

## SCIENTIFIC OPINION

### Scientific Opinion on the Substantiation of a health claim related to Iron and cognitive development of children 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>

European Food Safety Authority (EFSA), Parma, Italy

#### ABSTRACT

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 iron and cognitive development of children. The scope of the application was proposed to fall under claims referring to children's development and health. The food constituent that is the subject of the health claim is iron which is a well recognised nutrient and is measurable in foods by established methods. The Panel considers that the food constituent, iron, which is the subject of the health claim, is sufficiently characterised. The Panel considers that normal cognitive development is beneficial to children's health. The applicant provided also a number of reviews and reports on the biological functions of iron including cognitive function and cognitive development of children. The Panel considers that there is sufficient evidence from reviews, consensus opinions and from reports from authoritative bodies demonstrating the role of iron in the cognitive development of children. The Panel concludes that a cause and effect relationship has been established between the intake of iron and cognitive development of children and adolescents. Iron intakes may be inadequate in sub-groups of children and adolescents in some EU countries. The following wording reflects the scientific evidence: "iron contributes to normal cognitive development of children".

#### KEY WORDS

Iron, oxygen transport, cognitive function, children, adolescents, growth, health claims

---

1 On request from Transformation Laitière Française via the Competent Authority of France, Question No EFSA-Q-2008-325, adopted on 15 October 2009.

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](mailto:nda@efsa.europa.eu)

3 Acknowledgement: The Panel wishes to thank the members of the Working Group on Claims for the preparation of this opinion: 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.

This opinion is based on major contributions from: Wolfgang Gelbmann

For citation purposes: EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA); Scientific Opinion on the substantiation of a health claim related to Iron and necessary for the cognitive development of children pursuant to Article 14 of Regulation (EC) No 1924/2006. EFSA Journal 2009; 7(11):1360. [9 pp.]. doi:10.2903/j.efsa.2009.1360. Available online: [www.efsa.europa.eu](http://www.efsa.europa.eu)

## 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 iron and cognitive development of children.

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

The food constituent that is the subject of the health claim is iron which is a well recognised nutrient and is measurable in foods by established methods. Iron occurs naturally in foodstuffs in different oxidation states and in two forms, haem iron which is primarily derived from haemoglobin and myoglobin in flesh food and non-haem iron from plants foods. The Panel considers that the food constituent, iron, which is the subject of the health claim, is sufficiently characterised.

The claimed effect is that iron is "necessary for the cognitive development of children". The proposed target population for the health claim is children aged 3-18 years. The Panel considers that normal cognitive development is beneficial to children's health.

The applicant performed a literature search in the databases Medline, Pubmed and OVID platform. The applicant did not specify his search strategy. The search included clinical trials, meta-analyses, reviews and guidelines. In total the applicant identified 12 publications on human studies and 37 other publication to be pertinent to the claimed effect.

Iron is an essential trace element that has important metabolic functions, including oxygen transport and is involved in many redox reactions. The cognitive deficiency symptoms observed with iron-deficiency anaemia include deficits in attention, perceptual motor speed, memory and verbal fluency. Insufficient intake results in the deficiency conditions anaemia, impaired psychomotor development and cognitive performance. Reports from other authoritative bodies and reviews show that there is consensus on the importance of iron for the cognitive development. The Panel considers there is sufficient evidence from reviews, consensus opinions and from reports from authoritative bodies demonstrating the role of iron in the cognitive development of children.

The Panel concludes that a cause and effect relationship has been established between the intake of iron and cognitive development of children and adolescents. Iron intakes may be inadequate in sub-groups of children and adolescents in some EU countries.

The following wording reflects the scientific evidence: "iron contributes to normal cognitive development of children".

In order to bear the claim a food should be at least source of iron as per Annex to Regulation (EC) No 1924/2006. Such amounts can be easily consumed as part of a balanced diet. The target population is the general population. In 2004, EFSA considered that the available data were insufficient to establish a tolerable upper intake level for iron.

## TABLE OF CONTENTS

Abstract .....	1
Summary .....	2
Table of contents .....	3
Background as provided by the European Commission .....	4
Terms of reference as provided by the European Commission .....	4
EFSA Disclaimer.....	4
Information provided by the applicant .....	6
1. Assessment .....	6
1.1. Characterisation of the food/constituent.....	6
1.2. Relevance of the claimed effect to human health .....	6
1.3. Scientific substantiation of the claimed effect.....	7
1.4. Panel’s comments on the proposed wording .....	7
1.5. Conditions and restrictions of use .....	7
Conclusions .....	8
Documentation provided to EFSA .....	8
References .....	8

## BACKGROUND AS PROVIDED BY THE EUROPEAN COMMISSION

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 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 the 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 a health claim referring to disease risk reduction.
- During the check for completeness<sup>5</sup> of the application, the applicant was requested to provide missing information on 20/06/2008.
- The scientific evaluation procedure started on 15/05/2009.
- During the meeting on 15/10/2009, the NDA Panel, after having evaluated the overall data submitted, adopted an opinion on the scientific substantiation of a health claim related to iron and cognitive development of children.

## TERMS OF REFERENCE AS PROVIDED BY THE EUROPEAN COMMISSION

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: iron and cognitive development of.

## EFSA DISCLAIMER

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

---

<sup>4</sup> 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.

<sup>5</sup> In accordance with EFSA "Scientific and Technical guidance for the Preparation and Presentation of the Application for Authorisation of a Health Claim"

**ACKNOWLEDGEMENTS**

The European Food Safety Authority wishes to thank the members of the Working Group on claims for the preparation of this opinion: 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.

### **Information provided by the applicant**

**Applicant's name and address:** Association de la Transformation Laitiere Francaise (ATLA), 42 rue de Chateaudun, 75314 Paris Cedex 09, France.

### **Food/constituent as stated by the applicant**

Iron

### **Health relationship as claimed by the applicant**

Children require iron for the healthy development and function of their brain. Not only is iron needed to form myelin, a key component of the brain, but it is also needed for everyday synthesis of neurotransmitters and brain energy metabolism.

### **Wording of the health claim as proposed by the applicant**

“Iron is necessary for the cognitive development of children”

### **Specific conditions of use as proposed by the applicant**

The target population is children aged 3 to 18 years old.

## **1. Assessment**

### **1.1. Characterisation of the food/constituent**

The food constituent that is the subject of the health claims is iron which is a well recognised nutrient and is measurable in foods by established methods.

Iron occurs naturally in foods in two forms, haem iron which is primarily derived from haemoglobin and myoglobin in flesh food and non-haem iron from plants foods (IoM, 2001). Different forms of iron are authorised for addition to foods (Annex I of Regulation (EC) No 1925/2006<sup>6</sup> and Annex II of Directive 2002/46/EC<sup>7</sup>). This evaluation applies to iron naturally present in foods and those forms authorised for addition to foods (Annex II of the Regulation (EC) No 1925/2006 and Annex II of Directive 2002/46/EC).

The Panel considers that the food constituent, iron, which is the subject of the health claims, is sufficiently characterised.

### **1.2. Relevance of the claimed effect to human health**

The claimed effect is that iron is “necessary for the cognitive development of children”. The proposed target population for the health claim is children aged 3-18 years.

The Panel considers that normal cognitive development is beneficial to children's health.

---

<sup>6</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>7</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.

### 1.3. Scientific substantiation of the claimed effect

The applicant performed a literature search in the databases Medline, Pubmed and OVID platform. The applicant did not specify his search strategy. The search included clinical trials, meta-analyses, reviews and guidelines. In total the applicant identified 12 publications on human studies and 37 other publication to be pertinent to the claimed effect.

Five randomised controlled trials, one uncontrolled intervention trial and one observational study evaluated the effect of iron supplementation on haematological parameters, or studied endpoints of cognitive function, but did not address the role of iron in cognitive development (Mejia and Chew, 1988; Metallinos-Katsaras et al. 2004; Mwanri et al., 2000; Shankar et al., 2000; Smuts et al., 1995; Sungthong et al., 2002; Sungthong et al., 2004).

A systematic review evaluated the effect of iron supplementation on mental and motor development of children. Endpoints studied were psychomotor development, cognition, mental development, intelligence quotient, school performance. Iron supplementation improved mental development scores modestly in children above 7 years of age (Sachdev et al., 2004). The Panel considers this review to be pertinent to the claimed effect.

Hurtado et al. (1999) and Soewondo (1995) reported about an association between mental retardation and iron deficiency during infancy or early childhood. Another review studied the cognitive deficits induced by brain iron deficiency and the involvement of the dopamine-opiate system based on animal and human studies (Youbim and Yehuda, 2000).

The applicant also provided a number of reviews and reports on the biological functions of iron including cognitive function and cognitive development of children.

Iron is an essential trace element that has important metabolic functions, including oxygen transport and is involved in many redox reactions. The cognitive deficiency symptoms observed with iron-deficiency anaemia include deficits in attention, perceptual motor speed, memory and verbal fluency (Malestrom, 2002). Insufficient intake results in the deficiency conditions anaemia, impaired psychomotor development and cognitive performance (EFSA, 2004; EFSA, 2009). Reports from other authoritative bodies and reviews show that there is consensus on the importance of iron for the cognitive development (Grantham and Ani, 2001; Hunt, 2005; SACN, 2009; Schulze and Dreyfuss, 2005; WHO 2003).

The Panel considers that there is sufficient evidence from reviews, consensus opinions and from reports from authoritative bodies demonstrating the role of iron in the cognitive development of children.

The Panel concludes that a cause and effect relationship has been established between the intake of iron and cognitive development of children and adolescents. Iron intakes may be inadequate in sub-groups of children and adolescents in some EU countries.

### 1.4. Panel's comments on the proposed wording

Taking into account the scientific evidence presented, the Panel considers that the following wording reflects the scientific evidence:

“Iron contributes to normal cognitive development of children”.

### 1.5. Conditions and restrictions of use

In order to bear the claim a food should be at least a source of iron as per Annex to Regulation (EC) No 1924/2006. Such amounts can be easily consumed as part of a balanced diet. The target population

is the general population. In 2004, EFSA considered that the available data were insufficient to establish a tolerable upper intake level for iron (EFSA, 2004).

## CONCLUSIONS

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

- The food constituent, iron, that is the subject of the health claim (i.e., iron) is sufficiently characterised.
- The claimed effect is that iron is ‘necessary for the cognitive development of children’. Normal cognitive development is beneficial to children’s health.
- A cause and effect relationship has been established between the intake of iron and normal cognitive development of children.
- Iron intakes may be inadequate in sub-groups of children in some EU countries.
- The following wording reflects the scientific evidence: “iron contributes to normal cognitive development of children”.
- In order to bear the claim a food should be at least a source of iron as per Annex to Regulation 1924/2006. Such amounts can be easily consumed as part of a balanced diet. The target population is children and adolescents (up to 18 years).
- In 2004, EFSA considered that the available data were insufficient to establish a tolerable upper intake level for iron.

## DOCUMENTATION PROVIDED TO EFSA

Health claim application on iron and “necessary for the cognitive development of children” pursuant to Article 14 of Regulation (EC) No 1924/2006 (Claim serial No: 0162\_FR). May 2008. Submitted by Association de la Transformation Laitiere Francaise (ATLA).

## REFERENCES

- EFSA (European Food Safety Authority), 2004. Opinion of the Scientific Panel on Dietetic Products, Nutrition and Allergies on a request from the Commission related to the Tolerable Upper Intake Levels of Iron. *The EFSA Journal* (125), 1-34.
- EFSA (European Food Safety Authority), 2009. Opinion of the Scientific Panel on Dietetic Products, Nutrition and Allergies on the substantiation of health claims related to iron and formation of red blood cells and haemoglobin (ID 249, ID 1589), oxygen transport (ID 250, ID 254, ID 256), energy-yielding metabolism (ID 251, ID 1589), function of the immune system (ID 252, ID 259), cognitive function (ID 253) and cell division (ID 368) pursuant to Article 13(1) of Regulation (EC) No 1924/2006 on request from the European Commission. *EFSA Journal* 2009; 7(11):136. [9 pp.]. doi:10.2903/j.efsa.2009.1215.
- Grantham-McGregor S and Ani C (2001). A review of studies on the effect of iron deficiency on cognitive development on children. *J Nutr* 131: 649S-668S.
- Hunt JR (2005). Iron. In: *Encyclopedia of Human Nutrition*. Caballero B, Allen L, Prentice A (eds.). Oxford. Elsevier Ltd, 2nd ed.
- Hurtado EK, Claussen AH, Scott KG. Early childhood anaemia and mild and moderate mental retardation. *Am J Clin Nutr* 1999; 69: 115–119.

- IoM (Institute of Medicine), 2001. Dietary Reference Intakes for vitamin A, vitamin K, arsenic, boron, chromium, copper, iodine, iron, manganese, molybdenum, nickel, silicon, vanadium and zinc. Washington D.C. National Academy Press.
- Malestrom, 2002. Encyclopaedia of the human brain. Academic Press, New York.
- Metallinos-Katsaras E, Valassi-Adam E, Dewey KG, Lonnerdal B, Stamoulakatou A, Pollitt E. Effect of iron supplementation on cognition in Greek preschoolers. *Eur J Clin Nutr* 2004; 58(11): 1.532-1.542.
- Mejía L, Chew F. Hematological effects of supplementation of anaemic children with vitamin A alone and in combination with iron. *Am J Clin Nutr* 1988; 48: 595.
- Mwanri L, Worsley A., Ryan P, Masika J. Supplemental vitamin A improves anaemia and growth in anaemic school children in Tanzania. *J Nutr* 2000; 130(11): 2.691-2.696.
- SACN (Scientific Advisory Committee on Nutrition), 2009. Draft SACN Report on Iron and Health, 2009. [http://www.sacn.gov.uk/pdfs/draft\\_iron\\_and\\_health\\_report\\_complete\\_june\\_2009\\_consultation.pdf](http://www.sacn.gov.uk/pdfs/draft_iron_and_health_report_complete_june_2009_consultation.pdf)
- Sachdev H, Gera T, Nestel P. Effect of iron supplementation on mental and motor development in children: systematic review of randomised controlled trials. *Public Health Nutr* 2005; 8(2): 117-132.
- Schulze KJ and Dreyfuss ML (2005). Anemia. Iron-Deficiency Anemia Elsevier Ltd doi:10.1016/B0-12-226694-3/00015-6.
- Shankar N, Tandon OP, Bandhu R, Madan N, Gomber S. Brainstem auditory evoked potential responses in iron-deficient anaemic children. *Indian J Physiol Pharmacol* 2000; 44(3): 297-303.
- Smuts CM, Tichelaar HY, Van Jaarsveld PJ, Badenhorst CJ, Kruger M, Laubscher R, Mansvelt EP, Benade AJ. The effect of iron fortification on the fatty acid composition of plasma and erythrocyte membranes in primary school children with and without iron deficiency. *Prostaglandins Leukot Essent Fatty Acids* 1995; 52(1): 59-67.
- Soewondo S. The effect of iron deficiency and mental stimulation on Indonesian children's cognitive performance and development. *Kobe J Med Sci* 1995; 41(1-2): 1-17.
- Sungthong R, Mo-suwan L, Chongsuvivatwong V. Effects of haemoglobin and serum ferritin on cognitive function in school children. *Asia Pac J Clin Nutr* 2002; 11(2): 117-122.
- Sungthong R, Mo-suwan L, Chongsuvivatwong V, Geater AF. Once-weekly and 5-days a week iron supplementation differentially affect cognitive function but not school performance in Thai children. *J Nutr* 2004; 134(9): 2.349-2.354.
- WHO (World Health Organisation, 2003). Feeding and nutrition of infants and young children. WHO Regional Publications, European Series 2003; N° 87.
- Youdim MB, Yehuda S (2000). The neurochemical basis of cognitive deficits induced by brain iron deficiency: involvement of dopamine-opiate system. *Cell Mol Biol* 2000; 46: 491-500.