

## SCIENTIFIC OPINION

### Scientific Opinion on the substantiation of a health claim related to ♀EFAX™ and reduction of menstrual discomfort pursuant to Article 13(5) 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 Nutrilinks Sarl submitted for authorisation of a health claim pursuant to Article 13(5) of Regulation (EC) No 1924/2006 via the Competent Authority of Cyprus, the Panel on Dietetic Products, Nutrition and Allergies (NDA) was asked to deliver an opinion on the scientific substantiation of a health claim related to ♀EFAX™ and reduction of menstrual discomfort. The food, ♀EFAX™, which is standardised pure krill oil and is the subject of the health claim, is sufficiently characterised. The claimed effect, reduction of menstrual discomfort, is a beneficial physiological effect. No human intervention studies from which conclusions could be drawn for the scientific substantiation of the claim were provided by the applicant. A cause and effect relationship has not been established between the consumption of ♀EFAX™ and reduction of menstrual discomfort.

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#### KEY WORDS

♀EFAX, krill oil, menstrual discomfort, health claims.

<sup>1</sup> On request from the Competent Authority of Cyprus following an application by Nutrilinks Sarl, Question No EFSA-Q-2012-00591, adopted on 24 January 2013.

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## SUMMARY

Following an application from Nutrilinks Sarl submitted for authorisation of a health claim pursuant to Article 13(5) of Regulation (EC) No 1924/2006 via the Competent Authority of Cyprus, the Panel on Dietetic Products, Nutrition and Allergies (NDA) was asked to deliver an opinion on the scientific substantiation of a health claim related to ♀EFAX™ and reduction of menstrual discomfort.

The scope of the application was proposed to fall under a health claim based on newly developed scientific evidence.

The food that is the subject of the health claim is ♀EFAX™, which is standardised pure krill oil. The Panel considers that ♀EFAX™ is sufficiently characterised.

The claimed effect is “contributes to reduce menstrual discomfort”. The target population proposed by the applicant is “women presenting with physiological and emotional symptoms associated with the menstruation cycle”. The Panel considers that reduction of menstrual discomfort is a beneficial physiological effect.

The applicant performed a literature search and identified one published human intervention study as pertinent to the claim. This study was a double-blind, randomised, controlled parallel study in 70 women who fulfilled the Diagnostic and Statistical Manual of Mental Disorders-III-Revised (DSM-III-R) criteria for premenstrual syndrome (PMS) and were randomised to consume daily 2 g of either krill oil (n=36) or fish oil (18 % EPA, 12 % DHA; n=34) for one month, and thereafter for eight days prior to and two days during menstruation for the two subsequent menstruation cycles. The krill oil administered in the study was manufactured in line with the applicant’s specifications. Severity of symptoms associated with PMS (breast tenderness, feeling overwhelmed, stress, irritability, depression, joint pain, weight gain, abdominal pain, swelling and bloating) was assessed at baseline and at days 45 and 90 using a self-assessment questionnaire and by the quantity of analgesic consumption for menstrual pain. None of the subjects dropped out of the study. Between group differences were analysed at day 90 using analysis of variance.

The Panel notes that the information with respect to characterisation of the subjects recruited, and to the questionnaire used to assess changes in the severity of PMS symptoms, was insufficient to perform a full scientific evaluation; the Panel also notes the inadequate reporting and limitations of the statistical analysis. The Panel considers that no conclusions can be drawn from this study for the scientific substantiation of the claim.

The Panel notes that no human intervention studies from which conclusions could be drawn for the scientific substantiation of the claim were provided by the applicant.

The Panel concludes that a cause and effect relationship has not been established between the consumption of ♀EFAX™ and reduction of menstrual discomfort.

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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, Article 13(5) of this Regulation lays down provisions for the addition of claims (other than those referring to the reduction of disease risk and to children's development and health) which are based on newly developed scientific evidence, or which include a request for the protection of proprietary data, to the Community list of permitted claims referred to in Article 13(3).

According to Article 18 of this Regulation, an application for inclusion in the Community list of permitted claims referred to in Article 13(3) 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 21/05/2012.
- The scope of the application was proposed to fall under a health claim based on newly developed scientific evidence.
- On 12/06/2012 and on 18/07/2012, during the validation process of the application, EFSA sent a request to the applicant to provide missing information.
- The applicant provided the missing information on 24/07/2012 (which had been made available to EFSA in electronic format on 13/07/2012) and on 30/07/2012 (which had been made available to EFSA in electronic format on 25/07/2012).
- The scientific evaluation procedure started on 14/08/2012.
- On 25/10/2012, the Working Group on Claims of the NDA Panel agreed on a list of questions for the applicant to provide additional information to accompany the application. The clock was stopped on 30/10/2012 and restarted on 14/11/2012, in compliance with Article 18(3) of Regulation (EC) No 1924/2006.
- On 22/11/2012, EFSA received the requested information (which had been made available to EFSA in electronic format on 15/11/2012).
- During its meeting on 24/01/2013, the NDA Panel, having evaluated the data submitted, adopted an opinion on the scientific substantiation of a health claim related to “♀EFAX™” and reduction of menstrual discomfort.

## TERMS OF REFERENCE

EFSA is requested to evaluate the scientific data submitted by the applicant in accordance with Article 16(3) 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: ♀EFAX™ and reduction of menstrual discomfort.

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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.

**EFSA DISCLAIMER**

The present opinion does not constitute, and cannot be construed as, an authorisation for the marketing of ♀EFAX™, a positive assessment of its safety, nor a decision on whether ♀EFAX™ 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 18(4) of Regulation (EC) No 1924/2006.

## INFORMATION PROVIDED BY THE APPLICANT

**Applicant's name and address:** Nutrilinks Sarl, Chemin de Beau-rivage 7, P.O. Box 96, CH-1000 Lausanne 21, Switzerland.

### Food/constituent as stated by the applicant

According to the applicant, the food which is the subject of the claim is ♀EFAX™, a standardised pure krill oil extract.

### Health relationship as claimed by the applicant

According to the applicant, the health relationship refers to the contribution to the maintenance of a normal menstruation cycle. Upon request from EFSA, the applicant clarified the health relationship to be related to the contribution to reduce menstrual discomfort.

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

The applicant has proposed the following wordings for the health claim: “♀EFAX™ contributes to maintain a normal menstruation cycle”, “♀EFAX™ helps to reduce the severity of symptoms related to the premenstrual syndrome and dysmenorrhoea”, “♀EFAX™ contributes to maintain a normal menstruation cycle by reducing the intensity of emotional symptoms, such as irritability and stress experienced before menstruation”, and “♀EFAX™ contributes to maintain a normal menstruation cycle by reducing the intensity of physical symptoms, such as abdominal discomfort and joint sensitivity experiences before and during menstruation”.

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

According to the applicant, the target population is women presenting physiological and emotional symptoms associated with the menstruation cycle. The applicant proposed an intake of ♀EFAX™ of 2,000 mg/day preferably in the morning for one month during the first cycle and thereafter a dose of 2,000 mg/day for eight days prior to and two days during menstruation.

## ASSESSMENT

### 1. Characterisation of the food/constituent

The food that is the subject of the health claim is ♀EFAX™, which is standardised pure krill oil.

Krill oil is extracted from the crustacean *Euphausia superba* (Antarctic Krill). It has been authorised as a novel food ingredient<sup>5</sup>. The krill oil which is the subject of the claim complies with Commission Decision 2009/752/EC. The main constituents contained in the krill oil which is the subject of the claim are phospholipids ( $\geq 42.0$  g/100 g), omega-3 fatty acids ( $\geq 26.5$  g/100 g), comprising eicosapentaenoic acid (EPA, C20:5,  $\geq 14.2$  g/100 g) and docosahexaenoic acid (DHA, C22:6,  $\geq 8.5$  g/100 g), and saturated fatty acids ( $25.0 \pm 5$  g/100 g). The content of esterified astaxanthin amounts to around 1,000 to 1,500 mg/kg. Phospholipids, fatty acids and astaxanthin can be measured in foods by established methods. Information on the stability and the batch-to-batch variability of the product has been provided.

<sup>5</sup> 2009/752/EC: Commission Decision of 12 October 2009 authorising the placing on the market of a lipid extract from Antarctic Krill *Euphausia superba* as a novel food ingredient under Regulation (EC) No 258/97 of the European Parliament and of the Council (notified under document C(2009) 7647), OJ L 268, 13.10.2009, p. 33–34.

The Panel considers that the food, ♀EFAX™, which is the subject of the health claim, is sufficiently characterised.

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

The claimed effect is “contributes to reduce menstrual discomfort”. The target population proposed by the applicant is “women presenting with physiological and emotional symptoms associated with the menstruation cycle”.

Menstrual discomfort can be assessed as changes in the severity of symptoms related to the premenstrual syndrome and/or dysmenorrhoea using validated questionnaires.

The Panel considers that reduction of menstrual discomfort is a beneficial physiological effect.

## 3. Scientific substantiation of the claimed effect

The applicant performed a literature search in PubMed, ScienceDirect, Blackwell Synergy, Wiley InterScience, Mary Ann Liebert, Scirus, IBIDS, SciFinder Scholar, Pascal, Google and SCOPUS with the search terms [“Neptune krill oil”] AND [“premenstrual syndrome” OR “dysmenorrhoea”]. No time limits were applied to the search. Hand searches in specialised libraries and web research were also performed. The Panel notes the limitations of the literature search performed by the applicant.

The applicant identified one published human intervention study (Sampalis et al., 2003) as pertinent to the claim.

In the double-blind, randomised, controlled parallel study by Sampalis et al. (2003), 70 women (mean age approx. 33 years) who fulfilled the Diagnostic and Statistical Manual of Mental Disorders-III-Revised (DSM-III-R) criteria for premenstrual syndrome (PMS) were randomised to consume daily 2 g of either krill oil (n=36) or fish oil (18 % EPA, 12 % DHA; n=34) for one month and thereafter for eight days prior to and two days during menstruation for the two subsequent menstruation cycles. The applicant was invited to clarify whether subjects included in the study were diagnosed with late luteal phase dystrophic disorder (LPDD) to which the diagnostic criteria of the DSM-III-R relate. The applicant replied that according to the American College of Obstetricians and Gynecologists, the DSM set of criteria for diagnosing premenstrual dysphoric disorder (PMDD, or LPDD in DSM-III-R) is similar to the diagnostic criteria used for PMS, and that only subjects having less severe forms of PMS (not leading to functional impairment) were recruited for the study. The Panel considers that the characterisation of the study population with respect to the diagnosis of LPDD, a disorder typified in DSM-III-R, is unclear.

The krill oil administered in the study was manufactured in line with the applicant’s specifications. Subjects had to discontinue use of any food supplements two weeks prior to study initiation, but were allowed to continue use of analgesics and oral contraceptives throughout the study. The Panel notes that no information was provided about the use of oral contraceptives by the study subjects prior to or during the study. Severity of symptoms associated with PMS (breast tenderness, feeling overwhelmed, stress, irritability, depression, joint pain, weight gain, abdominal pain, swelling and bloating) was assessed at baseline and at days 45 and 90 using a self-assessment questionnaire in which symptom severity was rated on a 11-point Likert scale, and by the quantity of analgesic consumption for menstrual pain. The applicant was asked to clarify the origin of the questionnaire used in the study and to provide a copy of it, as well as information on its validation to assess changes in the severity of PMS symptoms. The applicant did not provide a copy of the questionnaire as requested, nor evidence for the validation of the questionnaire as used in the study to assess changes in the severity of PMS symptoms. The Panel notes that the validity of the questionnaire as used in the study to assess changes in the severity of PMS symptoms during an intervention is unclear. The Panel

also notes that the quantity of *ad libitum* analgesic consumption is not a direct measure of changes in the severity of PMS symptoms.

None of the subjects dropped out of the study. Between group differences were analysed at day 90 using analysis of variance (ANOVA). The applicant was invited to comment on why baseline values, medication use (analgesics and contraceptives) and repeated measures were not taken into account in the analysis. The applicant replied that baseline values and medication use were not considered in data analyses because they “appeared” to be “well-balanced” between the two treatment groups, and that between-group comparisons for PMS symptoms were only made at 90 days in order to limit multiple comparisons. The Panel notes the inadequate reporting and limitations of the statistical analysis performed (e.g. biological variability over time and differences in medication use between groups were not considered).

The Panel notes that the information with respect to characterisation of the subjects recruited and to the questionnaire used to assess changes in the severity of PMS symptoms is insufficient to perform a full scientific evaluation; the Panel also notes the inadequate reporting and limitations of the statistical analysis. The Panel considers that no conclusions can be drawn from this study for the scientific substantiation of the claim.

The Panel notes that no human intervention studies from which conclusions could be drawn for the scientific substantiation of the claim were provided by the applicant.

The Panel concludes that a cause and effect relationship has not been established between the consumption of ♀EFAX™ and reduction of menstrual discomfort.

## CONCLUSIONS

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

- The food, ♀EFAX™, which is standardised pure krill oil and is the subject of the claim, is sufficiently characterised.
- The claimed effect is “contributes to reduce menstrual discomfort”. The target population proposed by the applicant is “women presenting with physiological and emotional symptoms associated with the menstruation cycle”. Reduction of menstrual discomfort is a beneficial physiological effect.
- A cause and effect relationship has not been established between the consumption of ♀EFAX™ and reduction of menstrual discomfort.

## DOCUMENTATION PROVIDED TO EFSA

Health claim application on ♀EFAX™ and reduction of menstrual discomfort pursuant to Article 13(5) of Regulation (EC) No 1924/2006 (Claim serial No: 0354\_CY). July 2012. Submitted by Nutrilinks Sarl.

## REFERENCES

Sampalis F, Bunea R, Pelland MF, Kowalski O, Duguet N and Dupuis S, 2003. Evaluation of the effects of Neptune Krill Oil on the management of premenstrual syndrome and dysmenorrhea. *Alternative Medicine Review*, 8, 171-179.



## GLOSSARY AND ABBREVIATIONS

ANOVA	Analysis of variance
DHA	Docosahexaenoic acid
DSM-III-R	Diagnostic and Statistical Manual of Mental Disorders-III-Revised
EPA	Eicosapentaenoic acid
LPDD	Luteal phase dystrophic disorder
PMDD	Premenstrual dysphoric disorder
PMS	Premenstrual syndrome