumption of Q10 via dietary sorces of supplementation. 10-30mg per serving</li> <li>- 30 – 200 mg/day–With food–Naturidentes, fermentatives Q-10–Als Kapsel 30 – 200 mg/day–With food–Naturidentes, fermentatives Q-10–Als Kapsel 100 – 200 mg/day–With food–Naturidentes, fermentatives Q10 –Als Kapsel</li> </ul>			
ID	Food or Food constituent	Health Relationship	Proposed wording
1509	Coenzyme Q10 (Ubiquinone); Normal cardiovascular function	Heart health	<p>Supports normal blood pressure</p> <p>Contributes to a normal blood pressure</p>

	<p><b>Conditions of use</b></p> <ul style="list-style-type: none"> <li>- Amount of consumption 100 mg/Tag. Upper limit: 200 Milligramm (mg)</li> <li>- 100-200 mg per day</li> <li>- Für alle Bevölkerungsgruppen geeignet-Tagesdosis:–100 mg</li> <li>- Food supplement with 30-60mg of ubiquinone acid in the daily dose.</li> <li>- 15 mg/day, 15% of the lower therapeutic dose 100 mg.</li> <li>- 100-200 mg per day. Regular consumption of luetin via dietary sources or supplementation</li> </ul>		
ID	Food or Food constituent	Health Relationship	Proposed wording
1510	Coenzyme Q10 (Ubiquinone)	Antioxidant properties, Normal antioxidant activity	<p>Naturally occurring lipid soluble antioxidant in the body</p> <ul style="list-style-type: none"> <li>-helps to protect against lipid oxidation</li> <li>-antioxidant</li> <li>-helps to maintain healthy condition</li> <li>-helps to protect against free radicals which are mainly responsible for cellular ageing</li> </ul>
			<p><b>Conditions of use</b></p> <ul style="list-style-type: none"> <li>- Erwachsene. 30 – 200 Milligramm (mg)</li> <li>- 50 mg</li> <li>- Amount of consumption: 30 mg/Tag. Upper limit: 200 Milligramm (mg)</li> <li>- TD&gt;1 mg</li> <li>- 30-200 mg per day</li> <li>- Amount of consumption: 30 Milligramm (mg). Other conditions: 30 mg,was aber 5 Fach besser resorbiert wird</li> <li>- Amount of consumption: 30 Milligramm (mg). Upper limit: 60 Milligramm (mg)</li> <li>- Amount of consumption: Die in klinischen Studien verwendeten Tagesdosierungen liegen zwischen 50 und 240 mg.</li> <li>- Regular consumption of Q10 via dietary sources or supplementation</li> <li>- Food supplement with 30-60mg of ubiquinone acid in the daily dose.</li> <li>- Max 20 mg per day</li> <li>- 30-200 mg per day.Regular consumption of Q10 via dietary sources or supplementation</li> </ul>
ID	Food or Food constituent	Health Relationship	Proposed wording
1511	Coenzyme Q10	<p>Protection of healthy neurological system</p> <p><u>Clarification provided</u></p> <p>Maintain cognitive function: improves learning</p>	Coenzyme Q10 may help maintain healthy brain function.

	<p><b>Conditions of use</b></p> <ul style="list-style-type: none"> <li>- A minimum dose of 300mg is suggested with active neurological degeneration. Data indicates that doses of up to 2,400mg/day are safe. Stop use two weeks before procedures with bleeding risk e.g. surgery and do not use immediately after these procedures. Use with caution with anti-coagulant medication. Avoid if pregnant or breastfeeding.</li> </ul>		
ID	Food or Food constituent	Health Relationship	Proposed wording
1512	Q10 (Coenzyme Q, Ubiquinone)	<p>Ubiquinone takes part in electron-transferring in the respiratory chain</p> <p><u>Clarification provided</u></p> <p>Promotes energy production</p> <ul style="list-style-type: none"> <li>- is needed/important for energy production in the cell</li> <li>- is needed/important for the energy metabolism and the transformation of food into physiological energy</li> </ul> <p>Energy production, electron-transport (mitochondria) by transferring electrons from the primary substrates to the oxidase system at the same time Q10 transfers protons to the outside of the mitochondrial membrane. This transfer results in a proton gradient across the membrane. As the protons return to the interior through the enzymatic machinery for making ATP, they drive the formation of ATP.</p>	<p>Q10 is a component in the formation of energy</p> <p>Q10 contribute to the formation of energy in cells</p>
		<p><b>Conditions of use</b></p> <ul style="list-style-type: none"> <li>- 30 mg /day</li> <li>- 15 mg/nap, 15% of the lower therapeutic dose 100 mg);;the average daily intake is 3-5 mg based on an average Danish diet</li> </ul>	
ID	Food or Food constituent	Health Relationship	Proposed wording
1720	Co-Enzyme Q 10	For physiological energy	<p>Coenzyme Q10 is necessary for the energy metabolism and the transformation of food into physiological energy.</p> <p>Coenzyme Q10 supports energy production.</p>
			<p><b>Conditions of use</b></p> <ul style="list-style-type: none"> <li>- Regular consumption of Q10 via dietary sources or supplementation</li> </ul>

ID	Food or Food constituent	Health Relationship	Proposed wording
1721	Co-Enzyme Q 10	For maintenance and promotion of heart health	Coenzyme Q10 maintains a healthy heart.
			May help maintain healthy blood pressure.
<p>May help maintain healthy cholesterol levels</p>			
<b>Conditions of use</b>			
- Regular consumption of lutein via dietary sources or supplementation			
ID	Food or Food constituent	Health Relationship	Proposed wording
1911	Coenzyme Q10;ubiquinone	Blood pressure	Can contribute to maintain normal blood pressure
			<b>Conditions of use</b>
- 15 mg/day;(15% of the lower therapeutic dose 100 mg)			
ID	Food or Food constituent	Health Relationship	Proposed wording
1912	Coenzyme Q10;ubiquinone	Energy production, muscle function; <u>Clarification provided</u> Energy production, muscle function; Energy production, muscle function/for increased mental or physical performance/for the physiological energy/ for skeletal muscles, heart muscle	In case of increased energy needs of the body or for increased mental or physical performance or for supporting the energy supply of the overloaded muscles, such as skeletal muscles, heart muscle.
- 15 mg/ day;(15% of the lower therapeutic dose 100 mg)			
ID	Food or Food constituent	Health Relationship	Proposed wording
1913	Coenzyme Q10;(Ubiquinone)	Physical activity	Coenzyme Q10 may enhance the physical endurance.;Coenzyme Q10 may enhance sport performance in those who have reduced performance but are free from organic lesions.
			<b>Conditions of use</b>
- 90 mg/day up to 6 months			
ID	Food or Food constituent	Health Relationship	Proposed wording
4668	Coenzyme Q10	Energizing by stimulating the obtainance of adenosine triphosphate from the cellular energetic processes	Brings energy / Stimulates the psychical activity and improves the capacity of the intellectual effort. / Increases intracellular energetic mechanisms. / Helps in periods of convalescence. / Brings

			<p>energy in periods of prolonged physical and intellectual effort, in acute or chronic fatigue. / Prevents fatigue and sustains the organism's effort in periods of stress. / Reduces the incidence of neoplastic diseases. / Interferes in all metabolic chains, activating them. / Improves the quality of the life of the persons with cardiac diseases. / Increases the resistance to effort and reduces the frequency and intensity of the cardiac ache.</p>
<p><b>Conditions of use</b></p> <ul style="list-style-type: none"> <li>- 10 – 30 mg coenzyme Q10 per day</li> </ul>			

## GLOSSARY AND ABBREVIATIONS

ATP	Adenosine triphosphate
HDL	High-density lipoprotein
HMG CoA	3-hydroxy-3-methylglutaryl-coenzyme A
HPLC	High performance liquid chromatography
ISH	Isolated systolic hypertension
LDL	Low-density lipoproteins
MDA	Malondialdehyde
<sup>31</sup> P-NMR	Phosphorus-31 nuclear magnetic resonance
ROS	Reactive oxygen species
TBARS	Thiobarbituric acid reactive substances
TRAP	Total reactive antioxidant potential