EFSA NDA Panel (EFSA Panel on Dietetic Products, Nutrition and Allergies), 2013. Scientific Opinion on the substantiation of a health claim related to vitamin A and contribution to normal development and function of the immune system pursuant to Article 14 of Regulation (EC) No 1924/2006

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Scientific Opinion on the substantiation of a health claim related to vitamin A and contribution to normal development and function of the immune system pursuant to Article 14 of Regulation (EC) No 1924/20061

EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA)2, 3

European Food Safety Authority (EFSA), Parma, Italy

ABSTRACT

Following an application from IDACE, submitted pursuant to Article 14 of Regulation (EC) No 1924/2006 via the Competent Authority of France, the EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA) was asked to deliver an opinion on the scientific substantiation of a health claim related to vitamin A and contribution to normal development and function of the immune system. The food constituent, vitamin A, which is the subject of the health claim, is sufficiently characterised. Contribution to normal development and function of the immune system is a beneficial physiological effect for infants and young children. A claim on vitamin A and normal function of the immune system in the general population has already been assessed with a favourable outcome. The Panel notes that the role of vitamin A in the normal function of the immune system also applies to the developing immune system of infants and young children (from birth to three years). The Panel concludes that a cause and effect relationship has been established between dietary intake of vitamin A and contribution to normal development and function of the immune system. The following wording reflects the scientific evidence: “Vitamin A contributes to the normal function of the immune system”. The target population is infants and children up to three years.

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KEY WORDS

Vitamin A, infants, children, immune system, health claims

1 On request from the Competent Authority of France following an application by IDACE, Question No EFSA-Q-2008-160, adopted on 10 July 2013.
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3 Acknowledgement: The Panel wishes to thank the members of the Working Group on Claims: Carlo Agostoni, Jean-Louis Bresson, Susan Fairweather-Tait, Marina Heinonen, Ambroise Martin, Hildegard Przyrembel, Yolanda Sanz, Alfonso Siani, Anders Sjödin, Sean (J.J.) Strain, Inge Tetens, Hendrik Van Loveren, Hans Verhagen and Peter Willatts for the preparatory work on this scientific opinion.


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SUMMARY

Following an application from IDACE, submitted for authorisation of a health claim pursuant to Article 14 of Regulation (EC) No 1924/2006 via the Competent Authority of France, the EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA) was asked to deliver an opinion on the scientific substantiation of a health claim related to vitamin A and contribution to normal development and function of the immune system.

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 vitamin A, which is a well recognised nutrient and is measurable in foods by established methods. The Panel considers that vitamin A is sufficiently characterised.

The claimed effect proposed by the applicant is “necessary for the development and functioning of multiple aspects of the immune system”. The target population proposed by the applicant is “infants (from birth onwards) and young children (until three years of age)”. The Panel considers that contribution to normal development and function of the immune system is a beneficial physiological effect for infants and young children.

A claim on vitamin A and normal function of the immune system in the general population has already been assessed by the Panel with a favourable outcome. The conclusion from the Panel was based on the well-established role of vitamin A in regulating the proliferation of immune cells, on deficiency symptoms which included impaired phagocytic activity of macrophages and impaired antibody-mediated immunity in children, and on the effect of vitamin A supplementation on the incidence of infections in malnourished children.

The Panel notes that the role of vitamin A in the normal function of the immune system also applies to the developing immune system of infants and young children (from birth to three years).

The Panel concludes that a cause and effect relationship has been established between dietary intake of vitamin A and contribution to normal development and function of the immune system.

The following wording reflects the scientific evidence: “Vitamin A contributes to the normal function of the immune system”.

The Panel considers that, in order to bear the claim, follow-on formulae should comply with the criteria of composition of follow-on formulae as laid down in Directive 2006/141/EC; nutritionally complete foods for special medical purposes intended for use by infants and nutritionally complete foods for special medical purposes other than those intended for use by infants should comply with the criteria of composition of these foods as laid down in Directive 1999/21/EC; processed cereal-based foods for infants and young children should comply with the criteria of composition of these foods as laid down in Directive 2006/125/EC; other foodstuffs intended for infants and young children should provide at least 15 % of the reference values for nutrition labelling for foods intended for infants and young children as laid down in Directive 2006/125/EC. Such amounts can be easily consumed as part of a balanced diet. The target population is infants and children up to three years. A Tolerable Upper Intake Level for pre-formed vitamin A (retinol and retinyl esters) has been established for children, and has been set at 800 μg RE/day for children of 1-3 years of age.
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BACKGROUND

Regulation (EC) No 1924/2006 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 this Regulation, are authorised in accordance with this Regulation, and are included in the lists of authorised claims provided for in Articles 13 and 14 thereof. In particular, Articles 14 to 17 of this 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 this Regulation, an application for authorisation shall be submitted by the applicant to the national competent authority of a Member State, which will make the application and any supplementary information supplied by the applicant available to the European Food Safety Authority (EFSA).

STEPS TAKEN BY EFSA

- The application was received on 14/02/2008.
- The scope of the application was proposed to fall under a health claim referring to children’s development and health.
- On 26/03/2008, during the validation process of the application, EFSA sent a request to the applicant to provide missing information.
- On 08/05/2013, EFSA received the missing information as submitted by the applicant.
- The scientific evaluation procedure started on 20/06/2013.
- During its meeting on 10/07/2013, the NDA Panel, having evaluated the data submitted, adopted an opinion on the scientific substantiation of a health claim related to vitamin A and contribution to normal development and function of the immune system.

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: vitamin A and contribution to normal development and function of the immune system.

EFSA DISCLAIMER

The present opinion does not constitute, and cannot be construed as, an authorisation for the marketing of vitamin A, a positive assessment of its safety, nor a decision on whether vitamin A 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.

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.

INFORMATION PROVIDED BY THE APPLICANT

Applicant’s name and address: IDACE (Association of the Food Industries for Particular Nutritional Uses of the European Union), 194, rue de Rivoli, 75001, Paris, France.

Food/constituent as stated by the applicant

According to the applicant, the food constituent for which the claim is made is vitamin A (retinoids and carotenoids).

Health relationship as claimed by the applicant

According to the applicant, vitamin A is necessary for the development and functioning of multiple aspects of the immune system. In particular, infants and neonates have relatively immature immune systems which mostly accounts for their high susceptibility to infections and generally weaker response to vaccination when compared to children and adults. According to the applicant, given the importance of vitamin A in the development of the immune system and the greater susceptibility that infants have to developing vitamin A deficiency due to the low reserves of vitamin A that are present at birth, it is crucial that infants receive adequate amounts of vitamin A from their diet.

Wording of the health claim as proposed by the applicant

The applicant has proposed the following wording for the health claim: “Vitamin A helps support healthy immune function”.

As equivalent alternative wordings, the applicant has also proposed: “Vitamin A helps to support/is essential for the proper functioning of/babies natural defences/the immune system/the immune cells”.

Specific conditions of use as proposed by the applicant

According to the applicant, the target population is infants (from birth onwards) and young children (until three years of age) as defined in Directive 89/398/EEC on foodstuffs intended for particular nutritional uses. The claim should be used on foods that are exclusively intended for the category of infants and young children and in line with the composition laid down in the specific directives (Directive 2006/141/EC; Directive 2006/125/EC; Directive 1999/21/EC).

According to the applicant, the quantity needed to achieve the claimed effect is:

- For follow-on formulae, the content in vitamin A should be within the range set in Directive 2006/141/EC.
- For dietary foods for special medical purposes, the content in vitamin A should be within the range set in Directive 1999/21/EC.
- For processed cereal-based foods and baby foods, the content in vitamin A should be within the range set in Directive 2006/125/EC.
- For processed cereal-based foods and baby foods, the content in vitamin A should reach at least 15% of the Nutrient Reference Values set in Directive 2006/125/EC, i.e. 15% of 400 μg per 100 g or 100 ml or per serving, as reconstituted.
- For foods intended for infants and young children other than follow-on formulae, processed cereal-based foods and baby foods, the content in vitamin A should reach at least 15% of the
Vitamin A and normal development and function of the immune system

ASSESSMENT

1. **Characterisation of the food/constituent**

The food constituent, which is the subject of the health claim, is vitamin A (retinoids and carotenoids).

The term vitamin A describes a group of lipid soluble compounds related metabolically to all-trans-retinol. In the diet, vitamin A is found in products of animal origin as retinyl esters, mainly retinyl palmitate. Other esters (oleate, stearate, myristate) and retinol contribute to dietary vitamin A intake. Retinoic acids are considered as the molecular species responsible for all the functions attributed to vitamin A, with the exception of vision, where only retinal is able to exert an action. Some carotenoids (α- and β-carotenes, β-cryptoxanthine) can be cleaved into retinol via an enzymatic process in the small intestine (SCF, 2002).

Vitamin A is a well recognised nutrient and is measurable in foods by established methods.


The Panel considers that the food constituent, vitamin A, which is the subject of the health claim, is sufficiently characterised.

2. **Relevance of the claimed effect to human health**

The claimed effect proposed by the applicant is “necessary for the development and functioning of multiple aspects of the immune system”. The target population proposed by the applicant is “infants (from birth onwards) and young children (until three years of age)”. The Panel considers that contribution to normal development and function of the immune system is a beneficial physiological effect for infants and young children.

3. **Scientific substantiation of the claimed effect**

The applicant performed a literature search in PubMed covering a period from 2003 to 2008 and using the search terms “vitamin A OR retinol OR carotenoids” AND “immune* OR infection” in order to

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identify studies on the effect of vitamin A on the immune system in children from birth to three years of age. The applicant identified nine human intervention studies, one meta-analysis and one textbook chapter as being pertinent to the health claim. Five human intervention studies investigated the effect of vitamin A on the incidence and duration of infections in infants and children and/or on markers of the immune function (Long et al., 2006a, b, c; Long et al., 2007a, b), whereas four human intervention studies evaluated the effect of vitamin A on the antibody response to vaccination in infants and children (Cherian et al., 2003; Newton et al., 2005, 2007; Diness et al., 2007). The meta-analysis included randomised controlled trials which investigated the effect of vitamin A on the incidence of lower respiratory tract infections (Chen et al., 2008). A textbook chapter on the role of vitamin A in the function of the immune system was also provided by the applicant (Ramakrishnan et al., 2004).

The Panel has already assessed a claim on vitamin A and normal function of the immune system with a favourable outcome (EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA), 2009). The target population was the general population.

The conclusion from the Panel was based on the well-established role of vitamin A in regulating the proliferation of immune cells, on deficiency symptoms which included impaired phagocytic activity of macrophages and impaired antibody-mediated immunity in children, and on the effect of vitamin A supplementation on the incidence of infections in malnourished children (Field et al., 2002; Ruhl, 2007).

The Panel notes that the role of vitamin A in the normal function of the immune system also applies to the developing immune system of infants and young children (from birth to three years).

The Panel concludes that a cause and effect relationship has been established between dietary intake of vitamin A and contribution to normal development and function of the immune system.

4. Panel’s comments on the proposed wording

The Panel considers that the following wording reflects the scientific evidence: “Vitamin A contributes to the normal function of the immune system”.

5. Conditions and restrictions of use

The Panel considers that, in order to bear the claim:

- follow-on formulae should comply with the criteria of composition of follow-on formulae as laid down in Directive 2006/141/EC;

- nutritionally complete foods for special medical purposes intended for use by infants and nutritionally complete foods for special medical purposes other than those intended for use by infants should comply with the criteria of composition of these foods as laid down in Directive 1999/21/EC;\(^\text{10}\);

- processed cereal-based foods for infants and young children should comply with the criteria of composition of these foods as laid down in Directive 2006/125/EC;

- other foodstuffs intended for infants and young children should provide at least 15 % of the reference values for nutrition labelling for foods intended for infants and young children as laid down in Directive 2006/125/EC.

Such amounts can be easily consumed as part of a balanced diet. The target population is infants and children up to three years. A Tolerable Upper Intake Level (UL) for pre-formed vitamin A (retinol and retinyl esters) has been established for children, and has been set at 800 μg RE/day for children of 1-3 years of age (SCF, 2002).

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

- The food constituent, vitamin A, which is the subject of the health claim, is sufficiently characterised.
- The claimed effect proposed by the applicant is “necessary for the development and functioning of multiple aspects of the immune system”. The target population proposed by the applicant is “infants (from birth onwards) and young children (until three years of age)”. Contribution to normal development and function of the immune system is a beneficial physiological effect for infants and young children.
- A cause and effect relationship has been established between dietary intake of vitamin A and contribution to normal development and function of the immune system.
- The following wording reflects the scientific evidence: “Vitamin A contributes to the normal function of the immune system”.
- In order to bear the claim follow-on formulae should comply with the criteria of composition of follow-on formulae as laid down in Directive 2006/141/EC; nutritionally complete foods for special medical purposes intended for use by infants and nutritionally complete foods for special medical purposes other than those intended for use by infants should comply with the criteria of composition of these foods as laid down in Directive 1999/21/EC; processed cereal-based foods for infants and young children should comply with the criteria of composition of these foods as laid down in Directive 2006/125/EC; other foodstuffs intended for infants and young children should provide at least 15 % of the reference values for nutrition labelling for foods intended for infants and young children as laid down in Directive 2006/125/EC. Such amounts can be easily consumed as part of a balanced diet. The target population is infants and children up to three years. The UL has been set at 800 μg RE/day for children of 1-3 years of age.

DOCUMENTATION PROVIDED TO EFSA

REFERENCES

EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA), 2009. Scientific Opinion on the substantiation of health claims related to vitamin A and cell differentiation (ID 14), function of the immune system (ID 14), maintenance of skin and mucous membranes (ID 15, 17), maintenance of vision (ID 16), maintenance of bone (ID 13, 17), maintenance of teeth (ID 13, 17), maintenance of hair (ID 17), maintenance of nails (ID 17), metabolism of iron (ID 206), and protection of DNA, proteins and lipids from oxidative damage (ID 209) pursuant to Article 13(1) of Regulation (EC) No 1924/2006. EFSA Journal, 2009;7(9):1221, 25 pp. doi:10.2903/j.efsa.2009.1221


SCF (Scientific Committee on Food), 2002. Opinion of the Scientific Committee on Food (SCF) on the Tolerable Upper Intake Level of Preformed Vitamin A (retinol and retinyl esters).
Glossary/Abbreviations

UL \quad \text{Tolerable Upper Intake Level}