SCIENTIFIC OPINION

Scientific Opinion on the substantiation of health claims related to L-carnitine and faster recovery from muscle fatigue after exercise (ID 738, 1492, 1493), skeletal muscle tissue repair (ID 738, 1492, 1493), increase in endurance capacity (ID 4305, 4684), maintenance of normal blood LDL-cholesterol concentrations (ID 1494, 4684), contribution to normal spermatogenesis (ID 1822), "energy metabolism" (ID 1821), and increasing L-carnitine concentrations and/or decreasing free fatty acids in blood during pregnancy (ID 1495) 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

This scientific output, published on 14 July 2011, replaces the earlier version published on 30 June 2011[4].

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 L-carnitine and faster recovery from muscle fatigue after exercise, skeletal muscle tissue repair, increase in endurance capacity, maintenance of normal blood LDL-cholesterol concentrations, contribution to normal spermatogenesis, "energy metabolism", and increasing L-carnitine

[1] On request from the European Commission, Question No EFSA-Q-2008-1525, EFSA-Q-2008-2229, EFSA-Q-2008-2230, EFSA-Q-2008-2231, EFSA-Q-2008-2232, EFSA-Q-2008-2554, EFSA-Q-2008-2555, EFSA-Q-2010-00258, EFSA-Q-2010-00637, adopted on 08 April 2011.

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

[3] Acknowledgement: The Panel wishes to thank for the preparatory work on this scientific opinion: The members of the Working Group on Claims: Carlo Agostoni, Jean-Louis Bresson, Susan Fairweather-Tait, Albert Flynn, Ines Golly, Marina Heinonen, Hannu Korhonen, Martinus Løvik, Ambroise Martin, Hildegard Przyrembel, Seppo Salminen, Yolanda Sanz, Sean (J.J.) Strain, Inge Tetens, Hendrik van Loveren and Hans Verhagen. The members of the Claims Sub-Working Group on Weight Management/Satiety/Glucose and Insulin Control/Physical Performance: Kees de Graaf, Joanne Harrold, Mette Hansen, Mette Kristensen, Anders Sjödin and Inge Tetens.

[4] After publication of this opinion, the conclusion section of the opinion has been amended in order to reflect the conclusions of the NDA Panel as outlined in the main text of the opinion. Where changes have been made to the text of the opinion footnotes have been included to indicate the changes.

Suggested citation: EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA); Scientific Opinion on the substantiation of health claims related to L-carnitine and faster recovery from muscle fatigue after exercise (ID 738, 1492, 1493), skeletal muscle tissue repair (ID 738, 1492, 1493), increase in endurance capacity (ID 4305, 4684), maintenance of normal blood LDL-cholesterol concentrations (ID 1494, 4684), contribution to normal spermatogenesis (ID 1822), "energy metabolism" (ID 1821), and increasing L-carnitine concentrations and/or decreasing free fatty acids in blood during pregnancy (ID 1495) pursuant to Article 13(1) of Regulation (EC) No 1924/2006. EFSA Journal 2011;9(6):2212. [24 pp.]. doi:10.2903/j.efsa.2011.2212. Available online: www.efsa.europa.eu/efsajournal

© European Food Safety Authority, 2011

concentrations and/or decreasing free fatty acids in blood during pregnancy. The scientific substantiation is based on the information provided by the Member States in the consolidated list of Article 13 health claims and references that EFSA has received from Member States or directly from stakeholders.

The food constituent that is the subject of the health claims is carnitine (as L-carnitine). The Panel considers that L-carnitine is sufficiently characterised.

Faster recovery from muscle fatigue after exercise

The claimed effects are "fat metabolism" and "muscle metabolism/recovery after exercise". The target population is assumed to be adults performing strenuous exercise. In the context of the proposed wordings, the Panel assumes that the claimed effects refer to recovery from muscle fatigue after exercise. The Panel considers that faster recovery from muscle fatigue after exercise is a beneficial physiological effect.

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

On the basis of the data presented, the Panel concludes that a cause and effect relationship has not been established between the consumption of L-carnitine and faster recovery from muscle fatigue after exercise.

Skeletal muscle tissue repair

The claimed effects are "fat metabolism" and "muscle metabolism/recovery after exercise". The target population is assumed to be adults performing resistance exercise. In the context of the proposed wordings, the Panel assumes that the claimed effects refer to the rebuilding of structural protein within the skeletal muscle tissue after exercise which has caused muscle damage. The Panel considers that skeletal muscle tissue repair is a beneficial physiological effect.

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

On the basis of the data presented, the Panel concludes that a cause and effect relationship has not been established between the consumption of L-carnitine and skeletal muscle tissue repair.

Increase in endurance capacity

The claimed effects are "ergogenic role in sports and exercise", and "fat metabolism by mediating the transport of long-chain fatty acids across the inner mitochondrial membrane". The target population is assumed to be adults performing endurance exercise. In the context of the proposed wordings, the Panel assumes that the claimed effects refer to an increase in endurance capacity by promoting fat oxidation. The Panel considers that an increase in endurance capacity is a beneficial physiological effect.

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

On the basis of the data presented, the Panel concludes that a cause and effect relationship has not been established between consumption of L-carnitine and increase in endurance capacity.

Maintenance of normal blood LDL-cholesterol concentrations

The claimed effects are "heart health" and "fat metabolism by mediating the transport of long-chain fatty acids across the inner mitochondrial membrane". The target population is assumed to be the general population. In the context of the proposed wordings, the Panel assumes that the claimed

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

In weighing the evidence, the Panel took into account that the human intervention studies provided did not show a sustained effect of L-carnitine consumption on blood cholesterol concentrations, that results from studies in rats and rabbits cannot be extrapolated to humans because of major differences in lipid metabolism between species, and that no evidence for a mechanism by which L-carnitine could exert the claimed effect in humans has been provided.

On the basis of the data presented, the Panel concludes that a cause and effect relationship has not been established between the consumption of L-carnitine and maintenance of normal blood LDL-cholesterol concentrations.

Contribution to normal spermatogenesis

The claimed effect is "sexual organs, hormone activity". The target population is assumed to be the general male population. In the context of the proposed wordings, the Panel assumes that the claimed effect refers to contribution to normal spermatogenesis. The Panel considers that contribution to normal spermatogenesis is a beneficial physiological effect.

No human studies were provided from which conclusions could be drawn for the scientific substantiation of the claim.

On the basis of the data presented, the Panel concludes that a cause and effect relationship has not been established between the consumption of L-carnitine and contribution to normal spermatogenesis.

"Energy metabolism"

The claimed effect is "energy metabolism". The target population is assumed to be the general population.

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

Increasing L-carnitine concentrations and/or decreasing free fatty acids in blood during pregnancy

The claimed effect is "pregnancy". The target population is assumed to be pregnant women. In the context of the proposed wordings, the Panel assumes that the claimed effect relates to increasing L-carnitine concentrations and decreasing in free fatty acids in blood during pregnancy. The Panel considers that the evidence provided does not establish that increasing L-carnitine concentrations and/or decreasing free fatty acids in blood during pregnancy in the context of a protein adequate diet is a beneficial physiological effect *per se*.

On the basis of the data presented, the Panel concludes that a cause and effect relationship has not been established between the consumption of L-carnitine and a beneficial physiological effect related to increasing L-carnitine concentrations and/or decreasing free fatty acids in blood during pregnancy.

KEY WORDS

L-Carnitine, fatigue, skeletal muscle, endurance capacity, spermatogenesis, pregnancy, fatty acids, energy metabolism, health claims.

TABLE OF CONTENTS

BACKGROUND AS PROVIDED BY THE EUROPEAN COMMISSION

See Appendix A

TERMS OF REFERENCE AS PROVIDED BY THE EUROPEAN COMMISSION

See Appendix A

EFSA DISCLAIMER

See Appendix B

INFORMATION AS PROVIDED IN THE CONSOLIDATED LIST

The consolidated list of health claims pursuant to Article 13 of Regulation (EC) No 1924/2006[5] 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[6]. 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 carnitine (as L-carnitine).

Carnitine is a quaternary ammonium salt synthesised primarily in the liver and kidneys from amino acids, lysine and methionine. In living cells carnitine is required for the transport of fatty acids from the cytosol into the mitochondria for beta-oxidation. L-carnitine is the form commonly used in food supplements. The content of L-carnitine in foods can be measured by established methods. This opinion refers to the effects of L-carnitine when consumed as food supplements in addition to a protein adequate diet.

The Panel considers that the food constituent, L-carnitine, which is the subject of the health claims, is sufficiently characterised.

2. Relevance of the claimed effect to human health

2.1. Faster recovery from muscle fatigue after exercise (ID 738, 1492, 1493)

The claimed effects are "fat metabolism" and "muscle metabolism/recovery after exercise". The Panel assumes that the target population is adults performing strenuous exercise.

In the context of the proposed wordings, the Panel assumes that the claimed effects refer to recovery from muscle fatigue after exercise.

Fatigue can be defined as the loss of peak force or power output. Therefore, muscle fatigue recovery can be defined as the regain of maximal muscle strength or muscle power after performance of strenuous exercise which has induced muscle fatigue.

The Panel considers that faster recovery from muscle fatigue after exercise is a beneficial physiological effect.

[5] 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.

[6] EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA), 2011. General guidance for stakeholders on the evaluation of Article 13.1, 13.5 and 14 health claims. EFSA Journal, 9(4):2135, 24 pp.

2.2. Skeletal muscle tissue repair (ID 738, 1492, 1493)

The claimed effects are "fat metabolism" and "muscle metabolism/recovery after exercise". The Panel assumes that the target population is adults performing resistance exercise.

In the context of the proposed wordings, the Panel assumes that the claimed effects refer to the rebuilding of structural protein within the skeletal muscle tissue after exercise which has caused muscle damage.

The Panel considers that skeletal muscle tissue repair is a beneficial physiological effect.

2.3. Increase in endurance capacity (ID 4305, 4684)

The claimed effects are "ergogenic role in sports and exercise", and "fat metabolism by mediating the transport of long-chain fatty acids across the inner mitochondrial membrane". The Panel assumes that the target population is adults performing endurance exercise.

In the context of the proposed wordings, the Panel assumes that the claimed effects refer to an increase in endurance capacity by promoting fat oxidation. Endurance capacity refers to the exercise time to self-reported fatigue when exercising at a constant workload or speed.

The Panel considers that an increase in endurance capacity is a beneficial physiological effect.

2.4. Maintenance of normal blood LDL-cholesterol concentrations (ID 1494, 4684)

The claimed effects are "heart health" and "fat metabolism by mediating the transport of long-chain fatty acids across the inner mitochondrial membrane". The Panel assumes that the target population is the general population.

In the context of the proposed wordings, the Panel assumes that the claimed effects refer to the maintenance of normal blood LDL-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 (>4.1 mmol/L), may compromise the normal structure and function of the arteries.

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

2.5. Contribution to normal spermatogenesis (ID 1822)

The claimed effect is "sexual organs, hormone activity". The Panel assumes that the target population is the general male population.

In the context of the proposed wordings, the Panel assumes that the claimed effect refers to contribution to normal spermatogenesis.

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

2.6. "Energy metabolism" (ID 1821)

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

The claimed effect is not sufficiently defined, and no further details were given in the proposed wordings. No clarifications have been provided by Member States.

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

2.7. Increasing L-carnitine concentrations and/or decreasing free fatty acids in blood during pregnancy (ID 1495)

The claimed effect is "pregnancy". The Panel assumes that the target population is pregnant women.

In the context of the proposed wordings, the Panel assumes that the claimed effect relates to increasing L-carnitine concentrations, and to decreasing free fatty acids, in blood during pregnancy.

The Panel considers that the evidence provided does not establish that increasing L-carnitine concentrations and/or decreasing free fatty acids in blood during pregnancy in the context of a protein adequate diet is a beneficial physiological effect *per se*.

The Panel concludes that a cause and effect relationship has not been established between the consumption of L-carnitine and a beneficial physiological effect related to increasing L-carnitine concentrations and/or decreasing free fatty acids in blood during pregnancy.

3. Scientific substantiation of the claimed effect

3.1. Faster recovery from muscle fatigue after exercise (ID 738, 1492, 1493)

The references provided in relation to this claim included a number of narrative reviews, commentary papers, textbook chapters and animal studies. These references were either on food constituents (e.g. L-propionylcarnitine, and a combination of caffeine, carnitine and choline) unrelated to the food constituent which is the subject of the claim, or addressed outcomes (e.g. fatty acid oxidation, and muscle pain) unrelated to the claimed effect. The Panel considers that no conclusions can be drawn from these references for the scientific substantiation of the claim.

One reference reporting on a pilot human intervention study on the effects of L-carnitine supplementation on muscle recovery after exercise in six trained and six untrained subjects was provided as a symposium report. The report contained insufficient information regarding randomisation and statistical analyses for a full scientific evaluation (Maggini et al., 2000). The Panel considers that no conclusions can be drawn from this study for the scientific substantiation of the claim.

The Panel concludes that a cause and effect relationship has not been established between consumption of L-carnitine and faster recovery from muscle fatigue after exercise.

3.2. Skeletal muscle tissue repair (ID 738, 1492, 1493)

The references provided in relation to this claim included a number of narrative reviews, commentary papers, textbook chapters and animal studies. These references were either on food constituents (e.g. L-propionylcarnitine, and a combination of caffeine, carnitine and choline) unrelated to the food constituent which is the subject of the claim, or addressed outcomes (e.g. fatty acid oxidation, and muscle pain) unrelated to the claimed effect. The Panel considers that no conclusions can be drawn from these references for the scientific substantiation of the claim.

No references were provided which assessed the effects of L-carnitine consumption on muscle tissue repair after exercise.

The Panel concludes that a cause and effect relationship has not been established between the consumption of L-carnitine and skeletal muscle tissue repair.

3.3. Increase in endurance capacity (ID 4305, 4684)

The references provided in relation to the claim included narrative reviews and human studies which addressed outcomes (e.g. fatty acid oxidation, protein turnover, body weight and cardiac disorders) unrelated to the claimed effect.

One uncontrolled, open label human intervention study investigated the effect of L-carnitine supplementation (2 g/day for six weeks) on endurance capacity assessed using progressive treadmill tests until exhaustion in seven elite male marathon runners (Swart et al., 1997). The Panel notes the uncontrolled nature of the study, and considers that no conclusions can be drawn from this study for the scientific substantiation of the claim.

The Panel concludes that a cause and effect relationship has not been established between the consumption of L-carnitine and increase in endurance capacity.

3.4. Maintenance of normal blood LDL-cholesterol concentrations (ID 1494, 4684)

Some of the references provided were narrative reviews, and human, animal and *in vitro* studies, which reported on health outcomes (e.g. therapeutic efficacy in acute myocardial infarction, congestive heart failure and post-infarction; markers of recovery after exercise; electrocardiogram changes during exercise; delayed muscle pain after eccentric effort; long-chain fatty acid oxidation; protein turnover; glutathione redox state and mitochondrial enzymes in muscle and heart tissue) unrelated to the claimed effect. The Panel considers that no conclusions can be drawn from these references for the scientific substantiation of the claim.

Seven human intervention studies which investigated the effect of L-carnitine consumption on blood lipids were provided.

El-Metwally et al. (2003) and Vesela et al. (2001) assessed the effect of L-carnitine consumption on blood lipids in 24 children with chronic renal failure undergoing long-term haemodialysis, and in 12 dialysed adult patients, respectively. The Panel considers that the evidence provided does not establish that patients with chronic renal failure undergoing haemodialysis are representative of the general population with regard to blood lipids and lipid metabolism, and that the results obtained in these studies with respect to changes in LDL-cholesterol concentrations cannot be extrapolated to the general population. The Panel considers that no conclusions can be drawn from these references for the scientific substantiation of the claim.

In a one arm study (Stefanutti et al., 1998), the effect of L-carnitine consumption (3x1 g daily) on blood lipids was assessed in 24 subjects (aged 39-64 years) on a diet aiming to reduce blood cholesterol concentrations. The Panel notes the lack of a control group and considers that no conclusions can be drawn from this uncontrolled study for the scientific substantiation of the claim.

One parallel, randomised intervention study (Digiesi et al., 1994) in 37 subjects (mean age 60 years) with essential hypertension examined the effect of L-carnitine and antihypertensive medication on total cholesterol concentrations among other variables. Subjects received antihypertensive medication plus 2 g L-carnitine per day (group A1), antihypertensive medication only (group A2) or L-carnitine only (2 g/day, group B). Subjects in groups A1 and A2 (n=28) followed the intervention for 22 weeks,

and subjects in group B (n=9) for 10 weeks. The Panel notes the lack of a direct statistical comparison between the study groups, and thus the uncontrolled nature of the study, and considers that no conclusions can be drawn from this uncontrolled study for the scientific substantiation of the claim.

In a randomised, double-blind, placebo-controlled study with a parallel design (Pistone et al., 2003) 84 subjects (aged 70-92 years) with onset of fatigue after slight physical exercise were recruited to receive either L-carnitine (2x2 g/day, n=42) or placebo (n=42) for 30 days following a 2-week run-in phase in which subjects had followed a National Cholesterol Education Program (NCEP) Step 2 diet. All analyses were performed in the intent-to-treat population. In the L-carnitine group, total and LDL-cholesterol concentrations significantly decreased compared to placebo (-1.2 *vs.* +0.1 mmol/L, and -1.1 *vs.* -0.2 mmol/L, respectively, $p<0.01$). Total fat mass and total muscle mass also changed significantly in the L-carnitine compared to the placebo group (-3.1 *vs.* -0.5 kg and +2.1 *vs.* +0.2 kg, respectively, $p<0.01$). The Panel notes that this study showed an effect of L-carnitine on total and LDL-cholesterol concentrations when L-carnitine was consumed for 30 days. However, the Panel also notes that the constituents of the placebo were not reported, and that the study duration does not allow conclusions to be drawn on the sustainability of the effect.

In a double-blind, placebo-controlled intervention (Sirtori et al., 2000), 36 hyperlipidaemic subjects (mean age 55.9±9.3 years) with plasma Lp(a) ranging between 40 and 80 mg/dL and on isocaloric diets with a ratio of polyunsaturated/saturated fatty acids of 1.0 for the management of hyperlipidaemia were randomised to receive either L-carnitine (2 g/day, n=18) or placebo (n=18) for 12 weeks. Twelve subjects were taking low-dose acetylsalicylic acid and were on antihypertensive therapy, and eight subjects had either suffered from a myocardial infarction, had a transient ischaemic attack, or had stable angina or intermittent claudication and were taking medication (not specified) for these conditions. No statistically significant changes in total, LDL- or HDL-cholesterol concentrations were observed between groups. No body weight changes were observed during the study. The Panel notes that no information was provided on drop-outs during the study, or on the medication taken by some subjects. The Panel also notes that this study does not show an effect of L-carnitine on total, LDL- or HDL-cholesterol concentrations.

In a double-blind, placebo-controlled intervention study with a parallel design (Derosa et al., 2003), 94 hypercholesterolaemic subjects (mean age 51±6.5 years) with newly diagnosed type 2 diabetes mellitus managed with diet only were randomised after a 4-week placebo wash-out period to receive either L-carnitine (2x1 g/day, n=46) or placebo (n=48) for six months. Sixteen subjects were taking low-dose acetylsalicylic acid and were on antihypertensive therapy. Subjects were instructed to follow a standardised diet providing 1,400 to 1,600 kcal/day (55 % carbohydrates, 25 % proteins, 20 % fat, of which <7 % saturated fat), 105 mg cholesterol and 36 g fibre, and to perform aerobic exercise for at least 30 minutes on three to four days per week. Sample size calculations were not reported. It is unclear whether per protocol or intention-to-treat analyses were performed. No statistically significant changes in total or LDL-cholesterol concentrations were observed between groups. Body weight and BMI did not change significantly during the study in either group. The Panel notes that this study does not show an effect of L-carnitine on total or LDL-cholesterol concentrations.

The Panel notes that although one short-term human intervention study (30 days) reported a significant effect of L-carnitine consumption on the reduction of total and LDL-cholesterol concentrations, two human intervention studies of longer duration (12 weeks and six months, respectively) did not show an effect. The Panel considers that the human intervention studies provided did not show a sustained effect of L-carnitine consumption on blood cholesterol concentrations.

Two animal studies in rats (Mondola et al., 1988) and rabbits (Diaz et al., 2000) reported on the effects of L-carnitine on plasma lipoproteins and the apolipoprotein pattern. The Panel considers that results from studies in rats and rabbits cannot be extrapolated to humans because of major differences in lipid metabolism between species.

The Panel notes that no evidence for a plausible mechanism by which L-carnitine could exert the claimed effect in humans has been provided.

In weighing the evidence, the Panel took into account that the human intervention studies provided did not show a sustained effect of L-carnitine consumption on blood cholesterol concentrations, that results from studies in rats and rabbits cannot be extrapolated to humans because of major differences in lipid metabolism between species, and that no evidence for a mechanism by which L-carnitine could exert the claimed effect in humans has been provided.

The Panel concludes that a cause and effect relationship has not been established between the consumption of L-carnitine and maintenance of normal blood LDL-cholesterol concentrations.

3.5. Contribution to normal spermatogenesis (ID 1822)

Most of the references provided were not related to the food constituent which is the subject of the claim. One narrative review on sperm quality did not provide any original data for the substantiation of the claim. The Panel considers that no conclusions can be drawn from these references for the scientific substantiation of the claim.

One animal study examined the effect of L-carnitine on testicular ischaemic reperfusion injury in rats (Dokmeci et al., 2007). The Panel considers that evidence provided in animal studies is not sufficient to predict the occurrence of an effect of L-carnitine consumption on spermatogenesis in humans.

The Panel concludes that a cause and effect relationship has not been established between the consumption of L-carnitine and contribution to normal spermatogenesis.

CONCLUSIONS

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

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

Faster recovery from muscle fatigue after exercise (ID 738, 1492, 1493)

- The claimed effects are "fat metabolism" and "muscle metabolism/recovery after exercise". The target population is assumed to be adults performing strenuous exercise. In the context of the proposed wordings, it is assumed that the claimed effects refer to recovery from muscle fatigue after exercise. Faster recovery from muscle fatigue after exercise is a beneficial physiological effect.

- A cause and effect relationship has not been established between the consumption of L-carnitine and faster recovery from muscle fatigue after exercise.

Skeletal muscle tissue repair (ID 738, 1492, 1493)

- The claimed effects are "fat metabolism" and "muscle metabolism/recovery after exercise". The target population is assumed to be adults performing resistance exercise. In the context of the proposed wordings, it is assumed that the claimed effects refer to the rebuilding of structural protein within the skeletal muscle tissue after exercise which has caused muscle damage. Skeletal muscle tissue repair is a beneficial physiological effect.

- A cause and effect relationship has not been established between the consumption of L-carnitine and skeletal muscle tissue repair.

Increase in endurance capacity (ID 4305, 4684)

- The claimed effects are "ergogenic role in sports and exercise", and "fat metabolism by mediating the transport of long-chain fatty acids across the inner mitochondrial membrane". The target population is assumed to be adults performing endurance exercise. In the context of the proposed wordings, it is assumed that the claimed effects refer to an increase in endurance capacity by promoting fat oxidation. An increase in endurance capacity is a beneficial physiological effect.

- A cause and effect relationship has not been established between the consumption of L-carnitine and increase in endurance capacity[7].

Maintenance of normal blood LDL-cholesterol concentrations (ID 1494, 4684)

- The claimed effects are "heart health" and "fat metabolism by mediating the transport of long-chain fatty acids across the inner mitochondrial membrane". The target population is assumed to be the general population. In the context of the proposed wordings, it is assumed that the claimed effects refer to the maintenance of normal blood LDL-cholesterol concentrations. Maintenance of normal blood LDL-cholesterol concentrations is a beneficial physiological effect.

- A cause and effect relationship has not been established between the consumption of L-carnitine and maintenance of normal blood LDL-cholesterol concentrations.

Contribution to normal spermatogenesis (ID 1822)

- The claimed effect is "sexual organs, hormone activity". The target population is assumed to be the general male population. In the context of the proposed wordings, it is assumed that the claimed effect refers to contribution to normal spermatogenesis. Contribution to normal spermatogenesis is a beneficial physiological effect.

- A cause and effect relationship has not been established between the consumption of L-carnitine and contribution to normal spermatogenesis.

"Energy metabolism" (ID 1821)

- The claimed effect is "energy metabolism". 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.

Increasing L-carnitine concentrations and/or decreasing free fatty acids in blood during pregnancy (ID 1495)

- The claimed effect is "pregnancy". The target population is assumed to be pregnant women. The evidence provided does not establish that increasing L-carnitine concentrations and/or decreasing free fatty acids in blood during pregnancy in the context of a protein adequate diet is a beneficial physiological effect *per se*.

[7] Original text: "A cause and effect relationship has not been established between the consumption of L-carnitine and skeletal muscle tissue repair" and "skeletal muscle tissue repair" has been replaced with "increase in endurance capacity".

- A cause and effect relationship has not been established between the consumption of L-carnitine and a beneficial physiological effect related to increasing L-carnitine concentrations and/or decreasing free fatty acids in blood during pregnancy.

DOCUMENTATION PROVIDED TO EFSA

Health claims pursuant to Article 13 of Regulation (EC) No 1924/2006 (No: EFSA-Q-2008-1525, EFSA-Q-2008-2229, EFSA-Q-2008-2230, EFSA-Q-2008-2231, EFSA-Q-2008-2232, EFSA-Q-2008-2554, EFSA-Q-2008-2555, EFSA-Q-2010-00258, EFSA-Q-2010-00637). 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

Derosa G, Cicero AF, Gaddi A, Mugellini A, Ciccarelli L and Fogari R, 2003. The effect of L-carnitine on plasma lipoprotein(a) levels in hypercholesterolemic patients with type 2 diabetes mellitus. Clinical Therapeutics, 25, 1429-1439.

Diaz M, Lopez F, Hernandez F and Urbina JA, 2000. L-Carnitine effects on chemical composition of plasma lipoproteins of rabbits fed with normal and high cholesterol diets. Lipids, 35, 627-632.

Digiesi V, Cantini F, Bisi G, Guarino G and Brodbeck B, 1994. L-carnitine adjuvant therapy in essential hypertension. Clinica terapeutica, 144, 391-395.

Dokmeci D, Inan M, Basaran UN, Yalcin O, Aydogdu N, Turan FN and Uz YH, 2007. Protective effect of L-carnitine on testicular ischaemia-reperfusion injury in rats. Cell Biochemistry and Function, 25, 611-618.

El-Metwally TH, Hamed EA, Ahmad AR and Mohamed NA, 2003. Dyslipidemia, oxidative stress and cardiac dysfunction in children with chronic renal failure: effects of L-carnitine supplementation. Annals of Saudi Medicine, 23, 270-277.

Maggini S, Banziger KR and Walter P, 2000. L-Carnitine supplementation results in improved recovery after strenuous exercise: A preliminary study. Annals of Nutrition and Metabolism, 44, 86.

Mondola P, Belfiore A, Santangelo F and Santillo M, 1988. The effect of L-carnitine on the apolipoprotein pattern of rats fed a cholesterol-rich diet. Comparative Biochemistry and Physiology. B, Comparative Biochemistry, 89, 69-73.

Pistone G, Marino A, Leotta C, Dell'Arte S, Finocchiaro G and Malaguarnera M, 2003. Levocarnitine administration in elderly subjects with rapid muscle fatigue: effect on body composition, lipid profile and fatigue. Drugs and Aging, 20, 761-767.

Sirtori CR, Calabresi L, Ferrara S, Pazzucconi F, Bondioli A, Baldassarre D, Birreci A and Koverech A, 2000. L-carnitine reduces plasma lipoprotein(a) levels in patients with hyper Lp(a). Nutrition, Metabolism and Cardiovascular Diseases, 10, 247-251.

Stefanutti C, Vivenzio A, Lucani G, Di Giacomo S and Lucani E, 1998. Effect of L-carnitine on plasma lipoprotein fatty acids pattern in patients with primary hyperlipoproteinemia. Clinica terapeutica, 149, 115-119.

Swart I, Rossouw J, Loots JM and Kruger MC, 1997. The effect of L-carnitine supplementation on plasma carnitine levels and various performance parameters of male marathon athletes. Nutrition Research, 17, 405-414.

Vesela E, Racek J, Trefil L, Jankovy'ch V and Pojer M, 2001. Effect of L-carnitine supplementation in hemodialysis patients. Nephron, 88, 218-223.

APPENDICES

APPENDIX A

BACKGROUND AND TERMS OF REFERENCE AS PROVIDED BY THE EUROPEAN COMMISSION

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

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

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

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

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

b) psychological and behavioural functions; or

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

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

(i) based on generally accepted scientific evidence; and

(ii) well understood by the average consumer.

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

ISSUES THAT NEED TO BE CONSIDERED

IMPORTANCE AND PERTINENCE OF THE FOOD[9]

Foods are commonly involved in many different functions[10] of the body, and for one single food many health claims may therefore be scientifically true. Therefore, the relative importance of food e.g. nutrients in relation to other nutrients for the expressed beneficial effect should be considered: for functions affected by a large number of dietary factors it should be considered whether a reference to a single food is scientifically pertinent.

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

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 L-carnitine, including conditions of use from similar claims, as proposed in the Consolidated List.

ID	Food or Food constituent	Health Relationship	Proposed wording
738	Carnitine.	Fat metabolism.	Helps the energy production in the cell by transporting fatty acids in places where they are used and metabolised/contributes to the fat burning during exercise/contributes to increased fat oxidation/is important for the oxidation of fat/helps improve muscle recovery after exercise/helps mantain optimal repair of muscle tissue/transports long-chain fatty acids into the mitocondria/plays an important role in lipid metabolism/can support lipid metabolism converts fatty acids into energy/turns fat into energy/helps to increase fatty acid oxidation in healty humans.
	Conditions of use - Max 200 mg per day		
ID	**Food or Food constituent**	**Health Relationship**	**Proposed wording**
1492	Carnitine.	Fat metabolism.	Helps the energy production in the cell by transporting fatty acids in places where they are used and metabolised -contributes to the fat burning during exercise -contributes to increased fat oxidation -is important for the oxidation of fat -helps improve muscle recovery after exercise -helps maintain optimal repair of muscle tissue -plays an important role in lipid metabolism -can support lipid metabolism converts fatty acids into energy -helps to increase fatty acid oxidation in healthy humans

	Conditions of use - Erwachsene - Amount of consumption: 250 Milligramm (mg), 250-3500. Period of consumption: 14-30 Tage. Upper limit (value): 8000 Milligramm (mg). - Does claim rely on the presence/presence in a reduced quantity/absence of a nutrient or other substance: Presence of a nutrient or other substance. Number of nutrients/other substances that are essential to claimed effect: 4. Names of nutrient/other substances and Quantity in Average daily serving: 20mg Carnitine, 300mg Garcinia Cambogia, 50mg CLA, 66 micrograms Chromium Polynicotinate. Weight of average daily food serving: 60 miligram(s). Daily amount to be consumed to produce claimed effect: 400 miligram(s). Number of food portions this equates to in everyday food portions: 3. Are there factors that could interfere with bioavailability: Yes. Please give reason: do not store above 25 degrees C. Length of time after consumption for claimed effect to become apparent: It is apparent after a period of regular use. Number of days: 14. Is there a limit to the amount of food which should be consumed in order to avoid adverse health effects: Don't Know. - 200 mg/Tag. - bis 1000 mg pro Tag. - bis 250 mg pro Tag. - Tagesdosis: 500 mg. - 0,2 g pro Tag. - Sportler. - Min 200 mg per day; 100-500mg per day. - L-karnitiini sisaldus varieerub: 200 mg/100 g; 400 mg/100 g; 600 mg/100 g. - Ausdauersport–Tagesdosis ab 500 mg–L-Carnitin. Tagesdosis ab ca. 1 g–Erwachsene.		
ID	**Food or Food constituent**	**Health Relationship**	**Proposed wording**
1493	Carnitine.	Muscle metabolism / Recovery after exercise.	Helps improve muscle recovery after exercise -helps maintain optimal repair of muscle tissue -supports athletes in recovery from weight training -can help recreationally weight-trained in recovery from exercise -contributes to the reduction of muscle soreness from exercise in trained athletes
	Conditions of use - 200 mg/Tag; Upper limit (value): 500 mg. - Drink with 400mg/serving of L-carnitine. - 30 mg, (15% of the average daily intake 200 mg). - A minimum of 200-500 mg per day. 100-500mg per day. A minimum of 2g per day is required.		

ID	Food or Food constituent	Health Relationship	Proposed wording
1494	Carnitine.	Heart health.	Helps to maintain healthy blood cholesterol and plasma lipid levels in the elderly.
	Conditions of use - Erwachsene - 250 - 1.000 Milligramm (mg). - 200 mg/Tag. - Food supplement with 100 mg of L-carnitine in the daily dose. - Min 200 mg per day.		
ID	**Food or Food constituent**	**Health Relationship**	**Proposed wording**
1495	Carnitine.	Pregnancy.	Can increase L-Carnitine levels during pregnancy and lactation. Can help decrease free fatty acids during pregnancy. Can maintain normal L-Carnitine plasma levels during pregnancy.
	Conditions of use - Schwangere - 500mg/Tag. - Min. 500 mg/day.		
ID	**Food or Food constituent**	**Health Relationship**	**Proposed wording**
1821	L-carnitine.	Energy metabolism.	Makes energy metabolism more effective. Protects cell energy metabolism. Reduces changes in energy metabolism caused by ageing.
	Conditions of use - Food supplement with 100mg of L-carnitine in the daily dose.		
	Comments from Member States No further clarification received.		
ID	**Food or Food constituent**	**Health Relationship**	**Proposed wording**
1822	L-carnitine.	Sexual organs, hormone activity	Improves sperm quality.
	Conditions of use - Food supplement with 100mg of L-carnitine in the daily dose. - 1500 mg L-arginine per day.		
ID	**Food or Food constituent**	**Health Relationship**	**Proposed wording**
4305	Carnitine.	ERGOGENIC role in sports and exercise.	Helps to delay the onset of fatigue. Helps to maintain energy levels for prolonged periods during intense competition/exercise.

			Enhances endurance and helps to maintain peak effort during times of high physical demand.
	Conditions of use - Claim to be only used for Foods for sportpeople under the Dir. 89/398/EEC. Sports foods and food supplements providing minimum of 200-500mg carnitine per recommended daily consumption.		
ID	**Food or Food constituent**	**Health Relationship**	**Proposed wording**
4684	L/carnitine.	Fat metabolism by mediating the transport of long-chain fatty acids across the inner mitochondrial membrane.	Helps burn fat faster and thus improves physical performance. / Helpful in decreasing the LDL-colesterol level / Helpful in decreasing colesterol's blood levels / In diets, supplemented by a food diet and phisical exercices. / Accelerate the fatty acid import into mitochondria, which leads to a faster oxidation, favoring an efficient weight decrease as well as increasing of effort resistance.
	Conditions of use - 300 - 1200 mg/day.		

GLOSSARY AND ABBREVIATIONS

BMI	Body mass index
ECG	Electrocardiogram
HDL	High-density lipoproteins
LDL	Low-density lipoproteins