SCIENTIFIC OPINION

Scientific Opinion on the substantiation of a health claim related to increasing maternal folate status by supplemental folate intake and reduced risk of neural tube defects pursuant to Article 14 of Regulation (EC) No 1924/2006[1]

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

European Food Safety Authority (EFSA), Parma, Italy

ABSTRACT

Following an application from Rank Nutrition Ltd, submitted for authorisation of a health claim pursuant to Article 14 of Regulation (EC) No 1924/2006 via the Competent Authority of the United Kingdom, 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 increasing maternal folate status by supplemental folate intake and reduced risk of neural tube defects. The Panel considers that the food constituent, supplemental folate, which is the subject of the claim, is sufficiently characterised. Increasing maternal folate status by supplemental folate intake is a beneficial physiological effect in the context of reducing the risk of neural tube defects. In weighing the evidence, the Panel took into account that the association between low maternal folate intakes and an increased risk of neural tube defects is well established, and that a recent systematic review showed an effect of maternal folic acid intakes on the risk of neural tube defects. The Panel concludes that a cause and effect relationship has been established between increasing maternal folate status by supplemental folate intake and a reduced risk of neural tube defects.

KEY WORDS

Folate, neural tube defects, NTD, health claims

[1] On request from the Competent Authority of the United Kingdom following an application by Rank Nutrition Ltd, Question No EFSA-Q-2013-00265, 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 Rank Nutrition Ltd, submitted for authorisation of a health claim pursuant to Article 14 of Regulation (EC) No 1924/2006 via the Competent Authority of the United Kingdom, 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 increasing maternal folate status by supplemental folate intake and reduced risk of neural tube defects (NTD).

The scope of the application was proposed to fall under a health claim referring to disease risk reduction.

The food constituent that is the subject of the health claim is folic acid. Folic acid is used as synthetic folate in food supplements and in food fortification because of its stability, and becomes biologically active after reduction. Folate is the generic name for this B-vitamin and different forms of folate are authorised for addition to foods (Annex II of Regulation (EC) No 1925/2006 and Annex II of Directive 2002/46/EC). This evaluation applies to all forms of folate 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, supplemental folate, which is the subject of the health claim, is sufficiently characterised.

The claimed effect proposed by the applicant is "protective effect of folic acid against neural tube defects in the foetus, through beneficially raising maternal red blood cell folate". The target population proposed by the applicant is women of child-bearing age. The Panel considers that increasing maternal folate status by supplemental folate intake is a beneficial physiological effect in the context of reducing the risk of NTD.

In weighing the evidence, the Panel took into account that the association between low maternal folate intakes and an increased risk of NTD is well established, and that a recent systematic review showed an effect of maternal folic acid intakes on the risk of NTD.

The Panel concludes that a cause and effect relationship has been established between increasing maternal folate status by supplemental folate intake and a reduced risk of NTD.

The Panel considers that the following wording reflects the scientific evidence: "Supplemental folate intake increases maternal folate status. Increasing maternal folate status contributes to the reduction of the risk of NTD."

The Panel considers that in order to obtain the claimed effect 400 μg supplemental folate should be consumed daily for at least one month before and up to three months after conception. The target population is women of child-bearing age.

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BACKGROUND

Regulation (EC) No 1924/2006[4] 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 25/02/2013.
- The scope of the application was proposed to fall under a health claim referring to disease risk reduction.
- On 30/04/2013, during the validation process of the application, EFSA sent a request to the applicant to provide missing information.
- On 30/05/2013, EFSA received the missing information as submitted by the applicant.
- The scientific evaluation procedure started on 13/06/2013.
- 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 increasing maternal folate status by supplemental folate intake and reduced risk of neural tube defects.

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 increasing maternal folate status by supplemental folate intake and reduced risk of neural tube defects.

EFSA DISCLAIMER

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

[4] 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: Rank Nutrition Ltd, Long Barn, Etchden Court, Bethersden, Kent TN26 3DP, United Kingdom.

Food/constituent as stated by the applicant

According to the applicant, the food constituent, which is the subject of the claim, is folic acid.

Health relationship as claimed by the applicant

According to the applicant, the claimed effect relates to the protective effect of folic acid against neural tube defects in the foetus, through beneficially raising maternal red blood cell folate.

Wording of the health claim as proposed by the applicant

The applicant has proposed the following wording for the health claim: "Folic acid supplementation raises maternal red blood cell folate. Low maternal red blood cell folate is a risk factor for neural tube defects in the developing foetus".

Specific conditions of use as proposed by the applicant

According to the applicant, information should be given to the consumer that the beneficial effect is observed with a daily intake of 400 micrograms folic acid per day taken as a dietary supplement at least 12 weeks prior to conception and during the first 12 weeks of pregnancy. The target population proposed by the applicant is all women of child-bearing age.

ASSESSMENT

1. Characterisation of the food/constituent

The food constituent that is the subject of the health claim is folic acid.

Folic acid is used as synthetic folate in food supplements and in food fortification because of its stability, and becomes biologically active after reduction (SCF, 2000).

Folate is the generic name for this B-vitamin and different forms of folate are authorised for addition to foods (Annex II of Regulation (EC) No 1925/2006[5] and Annex II of Directive 2002/46/EC[6]). This evaluation applies to all forms of folate authorised for addition to foods (Annex II of Regulation (EC) No 1925/2006 and Annex II of Directive 2002/46/EC).

The Panel considers that the food constituent, supplemental folate, 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 "protective effect of folic acid against neural tube defects in the foetus, through beneficially raising maternal red blood cell folate". The target population proposed by the applicant is women of child-bearing age.

Neural tube defects (NTD) are the most common congenital malformations of the central nervous system resulting from fusion failure of the caudal neural tube (Román, 2006) up to 8-10 weeks of embryonic life. Some of these malformations are incompatible with life (anencephaly) and others (spina bifida) result in various disabilities.

[5] 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.

[6] 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.

While folate in serum or plasma is a sensitive marker of early changes in folate status (Herbert, 1987), red blood cell (RBC) folate is considered a reliable biomarker of long-term folate status as it reflects tissue folate stores (Wu et al., 1975) and decreases only weeks or months after the initial reduction of folate intake and the fall of serum folate concentrations (Eichner and Hillman, 1973).

The Panel considers that increasing maternal folate status by supplemental folate intake is a beneficial physiological effect in the context of reducing the risk of NTD.

3. Scientific substantiation of the claimed effect

There is consensus that low folate intakes are associated with an increased risk of NTD and that women of child-bearing age should consume supplemental folic acid at a level of 400 µg per day for at least one month before and up to three months after conception, in addition to consuming food folate from a varied diet in order to reduce the risk of NTD (IoM, 1998; NHMRC, 2006; SACN, 2006; D-A-CH, 2013).

This consensus is in line with a recent systematic review and meta-analysis (De-Regil et al., 2010) which included six randomised and quasi-randomised trials (Laurence et al., 1981; MRC Vitamin Study Research Group, 1991; Czeizel and Dudas, 1992; Kirke et al., 1992; Czeizel et al., 1994; Indian Council of Medical Research, 2000) in women who became or were <12 weeks pregnant at the time of the intervention and in which supplemental folic acid was administered vs. no treatment, placebo or other micronutrients without folic acid on the risk of occurrence or reoccurrence of NTD. These studies evaluated a total 3 066 births in the intervention and 3 039 births in the control groups, with 12 occurrences of NTD in the intervention and 45 occurrences in the control arms. Using a fixed effects model, the relative risk (RR) of NTD in the intervention arms was statistically significantly lower as compared to the control arms (mean RR 0.28 (95 % CI 0.15 to 0.52)).

In weighing the evidence, the Panel took into account that the association between low maternal folate intakes and an increased risk of NTD is well established, and that a recent systematic review showed an effect of maternal folic acid intakes on the risk of NTD.

The Panel concludes that a cause and effect relationship has been established between increasing maternal folate status by supplemental folate intake and a reduced risk of NTD.

4. Panel's comments on the proposed wording

The Panel considers that the following wording reflects the scientific evidence: "Supplemental folate intake increases maternal folate status. Increasing maternal folate status contributes to the reduction of the risk of NTD."

5. Conditions and restrictions of use

The Panel considers that in order to obtain the claimed effect, 400 µg supplemental folate should be consumed daily for at least one month before and up to three months after conception. The target population is women of child-bearing age.

CONCLUSIONS

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

- The food constituent, supplemental folate, which is the subject of the health claim, is sufficiently characterised.
- The claimed effect proposed by the applicant is "protective effect of folic acid against neural tube defects in the foetus, through beneficially raising maternal red blood cell folate". The target population proposed by the applicant is women of child-bearing age. Increasing

maternal folate status by supplemental folate intake is a beneficial physiological effect in the context of reducing the risk of NTD.

- A cause and effect relationship has been established between increasing maternal folate status by supplemental folate intake and a reduced risk of NTD.
- The following wording reflects the scientific evidence: "Supplemental folate intake increases maternal folate status. Increasing maternal folate status contributes to the reduction of the risk of NTD."
- In order to obtain the claimed effect, 400 µg supplemental folate should be consumed daily for at least one month before and up to three months after conception. The target population is women of child-bearing age.

DOCUMENTATION PROVIDED TO EFSA

Health claim application related to increasing maternal folate status by supplemental folate intake and reduced risk of neural tube defects pursuant to Article 14 of Regulation (EC) No 1924/2006 (Claim serial No: 0379_UK). May 2013. Submitted by Rank Nutrition Ltd.

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GLOSSARY AND ABBREVIATIONS

NTD Neural tube defects

RBC Red blood cell