European Food Safety Authority

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SCIENTIFIC OPINION

Animal protein and bone growth

Scientific substantiation of a health claim related to animal protein and bone growth 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-2008-326)

Adopted on 31 October 2008 by written procedure

PANEL MEMBERS

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SUMMARY

Following an application from the Association de la Transformation Laitière Française (ATLA) submitted pursuant to Article 14 of Regulation (EC) No 1924/2006 via the Competent Authority of France, the Panel on Dietetic Products, Nutrition and Allergies was asked to deliver an opinion on the scientific substantiation of a health claim related to proteins of animal origin and bone growth.

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

The health claim relates to food products containing proteins of animal origin. The applicant has proposed that the claim shall apply to all foods providing at least 12% of their energy value as protein. It is not stated whether this minimum value concerns protein of animal origin only. The Panel considers that the constituent (animal protein) which is the subject of the claim is sufficiently characterised.

The claimed effect is "contributes to children's bone growth". The target population is children and adolescents between 3 and 18 years of age. The Panel considers that normal growth and development of bone is beneficial to children's health.

The evidence provided by consensus opinions/reports from authoritative bodies and reviews shows that there is good consensus on the role of protein in growth and development of bone. It

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is well established that a source of protein is essential for allowing both growth and maintenance. Protein requirements of older infants, children and adolescents have recently been re-determined by the factorial method based on estimates of the maintenance requirements and the rates of protein deposition during periods of growth, corrected for interindividual variability and efficiency of utilisation. There is no evidence of benefit of additional protein above the amount found in otherwise nutritionally complete diets. No evidence of inadequate intakes of protein in European children has been provided. Provided that the requirements for total nitrogen and indispensable amino acids are fulfilled, there is no particular need for the consumption of animal protein for normal growth and development of bone.

Seven observational studies have been presented, investigating the relationship between protein consumption and bone mass assessed as bone mineral density (BMD), bone mineral content (BMC) or bone area (BA). Six observational studies in children and adolescents between 6 and 18 years of age show a positive association between dietary protein intake and markers of bone status. While in some of these studies statistical correlations were calculated separately for protein of animal origin, a positive relationship to total protein was more apparent. One observational study in children demonstrates that bone growth and size are negatively affected by protein-calorie malnutrition.

The applicant also presents a non-controlled 7-d intervention in 28 pre-pubertal boys on the effects of a high protein intake on markers of bone formation and bone resorption. This study indicates that high protein intake may have an impact on bone turnover, but does not supply data in support of a specific effect of protein of animal origin compared to protein of plant origin.

On the basis of the data presented, the Panel concludes that a cause and effect relationship has been established between total protein intake and normal growth and development of bone in children. Recommended intakes of protein to meet the requirements for growth and development of children, including normal growth and development of bone, have been established. Adequate intakes of protein can be obtained from various sources, including from animal origin. Provided that the requirements for total nitrogen and indispensable amino acids are fulfilled, there is no particular need for the consumption of animal protein. No evidence of inadequate intakes of protein in European children has been provided.

Key words: protein, animal origin, plant origin, growth, bone growth, bone mineral density, bone mineral content

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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 06/05/2008.
- The scope of the application was proposed to fall under claims 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 19/05/2008.
- The applicant provided the missing information on 20/06/2008.
- The scientific evaluation procedure started on 15/07/2008.
- On 31/10/2008 the NDA Panel, after having evaluated the overall data submitted, adopted by written procedure an opinion on the scientific substantiation of a health claim related to proteins of animal origin and bone growth.

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: proteins of animal origin and bone growth.

EFSA DISCLAIMER

The present opinion does not constitute, and cannot be construed as, an authorisation to the marketing of proteins of animal origin, a positive assessment of their safety, nor a decision on whether proteins of animal origin are, or are 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 and the proposed wording of the claim as considered by the EFSA in this opinion 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: Association de la Transformation Laitière Française (ATLA), 42 rue de Châteaudun, 75314 Paris Cedex 09, France.

1.1. Food/constituent as stated by the applicant

The health claim relates to food products containing proteins of animal origin.

1.2. Health relationship as claimed by the applicant

Children need a steady dietary intake of protein to ensure healthy bone growth. Indeed, proteins are used to form the scaffold upon which the bone matrix is built and represent approximately one third of a bone's mass. During childhood the growth process is highly active: as such, proteins are essential to bone growth and development during both childhood and adolescence.

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

Proteins of animal origin contribute to children's bone growth.

1.4 Specific conditions of use as proposed by the applicant

The target population for the products bearing this health claim is children aged 3 to18 years old. The food products bearing this health claim should contain the following minimum quantity to be considered as "source of protein" i.e.: 12% of the energy value of the food product, for protein, as specified in the Annex of the Regulation (EC) Nº 1924/2006.

2. Assessment

2.1. Characterisation of the food/constituent

The health claim relates to food products containing proteins of animal origin. The applicant has proposed that the claim shall apply to all foods providing at least 12% of their energy value as protein. It is not stated whether this minimum value concerns protein of animal origin only.

The Panel considers that the constituent (animal protein) which is the subject of the claim is sufficiently characterised.

2.2. Relevance of the claimed effect to human health

The claimed effect is: "contributes to children's bone growth". The target population is children and adolescents between 3 and 18 years of age.

The Panel considers that normal growth and development of bone is beneficial to children's health.

2.3. Scientific substantiation of the claimed effect

The applicant performed a literature search in Medline from 1950 onwards for publications in English using different combinations of the terms child, adolescents, protein, bone, supplement, clinical trial. In addition, the applicant, hand searched for expert reports from authoritative bodies, including FAO/WHO, the Institutes of Medicine or the EU Scientific Committee for Food. Of the 87 publications identified by the search, a total of 26 were considered as pertinent

by the applicant. These include 8 human studies (one intervention study and seven observational studies) and 18 guidelines, consensus opinions or textbook chapters.

The evidence provided by consensus opinions/reports from authoritative bodies and reviews shows that there is good consensus on the role of protein in growth and development of bone. It is well established that a source of protein is essential for allowing both growth and maintenance of bone. In man, normal growth is slow and the dietary requirement to support growth is small in relation to maintenance needs, except at very young ages, e.g. at 1 year of age, protein requirement for deposition is one sixth of the average total requirement, while at 18 years of age it is only 1-3%. Borderline inadequate protein intakes in infants and children are reflected in failure to grow in length or height. Protein requirements of older infants, children and adolescents have recently been re-determined by the factorial method based on estimates of the maintenance requirements and rates of protein deposition during periods of growth, corrected for interindividual variability and efficiency of utilisation (IoM, 2005; WHO, 2007). There is no evidence of benefit of additional protein above the amount found in otherwise nutritionally complete diets (WHO, 2007). No evidence of inadequate intakes of protein in European children has been provided.

Dietary proteins differ in amino acid composition from the composition of body proteins. While proteins of animal origin provide all indispensable amino acids, most proteins of plant origin tend to be deficient in one or more of the indispensable amino acids. A mixture of dietary proteins with different amino acid patterns will usually compensate for the deficiencies in particular amino acids of single protein sources. Provided that the requirements for total nitrogen and indispensable amino acids are fulfilled, there is no particular need for the consumption of animal protein for normal growth and development of bone.

Seven observational studies have been presented investigating the relationship between protein consumption and bone mass assessed as bone mineral density (BMD), bone mineral content (BMC) or bone area (BA).

One short observation describes a diminished thickness in cortical bones in 95 infants and children aged 6 months to 7 years with protein-calorie malnutrition in Guatemala. Nutritional rehabilitation was accompanied by increases in bone length and decreases in cortical thickness (Garn *et al.*, 1964).

A positive relationship between longitudinal intakes (from 2 to 8 years) of energy and protein (among others) assessed by 3-day dietary records and total body BMC was found in 52 eight-year old pre-pubertal children, while only intakes of protein were significantly related to bone mineral density BMD (Bounds *et al.*, 2005). Both BMD and BMC were assessed by dual-energy X-ray absorptiometry (DXA).

In a sample of 105 ten-year old pre-pubertal children which had participated in the Copenhagen cohort study, the influence of dietary factors assessed by 7-day food records on whole body bone measurements (BMC and BA assessed by DXA) was investigated (Hoppe *et al.*, 2000). In bivariate analyses, BMC and BA were strongly correlated with height, weight and with energy intake ($p<0.005$). Size-adjusted BMC was positively associated with calcium intake ($p=0.02$) in multivariate analysis, while size-adjusted BA was positively associated with protein intake ($p=0.003$) and negatively associated with sodium intake ($p=0.048$).

Budek *et al.* (2007a and 2007b) found in two cross-sectional studies in 109 Danish adolescents aged 17.3 ± 0.2 years (63 females) and also in 81 pre-pubertal boys aged 8.1 ± 0.1 years that total protein intake was positively associated with size-adjusted total body BMC, but only milk protein intake and not meat protein intake was found to be positively associated with total body BMC and lumbar spine BMC even after correction for calcium intake. They found a range of associations with various markers for bone turnover which differed according to the nature of

the protein of animal origin and its associated nutrients. Intake of protein from plant origin was assessed but it was not introduced in the regression analyses.

The relationship between physical activity levels and protein intakes on BMC measured at six different sites was assessed in 232 pre-pubertal boys (age 7.4 ± 0.4 years). Bone status parameters were positively associated with physical activity levels and protein intake in multiple regression analysis. When protein intake was higher than the median value (2 g/kg body weight/day), an increase in physical activity was associated with a greater mean BMC Z-score (+0.6, p=0.0005), while at a protein intake below the median level, increased physical activity had no significant effect on the BMC Z-score (Chevalley *et al.*, 2008).

Alexy *et al*. (2005) investigated the relationship between protein intake, dietary potential renal acid load (PRAL) and bone parameters in 229 children aged 6-18 years participating in a longitudinal study cohort (DONALD). Long-term protein intake (mean value 2 g/kg body weight/day in pre-pubertal children and 1.6 and 1.4 g/kg body weight per day in pubertal boys and girls, respectively) was positively associated with periosteal circumference, cortical area, BMC and polar strength strain index (an index for bone stability) of the radius. Dietary PRAL was significantly negatively associated with cortical area and BMC. These associations remained unchanged when growth velocity was introduced into the regression analysis. Overall protein intake and PRAL accounted for 3-6% and 2%, respectively, for the variation in bone indices, while muscle area accounted for 24-36%. A negative influence of protein intake on calcium balance is only of significance when calcium intake is low (Heaney, 2001).

In conclusion, six observational studies in children and adolescents between 6 and 18 years of age show a positive association between dietary protein intake and markers of bone status. While in some of these studies statistical correlations were calculated separately for protein of animal origin (e.g. Budek *et al.*, 2007a), a positive relationship to total protein was more apparent. One observational study in children demonstrates that bone growth and size are negatively affected by protein-calorie malnutrition.

The applicant also presents a non-controlled 7-d intervention in 28 pre-pubertal boys on the effects of a high protein intake on markers of bone formation and bone resorption (Budek *et al.*, 2007c). This study indicates that high protein intake may have an impact on bone turnover, but does not supply data in support of a specific effect of protein of animal origin compared to protein of plant origin. With regard to the mechanisms of action, insulin-like growth factor I has been proposed as a regulator of bone metabolism, a determinant of bone growth and mineral content, and possibly a mediator of the anabolic effects of dietary protein in muscle and bone (Ginty, 2003).

The Panel concludes that a cause and effect relationship has been established between total protein intake and normal growth and development of bone in children. Recommended intakes of protein to meet the requirements for growth and development of children, including normal growth and development of bone, have been established. Adequate intakes of protein can be obtained from various sources, including from animal origin. Provided that the requirements for total nitrogen and indispensable amino acids are fulfilled, there is no particular need for the consumption of animal protein. No evidence of inadequate intakes of protein in European children has been provided.

CONCLUSIONS

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

a) The food constituent which is the subject of the claim (i.e., protein of animal origin) is sufficiently characterised.

b) The claimed effect is: "contributes to children's bone growth". The target population is children and adolescents between 3 and 18 years of age. Normal growth and development of bone is beneficial to children's health.

c) A cause and effect relationship has been established between total protein intake and normal growth and development of bones in children.

d) Recommended intakes of protein to meet the requirements for growth and development of children, including normal growth and development of bone, have been established.

e) Adequate intakes of protein can be obtained from various sources, including from animal origin. Provided that the requirements for total nitrogen and indispensable amino acids are fulfilled, there is no particular need for the consumption of animal protein.

f) No evidence of inadequate intake of protein in European children has been provided.

DOCUMENTATION PROVIDED TO EFSA

Health claim application on animal protein and bone growth pursuant to Article 14 of the Regulation (EC) No 1924/2006 (Claim serial No: 0163_FR). June 2008. Submitted by the Association de la Transformation Laitière Française (ATLA).

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GLOSSARY / ABBREVIATIONS

BA	Bone area
BMC	Bone mineral content
BMD	Bone mineral density
DXA	Dual-energy x-ray absorptiometry
PRAL	Potential renal acid load