SCIENTIFIC OPINION

Scientific Opinion on the substantiation of health claims related to phosphatidyl serine (ID 552, 711, 734, 1632, 1927) 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 related to phosphatidyl serine. 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 phosphatidyl serine related to the following claimed effects: "memory and cognitive functioning in the elderly", "mental health/cognitive function" and "stress reduction and enhanced memory function". Nutritional phosphatidyl serine supplements can be derived from either animal or plant sources. The animal and plant sourced phosphatidyl serine differ in fatty acid composition. Bovine brain cortex- and soy-based phosphatidyl serine are different substances and might, therefore, have different biological activities. Thus, there is considerable uncertainty in generalising results from studies done with bovine brain cortex phosphatidyl serine as the test substance to soy-based phosphatidyl serine, and vice versa. The information in the consolidated list and the references provided do not allow the Panel to characterise the food constituent, phosphatidyl serine, that is the subject of the health claims. The Panel considers that phosphatidyl serine is not sufficiently characterised.

The Panel concludes that a cause and effect relationship cannot be established between the consumption of phosphatidyl serine and the claimed effects considered in this opinion.

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[1] On request from the European Commission, Question No EFSA-Q-2008-1339, EFSA-Q-2008-1498, EFSA-Q-2008-1521, EFSA-Q-2008-2368, EFSA-Q-2008-2660, adopted on 09 July 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 Mental/Nervous System: Jacques Rigo, Astrid Schloerscheidt, Barbara Stewart-Knox, Sean (J.J.) Strain, and Peter Willatts.

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KEY WORDS

Phosphatidyl serine, health claims.

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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

The approach used in the evaluation of Article 13(1) health claims is explained in the briefing document for stakeholders published by EFSA[6].

In assessing each specific food/health relationship that forms the basis of a health claim the NDA Panel considers the extent to which:

1. the food/constituent is defined and characterised;

2. the claimed effect is defined and is a beneficial physiological effect ("beneficial to human health");

3. a cause and effect relationship is established between the consumption of the food/constituent and the claimed effect (for the target group under the proposed conditions of use).

Substantiation of the claim is dependent on a favourable outcome of the assessment of 1, 2 and 3 above. Thus, a cause and effect relationship is considered not to be established if the outcome of any one of these assessments is unfavourable.

For a claim, each relationship between a food/constituent and a claimed effect is assessed separately and individual assessments are combined, as appropriate, to form coherent opinions.

Characterisation of the food/constituent (ID 552, 711, 734, 1632, 1927)

The food constituent that is the subject of this opinion is phosphatidyl serine related to the following claimed effects: "memory and cognitive functioning in the elderly", "mental health/cognitive function" and "stress reduction and enhanced memory function". Phosphatidyl serine is a phospholipid present in large quantities in the brains of animals. Dietary phosphatidyl serine supplements, however, can be derived from either animal or plant sources. The bovine brain cortex phosphatidyl serine is extracted from bovine cerebral tissue and purified (Calderini et al., 1985). The soy-based phosphatidyl serine is derived from soy lecithin that has been treated with serine and an enzyme to convert the phospholipids contained in soy to phosphatidyl serine (Sakai et al., 1996). The resulting phosphatidyl serine molecule comprises serine and two fatty acids. The animal and plant

[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] See footnote 5

sourced phosphatidyl serine differ in fatty acid composition. For example, the phosphatidyl serine from soy contains 7 % alpha-linolenic acid (n-3) and 47 % linoleic acid (n-6), while the phosphatidyl serine derived from bovine brain cortex contains mostly saturated and monounsaturated fatty acids besides 8 % docosahexaenoic acid (n-3) and 2 % arachidonic acid (n-6) (FDA, 2003).

Bovine brain cortex- and soy-based phosphatidyl serine are different substances and might, therefore, have different biological activities. Thus, there is considerable uncertainty in generalising results from studies done with bovine brain cortex phosphatidyl serine as the test substance to soy-based phosphatidyl serine, and vice versa (FDA, 2003).

The references provided do not allow the Panel to characterise the food constituent, phosphatidyl serine, that is the subject of the health claims. The Panel notes that the source of phosphatidyl serine has not been defined in the conditions of use for IDs 711, 734. In ID 552 and ID 1632, the Panel notes that the phosphatidyl serine in the conditions of use is given as a soy phosphatidyl serine extract which is part of a food bar containing other substances including vitamins. In ID 1632, the Panel notes that although the phosphatidyl serine source is identified as soy, it is in the form of a combination of phospholipids. In ID 1937, the Panel notes that the phosphatidyl serine is derived from a milk protein concentrate as part of a product containing other substances, including other phospholipids.

The Panel considers that the food constituent, phosphatidyl serine, which is the subject of this opinion is not sufficiently characterised in relation to the claimed effects considered in this opinion.

The Panel concludes that a cause and effect relationship cannot be established between the consumption of phosphatidyl serine and the claimed effects considered in this opinion.

CONCLUSIONS

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

- The constituent, phosphatidyl serine, which is the subject of this opinion, is not sufficiently characterised in relation to the claimed effects considered in this opinion.
- A cause and effect relationship cannot be established between the consumption of phosphatidyl serine and the claimed effects considered in this opinion.

DOCUMENTATION PROVIDED TO EFSA

Health claims pursuant to Article 13 of Regulation (EC) No 1924/2006 (No: EFSA-Q-2008-1339, EFSA-Q-2008-1498, EFSA-Q-2008-1521, EFSA-Q-2008-2368, EFSA-Q-2008-2660). 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

Calderini G, Aporti F, Bonetti AC, Zanotti A and Toffano G, 1985. Serine Phospholipids and Aging Brain. Progress in Clinical Biological Research, 192, 383-386.

Sakai M, Yamatoya H and Kudo S, 1996. Pharmacological effects of phosphatidylserine enzymatically synthesized from soybean lecithin on brain functions in rodents. Journal of Nutritional Science and Vitaminology, 42, 47-54.

FDA (Food and Drug Administration), 2003. Phosphatidylserine and Cognitive Dysfunction and Dementia (Qualified Health Claim: Final Decision Letter. Available from http://vm.cfsan.fda.gov/~dms/ds-ltr36.html.

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

ID	Food or Food constituent	Health Relationship	Proposed wording
552	Phosphatidyl serine	Memory and cognitive functioning in the elderly	May improve memory in the elderly May improve cognitive performance in the elderly. May improve memory and cognitive performance in the elderly Support of cognitive functions in young people Contributes to the maintenance of cognitive functions with aging Supports memory and brain performance in aging adults Plays an important role in healthy nerve function through the central nervous system including the brain Contributes to the resistance against stress Helps concentration and mental performance in cases of stress
	Conditions of use - Adults - 200 mg/day - 300 mg/day for minimum 6 weeks - 400 mg/day - 300 mg, upper level 400mg - 1000 mg - The product should contain at least 15% of the minimum effective dose, which is 300 mg/day. Thus, products containing =45 mg phosphatidyl-serine per 100 g or 100 mL would qualify to carry the proposed claims. - No adverse effects are associated with phosphatidyl-serine - Riegel - angereichert mit einem phosphatidxlserinhaltigen Sojalecithinextrakt und Vitaminen, 3 riegel pro woche - SUPER GEHIRN FORMEL: PS 150 mg;PC 150 mg; Acetyl-Lcarnitin 500 mg		
ID	**Food or Food constituent**	**Health Relationship**	**Proposed wording**
711	Phosphatidyl serine	Memory and cognitive functioning in the elderly	May improve memory in the elderly May improve cognitive performance in the elderly

			May improve memory and cognitive performance in the elderly PS is a naturally occurring phospholipid (lecithin) present in all cells. It is most concentrated in the brain where it plays a role in healthy brain functions PS is essential to the functioning of all cells of the body, but is most concentrated in the brain and can help maintain healthy brain function PS is a food ingredient intended to support brain function
	Conditions of use - Vor allem in Kombination mit anderen Aminosäuren wie z.B. Glutamin sowie den Vitaminen B12, B1, B2 und B6		
ID	**Food or Food constituent**	**Health Relationship**	**Proposed wording**
734	Phosphatidyl serine	Mental health / Cognitive function	Support of cognitive functions in young people Contributes to the maintenance of cognitive functions with aging Supports memory and brain performance in aging adults Plays an important role in healthy nerve function through the central nervous system including the brain Contributes to the resistance against stress Helps concentration and mental performance in cases of stress.
	Conditions of use - 300-400 mg per day		
ID	**Food or Food constituent**	**Health Relationship**	**Proposed wording**
1632	Phosphatidyl serine	Mental health / Cognitive function	Support of cognitive functions in young people Contributes to the maintenance of cognitive functions with aging Supports memory and brain performance in aging adults
	Conditions of use - Adults - 200-400 mg/day - Food supplement with 100-300mg of phophatidylserine in the daily dose		

	- 150mg Phospatidylserin je Portion (330ml Jogurt-Buttermilch bzw. 150g Jogurt) 300mg Phospatidylsein / Tag–(= 1 Packung Jogurt-Buttermilch bzw. 2 Packungen Jogurt - Riegel - angereichert mit einem phosphatidxlserinhaltigen Sojalecithinextrakt und Vitaminen / 3 Riegel pro Woche - 417 - 834 mg of phospholipids from soy containing 100 - 200 mg of phosphatidyl serine - SUPER GEHIRN FORMEL: PS 150 mg; PC 150 mg; Acetyl-Lcarnitin 500 mg - Upper level 400 mg		
ID	**Food or Food constituent**	**Health Relationship**	**Proposed wording**
1927	Lacprodan PL-20; Milk protein concentrate with a high content of phospholipids. (Effective component: Phosphatidyl serine)	Stress reduction and enhanced memory function	Reduce mental and emotional stress and enhance memory
	Conditions of use - 13.5 g Lacprodan PL-20 pr day for three weeks (~310 mg phosphatidyl serine pr day) - 200-600 mg phosphatidyl serine pr day for 30-60 days		