

SCIENTIFIC OPINION

Scientific Opinion on the substantiation of health claims related to cocoa flavanols and protection of lipids from oxidative damage (ID 652, 1372, 1506, 3143), and maintenance of normal blood pressure (ID 1507) pursuant to Article 13(1) of Regulation (EC) No 1924/2006¹

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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 cocoa flavanols and protection of lipids from oxidative damage, and maintenance of normal blood pressure. 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 cocoa flavanols. The Panel considers that cocoa flavanols is sufficiently characterised.

Protection of lipids from oxidative damage

The claimed effects are “antioxidant properties” and “oxidative stress reduction”. The target population is assumed to be the general population. In the context of the proposed wordings and the references provided, the Panel assumes that the claimed effect relates to the protection of lipids against oxidative damage. The Panel considers that the protection of lipids from oxidative damage may be a beneficial physiological effect.

¹ On request from the European Commission, Question No EFSA-Q-2008-1439, EFSA-Q-2008-2109, EFSA-Q-2008-2243, EFSA-Q-2008-2244, EFSA-Q-2008-3875, adopted on 10 September 2010.

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In weighing the evidence, the Panel took into account that, although one acute study reported significant changes in plasma concentrations of total F2-isoprostanes after a single administration of cocoa flavanols, this effect was not confirmed when cocoa flavanols were consumed daily for 3-6 weeks, and that no effect of cocoa flavanols was observed on plasma concentrations of oxidised LDL particles.

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

Maintenance of normal blood pressure

The claimed effect is “vascular health”. The target population is assumed to be the general population. In the context of the proposed wording, the Panel assumes that the claimed effect refers to the maintenance of a normal blood pressure. The Panel considers that maintenance of normal blood pressure is a beneficial physiological effect.

In weighing the evidence the Panel took into account that evidence from ten randomised controlled trials for a blood pressure-lowering effect of cocoa flavanols was inconsistent, that evidence from small and un-blinded studies with lower doses in favour of an effect was in conflict with evidence from adequately powered and well controlled studies with higher doses, and that evidence from blinded studies with lower doses was conflicting.

On the basis of the data presented, the Panel concludes that the evidence provided is insufficient to establish a cause and effect relationship between the consumption of cocoa flavanols and maintenance of normal blood pressure.

KEY WORDS

Cocoa flavanols, polyphenols, oxidative damage, blood pressure, health claims.

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BACKGROUND AS PROVIDED BY THE EUROPEAN COMMISSION

See Appendix A

TERMS OF REFERENCE AS PROVIDED BY THE EUROPEAN COMMISSION

See Appendix A

EFSA DISCLAIMER

See Appendix B

INFORMATION AS PROVIDED IN THE CONSOLIDATED LIST

The consolidated list of health claims pursuant to Article 13 of Regulation (EC) No 1924/2006⁴ 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 out⁵. 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 constituents that are the subject of the health claims are cocoa in chocolate, polyphenols and cocoa flavanols.

Cocoa (*Theobroma cacao* L.) contains a wide range of polyphenols, such as flavan-3-ols. No further information is provided on the nature and intakes of polyphenols in cocoa or dark chocolate to obtain the claimed effect. The conditions of use specify foods containing minimum 30 % of daily intakes of about 3000 to 5000 ORAC units per day (ID 652, 3143), which refers to the oxygen radical absorbance capacity (ORAC) measured *in vitro* in the food. An antioxidant capacity assay such as ORAC is not an acceptable way of characterising a food/food constituent which is the subject of a health claim because it is a non specific assay for substances capable of protecting a red photoreceptor pigment (β -phycoerythrin) from oxidation. The ORAC value of a food is not relevant for establishing a cause and effect relationship between the bioactive constituent (e.g. polyphenols) and the possible health effect. Therefore, the Panel considers that cocoa polyphenols *per se* are not sufficiently characterised, nor are the conditions of use specified appropriately.

The flavanol (i.e. procyanidins and catechins) content in cocoa, however, is measurable in foods by established methods and conditions of use are provided for flavanols naturally occurring in cocoa. This opinion will apply to flavanols naturally present in cocoa.

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

2. Relevance of the claimed effect to human health

2.1. Protection of lipids from oxidative damage (ID 652, 1372, 1506, 3143)

The claimed effects are “antioxidant properties” and “oxidative stress reduction”. The Panel assumes that the target population is the general population.

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>

In the context of the proposed wordings and the references provided, the Panel assumes that the claimed effect relates to the protection of body lipids from oxidative damage.

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

2.2. Maintenance of normal blood pressure (ID 1507)

The claimed effect is “vascular health”. The Panel assumes that the target population is the general population.

In the context of the proposed wording, the Panel assumes that the claimed effect refers to the maintenance of normal blood pressure.

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

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

3. Scientific substantiation of the claimed effect

3.1. Protection of lipids from oxidative damage (ID 652, 1372, 1506, 3143)

The majority of the references provided in the consolidated list were narrative reviews of the health effects of polyphenols in general (rather than specifically of flavanols naturally occurring in cocoa), compositional analysis of food phenolics, and human studies investigating the effects of cocoa polyphenols on health outcomes other than the claimed effect (e.g. insulin sensitivity, blood pressure, endothelial function). The Panel considers that no conclusions can be drawn from these references for the scientific substantiation of the claim.

Among the references provided, one systematic review and 11 intervention studies in humans reported on the effects of the food constituent on different markers of oxidative stress or antioxidant status.

A systematic review by Ding et al. (2006) on the effects of cocoa and chocolate on cardiovascular risk factors included nine publications reporting on LDL oxidation, other markers of lipid peroxidation, and/or antioxidant capacity of plasma among the outcomes (Fraga et al., 2005; Kondo et al., 1996; Mathur et al., 2002; Mursu et al., 2004; Osakabe et al., 2001; Serafini et al., 2003; Wan et al., 2001; Wang et al., 2000; Wiswedel et al., 2004). No statistical analysis of the effects of cocoa flavanols on any of the outcomes was provided in the review. All but one (Kondo et al., 1996) of the studies were provided in the references cited for the substantiation of the claimed effect.

Two acute studies (Wang et al., 2000; Wiswedel et al., 2004) and two chronic studies (Mathur et al., 2002; Mursu et al., 2004) reported on F2-isoprostanes, whereas one chronic study reported on *in vivo* LDL oxidation (Baba et al., 2007b).

Wang et al. (2000) observed no changes in plasma 8-isoprostane concentrations two hours after the ingestion of 27, 53 or 80 g of chocolate (5.3 mg of procyanidin/g of chocolate) in 20 healthy volunteers. Conversely, Wiswedel et al. (2004) observed a significant decrease in plasma concentrations of total F2-isoprostanes 2 and 4 h after the intake of a high-flavanol cocoa drink (187 mg flavan-3-ols/100 mL) versus a low-flavanol cocoa drink (14 mg/100 mL) in ten healthy subjects only when the high-flavanol cocoa drink was consumed after physical exercise.

In a three week clinical trial with parallel design, 45 healthy subjects received 75 g of either dark (365.5 mg catechins/100 g), white (0.3 mg catechins/100 g) or high-polyphenol chocolate (556.8 mg catechins/100 g). No significant differences in changes among study groups were observed with respect to plasma concentrations of F2-isoprostanes (Mursu et al., 2004). Similarly, supplementation of 25 healthy subjects for six weeks (randomised crossover design) with a chocolate bar or a cocoa powder drink (651 mg of flavanols per day) did not affect urinary F2-isoprostanes significantly (Mathur et al., 2002).

In the study by Baba et al. (2007b), 160 subjects were randomised to consume either 13, 19.5 or 26 g/day (corresponding approximately to 140, 190, and 280 mg of flavanols) of cocoa powder as beverage or placebo for four weeks and plasma oxidised LDL concentrations were measured by the ELISA method. In this study the control beverage was adjusted to account for the theobromine content of the cocoa drink. The Panel notes that changes in LDL oxidation during the study between the intervention groups and placebo were not assessed, and therefore no conclusions can be drawn for the scientific substantiation of the claimed effect owing to the uncontrolled nature of the statistical analysis. Dose-response relationships were not reported.

The remaining human intervention studies presented reported on the effects of a single dose of flavanol-containing chocolate/cocoa on the antioxidant capacity of plasma (Serafini et al., 2003; Wang et al., 2000), TBARS (Wang et al., 2000), on the oxidation lag time of LDL *ex vivo* (Kondo et al., 1996; Hirano et al., 2000), on the effects of daily chocolate/cocoa consumption with different flavanol content (140-651 mg flavanols per day) on oxidation lag time of LDL *ex vivo* (Osakabe et al., 2001; Wan et al., 2001; Mathur et al., 2002; Mursu et al., 2004; Baba et al., 2007a) or on malondialdehyde (MDA) (Fraga et al., 2005). The Panel considers that these studies, because of the unreliability of the markers used, are not a source of data on their own for the substantiation of the claimed effect (Griffiths et al., 2002; Lykkesfeldt, 2007; Knasmüller et al., 2008).

In weighing the evidence, the Panel took into account that, although one acute study reported significant changes in plasma concentrations of total F2-isoprostanes after a single administration of cocoa flavanols, this effect was not confirmed when cocoa flavanols were consumed daily for 3-6 weeks, and that no effect of cocoa flavanols was observed on plasma concentrations of oxidised LDL particles.

The Panel concludes that a cause and effect relationship has not been established between the consumption of cocoa flavanols and protection of lipids from oxidative damage.

3.2. Maintenance of normal blood pressure (ID 1507)

Some of the references provided reported on vascular outcomes other than blood pressure (e.g. flow-mediated dilation, endothelial function), had methodological weaknesses (e.g. ecological study design), were narrative reviews or reported on personal opinions that were not based on a systematic review of the literature. The Panel considers that no conclusions can be drawn from these references for the scientific substantiation of the claim.

The references cited in the list also included two meta-analysis (Taubert et al., 2007a; Hooper et al., 2008) and two systematic reviews (Ding et al., 2006; Erdman et al., 2008) addressing the effects of

cocoa flavanols on blood pressure. Furthermore, the list included nine relevant RCTs (Taubert et al., 2003, 2007b; Engler et al., 2004; Fraga et al., 2005; Grassi et al., 2005a, b; Allen et al., 2008; Davison et al., 2008; Faridi et al., 2008), of which three RCTs (Allen et al., 2008; Davison et al., 2008; Faridi et al., 2008) had not been included in the meta-analyses. Apart from RCTs, there was one observational study that was pertinent to the claim (Buijsse et al., 2006).

Taubert et al. (2007a) performed a meta-analysis of five RCTs on cocoa intake and blood pressure (total of 173 subjects) with a median duration of two weeks and which were published before October 2006. Pooling of the five RCTs resulted in a blood pressure change estimate of -4.7 mmHg systolic and -2.8 mmHg diastolic for cocoa intake, which was statistically significant. The five RCTs included in the meta-analysis are described in more detail below. In three RCTs (Taubert et al., 2003; Grassi et al., 2005a, b) the blood pressure effect of dark versus white chocolate (100 g/d) was examined and yielded an 88 mg/d difference between groups in flavanol intake (22 mg catechin + 66 mg epicatechin). The RCT by Taubert et al. (2003) in 13 untreated hypertensive men and women (age ~59 y) showed a significant change in blood pressure of -5.1/-1.9 mmHg for dark versus white chocolate. The RCT by Grassi et al. (2005a) in 20 men and women (age ~44 y) with high-normal blood pressure showed a larger effect of dark versus white chocolate on blood pressure (-10.5/-5.9 mmHg). Another RCT by the same group in 15 normotensive men and women (age ~34 y) showed a blood pressure-lowering effect of -5.4/-3.5 mmHg following consumption of dark chocolate compared to white chocolate (Grassi et al., 2005b). In the remaining two studies, high versus low flavanol chocolates were compared (Fraga et al., 2005; Engler et al., 2004). Fraga et al. (2005) compared the blood pressure effect of high flavanol milk chocolate (105 g/d, 168 mg flavanols) with low flavanol chocolate (flavanols <5 mg/d) in 28 young normotensive men. Flavanol intake in this study was related to a blood pressure change of -4.0/-4.0 mmHg. Finally, the meta-analysis included a RCT by Engler et al. (2004) in 21 normotensive men and women (age ~32 y) who were randomised to dark chocolate with either high or low flavanol content. Subjects who consumed flavonoid-rich chocolate had a 213 mg higher daily intake of procyanidins, including 46 mg epicatechins. After 2 weeks of intake a significant increase in plasma epicatechin concentrations was seen in these subjects (from ~30 to 210 mmol/L). In contrast to other RCTs, blood pressure slightly increased (+1.8/ +1.0 mmHg) in subjects with a high compared to low flavonoid intake.

Another meta-analysis by Hooper et al. (2008) included RCTs published before June 2007. This meta-analysis included four (Taubert et al., 2003; Grassi et al., 2005a, b; Fraga et al., 2005) out of the five RCTs described above. The study by Engler et al. (2004) was excluded for reporting large differences in saturated fat intakes between the intervention and control arms. Instead, a more recent intervention study by Taubert et al. (2007b) was included. In that study, 44 men and women (age ~64 y) with untreated (pre)hypertension were randomly assigned to a daily intake of 6.3 g of polyphenol-rich dark chocolate or 5.6 g polyphenol-free white chocolate (isocaloric) for 18 weeks. The dark chocolate group had a 7.1 mg/d higher intake of catechins (catechin, epicatechin, and epicatechin-gallate) and a 21.2 mg/d higher intake of procyanidins. Dark chocolate intake significantly reduced blood pressure by -2.9/-1.9 mmHg after 18 weeks, and the prevalence of hypertension declined from 86 % to 68 %.

Overall, the meta-analysis included 97 subjects in the intervention and 97 subjects in the control groups and observed a statistically significant reduction in systolic blood pressure (by 5.88 mmHg; 95 % CI: -9.55, -2.21; 5 studies; P for heterogeneity=0.0003, $I^2=81$ %) and in diastolic blood pressure (by 3.30 mmHg; 95 % CI: -5.77, -0.83; four studies; P for heterogeneity=0.009, $I^2=70$ %) in the cocoa flavanol group compared to controls. The clear heterogeneity in these analyses is partly explained by dose and duration, so that sub-grouping by dose or duration reduces apparent levels of heterogeneity (effects appear greater in studies with higher doses and shorter duration; data not shown). There are only five data points, but the funnel plot suggested that small studies showing large systolic blood pressure reductions may have been over-represented.

Three recent RCTs provided in the list were not included in the above-mentioned meta-analyses (Allen et al., 2008; Faridi et al., 2008; Davison et al., 2008).

Allen et al. (2008) assigned 44 untreated normotensive men and women (aged 24-70 y) with mildly elevated serum total cholesterol to 2x4 weeks use of cocoa flavanol-containing dark chocolate with or without plant sterols, using a randomised cross-over design. The daily dose of cocoa flavanols from chocolate bars was 360 mg/d. However, intervention periods were controlled for sterol ester intake and not for cocoa flavanol intake. Therefore, the blood pressure effect of flavanols could not be adequately assessed in this RCT and no conclusions can be drawn for the scientific substantiation of the claim.

Faridi et al. (2008) randomly assigned 45 normotensive men and women (age ~53 y) who were overweight/obese (BMI ~30 kg/m²) to a dark chocolate bar or a cocoa-free placebo bar per day. The cocoa bar contained 821 mg flavanols (of which 32 mg catechin + epicatechin) versus 0 mg in the placebo bar. The trial was repeated using sugar-containing versus sugar-free cocoa. Postprandial blood pressure was assessed two hours after intake. This study did not address the effects of chronic administration of cocoa flavanols on blood pressure and therefore no conclusions can be drawn for the scientific substantiation of the claimed effect.

In another RCT by Davison et al. (2008), 49 normotensive men and women (age ~49 y) were randomised to a high-flavanol cocoa drink (451 mg flavanols) or a low-flavanol cocoa drink (18 mg flavanols) daily for 12 weeks. Within these groups, subjects were additionally randomised to an exercise programme. Changes in blood pressure were found of approximately +1.5/+1.2 mmHg for the low flavanol group and -0.2/-1.5 mmHg for the high flavanol group when combining data from both exercise groups at the end of the study. Differences between groups were only statistically significant for diastolic blood pressure when measurements at 6 and 12 weeks were combined in a nested analysis. No significant differences between groups were observed for systolic blood pressure at any time point.

Three recently published RCTs on the effects of cocoa flavanols on blood pressure were also considered by the Panel (Muniyappa et al., 2008; Crews et al., 2008; Grassi et al., 2008).

Muniyappa et al. (2008) randomly assigned 29 untreated men and women (age ~51 y) with mild-to-moderate hypertension and obesity (BMI ~33 kg/m²) to daily consumption of cocoa drinks (900 mg/d flavanols) or placebo drinks (28 mg/d flavanols) in a double-blind manner. Drinks were matched for calories and content of other nutrients and appearance (calories, fat, macronutrients, mineral content, theobromine, caffeine, colour, taste and packaging) to test the effects of cocoa flavanols *per se* and to eliminate ascertainment or expectation bias. A 2x2 week cross-over design was used, interrupted by a one week wash-out period. A sample size of 20 is sufficient to detect a 5 mmHg change in systolic blood pressure with > 90 % power and a 2 mmHg change in diastolic blood pressure with >90 % power and a 2-sided $\alpha=0.05$. No intention-to-treat analysis was applied, and only subjects who completed the study (n=20) were included in the data-analysis. No significant differences in blood pressure were observed between the cocoa and placebo periods. There was no evidence of a carryover effect of either cocoa or placebo.

Crews et al. (2008) performed a large RCT in 101 untreated men and women (age ~69 y) with normal to high-normal blood pressure who randomly received a 37 g dark chocolate bar and 237 mL of aspartame-sweetened cocoa drink daily, or low-polyphenol matched (for appearance, smell, taste, and caloric content) placebo products, for 6 weeks. The chocolate bar (11 g of natural cocoa) contained 397.3 mg of total proanthocyanins. The cocoa beverage (12 g dry weight, of which 11 g of natural cocoa) contained 357.4 mg proanthocyanins. Matching placebo products contained 0.2 mg and 40.9 mg proanthocyanins, respectively. Pre-treatment systolic blood pressure was on average 2 mmHg higher in the cocoa group (128.6 mmHg) than in the placebo group (126.7 mmHg). During the

intervention, blood pressure decreased both in the cocoa group (-3.6/-0.5 mmHg) and in the placebo group (-3.1/-0.6 mmHg), with no statistical differences between groups.

In another randomised, controlled cross-over study by Grassi et al. (2008), 19 subjects with hypertension and impaired glucose tolerance who were not on pharmacological treatment for hypertension consumed 100 g/d of dark (147 mg flavanols) versus white (flavanol-free) chocolate for 15 days each with one week wash-out period in between. Systolic and diastolic blood pressure significantly decreased during the dark chocolate consumption compared to the white chocolate after 15 days of intervention (-3.8 and -3.9 mmHg, respectively).

One observational, epidemiological study was cited in relation to the claim. In 470 elderly Dutch men the intake of cocoa-containing foods (among others) was repeatedly assessed between 1985 and 1995, and blood pressure was monitored (Buijsse et al., 2006). In 1985, one-third of the men did not consume cocoa, one-third had a median intake of 0.9 g/d and one-third had an intake of 4.2 g/d. After adjustment for potential confounders, the mean systolic blood pressure in the top tertile of cocoa intake was -3.7 mmHg lower (95 % confidence interval, -7.1 to -0.3 mmHg) and the mean diastolic blood pressure was -2.1 mmHg lower (-4.0 to -0.2 mmHg) compared with the bottom tertile. Data on the actual intake of cocoa flavanols, however, were not available and residual confounding by other dietary and lifestyle factors inherent to the observational study design cannot be excluded.

The Panel notes that 10 of the above-mentioned RCTs allowed conclusions to be drawn in relation to the substantiation of the claimed effect (Taubert et al., 2003, 2007b; Grassi et al., 2005a, b, 2008; Fraga et al., 2005, Engler et al., 2004; Davison et al., 2008; Muniyappa et al., 2008; Crews et al., 2008). Of these, five small RCTs by two different research groups (Taubert et al., 2003, 2007b, Grassi et al., 2005a, b, 2008) were performed in normotensive and untreated hypertensive subjects who consumed either dark or white chocolate during 2-18 weeks. Flavanol doses in these five RCTs were low (<150 mg/d). Significant blood pressure reductions, ranging from -3/-2 mmHg to -11/-6 mmHg, were found which were not clearly related to pre-treatment blood pressure levels. The Panel notes that these low-dose RCTs suffer from lack of blinding, which could have influenced the results. In three other small RCTs in normotensive subjects, higher flavanol doses (168-433 mg/d) were administered via flavanol-rich chocolate or beverages. These studies, which aimed to be double-blinded, showed either a reduction in systolic and diastolic blood pressure (-2/-3 mmHg and -4/-4 mmHg; Fraga et al., 2005), a decrease in diastolic blood pressure only (-2.5 mmHg; Davison et al., 2008), or an increase in blood pressure (+2/+1 mmHg; Engler et al., 2004) associated with cocoa flavanol consumption. Another small but well controlled and adequately powered double-blind RCT (Muniyappa et al., 2008) was performed in untreated hypertensive subjects with a relatively high flavanol dose (872 mg/d), and showed no effect on blood pressure (-1/+1 mmHg). Finally, a large RCT by Crews et al. (2008) with very high daily doses of cocoa flavanols (>750 mg proanthocyanidins) showed no effect on blood pressure.

Thus, double-blind RCTs on the effects of cocoa flavanols on blood pressure are inconsistent, showing a tendency to reduce blood pressure at lower levels of flavanol intake (<500 mg/d) and showing no effect on blood pressure at higher intakes. The Panel notes that, at low doses of cocoa flavanol intake, small and un-blinded studies tend to show an effect on blood pressure (Taubert et al., 2003, 2007b, Grassi et al., 2005a, b, 2008), whereas studies aiming to be double-blinded show conflicting results (Fraga et al., 2005; Davison et al., 2008; Engler et al., 2004). The Panel also notes that adequately powered and well controlled intervention studies at higher doses (>750 mg proanthocyanidins) do not show an effect of cocoa flavanols on blood pressure (Muniyappa et al., 2008; Crews et al., 2008), and that these studies were not considered in the meta-analyses by Taubert et al. (2007) and Hooper et al. (2008). The Panel considers that the evidence from RCTs for a blood pressure-lowering effect of cocoa flavanols is inconsistent and notes that adequately powered and well controlled studies with higher doses did not confirm the effect observed in small and un-blinded

studies with lower doses, and that the findings from blinded studies with lower doses were conflicting.

In weighing the evidence the Panel took into account that evidence from 10 RCTs for a blood pressure-lowering effect of cocoa flavanols was inconsistent, that evidence from small and un-blinded studies with lower doses in favour of an effect was in conflict with evidence from adequately powered and well controlled studies with higher doses, and that evidence from blinded studies with lower doses was conflicting.

The Panel concludes that the evidence provided is insufficient to establish a cause and effect relationship between the consumption of cocoa flavanols and maintenance of normal blood pressure.

CONCLUSIONS

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

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

Protection of lipids from oxidative damage (ID 652, 1372, 1506, 3143)

- The claimed effects are “antioxidant properties” and “oxidative stress reduction”. The target population is assumed to be the general population. Protection of lipids from oxidative damage may be a beneficial physiological effect.
- A cause and effect relationship has not been established between the consumption of cocoa flavanols and protection of lipids from oxidative damage.

Maintenance of normal blood pressure (ID 1507)

- The claimed effect is “vascular health”. The target population is assumed to be the general population. Maintenance of normal blood pressure is a beneficial physiological effect.
- The evidence provided is insufficient to establish a cause and effect relationship between the consumption of cocoa flavanols and maintenance of normal blood pressure.

DOCUMENTATION PROVIDED TO EFSA

Health claims pursuant to Article 13 of Regulation (EC) No 1924/2006 (No: EFSA-Q-2008-1439, EFSA-Q-2008-2109, EFSA-Q-2008-2243, EFSA-Q-2008-2244, EFSA-Q-2008-3875). The scientific substantiation is based on the information provided by the Member States in the consolidated list of Article 13 health claims and references that EFSA has received from Member States or directly from stakeholders.

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

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APPENDICES

APPENDIX A

BACKGROUND AND TERMS OF REFERENCE AS PROVIDED BY THE EUROPEAN COMMISSION

The Regulation 1924/2006 on nutrition and health claims made on foods⁶ (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 FOOD⁷

Foods are commonly involved in many different functions⁸ of the body, and for one single food many health claims may therefore be scientifically true. Therefore, the relative importance of food e.g. nutrients in relation to other nutrients for the expressed beneficial effect should be considered: for functions affected by a large number of dietary factors it should be considered whether a reference to a single food is scientifically pertinent.

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

⁶ OJ L12, 18/01/2007

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

⁸ The term 'function' when used in this Terms of Reference refers to health claims in Article 13(1)(a), (b) and (c).

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 cocoa flavanols, including conditions of use from similar claims, as proposed in the Consolidated List.

ID	Food or Food constituent	Health Relationship	Proposed wording
652	Polyphenols.	Oxidative stress reduction.	Polyphenols are antioxidants, which naturally occur in cocoa and therefore in dark chocolate. They help to protect our body cells against free radicals.
	Conditions of use - Min. 30 % of intakes per day (Intakes are 3000 to 5000 ORAC unit per day).		
ID	Food or Food constituent	Health Relationship	Proposed wording
1372	chocolate	Cocoa in chocolate may be a major dietary source of antioxidants. Cocoa flavanols show antioxidative effects and help protect the cells against oxidative stress & help protect from radicals. Target group: All adults aged 18 years and over.	Exact wording of claim as it appears on product: Cocoa beans naturally contain polyphenols. Cocoa polyphenols are known for their antioxidant properties. Examples of any alternative wording that may be used in relation to claim: Cocoa flavonols show antioxidative effects and help protect the cells against oxidative stress, help protect you from radicals which cause cell damage, help strengthen our body's natural defences against oxidative stress. Description of picture: A cocoa bean.
			Conditions of use - Quantity in Average daily serving: 188 mg cocoa flavonols. Weight of average daily food serving: 30 gram(s). Daily amount to be consumed to produce claimed effect: 60 gram(s). Number of food portions this equates to in everyday food portions: 2. Length of time after consumption for claimed effect to become apparent: There are short-term and long-term effects. Is there a limit to the amount of food which should be consumed in order to avoid adverse health effects: Yes. State the maximum limit in mg/kg body weight/day: 30.00. Potential adverse health effects: There is no adverse effect expected regarding antioxidant intake with this product in amounts which can be reasonably consumed; however, for a snack product, such as chocolate, which delivers energy, fat and sugar as well, an average daily serving would be 30 grams per day. Other conditions for use: Antioxidant is a term used to describe a large family of many different compounds with antioxidative properties, which are naturally present in foods. Flavonols are the most important antioxidants in cocoa.

ID	Food or Food constituent	Health Relationship	Proposed wording
1506	Cocoa flavanols.	Antioxidative properties.	<ul style="list-style-type: none"> - helps protect you from free radicals; - helps promote healthy cells by minimising free radicals; - helps to promote healthy cells by neutralising free radicals. - antioxidant(s).
	Conditions of use <ul style="list-style-type: none"> - At least 168 mg per day 		
ID	Food or Food constituent	Health Relationship	Proposed wording
1507	Cocoa flavanols.	Vascular health.	Maintenance and promotion of a normal blood pressure.
	Conditions of use <ul style="list-style-type: none"> - At least 88 mg of cocoa flavonols per day - At least 168 mg per day 		
ID	Food or Food constituent	Health Relationship	Proposed wording
3143	Polyphenols.	Antioxidant properties.	Polyphenols are antioxidants, which naturally occur in cocoa and therefore in dark chocolate. They help to protect our body cells against free radicals.
	Conditions of use <ul style="list-style-type: none"> - Min. 30 % of intakes per day (Intakes are 3000 to 5000 ORAC unit per day) 		

GLOSSARY AND ABBREVIATIONS

BMI	Body mass index
DNA	Deoxyribonucleic acid
ELISA	Enzyme-Linked ImmunoSorbent Assay
HDL	High-density lipoprotein
LDL	Low-density lipoprotein
MDA	Malondialdehyde
ORAC	Oxygen Radical Absorbance Capacity
RCT	Randomised controlled trial
ROS	Reactive oxygen species
TBARS	Thiobarbituric acid reactive substances