SCIENTIFIC OPINION

Scientific Opinion on the substantiation of health claims related to isoleucine-proline-proline (IPP) and valine-proline-proline (VPP) and maintenance of normal blood pressure (ID 615, 661, 1831, 1832, 2891), and maintenance of the elastic properties of the arteries (ID 1832) pursuant to Article 13(1) of Regulation (EC) No 1924/2006[1]

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

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 1924/2006. This opinion addresses the scientific substantiation of health claims in relation to the tripeptides isoleucine-proline-proline (IPP) and valine-proline-proline (VPP) and the following claimed effects: maintenance of blood pressure and maintenance of the elastic properties of the arteries. 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 Panel assumes that the food constituent that is the subject of the health claims is the tripeptides isoleucine-proline-proline (IPP) and valine-proline-proline (VPP), which can be measured in foods by established methods. The Panel considers that the food constituent, tripeptides IPP and VPP, which is the subject of the health claims is sufficiently characterised.

Maintenance of normal blood pressure (ID 615, 661, 1831, 1832, 2861)

The claimed effects are "blood pressure", "cardiovascular system" and "ACE inhibitor". The Panel assumes that the target population is the general population. In the context of the proposed wordings, the Panel notes that the claimed effect relates to the maintenance of a normal blood pressure. The Panel considers that maintenance of a normal blood pressure is beneficial to human health.

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1 On request from the European Commission, Question No EFSA-Q-2008-1402, EFSA-Q-2008-1448, EFSA-Q-2008-2564, EFSA-Q-2008-2565, EFSA-Q-2008-3624 adopted on 02 July 2009.

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In weighing the evidence, the Panel took into account that, although some small studies have observed a significant decrease in systolic blood pressure with the administration of lactotripeptides at doses around 5mg/d in untreated pre-hypertensive or moderately hypertensive subjects, these results have not been supported by large intervention trials providing daily doses of lactotripeptides in the range of 2.7 mg to 14 mg in either normotensive or untreated hypertensive subjects.

On the basis of the data available, the Panel concludes that the evidence presented is insufficient to establish a cause and effect relationship between the consumption of the tripeptides VPP and IPP and the maintenance of normal blood pressure.

Maintenance of the elastic properties of the arteries (ID 1832)

The claimed effect is "cardiovascular system". The Panel assumes that the target population is the general population. In the context of the proposed wordings, the Panel notes that the claimed effect relates to the maintenance of the elastic properties of the arteries. The Panel considers that the maintenance of the elastic properties of the arteries is beneficial to human health.

Only one scientific reference has been cited reporting the effects of the tripeptides IPP and VPP on measures of arterial stiffness in humans. The study did not use a generally accepted method for the assessment of arterial stiffness, differences in changes between the intervention and the control groups were not reported, and the study was not sufficiently controlled for confounders.

On the basis of the data available, the Panel concludes that a cause and effect relationship has not been established between the consumption of the tripeptides VPP and IPP and the maintenance of the elastic properties of the arteries .

KEY WORDS

Tripeptides, isoleucine-proline-proline (IPP) and valine-proline-proline (VPP), blood pressure, arteries, health claims.

TABLE OF CONTENTS

BACKGROUND AS PROVIDED BY THE EUROPEAN COMMISSION

See Appendix A

TERMS OF REFERENCE AS PROVIDED BY THE EUROPEAN COMMISSION

See Appendix A

EFSA DISCLAIMER

See Appendix B

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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.

INFORMATION AS PROVIDED IN THE CONSOLIDATED LIST

The consolidated list of health claims pursuant to Article 13 of Regulation (EC) No 1924/2006[3] submitted by Member States contains main entry claims with corresponding conditions of use and literature from similar health claims. The information provided in the consolidated list for the health claims subject to 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 "special hydrolysed milk proteins", "lactotripeptides", "milk products fermented with *L. Helveticus* lactic acid bacteria", "the peptides isoleucine-proline-proline (IPP) and valine-proline-proline (VPP)".

The information provided on "special hydrolysed milk proteins", "lactotripeptides" and "milk products fermented with *L. Helveticus* lactic acid bacteria" is insufficient to allow a full characterisation of these foods or food constituents.

The Panel assumes that the food constituent for which the claims are made is the tripeptides isoleucine-proline-proline (IPP) and valine-proline-proline (VPP), which can be obtained through the fermentation of milk by certain lactic acid bacteria, by enzymatic hydrolysis of casein or by chemical synthesis. All clinical studies presented have been conducted with either directly fermented milk, with powdered fermented milk, or with powdered enzymatically hydrolysed tripeptides. IPP and VPP can be measured in foods by established methods. Bioavailability of intact IPP has been demonstrated in animals and humans (Jauhiainen et al., 2007a; Foltz et al., 2007).

The Panel considers that the food constituent, tripeptides IPP and VPP, which is the subject of the health claims, is sufficiently characterised.

2. Relevance of the claimed effect to human health

2.1. Maintenance of normal blood pressure (ID 615, 661, 1831, 1832, 2891)

The claimed effects are "blood pressure", "cardiovascular system" and "ACE inhibitor". The Panel assumes that the target population is the general population.

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

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

The Panel considers that maintenance of normal blood pressure is beneficial to human health.

[3] 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.

2.2. Maintenance of the elastic properties of the arteries (ID 1832)

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

In the context of the proposed wordings, the Panel notes that the claimed effect relates to the maintenance of the elastic properties of the arteries.

The Panel considers that the maintenance of the elastic properties of the arteries is beneficial to human health.

3. Scientific substantiation of the claimed effect

3.1. Maintenance of normal blood pressure (ID 615, 661, 1831, 1832, 2891)

A total of 70 different references were provided to substantiate this claimed effect. Human intervention studies either conducted in hypertensive subjects on pharmacological treatment for hypertension, reporting clinical outcomes other than BP, or not reporting the daily dose of IPP and VPP used in the intervention were not considered as pertinent to substantiate the claimed effect.

Most of the human intervention studies provided investigated the effects of known doses of IPP and VPP on BP in normotensive, pre-hypertensive or untreated hypertensive subjects were reviewed in a meta-analysis of randomised controlled trials (RCTs) published in 2008 (Xu et al., 2008). This meta-analysis included all RCTs published between 1996 and 2005. The total number of subjects in these studies was 623 (316 in the intervention groups and 307 in the control groups). The authors identified nine publications in which VPP (ranging from 1.5 to 3.3mg/d) and IPP (ranging from 1.1. to 2.5 mg/day) were administered for 4 weeks or longer (Aihara et al., 2005; Jauhiainen et al., 2005; Mizuno et al., 2005; Sano et al., 2005; Mizushima et al., 2004; Tuomilehto et al., 2004; Seppo et al., 2002; Seppo et al., 2003; Hata et al., 1996). The Panel notes that, in the original publication by Jauhiainen et al. (2005), the reported daily doses of IPP and VPP were 22.5mg and 30mg, respectively.

In the studies by Aihara et al. (2005) and Mizuno et al. (2005), subjects with pre-hypertension and subjects with hypertension were randomised and analysed separately and these two populations were included as separate studies in the meta-analysis. Also, the two phases of the cross-over intervention by Tuomilehto et al. (2004) were included as independent studies. The Panel notes that, in phase II of this cross-over study, subjects were the same as in phase I and therefore cannot be analysed independently. Also, baseline BP values at the beginning of phase II were not comparable between intervention and control groups, so that the randomisation in phase I did not hold for the second part of the study.

Out of the 12 interventions considered in the meta-analysis, 6 were conducted in Japan and 5 in Finland. The overall pooled estimate of the effects of IPP and VPP consumption on systolic BP (SBP) was a significant change of -4.8 mmHg (95% confidence interval -6.0 to -3.7) and for diastolic BP (DBP) a significant change of -2.2 mmHg (95% confidence interval -3.1 to -1.3). No linear relationship was observed between the amount of tripeptides consumed and the decrease in BP.

Six additional RCTs have been published (not included in the meta-analysis above) on the effects of IPP and VPP on BP in humans (Hirota et al., 2007; van der Zander et al., 2008a and 2008b; Engberink et al., 2008; de Leeuw et al., 2009; van Mierlo et al., 2009).

In the placebo-controlled, double-blind crossover study by Hirota et al. (2007) conducted on 25 male adults with mild hypertension, the consumption of 3.42 mg of VPP and of 3.87 mg of IPP daily for 1 week did not lead to any significant changes in BP compared to placebo. The Panel acknowledges the

short duration of the study, which was originally designed to test the effects of VPP and IPP intake on endothelial function (primary outcome).

In a double-blind, randomised crossover design, 42 participants consumed for 4 weeks a fermented IPP (15.9mg/d) and VPP (18.7mg/d)-containing product or a placebo product, with a 4-week washout period in between (van der Zander et al., 2008a). Sample size was calculated with SBP as primary outcome. When all subjects were considered together, no differences between the active and the placebo interventions were observed either at the beginning or at the end of the study. In a post hoc subgroup analysis, treatment with IPP and VPP-containing milk showed significant decreases in both SBP and DBP in participants with SBP>130mmHg at the start of the study, but no differences were observed in those with SBP≤130mmHg. The Panel notes that no interaction analysis between SBP values at baseline and SBP changes during the intervention was performed to justify such post hoc analysis, and that the number of subjects with SBP>130mmHg (and with SBP≤130mmHg) has not been reported. No changes were observed in plasma concentrations of angiontensin I, angiotensin II, ACE activity or active plasma renin concentrations.

In a double-blind, parallel, placebo-controlled trial, 135 Dutch subjects with elevated SBP randomly received a daily dose of 200 mL dairy drink with 14 mg IPP+VPP (obtained by either concentrating fermented milk, by enzymatic hydrolysis, or by chemical synthesis) or placebo for 8 weeks (Engberink et al., 2008). The primary outcome was 8-week change in office SBP. Secondary outcomes were changes in DBP, home BP, 24-hour ambulatory BP, plasma ACE-activity, and plasma angiotensin II. Consumption of IPP and VPP did not affect SBP or DBP compared with placebo, regardless of the method by which IPP and VPP were obtained. Consumption of IPP and VPP also did not have a significant effect on secondary outcome measures.

In a multicentre, double-blind, parallel, placebo-controlled trial, 275 hypertensive subjects were randomised to consume either a yogurt beverage providing 5.8 mg IPP and 4.4 mg VPP daily (10.2mg/d in total) or a control yogurt for 8 weeks (van der Zander et al., 2008b). BP and body weight were measured on several days at baseline and at weeks 4 and 8 of the intervention between 2.5 and 3 h after intake of the test product. No significant changes in SBP or DBP were observed with the consumption of the test food as compared to placebo.

An additional publication reports the results of two multicentre, placebo-controlled, randomised, crossover studies, each consisting of two 4-week intervention periods separated by a 4-week washout period (van Mierlo et al., 2009). In study 1, 69 subjects received 200 g/d of a dairy drink with 5.8 mg IPP and 4.4 mg VPP (10.2mg/d in total) or placebo. In study 2, 93 subjects received either 100 g/d of a dairy drink containing 2.7 mg IPP, 1.9 mg VPP, and 350 mg added potassium or placebo. Subjects had high normal or grade I hypertension and were randomly assigned to the order of the intervention according to their daytime ambulatory BP. No significant differences between treatments in either study were observed for mean 24-h SBP or DBP. Office BP decreased over the course of both studies, but differences between intervention groups and placebo were not significant. In both studies, night-time BP dipped during all treatments but was statistically more significant with placebo.

Finally, in a randomised, double-blind, parallel-group, dose-response intervention, 166 subjects with diagnosis of hypertension received either a milk product containing IPP and VPP (1.13 mg and 1.17 mg in the low-dose product, 2.30 mg and 2.26 mg in the medium dose product, and 4.56 mg and 4.47 mg in the high dose product, corresponding to total daily doses of tripeptides of 2.3 mg, 4.6 mg and 9 mg, respectively) or placebo for 8 weeks. Results indicated that test products containing IPP and VPP lowered DPB (but not SBP) dose-dependently. When the results over 8 weeks were corrected for the placebo response, neither SBP not DBP changed significantly in either intervention group. The percentages of subjects who showed a fall in SBP >3 mmHg or who attained an SBP below 140 mmHg were 54% (placebo), 64% (low), 76% (medium) and 71% (high dose) respectively, with a significant p-per-trend across groups. This effect could only be demonstrated for office BP and

not for home or ambulatory BP. Results also suggested that the magnitude of the fall in BP was a function of baseline BP (de Leeuw et al., 2009).

The Panel notes that, although some small studies have observed a significant decrease in SBP with the administration of lactotripeptides at doses around 5mg/d in untreated pre-hypertensive or moderately hypertensive subjects, these results have not been supported by large intervention trials providing daily doses of lactotripeptides in the range of 2.7 mg to 14 mg in either normotensive or untreated hypertensive subjects.

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

3.2. Maintenance of the elastic properties of the arteries (ID 1832)

11 references have been cited to substantiate the claim, but only one published reference was related to the effects of the tripeptides IPP and VPP on measures of arterial stiffness (Jauhiainen et al., 2007b).

In that intervention study, 94 (60 women) hypertensive volunteers not on antihypertensive medication were randomised to consume either 150mL of milk containing the milk tripeptides Ile-Pro-Pro and Val-Pro-Pro or 150mL or a control milk twice daily for 10 weeks with a double-blind design. Daily doses of tripeptides in the intervention group were 52.5mg, about 10 times higher than the daily doses proposed in the conditions of use. 24-h ambulatory BP monitoring (24-h ABPM) using an automatic BP recorder was assessed at the beginning and end of the study. Arterial stiffness was calculated as ambulatory arterial stiffness index (AASI) from 24-h ABPM measurements. Changes in BP were the primary outcome of the study. At the end of the 10-wk intervention period, AASI decreased significantly from baseline in the intervention group but not in the placebo group. Differences in AASI changes between the intervention and control groups were not reported.

The Panel notes a number of weaknesses in this study: AASI is not a generally accepted method for the assessment of arterial stiffness (Laurent et al., 2006; Hamilton et al., 2007), differences in AASI changes between the intervention and the control groups were not reported, and the study was not sufficiently controlled for confounders that could potentially have affected the outcome (e.g., background diet and physical activity).

The Panel concludes that a cause and effect relationship has not been established between the consumption of the tripeptides VPP and IPP and the maintenance of the elastic properties of the arteries.

CONCLUSIONS

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

- The food constituent, tripeptides IPP and VPP, which is the subject of the health claims is sufficiently characterised.

Maintenance of a normal blood pressure (ID 615, 661, 1831, 1832, 2861)

- The claimed effects are “blood pressure”, “cardiovascular system” and “ACE inhibitor”. The target population is the general population. Maintaining a normal blood pressure is beneficial to human health.

- The evidence presented is not sufficient to establish a cause and effect relationship between the consumption of the tripeptides VPP and IPP and the maintenance of normal blood pressure.

Maintenance of the elastic properties of the arteries (ID 1832)

- The claimed effect is "cardiovascular system". The target population is the general population. The maintenance of the elastic properties of the arteries is beneficial to human health.

- A cause and effect relationship has not been established between the consumption of the tripeptides VPP and IPP and the maintenance of the elastic properties of the arteries.

DOCUMENTATION PROVIDED TO EFSA

Health claims pursuant to Article 13 of Regulation (EC) No 1924/2006 (No: EFSA-Q-2008-1402, EFSA-Q-2008-1448, EFSA-Q-2008-2564, EFSA-Q-2008-2565, EFSA-Q-2008-3624). The scientific substantiation is based on the information provided by the Members States in the consolidated list of Article 13 health claims and references that EFSA has received from Member States or directly from stakeholders.

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

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APPENDICES

APPENDIX A

BACKGROUND AND TERMS OF REFERENCE AS PROVIDED BY THE EUROPEAN COMMISSION

The Regulation 1924/2006 on nutrition and health claims made on foods[4] (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[5]

Foods are commonly involved in many different functions[6] 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.

[4] OJ L12, 18/01/2007
[5] The term 'food' when used in this Terms of Reference refers to a food constituent, the food or the food category.
[6] 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 DISCAIMER

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

ID	Food or Food constituent	Health Relationship	Proposed wording
615	Special hydrolysed milk proteins	ACE inhibitor	- good for your blood pressure - supports a healthy blood pressure - helps maintain a healthy blood pressure - helps maintain a normal blood pressure
	Conditions of use - 1,7 g per day, max 3,4 g per day		
661	**Food or Food constituent**	**Health Relationship**	**Proposed wording**
	Lactotripeptides	Blood pressure	Can help to maintain a healthy blood pressure/can contribute to a healthy blood pressure
	Conditions of use - Minimum 3 mg/day - Peptide aus der Milch		
1831	**Food or Food constituent**	**Health Relationship**	**Proposed wording**
	Peptides (milk products fermented with L. Helveticus lactic acid bacteria)	Cardiovascular system	Helps/help to control blood pressure
	Conditions of use - Milk drink fermented with L. Helveticus lactic acid bacteria and containing 2.5-5mg/100g, 5mg/serving of valine-proline-proline (VPP) and isoleucine-proline-proline (IPP).According to the respondent, there are no factors that could weaken absorption of peptides or their usefulness because the study showed that IPP is absorbed (Jauhiainen et al. 2007). There are also references to peptide absorption in earlier studies (Masuda et al. 1996)		

	Food or Food constituent	Health Relationship	Proposed wording
1832	Peptides (isoleucine-proline-proline, IPP + valine-proline-proline, VPP)	Cardiovascular system	Peptides help to control blood pressure / Bioactive peptides help to control blood pressure. Peptides help to control blood pressure and reduce arterial stiffness. / Bioactive peptides help to control blood pressure and help to reduce arterial stiffness. Helps to control blood pressure. Helps to improve arterial elasticity / Reduces arterial stiffness. Has a positive effect on arterial function.
	Conditions of use - Butter milk and yoghurt with a peptide (isoleucine-proline-proline , IPP + valine-proline-proline, VPP content of 1.7 g /100 g, 5 g /300 g of butter milk or 200 g of yoghurt = serving. In an absorption study, the IPP peptide was found to be absorbed in an experimental model (Jauhiainen et al. 2007) and in people (Foltz et al. 2007).		
	Food or Food constituent	**Health Relationship**	**Proposed wording**
2891	Lactotripeptides	Blood pressure	Helps to maintain a healthy blood pressure/contributes to a healthy blood pressure/helps to keep/control blood pressure at healthy levels/Helps to control blood pressure
	Conditions of use No conditions of use provided.		

GLOSSARY AND ABBREVIATIONS

AASI	ambulatory arterial stiffness index
ABPM	ambulatory blood pressure monitoring
BP	blood pressare
DBP	diastolic blood pressure
IPP	isoleucine-proline-proline
RCT	randomised controlled trial
SBP	systolic blood pressure
VPP	valine-proline-proline