European Food Safety Authority

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SCIENTIFIC OPINION

Scientific Opinion on the substantiation of health claims related to lycopene and protection of DNA, proteins and lipids from oxidative damage (ID 1608, 1609, 1611, 1662, 1663, 1664, 1899, 1942, 2081, 2082, 2142, 2374), protection of the skin from UV-induced (including photo-oxidative) damage (ID 1259, 1607, 1665, 2143, 2262, 2373), contribution to normal cardiac function (ID 1610, 2372), and maintenance of normal vision (ID 1827) pursuant to Article 13(1) of Regulation (EC) No 1924/2006[1]

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

European Food Safety Authority (EFSA), Parma, Italy

SUMMARY

Following a request from the European Commission, the Panel on Dietetic Products, Nutrition and Allergies was asked to provide a scientific opinion on a list of health claims pursuant to Article 13 of Regulation (EC) No 1924/2006. This opinion addresses the scientific substantiation of health claims in relation to lycopene and protection of DNA, proteins and lipids from oxidative damage, protection of the skin from UV-induced (including photo-oxidative) damage, contribution to normal cardiac function, and maintenance of normal vision. 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 lycopene. The present opinion applies to lycopene from all sources with appropriate bioavailability in the specified amounts. The Panel considers that lycopene is sufficiently characterised.

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[1] On request from the European Commission, Question No EFSA-Q-2008-1997, EFSA-Q-2008-2343, EFSA-Q-2008-2344, EFSA-Q-2008-2345, EFSA-Q-2008-2346, EFSA-Q-2008-2347, EFSA-Q-2008-2398, EFSA-Q-2008-2399, EFSA-Q-2008-2400, EFSA-Q-2008-2401, EFSA-Q-2008-2560, EFSA-Q-2008-2632, EFSA-Q-2008-2675, EFSA-Q-2008-2814, EFSA-Q-2008-2815, EFSA-Q-2008-2875, EFSA-Q-2008-2876, EFSA-Q-2008-2995, EFSA-Q-2008-3105, EFSA-Q-2008-3106, EFSA-Q-2008-3107, adopted on 12 November 2010.

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

[3] Acknowledgement: The Panel wishes to thank for the preparatory work on this scientific opinion: The members of the Working Group on Claims: Carlo Agostoni, Jean-Louis Bresson, Susan Fairweather-Tait, Albert Flynn, Ines Golly, Marina Heinonen, Hannu Korhonen, Martinus Løvik, Ambroise Martin, Hildegard Przyrembel, Seppo Salminen, Yolanda Sanz, Sean (J.J.) Strain, Inge Tetens, Hendrik van Loveren and Hans Verhagen. The members of the Claims Sub-Working Group on Cardiovascular Health/Oxidative Stress: Antti Aro, Marianne Geleijnse, Marina Heinonen, Ambroise Martin, Wilhelm Stahl and Henk van den Berg. The members of the Claims Sub-Working Group on Mental/Nervous System: Jacques Rigo, Astrid Schloerscheidt, Barbara Stewart-Knox, Sean (J.J.) Strain, and Peter Willatts.

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Protection of DNA, proteins and lipids from oxidative damage

The claimed effects are "antioxidant properties", "antioxidant properties/cell and DNA protection", "antioxidant properties/protection of DNA", "oxidative stress control", "for antioxidant protection system/protection of DNA", "maintains cardiovascular health", "prostate health" and "maintains prostate health". 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 refer to the protection of DNA, proteins and lipids from oxidative damage. The Panel considers that 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 none of the studies provided reported a significant effect of lycopene consumption on reliable markers of oxidative damage to DNA, lipids or proteins compared to control.

On the basis of the data presented, the Panel concludes that a cause and effect relationship has not been established between the consumption of lycopene and protection of DNA, proteins and lipids from oxidative damage.

Protection of the skin from UV-induced (including photo-oxidative) damage

The claimed effects are "skin health", "maintains skin health", and "for skin health". 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 refer to the protection of the skin from UV-induced damage, including photo-oxidative damage. The Panel considers that the protection of the skin from UV-induced (including photo-oxidative) damage is a beneficial physiological effect.

None of the studies provided addressed the effects of lycopene consumption on reliable markers of UV-induced (including photo-oxidative) damage to the skin.

On the basis of the data presented, the Panel concludes that a cause and effect relationship has not been established between the consumption of lycopene and protection of the skin from UV-induced (including photo-oxidative) damage.

Contribution to normal cardiac function

The claimed effects are "heart health" and "cardio-vascular health". 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 refer to the maintenance of normal cardiac function. The Panel considers that contribution to normal cardiac function is a beneficial physiological effect.

In weighing the evidence, the Panel took into account that one observational study did not show an association between lycopene dietary intakes and risk of myocardial infarction, and that the nature of the relationship between dietary lycopene and blood concentrations of lycopene was not established in the two observational studies provided, which did not report on lycopene intakes.

On the basis of the data presented, the Panel concludes that a cause and effect relationship has not been established between the consumption of lycopene and contribution to normal cardiac function.

Maintenance of normal vision

The claimed effect is "eyes". The target population is assumed to be the general population. In the context of the proposed wording and from the information provided, the Panel assumes that the

claimed effect refers to the maintenance of normal vision. The Panel considers that maintenance of normal vision 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 lycopene and maintenance of normal vision.

KEY WORDS

Lycopene, oxidative damage, UV-induced damage, skin, cardiac function, vision, health claims.

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EFSA DISCLAIMER

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INFORMATION AS PROVIDED IN THE CONSOLIDATED LIST

The consolidated list of health claims pursuant to Article 13 of Regulation (EC) No 1924/2006[4] submitted by Member States contains main entry claims with corresponding conditions of use and literature for similar health claims. EFSA has screened all health claims contained in the original consolidated list of Article 13 health claims which was received by EFSA in 2008 using six criteria established by the NDA Panel to identify claims for which EFSA considered sufficient information had been provided for evaluation and those for which more information or clarification was needed before evaluation could be carried out[5]. The clarifications which were received by EFSA through the screening process have been included in the consolidated list. This additional information will serve as clarification to the originally provided information. The information provided in the consolidated list for the health claims which are the subject of this opinion is tabulated in Appendix C.

ASSESSMENT

1. Characterisation of the food/constituent

The food constituent that is the subject of the health claims is lycopene (psi, psi-carotene).

Lycopene is a well recognised dietary constituent and is measurable in foods, blood and tissues by established methods. Major dietary sources of lycopene are tomatoes and tomato products. Lycopene is also the natural red colorant of water melons, pink grapefruit and rose hips. Dietary sources of lycopene, or lycopene preparations from natural sources, usually contain other food constituents (e.g. other carotenoids and/or polyphenols) which may contribute to the claimed effects. Synthetic lycopene has recently been authorised in the EU as a novel food ingredient[6]. The present opinion applies to lycopene from all sources with appropriate bioavailability in the specified amounts.

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

2. Relevance of the claimed effect to human health

2.1. Protection of DNA, proteins and lipids from oxidative damage (ID 1608, 1609, 1611, 1662, 1663, 1664, 1899, 1942, 2081, 2082, 2142, 2374)

The claimed effects are “antioxidant properties”, “antioxidant properties/cell and DNA protection”, “antioxidant properties/protection of DNA”, “oxidative stress control”, “for antioxidant protection system/protection of DNA”, “maintains cardiovascular health”, “prostate health” and “maintains prostate health”. The Panel assumes that the target population is the general population.

In the context of the proposed wordings and clarifications provided by Member States, the Panel assumes that the claimed effects refer to the protection of DNA, proteins and lipids from oxidative damage.

The Panel considers that claims made on the antioxidant capacity/content of lycopene-containing foods based on their capability to scavenge free radicals *in vitro* refer to a property of the food/food

[4] Regulation (EC) No 1924/2006 of the European Parliament and of the Council of 20 December 2006 on nutrition and health claims made on foods. OJ L 404, 30.12.2006, p. 9–25.

[5] Briefing document for stakeholders on the evaluation of Article 13.1, 13.5 and 14 health claims: http://www.efsa.europa.eu/en/ndameetings/docs/nda100601-ax01.pdf

[6] 2009/362/EC: Commission Decision of 30 April 2009 authorising the placing on the market of lycopene as novel food ingredient under Regulation (EC) No 258/97 of the European Parliament and of the Council (notified under document number C(2009) 3149) OJ L 110, 1.5.2009, p. 54–57

constituent measured in model systems, and that the information provided does not establish that this exerts a beneficial physiological effect in humans as required by Regulation (EC) No 1924/2006.

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

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

2.2. Protection of the skin from UV-induced (including photo-oxidative) damage (ID 1259, 1607, 1665, 2143, 2262, 2373)

The claimed effects are "skin health", "maintains skin health", and "for skin health". The Panel assumes that the target population is the general population.

In the context of the proposed wordings and clarifications provided by Member States, the Panel assumes that the claimed effects refer to the protection of the skin from UV-induced damage, including photo-oxidative damage.

The Panel considers that protection of the skin from UV-induced (including photo-oxidative) damage is a beneficial physiological effect.

2.3. Contribution to normal cardiac function (ID 1610, 2372)

The claimed effects are "heart health" and "cardio-vascular health". The Panel assumes that the target population is the general population.

In the context of the proposed wordings and clarifications provided by Member States, the Panel assumes that the claimed effects refer to the maintenance of normal cardiac function.

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

2.4. Maintenance of normal vision (ID 1827)

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

In the context of the proposed wording and from the information provided, the Panel assumes that the claimed effect refers to the maintenance of normal vision.

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

3. Scientific substantiation of the claimed effect

3.1. Protection of DNA, proteins and lipids from oxidative damage (ID 1608, 1609, 1611, 1662, 1663, 1664, 1899, 1942, 2081, 2082, 2142, 2374)

A number of the references provided were narrative reviews or consensus opinions on the health effects of lycopene that did not allow evaluation of original data, reports on intervention studies that assessed the effects of other carotenoids or antioxidant vitamins, either alone or in combination with

lycopene, or human studies assessing the effects of lycopene intake and related products on health outcomes unrelated to the claimed effect (e.g. UV-induced erythema, UV-induced immunomodulation and the risk of chronic disease, such as prostate cancer). The Panel considers that no conclusions can be drawn from these references for the scientific substantiation of the claimed effect.

Some experimental, and generally small-scale, human studies investigated the effects of lycopene consumption on the total antioxidant activity of plasma measured by various assays (i.e. trolox-equivalent antioxidant capacity (TEAC), total reactive antioxidant potential (TRAP), and a chemiluminescent assay using 2, 2'-azinobis (3-ethylbenzothiazoline-6-sulfonate) (ABTS) as a reagent (Bohm and Bitsch, 1999; Neyestani et al., 2007; Tyssandier et al., 2004)); on GSH concentrations and antioxidant metalloenzyme activities (Hininger et al., 2001); on DNA strand breaks (Briviba et al., 2004a; Pool-Zobel et al., 1997; Porrini et al., 2005; Zhao et al., 2006); on *ex vivo* DNA oxidation (e.g. to lymphocytes) measured by different modifications of the comet assay (e.g. after challenge with Fe^{2+} or with hydrogen peroxide before electrophoresis (Riso et al., 1999; 2004; Torbergsen and Collins, 2000; Zhao et al., 2006)); on *ex vivo* susceptibility of LDL to Cu-ion induced oxidation (Briviba et al., 2004b; Carroll et al., 2000; Fuhrman et al., 2000; Hininger et al., 2001; Maruyama et al., 2001; Silaste et al., 2007; Visioli et al., 2003); on LDL conjugated dienes (Agarwal and Rao, 1998), on the formation of malondialdehyde (MDA) measured as thio-barbituric acid reactive substances (TBARS) (Agarwal and Rao, 1998; Briviba et al., 2004b; Neyestani et al., 2007; Rao and Agarwal, 1998; Rao and Shen, 2002); and on protein thiol concentrations (Hininger et al., 2001; Rao and Agarwal, 1998). The Panel notes that measurements of the total antioxidant activity/potential of plasma, and/or of GSH concentrations, and/or of antioxidant enzyme activities are not considered to be markers of oxidative damage, that the formation of MDA measured as TBARS, as well as the resistance of LDL to oxidation, are not suitable markers to assess lipid peroxidation, that the variants of the comet assay which measure unspecified DNA damage do not reflect DNA oxidative damage but general DNA strand breaks independent of their origin, that the *ex vivo* DNA resistance to oxidation after oxidative challenge does not reflect *in vivo* DNA oxidative damage, and that measurement of protein thiol concentrations is not a reliable marker of oxidative damage to proteins (Dalle-Donne et al., 2006; Dragsted, 2008; Griffiths et al., 2002; Knasmuller et al., 2008; Mayne, 2003). In addition, a number of the human studies provided were uncontrolled interventions with lycopene or tomato products (Agarwal and Rao, 1998; Bohm and Bitsch, 1999; Bowen et al., 2002; Hadley et al., 2003; Pool-Zobel et al., 1997; Porrini and Riso, 2000; Rao and Shen, 2002; Riso et al., 2004; Tyssandier et al., 2004; Visioli et al., 2003). The Panel considers that no conclusions can be drawn from these references for the scientific substantiation of the claimed effect.

Rao and Agarwal (1998) performed a controlled, randomised, cross-over study with five different sources of lycopene in 19 healthy subjects (9 females/10 males), who were non-smokers aged 25-40 years. The duration of the study was one week with each source providing lycopene at 20.5 mg/day (spaghetti sauce A), 39.2 mg/day (spaghetti sauce B), 50.4 mg/day (tomato juice), 75 mg/day (tomato oleoresin A) and 150 mg/day (tomato oleoresin B). Controls received a placebo which was not further specified. As a marker of DNA damage, 8-oxodG in lymphocytes was measured by HPLC with EC detection. For lipid peroxidation, TBARS were determined in serum, and protein oxidation was estimated by loss of free thiol groups in serum measured with beta dystrobrevin (5,5'-Dithio-bis (2-nitrobenzoic acid), DTNB). There was no statistically significant difference in DNA oxidation between the different verum groups and placebo. The Panel notes that TBARS and loss of free thiol groups in serum measured with DTNB are not reliable markers of oxidative damage to protein and lipids, respectively.

Kucuk et al. (2002) performed a randomised, two-arm clinical intervention study in patients with prostate cancer scheduled for radical prostatectomy. Data were collected from 26 patients and the intervention group took 30 mg of lycopene as tomato oleoresin for three weeks. Levels of 5-OHmdU (5-hydroxy-methyl-desoxy-uridine) in peripheral blood lymphocytes were not significantly different between groups before and after intervention.

In weighing the evidence, the Panel took into account that none of the studies provided reported a significant effect of lycopene consumption on reliable markers of oxidative damage to DNA, lipids or proteins compared to control.

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

3.2. Protection of the skin from UV-induced (including photo-oxidative) damage (ID 1259, 1607, 1665, 2143, 2262, 2373)

A number of the references provided were narrative reviews or consensus opinions on the health effects of lycopene which did not allow evaluation of original data, or reports on intervention studies which assessed the effects of other carotenoids or antioxidant vitamins, either alone or in combination with lycopene, on health outcomes unrelated to the claimed effect. The Panel considers that no conclusions can be drawn from these references for the scientific substantiation of the claimed effect.

Among the references provided, three reported on human intervention studies on the effects of lycopene on measures of UV-induced damage to the skin (Aust et al., 2005; Stahl et al., 2001; 2006).

The study by Aust et al. (2005) was an uncontrolled intervention where the effects of synthetic (pure) lycopene were compared to those of lycopene in a tomato extract. The Panel considers that no conclusions can be drawn from this study for the scientific substantiation of the claimed effect.

Stahl et al. (2001) reported on a controlled, non-blinded human study with lycopene from tomato paste in 22 healthy adults (26-67 years; 14 female), skin type II, over a period of 10 weeks. The verum group (n=9 finished) consumed 40 g tomato paste with 10 g of olive oil per day providing 16 mg/day of lycopene; controls (n=10 finished) received olive oil only. At day 0, and at 4 and 10 weeks, serum lycopene and skin carotenoid concentrations were measured. Erythema formation (skin reddening) in response to 1.25 minimal erythemal dose (MED) was measured at the same time by chromametry. Serum concentrations of lycopene and skin carotenoids significantly increased in supplemented subjects. At week 10, erythema formation significantly decreased in the group which consumed tomato paste compared to controls, whereas no significant difference between groups was found at week 4 of the intervention. The Panel notes the small number of subjects recruited and that the study was not blinded. The Panel also notes that UV-induced erythema (sunburn or skin reddening) is a primary reaction of the skin following overexposure to UV (sun)light, and that it represents an inflammatory response of cutaneous tissue as a consequence of light-dependent molecular and cellular damage. However, whereas a reduction in skin erythema may indicate a reduction in UV-induced skin damage, it can also reflect a reduction in the capacity of the skin to react to molecular and cellular damage, and the data provided in this study did not allow such effects to be distinguished. The Panel considers that no conclusions can be drawn from this study for the scientific substantiation of the claimed effect.

The review by Stahl et al. (2006) reported on the studies by Stahl et al. (2001) and Aust et al. (2005), and presented data from a non-controlled intervention with a lycopene-rich carrot juice. The juice contained considerable amounts of beta-carotene (10 mg lycopene plus 5 mg beta-carotene/day). The Panel considers that no conclusions can be drawn from this reference for the scientific substantiation of the claimed effect.

The Panel notes that none of the studies provided addressed the effects of lycopene consumption on reliable markers of UV-induced (including photo-oxidative) damage to the skin.

The Panel concludes that a cause and effect relationship has not been established between the consumption of lycopene and protection of the skin from UV-induced (including photo-oxidative) damage.

3.3. Contribution to normal cardiac function (ID 1610, 2372)

A number of the references provided were narrative reviews or consensus opinions on the health effects of lycopene which did not allow evaluation of original data, or reports on intervention studies which assessed the effects of other carotenoids or antioxidant vitamins, either alone or in combination with lycopene, on health outcomes unrelated to the claimed effect, e.g. on lipid peroxidation and on the susceptibility of lipoproteins to oxidative stress. The three animal studies provided reported on health outcomes unrelated to the claimed effect, i.e. on the effect of probucol on atherosclerosis in rabbits, on the role of lycopene on adriamycin-induced heart and kidney toxicity in rats, and on the effect of lycopene in a rat model of myocardial ischemia-reperfusion injury. The three *in vitro* studies provided related to the involvement of reactive oxygen species in the generation of mitochondrial DNA lesions in human fibroblasts, to the effect of carotenoids on macrophage cholesterol metabolism, and to the ageing of cultured retinal pigment epithelial cells. The Panel considers that no conclusions can be drawn from these references for the scientific substantiation of the claimed effect.

Among the references provided, three human observational studies addressed the association between blood concentrations of lycopene and combined risk for coronary heart disease and stroke (Rissanen et al., 2001; Sesso et al., 2004), intima-media thickness (Rissanen et al., 2001), or blood concentrations of C-reactive protein and E-selectin (Rowley et al., 2003). None of these studies reported on dietary intakes of lycopene. The Panel considers that no conclusions can be drawn from these references for the scientific substantiation of the claimed effect.

Three human observational studies addressed the association between blood concentrations of lycopene and risk of coronary heart disease (Ito et al., 2006; Kristenson et al., 1997; Sesso et al., 2003). The Panel notes that in one prospective cohort study (Ito et al., 2006) and in one cross-sectional study (Kristenson et al., 1997) lycopene dietary intakes were not reported, and that the nature of the relationship between dietary lycopene and blood concentrations of lycopene has not been established in these studies. The Panel considers that no conclusions can be drawn from these references for the scientific substantiation of the claimed effect.

Only one of the three human observational studies reported on lycopene dietary intakes (Sesso et al., 2003).

Sesso et al. (2003) reported on a prospective cohort study of 39,876 middle-aged and older women initially free of cardiovascular disease and cancer. Dietary lycopene intakes were divided into quintiles, and primary lycopene food sources (total tomato-based products, including tomatoes, tomato juice, tomato sauce and pizza) were categorised. During 7.2 years of follow-up, 719 cardiovascular disease cases (including myocardial infarction, stroke, revascularisation and cardiovascular disease death) occurred. Compared with women in the 1st quintile of lycopene intake, multivariate relative risks (95 % CI) for increasing quintiles of lycopene intake in relation to myocardial infarction were 1.10 (0.72-1.69), 1.01 (0.65-1.57), 0.90 (0.57-1.44) and 0.69 (0.41-1.15) (p for trend=0.09). For the consumption of tomato-based products, women consuming 1.5 to <4, 4 to <7, 7 to <10 and ≥ 10 servings/week had relative risks (95 % CI) for myocardial infarction of 0.94 (0.65-1.37), 0.67 (0.43-1.06), 0.70 (0.38-1.29) and 0.39 (0.12-1.30) (p for trend=0.033) compared with women consuming <1.5 servings/week. The Panel notes that lycopene intake was not associated with a decreased risk of myocardial infarction in this study.

In weighing the evidence, the Panel took into account that one observational study did not show an association between lycopene dietary intakes and risk of myocardial infarction (Sesso et al., 2003),

and that the nature of the relationship between dietary lycopene and blood concentrations of lycopene was not established in the two observational studies provided, which did not report on lycopene intakes (Ito et al., 2006; Kristenson et al., 1997).

The Panel concludes that a cause and effect relationship has not been established between the consumption of lycopene and contribution to normal cardiac function.

3.4. Maintenance of normal vision (ID 1827)

Three references have been provided in relation to the claimed effect.

One reference (Cardinault et al., 2005) reported on the determination of carotenoids, including lycopene, in serum and lipoprotein fractions in 34 subjects diagnosed for age-related macular degeneration, compared to 21 control subjects. Another reference (Simonelli et al., 2002) reported on the measurement of carotenoids (including serum lycopene) in 48 patients with age-related maculopathy, compared to 46 controls. The Panel considers that the nature of the relationship between dietary lycopene and blood concentrations of lycopene has not been established in these studies, and notes that there was no measurement of dietary lycopene.

The Panel notes that no human studies have been provided from which conclusions can be drawn for the scientific substantiation of the claimed effect.

The remaining reference (Nilsson et al., 2003) was an *in vitro* study undertaken in cultured retinal pigment epithelial cells. The Panel considers that evidence provided in *in vitro* studies alone is not sufficient to predict the occurrence of an effect of lycopene consumption on maintenance of normal vision in humans.

The Panel concludes that a cause and effect relationship has not been established between the consumption of lycopene and maintenance of normal vision.

CONCLUSIONS

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

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

Protection of DNA, proteins and lipids from oxidative damage (ID 1608, 1609, 1611, 1662, 1663, 1664, 1899, 1942, 2081, 2082, 2142, 2374)

- The claimed effects are “antioxidant properties”, “antioxidant properties/cell and DNA protection”, “antioxidant properties/protection of DNA”, “oxidative stress control”, “for antioxidant protection system/protection of DNA”, “maintains cardiovascular health”, “prostate health” and “maintains prostate health”. 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 lycopene and protection of DNA, proteins and lipids from oxidative damage.

Protection of the skin from UV-induced (including photo-oxidative) damage (ID 1259, 1607, 1665, 2143, 2262, 2373)

- The claimed effects are “skin health”, “maintains skin health”, and “for skin health”. The target population is assumed to be the general population. In the context of the proposed

wordings and clarifications provided by Member States, it is assumed that the claimed effects refer to the protection of the skin from UV-induced damage, including photo-oxidative damage. Protection of the skin from UV-induced (including photo-oxidative) damage is a beneficial physiological effect.

- A cause and effect relationship has not been established between the consumption of lycopene and protection of the skin from UV-induced (including photo-oxidative) damage.

Contribution to normal cardiac function (ID 1610, 2372)

- The claimed effects are "heart health" and "cardio-vascular health". The target population is assumed to be the general population. Contribution to normal cardiac function is a beneficial physiological effect.
- A cause and effect relationship has not been established between the consumption of lycopene and contribution to normal cardiac function.

Maintenance of normal vision (ID 1827)

- The claimed effect is "eyes". The target population is assumed to be the general population. Maintenance of normal vision is a beneficial physiological effect.
- A cause and effect relationship has not been established between the consumption of lycopene and maintenance of normal vision.

DOCUMENTATION PROVIDED TO EFSA

Health claims pursuant to Article 13 of Regulation (EC) No 1924/2006 (No: EFSA-Q-2008-1997, EFSA-Q-2008-2343, EFSA-Q-2008-2344, EFSA-Q-2008-2345, EFSA-Q-2008-2346, EFSA-Q-2008-2347, EFSA-Q-2008-2398, EFSA-Q-2008-2399, EFSA-Q-2008-2400, EFSA-Q-2008-2401, EFSA-Q-2008-2560, EFSA-Q-2008-2632, EFSA-Q-2008-2675, EFSA-Q-2008-2814, EFSA-Q-2008-2815, EFSA-Q-2008-2875, EFSA-Q-2008-2876, EFSA-Q-2008-2995, EFSA-Q-2008-3105, EFSA-Q-2008-3106, EFSA-Q-2008-3107). 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

Agarwal S and Rao AV, 1998. Tomato lycopene and low density lipoprotein oxidation: a human dietary intervention study. Lipids, 33, 981-984.

Aust O, Stahl W, Sies H, Tronnier H and Heinrich U, 2005. Supplementation with tomato-based products increases lycopene, phytofluene, and phytoene levels in human serum and protects against UV-light-induced erythema. International Journal for Vitamin and Nutrition Research, 75, 54-60.

Bohm V and Bitsch R, 1999. Intestinal absorption of lycopene from different matrices and interactions to other carotenoids, the lipid status, and the antioxidant capacity of human plasma. European Journal of Nutrition, 38, 118-125.

Bowen P, Chen L, Stacewicz-Sapuntzakis M, Duncan C, Sharifi R, Ghosh L, Kim HS, Christov-Tzelkov K and van Breemen R, 2002. Tomato sauce supplementation and prostate cancer: lycopene accumulation and modulation of biomarkers of carcinogenesis. Experimental Biology and Medicine (Maywood), 227, 886-893.

Briviba K, Kulling SE, Moseneder J, Watzl B, Rechkemmer G and Bub A, 2004a. Effects of supplementing a low-carotenoid diet with a tomato extract for 2 weeks on endogenous levels of DNA single strand breaks and immune functions in healthy non-smokers and smokers. Carcinogenesis, 25, 2373-2378.

Briviba K, Schnabele K, Rechkemmer G and Bub A, 2004b. Supplementation of a diet low in carotenoids with tomato or carrot juice does not affect lipid peroxidation in plasma and feces of healthy men. Journal of Nutrition, 134, 1081-1083.

Cardinault N, Abalain JH, Sairafi B, Coudray C, Grolier P, Rambeau M, Carre JL, Mazur A and Rock E, 2005. Lycopene but not lutein nor zeaxanthin decreases in serum and lipoproteins in age-related macular degeneration patients. Clinica Chimica Acta, 357, 34-42.

Carroll YL, Corridan BM and Morrissey PA, 2000. Lipoprotein carotenoid profiles and the susceptibility of low density lipoprotein to oxidative modification in healthy elderly volunteers. European Journal of Clinical Nutrition, 54, 500-507.

Dalle-Donne I, Rossi R, Colombo R, Giustarini D and Milzani A, 2006. Biomarkers of oxidative damage in human disease. Clinical Chemistry, 52, 601-623.

Dragsted LO, 2008. Biomarkers of exposure to vitamins A, C, and E and their relation to lipid and protein oxidation markers. European Journal of Nutrition, 47 Suppl 2, 3-18.

Fuhrman B, Volkova N, Rosenblat M and Aviram M, 2000. Lycopene synergistically inhibits LDL oxidation in combination with vitamin E, glabridin, rosmarinic acid, carnosic acid, or garlic. Antioxidants and Redox Signalling, 2, 491-506.

Griffiths HR, Moller L, Bartosz G, Bast A, Bertoni-Freddari C, Collins A, Cooke M, Coolen S, Haenen G, Hoberg AM, Loft S, Lunec J, Olinski R, Parry J, Pompella A, Poulsen H, Verhagen H and Astley SB, 2002. Biomarkers. Molecular Aspects of Medicine, 23, 101-208.

Hadley CW, Clinton SK and Schwartz SJ, 2003. The consumption of processed tomato products enhances plasma lycopene concentrations in association with a reduced lipoprotein sensitivity to oxidative damage. Journal of Nutrition, 133, 727-732.

Hininger IA, Meyer-Wenger A, Moser U, Wright A, Southon S, Thurnham D, Chopra M, Van Den Berg H, Olmedilla B, Favier AE and Roussel AM, 2001. No significant effects of lutein, lycopene or beta-carotene supplementation on biological markers of oxidative stress and LDL oxidizability in healthy adult subjects. Journal of the American College of Nutrition, 20, 232-238.

Ito Y, Kurata M, Suzuki K, Hamajima N, Hishida H and Aoki K, 2006. Cardiovascular disease mortality and serum carotenoid levels: a Japanese population-based follow-up study. Journal of Epidemiology, 16, 154-160.

Knasmuller S, Nersesyan A, Misik M, Gerner C, Mikulits W, Ehrlich V, Hoelzl C, Szakmary A and Wagner KH, 2008. Use of conventional and -omics based methods for health claims of dietary antioxidants: a critical overview. British Journal of Nutrition, 99 E Suppl 1, ES3-52.

Kristenson M, Zieden B, Kucinskiene Z, Elinder LS, Bergdahl B, Elwing B, Abaravicius A, Razinkoviene L, Calkauskas H and Olsson AG, 1997. Antioxidant state and mortality from coronary heart disease in Lithuanian and Swedish men: concomitant cross sectional study of men aged 50. British Medical Journal, 314, 629-633.

Kucuk O, Sarkar FH, Djuric Z, Sakr W, Pollak MN, Khachik F, Banerjee M, Bertram JS and Wood DP, Jr., 2002. Effects of lycopene supplementation in patients with localized prostate cancer. Experimental Biology and Medicine (Maywood), 227, 881-885.

Maruyama C, Imamura K, Oshima S, Suzukawa M, Egami S, Tonomoto M, Baba N, Harada M, Ayaori M, Inakuma T and Ishikawa T, 2001. Effects of tomato juice consumption on plasma and

lipoprotein carotenoid concentrations and the susceptibility of low density lipoprotein to oxidative modification. Journal of Nutritional Science and Vitaminology, 47, 213-221.

Mayne ST, 2003. Antioxidant nutrients and chronic disease: use of biomarkers of exposure and oxidative stress status in epidemiologic research. Journal of Nutrition, 133 Suppl 3, 933S-940S.

Neyestani TR, Shariat-Zadeh N, Gharavi A, Kalayi A and Khalaji N, 2007. The opposite associations of lycopene and body fat mass with humoral immunity in type 2 diabetes mellitus: a possible role in atherogenesis. Iranian Journal of Allergy, Asthma, and Immunology, 6, 79-87.

Nilsson SE, Sundelin SP, Wihlmark U and Brunk UT, 2003. Aging of cultured retinal pigment epithelial cells: oxidative reactions, lipofuscin formation and blue light damage. Documenta Ophthalmologica, 106, 13-16.

Pool-Zobel BL, Bub A, Muller H, Wollowski I and Rechkemmer G, 1997. Consumption of vegetables reduces genetic damage in humans: first results of a human intervention trial with carotenoid-rich foods. Carcinogenesis, 18, 1847-1850.

Porrini M and Riso P, 2000. Lymphocyte lycopene concentration and DNA protection from oxidative damage is increased in women after a short period of tomato consumption. Journal of Nutrition, 130, 189-192.

Porrini M, Riso P, Brusamolino A, Berti C, Guarnieri S and Visioli F, 2005. Daily intake of a formulated tomato drink affects carotenoid plasma and lymphocyte concentrations and improves cellular antioxidant protection. British Journal of Nutrition, 93, 93-99.

Rao AV and Agarwal S, 1998. Bioavailability and in vivo antioxidant properties of lycopene from tomato products and their possible role in the prevention of cancer. Nutrition and Cancer, 31, 199-203.

Rao AV and Shen H, 2002. Effect of low dose lycopene intake on lycopene bioavailability and oxidative stress. Nutrition Research, 22, 1125-1131.

Riso P, Pinder A, Santangelo A and Porrini M, 1999. Does tomato consumption effectively increase the resistance of lymphocyte DNA to oxidative damage? American Journal of Clinical Nutrition, 69, 712-718.

Riso P, Visioli F, Erba D, Testolin G and Porrini M, 2004. Lycopene and vitamin C concentrations increase in plasma and lymphocytes after tomato intake. Effects on cellular antioxidant protection. European Journal of Clinical Nutrition, 58, 1350-1358.

Rissanen TH, Voutilainen S, Nyyssonen K, Lakka TA, Sivenius J, Salonen R, Kaplan GA and Salonen JT, 2001. Low serum lycopene concentration is associated with an excess incidence of acute coronary events and stroke: the Kuopio Ischaemic Heart Disease Risk Factor Study. British Journal of Nutrition, 85, 749-754.

Rowley K, Walker KZ, Cohen J, Jenkins AJ, O'Neal D, Su Q, Best JD and O'Dea K, 2003. Inflammation and vascular endothelial activation in an Aboriginal population: relationships to coronary disease risk factors and nutritional markers. Medical Journal of Australia, 178, 495-500.

Sesso HD, Liu S, Gaziano JM and Buring JE, 2003. Dietary lycopene, tomato-based food products and cardiovascular disease in women. Journal of Nutrition, 133, 2336-2341.

Sesso HD, Buring JE, Norkus EP and Gaziano JM, 2004. Plasma lycopene, other carotenoids, and retinol and the risk of cardiovascular disease in women. American Journal of Clinical Nutrition, 79, 47-53.

Silaste ML, Alfthan G, Aro A, Kesaniemi YA and Horkko S, 2007. Tomato juice decreases LDL cholesterol levels and increases LDL resistance to oxidation. British Journal of Nutrition, 98, 1251-1258.

Simonelli F, Zarrilli F, Mazzeo S, Verde V, Romano N, Savoia M, Testa F, Vitale DF, Rinaldi M and Sacchetti L, 2002. Serum oxidative and antioxidant parameters in a group of Italian patients with age-related maculopathy. Clinica Chimica Acta, 320, 111-115.

Stahl W, Heinrich U, Wiseman S, Eichler O, Sies H and Tronnier H, 2001. Dietary tomato paste protects against ultraviolet light-induced erythema in humans. Journal of Nutrition, 131, 1449-1451.

Stahl W, Heinrich U, Aust O, Tronnier H and Sies H, 2006. Lycopene-rich products and dietary photoprotection. Photochemical and Photobiological Sciences, 5, 238-242.

Torbergsen AC and Collins AR, 2000. Recovery of human lymphocytes from oxidative DNA damage; the apparent enhancement of DNA repair by carotenoids is probably simply an antioxidant effect. European Journal of Nutrition, 39, 80-85.

Tyssandier V, Feillet-Coudray C, Caris-Veyrat C, Guilland JC, Coudray C, Bureau S, Reich M, Amiot-Carlin MJ, Bouteloup-Demange C, Boirie Y and Borel P, 2004. Effect of tomato product consumption on the plasma status of antioxidant microconstituents and on the plasma total antioxidant capacity in healthy subjects. Journal of the American College of Nutrition, 23, 148-156.

Visioli F, Riso P, Grande S, Galli C and Porrini M, 2003. Protective activity of tomato products on in vivo markers of lipid oxidation. European Journal of Nutrition, 42, 201-206.

Zhao X, Aldini G, Johnson EJ, Rasmussen H, Kraemer K, Woolf H, Musaeus N, Krinsky NI, Russell RM and Yeum KJ, 2006. Modification of lymphocyte DNA damage by carotenoid supplementation in postmenopausal women. American Journal of Clinical Nutrition, 83, 163-169.

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[7] (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[8]

Foods are commonly involved in many different functions[9] 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.

[7] OJ L12, 18/01/2007
[8] The term 'food' when used in this Terms of Reference refers to a food constituent, the food or the food category.
[9] 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 lycopene, including conditions of use from similar claims, as proposed in the Consolidated List.

ID	Food or Food constituent	Health Relationship	Proposed wording
1259	Guava.	Skin health.	Guava is a major source of lycopene. Lycopene from dietary sources contributes to the maintenance of healthy skin.
	Conditions of use - at least 120 g per day.		
	No clarification provided by Member States **Comments from Member States** Guava is a major source of lycopene / Lycopene from dietary sources contributes to the maintenance of healthy skin.		
ID	**Food or Food constituent**	**Health Relationship**	**Proposed wording**
1607	Lycopene	Skin health <u>Clarification provided</u> Skin Health. Contributes to the maintenance of healthy skin when exposed to sun light thanks to its antioxidant effects.	Contributes to the maintenance of healthy skin when exposed to sun light. (Avoid sunburns by using an effective sun screen. Lycopene is not a replacement for sun screens).
	Conditions of use - Food supplement with 30mg of lycopene in the daily dose. - Min. 6 mg/day; 7-16 mg/day - Min. 6 mg/day		
	Comments from Member States Italy's proposal is identical to Dutch proposal/ UK proposal is identical to Dutch proposal/ FI: no further clarification received. Dutch proposal OK.		
ID	**Food or Food constituent**	**Health Relationship**	**Proposed wording**
1608	Lycopene.	Antioxidant properties.	Lycopenes contained in this product ensure antioxidant action. Ensure protective effect on the organism. Contribute to the protection of the cellular membranes from oxidation.

	Conditions of use - 7-16 mg/day. - Up to 12 mg/day. 7-16 mg/day - Food supplement with 2.5 mg of lycopene in the daily dose. - Food supplement with 30 mg of lycopene in the daily dose. - 10 mg Tagesdosis. Für alle Bevölkerungsgruppen geeignet.		
ID	**Food or Food constituent**	**Health Relationship**	**Proposed wording**
1609	Lycopene	Prostate health	Contributes to the normal functioning of the prostate/helps to maintain a healthy prostate/helps to keep your prostate in shape/helps to reduce oxidative damage of prostate cells and tissue/helps to maintain intact DNA in prostate tissue
	Conditions of use - 6-8 mg per day. 7-16 mg/day - Gemeinsam mit einer fetthaltigen Mahlzeit–Tagesdosis Lycopin: 6 mg–Männer - Food supplement with 30mg of lycopene in the daily dose.		
ID	**Food or Food constituent**	**Health Relationship**	**Proposed wording**
1610	Lycopene.	Heart health. <u>Clarification provided</u> Lycopene can contribute to maintain a healthy heart and cardiovascular system by protecting the arteries from narrowing and hardening, helping to maintain a normal blood flow, to help maintain healthy blood lipid levels and artery wall thickness.	Helps to maintain a healthy heart/contributes to maintain a healthy cardiovascular system/contributes to protect the arteries from narrowing and hardening/contributes to keep the arteries healthy/helps to maintain a normal blood flow.
	Conditions of use - Food supplement with 30mg of lycopene in the daily dose. - Food supplement with 2.5mg of lycopene in the daily dose. - 40-60 mg per day. 7-16 mg/day.		
ID	**Food or Food constituent**	**Health Relationship**	**Proposed wording**
1611	Lycopenes from tomato juices	Antioxidant properties	Lycopenes contained in this product ensure antioxidant action/lycopenes contained in this product ensure protective effect on the organism; antioxidant/s.

	Conditions of use - Estimated suficient intakes: 6 to 10 mg per day - 7-10 mg/day - Tagesdosis > 0,4 mg		
ID	**Food or Food constituent**	**Health Relationship**	**Proposed wording**
1662	Tomato extract containing lycopene.	Maintains cardiovascular health. Clarification provided Cardiovascular system - supports a healthy lipid profile whilst antioxidant action helps prevent the oxidation of harmful LDL cholesterol.	Contributes to the maintenance of a healthy cardiovascular system. Maintains cardiovascular health.
	Conditions of use - 5-15 mg, Maximum 40-60 mg lycopene in the daily portion of the product. - 250mg extract/day (providing up to 15 mg lycopene/day).		
ID	**Food or Food constituent**	**Health Relationship**	**Proposed wording**
1663	Tomato extract containing lycopene.	Antioxidant properties/cell and DNA protection. Clarification provided Antioxidant properties/cell and DNA protection; Helps to maintain intact cells/protects cells, cellular membranes, DNA from oxidative damage.	Helps to maintain intact cells.
	Conditions of use - 5-15 mg lycopene in the daily portion of the product. - 166-250mg extract/day (providing 10-15 mg lycopene).		
	Comments from Member States We think that this health relationship needs no further clarification. EFSA accepted similar relationships, under HR_ID 1608, 1611, 1899, 1942, 2081 and the same relationship under 2082 without any comment.		
ID	**Food or Food constituent**	**Health Relationship**	**Proposed wording**
1664	Tomato extract containing lycopene	Maintains prostate health. Clarification provided Prostate health - Can contribute to the maintenance of prostate health and function by participating in the protection of prostate cells	Helps to maintain normal prostate health. Helps to maintain a healthy prostate.

		and tissue from oxidative damage. Can help to maintain intact prostate DNA and balanced tissue growth in prostate.	
	Conditions of use - 6-8 mg lycopene in the daily portion of the product. - 250mg extract/day (providing up to15 mg lycopene).		
	Comments from Member States HU comment: EFSA has accepted similar relationship, under HR_ID 1609 without comment.		
ID	**Food or Food constituent**	**Health Relationship**	**Proposed wording**
1665	Tomato extract containing lycopene.	Maintains skin health. Clarification provided Skin health - can contribute to the maintenance of skin health when exposed to the sun/UV radiation/UV induced oxidative damage due to its antioxidant effect, thus supporting endogenous photoprotection.	Helps to maintain healthy appearance and structure of the skin when exposed to sun. Helps protect the skin from exposure to sun.
	Conditions of use - 250mg extract/day (providing up to15 mg lycopene). - Minimum 6 mg lycopene in the daily portion of the product.		
	Comments from Member States HU comment: EFSA has accepted the same or similar relationships under HR ID 1796, 2143, 2373 without any comments.		
ID	**Food or Food constituent**	**Health Relationship**	**Proposed wording**
1827	Lycopene	Eyes	Good for the eye health of older people.
	Conditions of use - Food supplement with 2.5mg of lycopene in the daily dose.		
	Comments from Member States No further clarification received		
ID	**Food or Food constituent**	**Health Relationship**	**Proposed wording**
1899	Lycopenes from tomato pulp and sauces	Antioxidant Properties	Tomato is as almost unique as a source of a specific carotene named: Lycopene; Therefore use it always is any conditions for its nutritional qualities
	Conditions of use		

	- Estimated sufficient intakes: 6 to 10mg per day		
ID	**Food or Food constituent**	**Health Relationship**	**Proposed wording**
1942	Lycopenes from tomato juice	Oxidative stress control	(Lycopenes from) tomato juice: - plays an important antioxidative function - protect cells against oxidative damages - strengthen the immune system - strengthen the body's defences
	Conditions of use - 1 Portion of tomatoes or tomato products per day is recommended		
ID	**Food or Food constituent**	**Health Relationship**	**Proposed wording**
2081	Lycopene (from Tomato extract)	Antioxidant properties	Lycopene from tomato extract has an antioxidant effect. Lycopenes contained in this product have an antioxidant action/ ensure a protective effect on the organism/contribute to the protection of the cellular membranes from oxidation.
	Conditions of use - 6 Milligramm /Tag. Upper limit: 10 Milligramm - 7-16 mg/day		
ID	**Food or Food constituent**	**Health Relationship**	**Proposed wording**
2082	Lycopene (from Tomato extract)	Antioxidant properties / protection of DNA	lycopene is an antioxidant and helps to protect the body’s cells/helps to maintain intact body cells. Lycopene or a diet rich in lycopene helps to maintain intact cell DNA/contributes to healthy ageing by maintaining intact cell DNA/
	Conditions of use - 5-15 mg lycopene in the daily portion of the product - up to 15 mg/day		

ID	Food or Food constituent	Health Relationship	Proposed wording
2142	Standardized tomato extract [Oleoresin extracted from ripe fruits of Licopersicum aesculentum, solvent of extraction Ethyl acetate, 5% lycopene	For antioxidant protection system/protection of DNA	Contains naturally occurring antioxidants /for cells protection/helps protect cells from free radical damage, Lycopene is an antioxidant and helps to maintain intact cell DNA, it contributes to healthy ageing, by maintaining intact cell DNA
	Conditions of use - 25-50 mg		
ID	**Food or Food constituent**	**Health Relationship**	**Proposed wording**
2143	Standardized tomato extract [Oleoresin extracted from ripe fruits of Licopersicum aesculentum, solvent of extraction Ethyl acetate, 5% lycopene	For skin health	Helps to protect the skin from UV-induced oxidative damage, Helps to protect against UV-induced erythema, Helps to reduce skin reddening when exposed to sun
	Conditions of use - 25-50 mg - 25-50 mg WARNING: Avoid sunburns by using an effective sun screen. This product is not a replacement for sun screens		
ID	**Food or Food constituent**	**Health Relationship**	**Proposed wording**
2262	Guava	Skin health	Guava is a major source of lycopene/ Lycopene from dietary sources contributes to the maintenance of healthy skin, when exposed to sun light (Avoid sunburns by using an effective sun screen. Lycopene is not a replacement for sun screens)/ helps to reduce skin reddening when exposed to sun light (Avoid sunburns by using an effective sun screen. Lycopene is not a replacement for sun screens)
	Conditions of use - at least 120 g per day. WARNING: (Avoid sunburns by using an effective sun screen. Lycopene is not a replacement for sun screens. - At least 120 g / Used as part of a multibotanical combination.		

	Comments from Member States Helps to protect the skin from the effects of UV radiation. Reduces the skin's susceptibility to burning. Increases the skin's sun tolerance. (EFSA published list of health claims - Nr.1796)		
ID	**Food or Food constituent**	**Health Relationship**	**Proposed wording**
2372	Lycopene.	Cardio-vascular health.	Can help in the maintenance of the healthy function of the cardiovascular system.
	Conditions of use - 25-50 mg - 5-15 mg, Maximum 40-60 mg lycopene in the daily portion of the product		
	Comments from Member States No clarifications were submitted in any MS concerned.		
ID	**Food or Food constituent**	**Health Relationship**	**Proposed wording**
2373	Tomato extract containing lycopene	Skin health	Can contribute to the maintenance of skin health when exposed to sun.; Can help in the maintenance of healthy structure of the skin;
	Conditions of use - Minimum 6 mg lycopene in the daily portion of the product		
ID	**Food or Food constituent**	**Health Relationship**	**Proposed wording**
2374	Tomato extract containing lycopene.	Prostate health. Clarification provided Prostate health; Lycopene helps defend prostate cells and tissues from oxidative deamge, can contribute to a balanced tissue growth in prostate; Can help to maintain intact prostate DNA and balanced tissue growth in prostate.	Can contribute to the maintenance of prostate health; Can contribute to the maintenance of the healthy function of prostate.
	Conditions of use - 6-8 mg lycopene in the daily portion of the product.		
	Comments from Member States EFSA has accepted similar relationship, under HR_ID 1609 without comment.		

GLOSSARY AND ABBREVIATIONS

5-OhmdU	5-hydroxy-methyl-desoxy-uridine
ABTS	2, 2'-azinobis (3- ethylbenzothiazoline-6-sulfonate)
DNA	Deoxyribonucleic acid
DTNB	5,5'-Dithio-bis (2-nitrobenzoic acid)
GSH	Glutathione
HPLC-EC	High pressure liquid chromatography/electrochemical detection
LDL	Low-density lipoproteins
MDA	Malondialdehyde
MED	Minimal erythemal dose
ROS	Reactive oxygen species
TBARS	Thio-barbituric acid reactives substances
TEAC	Trolox-equivalent antioxidant capacity
TRAP	Total reactive antioxidant potential
UV	Ultra-violet