

SCIENTIFIC OPINION

Scientific Opinion on the substantiation of a health claim related to Catalgine[®] bouffées de chaleur and contributes to the reduction in the number of hot flushes pursuant to Article 13(5) of Regulation (EC) No 1924/2006¹

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

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ABSTRACT

Following an application from Laboratoire Vie et Santé submitted pursuant to Article 13(5) 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 based on newly developed science and including proprietary data related to Catalgine[®] and contributes to the reduction in the number of hot flushes. Catalgine[®] bouffées de chaleur (also called OM3[®] menopause) is a dietary supplement made with concentrated wild fish oil that is sufficiently characterised. The reduction in the frequency of episodes of hot flushes is considered beneficial to the health of peri- and post-menopausal women. Two publications (three studies) were identified by the applicant as being pertinent to the claim. Two studies were uncontrolled with respect to the supplement. The third was a post-hoc analysis of a subsample of women participating in a randomised, placebo controlled intervention evaluating the effects of Catalgine[®] on psychological distress. A number of weaknesses in this study, including unsuccessful blinding and limited power, greatly limit its value as a source of data to substantiate the claimed effect. The Panel concludes that a cause and effect relationship has not been established between the consumption of Catalgine[®] bouffées de chaleur and the reduction in the frequency of episodes of hot flushes.

KEY WORDS

Catalgine[®] bouffées de chaleur, eicosapentaenoic acid, docosahexaenoic acid, n-3 polyunsaturated fatty acids, hot flushes, peri-menopausal women, post-menopausal women, health claims.

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SUMMARY

Following an application from Laboratoire Vie et Santé submitted pursuant to Article 13(5) 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 Catalgine[®] and contributes to the reduction in the number of hot flushes.

The scope of the application was proposed to fall under a health claim based on newly developed scientific evidence and including a request for the protection of proprietary data.

The food constituent that is the subject of the health claim is Catalgine[®] bouffées de chaleur (also called OM3[®] menopause). The product is described as a dietary supplement made with concentrated wild fish oil from sardines and anchovies. The amount of fish oil per capsule is 500 mg with total n-3 fatty acids being about 90 % by weight, eicosapentaenoic acid (EPA) about 73 % (688.6 mg/g) and docosahexaenoic acid (DHA) about 13 % (123.4 mg/g) expressed as ethyl esters. The Panel considers that the food constituent, Catalgine[®] bouffées de chaleur, which is the subject of the health claim, is sufficiently characterised.

The claimed effect is “management of vasomotor symptoms, particularly hot flushes”. The target population is middle aged women prone to hot flushes during the peri- and the post-menopausal period. From the proposed wording, the Panel assumes that the claimed effect relates to the reduction in the number of episodes of hot flushes. The Panel considers that the reduction in the frequency of episodes of hot flushes is beneficial to the health of peri- and post-menopausal women.

Two publications were identified by the applicant as being pertinent to the claim. The first publication reported on two double-blinded randomised controlled trials (RCT) with cross-over design of 24 week duration. The Panel notes that no conclusions can be drawn from these studies to substantiate the claim as they were uncontrolled with respect to the PUFA supplement, which also differed substantially from the PUFA profile of the product that is the subject of the health claim.

The second publication reported on a double-blinded RCT with parallel design in middle aged women suffering from hot flushes (HF) who were part of a larger clinical trial aimed at evaluating the effects of OM3[®] (identical to Catalgine[®] bouffées de chaleur) on psychological distress. A total of 29 women (n=14 OM3[®] group, n=15 placebo) did not have any HF symptoms during the study and were excluded from the secondary post-hoc analysis, which included data from 43 (OM3[®] group) and 39 (placebo group) women, respectively. Secondary outcomes of the study were changes in HF frequency (number of HF/d), HF intensity, HF score (frequency x intensity), and changes in the proportion of HF responders defined as a reduction in HF frequency of 50 % or more. HF frequency and intensity were reported by means of a self-administered questionnaire. A significantly higher percentage of women in the OM3[®] group than in the placebo group declared a fish taste of the capsules (46.5 % vs 5.1 %). After 8 weeks of supplementation, HF frequency and HF score decreased significantly in the supplemented group compared to placebo. The odds of being a responder among those taking the supplement were 2.7 times greater than among those taking placebo. Changes in HF intensity were not significantly different between the groups. Post-hoc power analysis indicated a power of 66 % to detect the observed difference of 1.1 HF/d between groups.

The Panel notes a number of weaknesses in this study: a significantly higher percentage of women in the OM3[®] group declared a fish taste of the capsules compared to the placebo group indicating a failure in the subjects' blinding, which is a major drawback for self-reported outcomes such as HF frequency and intensity; the study reported a post-hoc analysis on a secondary outcome in a sub-group of women who were selected only post-randomisation on the basis of suffering from HF. The Panel considers that the significant weaknesses of this study greatly limit its value as a source of data to substantiate the claimed effect.

The Panel concludes that a cause and effect relationship has not been established between the consumption of Catalgine[®] bouffées de chaleur and the reduction in the frequency of episodes of hot flushes.

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BACKGROUND AS PROVIDED BY THE EUROPEAN COMMISSION

Regulation (EC) No 1924/2006⁴ 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, Article 13(5) of that Regulation lays down provisions for 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 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 that Regulation, an application for authorisation or inclusion in the Community list of permitted claims referred to in Art 13(3) 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 06/10/2009.
- The scope of the application was proposed to fall under a health claim based on newly developed scientific evidence and including a request for the protection of proprietary data.
- The scientific evaluation procedure started on 20/10/2009.
- During the meeting on 04/12/2009, the NDA Panel, after having evaluated the overall data submitted, adopted an opinion on the scientific substantiation of a health claim related to Catalgine[®] and contributes to the reduction in the number of hot flushes.

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(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: Catalgine[®] bouffées de chaleur and contributes to the reduction in the number of hot flushes.

EFSA DISCLAIMER

The present opinion does not constitute, and cannot be construed as, an authorisation to the marketing of Catalgine[®] bouffées de chaleur (also called OM3[®]menopause), a positive assessment of its safety, nor a decision on whether Catalgine[®] bouffées de chaleur (also called OM3[®]menopause) 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.

⁴ 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.

INFORMATION PROVIDED BY THE APPLICANT

Applicant's name and address: Laboratoire Vie et Santé, 8 rue Christophe Colomb, 75008 Paris, France

The application includes a request for the protection of proprietary data in accordance with Article 21 of Regulation (EC) No 1924/2006.

Food/constituent as stated by the applicant

The Catalgine[®] bouffées de chaleur (also called OM3[®] menopause) product contains concentrated wild fish oil (sardines and anchovies), rich in omega-3 fatty acids (minimum 90 %).

Health relationship as claimed by the applicant

The applicant states that vasomotor instability causes symptoms like hot flushes, resulting from disruption of temperature regulatory mechanisms and associated vasodilatation. Hot flushes manifest as intense heat and intense sweating followed by a cold, clammy sensation. They are mostly caused by the hormonal changes of menopause, but can also be affected by lifestyle and medications. Dietary omega-3 from fish oil could play a role in the management of vasomotor symptoms, particularly hot flushes.

Wording of the health claim as proposed by the applicant

“Contributes to the reduction in the number of hot flushes”.

Specific conditions of use as proposed by the applicant

Three capsules per day in three catches, preferably at the beginning of each meal, for an 8-week period.

ASSESSMENT

1. Characterisation of the food/constituent

The food constituent that is the subject of the health claim is Catalgine[®] bouffées de chaleur (also called OM3[®] menopause). The product is described as a dietary supplement made with concentrated wild fish oil from sardines and anchovies. The amount of fish oil per capsule is 500 mg with total n-3 fatty acids being about 90 % by weight, eicosapentaenoic acid (EPA) about 73 % (688.6 mg/g) and docosahexaenoic acid (DHA) about 13 % (123.4 mg/g) expressed as ethyl esters. The total lipids are comprised of polyunsaturated fatty acids (489 mg/capsule), monounsaturated fatty acids (10 mg/capsule) and saturated fatty acids (1 mg/capsule). Each capsule also contains protein (147 mg) and carbohydrates (25 mg), and vitamin E (1.25 mg, at least 70 % as alpha tocopherols) is added as an antioxidant. The total energy content is 5.2 kcal (21.7 kJ). A certificate of analysis, a scheme detailing the manufacturing process, stability information and quality control procedures are supplied along with data which indicate that there is no significant difference in bioavailability between the ethyl ester preparations of the n-3 fatty acids (purported active ingredients) and the corresponding triacylglycerols.

The Panel considers that the food constituent, Catalgine[®] bouffées de chaleur, which is the subject of the health claim, is sufficiently characterised.

2. Relevance of the claimed effect to human health

The claimed effect is “management of vasomotor symptoms, particularly hot flushes”. The target population is middle aged women prone to hot flushes during the peri- and the post-menopausal period.

From the proposed wording, the Panel assumes that the claimed effect relates to the reduction in the number of episodes of hot flushes. Hot flushes are episodes of intense heat and sweating with increased heart rate followed by a cold, clammy sensation. The hormonal changes of menopause appear to cause the symptoms. The symptoms of hot flushes cause considerable discomfort to those who are affected.

The Panel considers that the reduction in the frequency of episodes of hot flushes is beneficial to the health of peri- and post-menopausal women.

3. Scientific substantiation of the claimed effect

The applicant searched the databases American Chemical Society, Cochrane, Ovid, Pascal, Pubmed/Medline, Science Direct, Scirus, SpringerLink, Wiley InterScience using the terms [“fish oil” OR fish OR EPA OR DHA] AND [“hot flashes” OR “hot flushes” OR vasomotor OR thermoregulation]. In total two studies were identified.

The first publication (Campagnoli et al., 2005) reports on two double-blinded randomised controlled trials with cross-over design of 24 week duration. Although the active food constituent in each study was isoflavones, a PUFA supplement containing a mix of n-6 and n-3 fatty acids was given daily to each postmenopausal woman for the entire 24 week period. The Panel notes that no conclusions can be drawn from these studies to substantiate the claim as they were uncontrolled with respect to the PUFA supplement, which also differed substantially from the PUFA profile of the product that is the subject of the health claim.

The second publication (presented as an unpublished study report in the application but now published as a full-text article, Lucas et al., 2009), reports on a double-blinded randomised controlled trial with parallel design in middle aged women suffering from hot flushes (HF) who were part of a larger clinical trial aimed at evaluating the effects of OM3[®] (identical to Catalgine[®] bouffées de chaleur) on psychological distress (n=59 supplement, n=61 placebo). Women were considered for participation if they were between 40-55 years of age and had moderate to severe psychological distress, defined as a score of ≥ 72 on the Psychological General Well-Being Schedule. A range of appropriate exclusion criteria for a trial evaluating the effects of a n-3 PUFA supplement on psychological distress were also employed. As the main objective of the study was to compare the mean change in the Psychological General Well-Being Schedule score after 8 weeks of intervention with the product against a sunflower oil placebo, not all of the women had HF symptoms at baseline. A total of 29 (n=14 supplement, n=15 placebo) did not have any HF symptoms during the study and were excluded from the secondary post-hoc analysis which included data from 45 and 43 (supplemented group) and 46 and 39 (placebo group) women at baseline and week 8 of supplementation, respectively. Secondary outcomes of the study were changes from baseline (average number of HF=2.8/d) to week 8 post-intervention in HF frequency (number of HF/d), HF intensity, HF score (frequency x intensity), and changes in the proportion of HF responders defined as a reduction of 50 % or more in the HF frequency between baseline and week 8. HF frequency and intensity were reported by means of a self-administered questionnaire. HF included daytime episodes as well as night sweats. The proportion of compliers (taking >80 % of the prescribed capsules) was not different between groups, but a significantly higher percent of women in the OM3[®] group declared a fish taste of the capsules (46.5 % vs 5.1 %). The percentage of women being in post-menopause defined as 12 months of amenorrhea following the final menstrual period was not significantly different between groups (31.1 % in the intervention vs 50.0 % in controls, p=0.07).

After 8 weeks of supplementation, HF frequency and HF score decreased significantly in the supplemented group compared to placebo; mean decreases in HF frequency were -1.58/d (95 % CI, -2.18 to -0.98) and -0.50/d (95 % CI, -1.20 to 0.20) in the supplemented group and placebo (mean difference change = -1.1, 95 % CI, -2.0 to -0.2), respectively. The odds of being a responder among those taking the supplement were 2.7 times greater (95 % CI, 1.03 to 7.03; $p=0.04$) than among those taking placebo. Changes in HF intensity were not significantly different between the groups. Post-hoc power analysis using the mean HF frequency change at week 8 and SD (two-tailed significance, $\alpha=0.05$) indicated a power of 66 % to detect the observed difference of 1.1 HF/d between groups.

The Panel notes a number of weaknesses in this study: a significantly higher percentage of women in the OM3[®] group declared a fish taste of the capsules compared to the placebo group (46.5 % vs 5.1 %) indicating a failure in the subjects' blinding, which is a major drawback for self-reported outcomes such as HF frequency and intensity; the study reported a post-hoc analysis on a secondary outcome in a subgroup of women who were selected only post-randomisation on the basis of suffering from HF, such analyses being at high risk of bias (Rothwell, 2005; Schulz and Grimes, 2005; Wang et al., 2007). The Panel considers that the significant weaknesses of this study greatly limit its value as a source of data to substantiate the claimed effect.

The Panel concludes that a cause and effect relationship has not been established between the consumption of Catalgine[®] bouffées de chaleur and the reduction in the frequency of episodes of hot flushes.

CONCLUSIONS

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

- The food constituent, Catalgine[®] bouffées de chaleur, that is the subject of the health claim, is sufficiently characterised.
- The claimed effect is “management of vasomotor symptoms, particularly hot flushes”. The target population is middle aged women prone to hot flushes during the peri- and the post-menopausal period. The reduction in the frequency of episodes of hot flushes is beneficial to the health of peri- and post-menopausal women.
- A cause and effect relationship has not been established between the consumption of Catalgine[®] bouffées de chaleur and the reduction in the frequency of episodes of hot flushes.

DOCUMENTATION PROVIDED TO EFSA

Health claim application on Catalgine[®] and contributes to the reduction in the number of hot flushes pursuant to Article 13(5) of Regulation (EC) No 1924/2006 (Claim serial No: 0262_FR). October 2009. Submitted by Laboratoire Vie et Santé.

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GLOSSARY / ABBREVIATIONS

DHA	docosahexaenoic acid
EPA	eicosapentaenoic acid
HF	hot flushes
PUFA	polyunsaturated fatty acids