European Food Safety Authority

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SCIENTIFIC OPINION

ALA and contribution to brain development

Scientific substantiation of a health claim related to ALA and contribution to brain development pursuant to Article 14 of Regulation (EC) No 1924/2006[1]

Scientific Opinion of the Panel on Dietetic Products, Nutrition and Allergies

(Question No EFSA-Q-2008-666)

Adopted on 13 March 2009

PANEL MEMBERS[*]

Jean-Louis Bresson, Albert Flynn*, Marina Heinonen, Karin Hulshof, Hannu Korhonen, Pagona Lagiou, Martinus Løvik, Rosangela Marchelli, Ambroise Martin, Bevan Moseley, Hildegard Przyrembel, Seppo Salminen, Sean (J.J.) Strain, Stephan Strobel, Inge Tetens, Henk van den Berg, Hendrik van Loveren and Hans Verhagen.

SUMMARY

Following an application from Kraft Biscuits Europe R&D submitted pursuant to Article 14 of Regulation (EC) No 1924/2006 via the Competent Authority of Belgium, the Panel on Dietetic Products, Nutrition and Allergies was asked to deliver an opinion on the scientific substantiation of a health claim related to ALA and contribution to brain development.

The scope of the application was proposed to fall under a health claim referring to children's development and health.

The food constituent that is the subject of the health claim is alpha-linolenic acid (ALA), a well recognised nutrient that is measurable in foods by established methods. This fatty acid is well absorbed when consumed in the form of triglycerides. Sufficient information is provided on the stability of ALA in processed foods. This evaluation will apply to all appropriate sources of ALA in the specified amounts. The panel considers that ALA is sufficiently characterised.

[1] For citation purposes: Scientific Opinion of the Panel on Dietetic Products, Nutrition and Allergies on a request from Kraft Biscuits Europe R&D on ALA and contribution to brain development. *The EFSA Journal* (2009) 1005, 1-9

[*] One member of the Panel did not participate in the discussion on the subject referred to above because of possible conflicts of interest.

The claimed effect is that ALA contributes to brain development and the target population is children aged 3 to 6 years. The Panel considers that normal brain development is beneficial for the development of children.

A total of one human study and 20 non-human studies were identified and considered as pertinent by the applicant.

The human study was a case report of ALA deficiency in a 6 year old girl maintained on total parenteral nutrition (TPN) containing safflower oil (devoid of ALA but with a very high content of linoleic acid) for five months. The girl developed neurological and visual problems: episodes of numbness, paresthesia, weakness, inability to walk, pain in the legs, blurring of vision. After switching to another TPN preparation containing soybean oil (adequate in both ALA and linoleic acid), the neurological symptoms disappeared in a few months. The panel notes that this study does not provide any information on a dose-response relationship between ALA intake and brain development. The Panel also notes that no dietary epidemiological or intervention studies involving ALA were presented to substantiate the claimed effect.

Those non-human studies that the applicant identified as being pertinent to the claimed effect were concerned primarily with brain fatty acid synthesis, content and structural effects in the brain of rhesus monkeys and rats. The Panel considers that these data are sufficient to establish that ALA is a precursor of docosahexaenoic acid (DHA), the major fatty acid in mammalian brain. The Panel notes that no data are provided on the efficacy of conversion of dietary ALA to DHA and on the relative importance of dietary ALA (compared with other n-3 fatty acid sources) as a precursor of DHA in the target population.

On the basis of the data presented, the Panel concludes that a cause and effect relationship has been established between ALA and "contribution to brain development". However, dietary deficiency of ALA leading to impaired brain development has never been demonstrated in human populations.

The wording "alpha-linolenic acid contributes to brain development" reflects the scientific evidence.

The Panel considers that the evidence provided does not establish a benefit for brain development in children of ALA intake greater than about 0.2% of total energy. This quantity is consumed as part of a balanced diet.

Key words: ALA, brain development, children

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BACKGROUND

Regulation (EC) No 1924/2006[2] harmonises the provisions that relate to nutrition and health claims and establishes rules governing the Community authorisation of health claims made on foods. As a rule, health claims are prohibited unless they comply with the general and specific requirements of that Regulation and are authorised in accordance with this Regulation and included in the lists of authorised claims provided for in Articles 13 and 14 thereof. In particular, Articles 14 to 17 of that Regulation lay down provisions for the authorisation and subsequent inclusion of reduction of disease risk claims and claims referring to children's development and health in a Community list of permitted claims.

According to Article 15 of that Regulation, an application for authorisation shall be submitted by the applicant to the national competent authority of a Member State, who will make the application and any supplementary information supplied by the applicant available to European Food Safety Authority (EFSA).

Steps taken by EFSA:

- The application was received on 13/08/2008.
- The scope of the application was proposed to fall under a health claim referring to children's development and health.
- During the check for completeness[3] of the application, the applicant was requested to provide missing information on 25/09/2008.
- The applicant provided the missing information on 02/10/2008.
- The scientific evaluation procedure started on 15/10/2008.
- During the meeting on 13/03/2009 the NDA Panel, after having evaluated the overall data submitted, adopted an opinion on the scientific substantiation of a health claim related to ALA and contribution to brain development.

TERMS OF REFERENCE

EFSA is requested to evaluate the scientific data submitted by the applicant in accordance with Article 16 of Regulation (EC) No 1924/2006. On the basis of that evaluation, EFSA will issue an opinion on the scientific substantiation of a health claim related to: ALA and "contribution to brain development".

EFSA DISCLAIMER

The present opinion does not constitute, and cannot be construed as, an authorisation to the marketing of ALA, a positive assessment of its safety, nor a decision on whether ALA is, or is not, classified as a foodstuff. It should be noted that such an assessment is not foreseen in the framework of Regulation (EC) No 1924/2006.

[2] European Parliament and Council (2006). 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. Official Journal of the European Union OJ L 404, 30.12.2006. Corrigendum OJ L 12, 18.1.2007, p. 3–18.

[3] In accordance with EFSA "Scientific and Technical guidance for the Preparation and Presentation of the Application for Authorisation of a Health Claim".

It should also be highlighted that the scope, the proposed wording of the claim and the conditions of use as proposed by the applicant may be subject to changes pending the outcome of the authorisation procedure foreseen in Article 17 of Regulation (EC) No 1924/2006.

ACKNOWLEDGEMENTS

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1. Information provided by the applicant

Applicant's name and address: Kraft Biscuits Europe R&D, RD128, 91767 Palaiseau Cedex, France

1.1. Food/constituent as stated by the applicant

ALA (alpha-linolenic acid).

1.2. Health relationship as claimed by the applicant

Metabolisation of ALA into constituents of brain membrane that are essential for brain development during the first 6 years of growth of children.

1.3. Wording of the health claim as proposed by the applicant

ALA contributes to the brain development.

1.4. Specific conditions of use as proposed by the applicant

The target population is children from 3 until 6 years old.

Minimum 0.6 g ALA per 100 g or 100 mL or 100 kcal of food. A ratio omega 6/omega 3 < or = 5. Study of the oxidative stability of ALA in food matrix during the shelf-life.

2. Assessment

2.1. Characterisation of the food/constituent

The food constituent, alpha-linolenic acid (ALA), which is the subject of the health claim is a well recognised nutrient that is measurable in foods by established methods. This fatty acid is well absorbed when consumed in the form of triglycerides. Sufficient information is provided on the stability of ALA in processed foods. This evaluation will apply to all appropriate sources of ALA in the specified amounts.

The panel considers that the food constituent, ALA, that is the subject of the claim is sufficiently characterised.

2.2. Relevance of the claimed effect to human health

The claimed effect is "contribution to brain development". The target population is children aged 3 to 6 years old.

The Panel considers that normal brain development is beneficial for the development of children.

2.3. Scientific substantiation of the claimed effect

The applicant searched six databases (Medline [from1950]; Medline In-Process [most recent 8 weeks of MEDLINE]; Embase [from 1974]; Biosis [from 1926]; Pascal [from 1984] and CAB abstracts [from 1990]) using key words of alpha-linolenic acid or derivatives thereof

(but NOT alanine or derivatives thereof) AND children (truncation, toddlers, preschool) AND brain (cerebal, cortex, encephal, cortical or cerebellum) AND deficient/ deprivation/ malnutrition AND erythrocytes/red blood cells. Pertinent publications were selected using the inclusion criteria: studies on children from 1-6 years of ages; ALA is the only acceptable source of omega 3; studies examining the relationship between ALA dietary intakes and brain or erythrocyte DHA content; studies reporting neurological symptoms following an ALA deficiency. Exclusion criteria included studies examining the effect of ALA on behavioural abnormalities etc and studies examining only the effects of ALA on cognitive performance, learning capacity, visual acuity, retinal development, etc.

Only one human study (of a total of 31 publications identified) was considered by the applicant as being pertinent to the claimed effect. Some 20 non-human studies were identified by the applicant using similar search strategies and 8 of the main non-human studies were summarised as being pertinent to support the claimed effect.

The study of Holman *et al*. (1982) was a case report of ALA deficiency in a 6 year old girl maintained on total parenteral nutrition (TPN) containing safflower oil (devoid of ALA but with a very high content of linoleic acid) for five months. The girl developed neurological and visual problems: episodes of numbness, paresthesia, weakness, inability to walk, pain in the legs, blurring of vision. After switching to another TPN preparation containing soybean oil (adequate in both ALA and linoleic acid), the neurological symptoms disappeared in a few months. The panel notes that this study does not provide any information on a dose-response relationship between ALA intake and brain development The Panel also notes that no dietary epidemiological or intervention studies involving ALA were presented to substantiate the claimed effect.

Those non-human feeding studies that the applicant identified as being pertinent to the claimed effect were concerned primarily with brain fatty acid synthesis, content and structural effects in the brain of rhesus monkeys (Neuringer *et al.*, 1986) and rats (Menard *et al*., 1998; Murthy *et al*., 2002; Rapoport *et al.*, 2007; Poumes-Ballihaut *et al.*, 2001; Xiao *et al.*, 2005). The Panel considers that these data are sufficient to establish that ALA is a precursor of docosahexaenoic acid (DHA), the major fatty acid in mammalian brain. In the absence of preformed DHA in the diet, ALA is essential. The Panel notes that no data are provided on the efficacy of conversion of dietary ALA to DHA and on the relative importance of dietary ALA (compared with other n-3 fatty acid sources) as a precursor of DHA in the target population.

The Panel concludes that a cause and effect relationship has been established between ALA and "contribution to brain development". However, dietary deficiency of ALA leading to impaired brain development has never been demonstrated in human populations.

The applicant provided intake data on ALA in European populations that overlap in age with the target population (AFSSA, 2003; Sioen *et al*., 2007). The Panel considers that the evidence provided does not establish that intakes of ALA are inadequate for brain development of children in the EU population.

2.4. Panel's comments on the proposed wording

The Panel considers that the wording "alpha-linolenic acid contributes to brain development" reflects the scientific evidence.

2.5. Panel's comments on the conditions of use

The applicant proposes a minimum of 0.6 g ALA per 100 g or 100 ml or 100 kcal. The Panel considers that the evidence provided does not establish a benefit for brain development in children of an ALA intake greater than about 0.2% of total energy (see also EFSA, 2008). This quantity can be consumed as part of a balanced diet.

CONCLUSIONS

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

- The food constituent (ALA) that is the subject of the claim is sufficiently characterised.
- The claimed effect is "contribution to brain development". The target population is children aged 3 to 6 years old. Normal brain development is beneficial for the development of children.
- A cause and effect relationship has been established between ALA and "contribution to brain development".
- Dietary deficiency of ALA leading to impaired brain development has never been demonstrated in human populations.
- The wording "alpha-linolenic acid contributes to brain development" reflects the scientific evidence.
- The evidence provided does not establish a benefit for brain development in children of ALA intake greater than about 0.2% of total energy. This quantity is consumed as part of a balanced diet.

DOCUMENTATION PROVIDED TO EFSA

Health claim application on ALA and contribution to brain development pursuant to Article 14 of Regulation (EC) No 1924/2006 (Claim serial No: 0214_BE). August 2008. Submitted by Kraft Biscuits Europe R&D.

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GLOSSARY / ABBREVIATIONS

ALA	alpha-linolenic acid
DHA	docosahexaenoic acid
LA	linoleic acid
TPN	total parenteral nutrition