

## SCIENTIFIC OPINION

### 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<sup>1</sup>

EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA)<sup>2,3</sup>

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#### 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

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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<sup>4</sup> 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.

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<sup>4</sup> 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.

## **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

Nutrient Reference Values set in Directive 2006/141/EC (replacing Directive 91/321/EC), i.e. 15 % of 400 µg per 100 ml product ready for use.

## 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 ( $\alpha$ - and  $\beta$ -carotenes,  $\beta$ -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.

Vitamin A occurs naturally in foods and is authorised for addition to foods (Annex I of Regulation (EC) No 1925/2006<sup>5</sup>, Annex I of Directive 2002/46/EC<sup>6</sup>, Annex III of Directive 2006/141/EC<sup>7</sup>, Annex IV of Directive 2006/125/EC<sup>8</sup>, Directive 2001/15/EC<sup>9</sup>). This evaluation applies to Vitamin A naturally present in foods and those forms authorised for addition to foods (Annex II of Regulation (EC) No 1925/2006, Annex II of Directive 2002/46/EC, Annex III of Directive 2006/141/EC, Annex IV of Directive 2006/125/EC, Directive 2001/15/EC). The forms authorised in these regulations are retinol, retinyl acetate, retinyl palmitate, and  $\beta$ -carotene.

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

<sup>5</sup> Regulation (EC) No 1925/2006 of the European Parliament and of the Council of 20 December 2006 on the addition of vitamins and minerals and of certain other substances to foods. OJ L 404, 30.12.2006, p. 26–38.

<sup>6</sup> Directive 2002/46/EC of the European Parliament and of the Council of 10 June 2002 on the approximation of the laws of the Member States relating to food supplements. OJ L 183, 12.7.2002, p. 51–57.

<sup>7</sup> Commission Directive 2006/141/EC of 22 December 2006 on infant formulae and follow-on formulae and amending Directive 1999/21/EC Text with EEA relevance. OJ L 401, 30.12.2006, p. 1–33.

<sup>8</sup> Commission Directive 2006/125/EC of 5 December 2006 on processed cereal-based foods and baby foods for infants and young children. OJ L 339, 6.12.2006, p. 16–35.

<sup>9</sup> Commission Directive 2001/15/EC of 15 February 2001 on substances that may be added for specific nutritional purposes in foods for particular nutritional uses. OJ L 52, 22.2.2001, p. 19–25.

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<sup>10</sup>;
- 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.

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<sup>10</sup> Commission Directive 1999/21/EC of 25 March 1999 on dietary foods for special medical purposes. OJ L 91, 7.4.1999, p. 29–36.

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

Health claim application on vitamin A and the normal development and function of the immune system pursuant to Article 14 of Regulation (EC) No 1924/2006 (Claim serial No: 0080\_FR). February 2008. Submitted by IDACE.

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## GLOSSARY/ABBREVIATIONS

UL                    Tolerable Upper Intake Level