Maisons-Alfort, 16 November 2011

OPINION
of the French Agency for Food, Environmental and Occupational Health & Safety

regarding an application for marketing authorisation for a novel food or novel food ingredient: krill oil - extension of uses

ANSES undertakes independent and pluralistic scientific expert assessments.
ANSES primarily ensures environmental, occupational and food safety as well as assessing the potential health risks they may entail.
It also contributes to the protection of the health and welfare of animals, the protection of plant health and the evaluation of the nutritional characteristics of food.
It provides the competent authorities with all necessary information concerning these risks as well as the requisite expertise and scientific and technical support for drafting legislative and statutory provisions and implementing risk management strategies (Article L.1313-1 of the French Public Health Code).
Its opinions are made public.

1. REVIEW OF THE REQUEST

On 3 October 2001, the French Agency for Food, Environmental and Occupational Health & Safety (ANSES) received a request from the Directorate-General for Competition, Consumer Affairs and Fraud Control (DGCCRF) for an Opinion relating to an application for marketing authorisation for a food ingredient: krill oil - extension of uses.

2. BACKGROUND AND PURPOSE OF THE REQUEST

In 2007, the applicant submitted the first application for marketing authorisation for a novel food ingredient (NI), namely krill oil, in the following products: dairy products, fruit juices, protein bars, meal substitutes, food supplements and dietary foods for special medical purposes.

This application received an overall positive opinion from the Finnish authorities (the Novel Food Board of the Finnish Ministry of Agriculture and Forestry) which performed the initial assessment of the NI, and from the European Food Safety Authority (EFSA). The French Food Safety Agency (AFSSA) also issued a favourable opinion, but stressed the need to assess the effects of excessive consumption of the NI, given the possibility of cumulative intake from a number of different products. AFSSA also felt that 'consideration should be given to limiting the range of products and the levels of enrichment'. The application for marketing authorisation was officially accepted under Commission Decision 2009/752/EC, granting authorisation for use of the NI in the following products:

- Dairy products except milk-based drinks
- Dairy analogues except drinks
- Spreadable fat and dressings
- Breakfast cereals

- Food supplements
- Dietary foods for special medical purposes

The applicant is now applying for an extension of uses of krill oil to include products authorised to contain oils of a similar composition to that of the NI, namely microalgae oils (Commission Decisions 2009/777/EC and 2009/778/EC). The applicant is also requesting an increase in the maximum content of the NI in food supplements.

3. ORGANISATION OF THE EXPERT APPRAISAL

The expert appraisal was carried out in accordance with French standard NF X 50-110 "Quality in Expert Appraisals – General requirements of Competence for Expert Appraisals (May 2003)".

The collective expert appraisal was conducted by the Expert Committee (CES) on human nutrition based on the initial reports written by two rapporteurs. Due to the very short regulatory deadlines, the opinion was validated by correspondence by the CES on human nutrition.

4. ANALYSIS AND CONCLUSIONS OF THE CES

■ Specification of the NI

The novel ingredient is a lipid extract from the crustacean Antarctic Krill (*Euphausia superba)*. The specifications for this ingredient have already been subject to an assessment by AFSSA (Request 2007-SA-0080). These correspond to the specifications authorised and described in Commission Decision 2009/752/EC, i.e.:

Description: Lipid extract is produced from crushed deep-frozen Antarctic Krill (*Euphausia superba*) by acetone extraction. Proteins and krill material are removed from the lipid extract by filtration. The acetone and residual water are removed by evaporation.	
Test	**Specification**
Saponification value	Not more than 185 mg KOH/g
Peroxide value (PV)	Not more than 0.2 meq O_2/kg oil
Moisture and volatiles	Not more than 0.9%
Phospholipids	Not more than 50%
Trans-fatty acids	Not more than 1%
EPA (eicosapentaenoic acid)	Not less than 15%
DHA (docosahexaenoic acid)	Not less than 7%

■ Outcome of the production process applied to the NI

The production process is the same as that previously assessed by AFSSA (Opinion 2007-SA-0080), which was considered to be acceptable.

■ Previous use of the organism used as the source of the NI

The previous use of Antarctic Krill was explained when the first application for marketing authorisation was submitted in 2007. Antarctic Krill is found in the Antarctic waters of the Southern Ocean. In phylogenetic terms, Antarctic Krill is similar to the common shrimp.

This point did not give rise to any comments from the Finnish authorities or AFSSA in 2007.

■ **Consumption/level of use of the NI envisaged**

- Extension of use of the NI

Use of the NI in a number of products was authorised by Commission Decision 2009/752/EC. The applicant is now proposing that this be extended to products for which the inclusion of DHA-rich microalgae oils was authorised by Commission Decisions 2009/778/EC (*Schizochytrium sp*) and 2009/777/EC (*Ulkenia sp*).

The applicant now wishes to extend the list of authorised products to include:

- bakery products, with a maximum content of DHA and EPA of 200 mg/100 g;
- breads and rolls, with a maximum content of DHA and EPA of 200 mg/100 g;
- diet bars, with a maximum content of DHA and EPA of 500 mg/100 g;
- non-alcoholic beverages, with a maximum content of DHA and EPA of 60 mg/100 ml;
- milk-based drinks and analogues, with a maximum content of DHA and EPA of 60 mg/100 ml.

The applicant has stated that the maximum levels of the NI added to these new products are calculated in such a way that the sum of the DHA and EPA content corresponds to the levels of DHA authorised by Commission Decisions 2009/778/EC and 2009/777/EC for microalgae oils.

The applicant has given two estimates of the maximum intake of EPA and DHA. The first estimate is calculated using the gross values of food consumption reported by the UK's National Diet and Nutrition Survey (NDNS). This estimate is based on the hypothesis that consumers would consume each of the foodstuffs on the list of authorised products, in the enriched version, to the maximum authorised levels of EPA and DHA. This scenario therefore takes eating habits into account. According to this scenario, the average EPA and DHA exposure levels are 435 mg for young children aged between 1.5 and 4.5 years, 678 mg for children aged between 4.5 and 10 years, 703 mg for female adolescents, 898 mg for male adolescents (11-18 years), 653 mg for adult women and 831mg for adult men. The intake levels for the 97.5th percentile range from 835 mg for young children to 1697 mg for adult men.

The second estimate uses actual market data to estimate consumption per person throughout Europe. This estimate is based on the hypothesis that all products that could be enriched with EPA/DHA are done so to the maximum levels. According to this estimate, the maximum daily intake would be 1500 mg of EPA and DHA.

The applicant feels that these two estimates are calculated on the basis of a 'worst case scenario' and that they overestimate intake. It takes the view that it is unlikely that a consumer would choose all the foodstuffs enriched with EPA/DHA on a daily basis, that they would consume maximum quantities of everything or that these products would be enriched to the maximum authorised levels. It imagines that the consumer would instead choose one or two categories of enriched products. According to this hypothesis, the intake levels of the 97.5th percentile would be between 600 mg and 700 mg per day.

The applicant also points out that international dietary recommendations for EPA and DHA range from 200 mg to 500 mg per day for the sum of the two fatty acids.

The estimates do not take into account food supplements or dietary foods for special medical purposes. According to the applicant, special dietary foods do not form part of the day-to-day diet. With regard to the food supplements, the applicant feels that it is unlikely that a consumer would buy food supplements or foodstuffs enriched with EPA/DHA on a regular basis.

- Increase in the NI content of food supplements

The applicant also wishes to increase the EPA/DHA content of food supplements from 200 mg per day to 250 mg per day.

To support its application, the applicant states that 250 mg per day is the dose at which the beneficial impacts on health have been proven. On assessing these alleged benefits, EFSA issued a favourable opinion for an intake of between 250 mg and 3000 mg per day of EPA + DHA, according to the applicant.

The Finnish authorities point out that the products to which the applicant wishes to add the NI are already authorised to contain n-3-rich PUFA microalgae oils. It is their opinion that the nature of the source ingredient of the n-3 PUFA is not as important a criterion as the intake levels. Therefore, they feel that the EPA and DHA-rich NI may be used for the same purposes as the oils from the DHA-rich microalgae.

The Finnish authorities note that the increase in the EPA/DHA content of food supplements from 200 mg per day to 250 mg per day should not lead to a significant rise in the intake of these fatty acids. They stressed that there are many food supplements on the market that contain levels of n-3 PUFA from fish oil that exceed 250 mg per day. They therefore feel that food supplements containing the NI will replace the EPA and DHA-rich food supplements already on the market.

The CES on human nutrition agrees with the Finnish authorities that the NI could be used for the same purposes as the oils from the DHA-rich microalgae. In its opinion regarding the microalgae oils (Request 2008-SA-0316), AFSSA stressed that 'this oil does not contain EPA and alone could not replace the fish oils that contain the nutritional fatty acids EPA and DHA'. The profile of the NI as a fatty acid similar to that contained in fish oils could mean that it is considered as an alternative to help reach the advised intake of EPA and DHA.

With regard to the estimates of the maximum EPA and DHA intake levels provided by the NI, the CES on human nutrition considers that the two methods used reach estimates on the maximum intake that are coherent and below levels observed in certain sections of the population that consume a lot of fish (2.8g/day) (Leblanc, 2006). However, it regrets that these intake estimates do not take into account the basal level of exposure or consumption of EPA/DHA-rich food supplements, which vary enormously depending on the level of consumption of seafood products, in particular. Consumption of enriched products by heavy consumers of fish could lead to very high EPA/DHA intake levels, the long-term effects of which are as yet unknown. As AFSSA pointed out in its Opinion regarding the microalgae oils (Request 2008-SA-0316), a high intake of DHA could be harmful in terms of the peroxidation process which could occur in foodstuffs. This process varies in intensity, due largely to the food matrix or cooking/storage method (AFSSA, 2003). These peroxidation reactions generate different compounds, in particular hydroxy-alkenals, the biological effects of which have yet to be assessed (Surh et al., 2007). Despite this, no mention is made of studying the product's stability in the different food matrices proposed. The uncertainty regarding a high intake of long-chain n-3 PUFA by children is even greater, as fewer studies have been carried out in this regard.

Nevertheless, the CES on human nutrition feels that correct labelling of the NI on the enriched products should prevent heavy consumers of seafood products from consuming EPA and DHA-enriched foodstuffs.

With regard to the increase in the NI content of food supplements, the CES on human nutrition agrees with the Finnish authorities that an increase in the EPA and DHA content of food supplements from 200 mg per day to 250 mg per day should not lead to a significant rise in the intake of these fatty acids.

■ **Information on previous human exposure to the NI or source thereof**

The applicant points out that authorisation has been granted for a number of foodstuffs and food supplements to contain the NI in the European Union. Furthermore, oils of a similar composition, extracted from Antarctic krill and intended for use in the same foodstuffs, have been placed on the market in accordance with the notification procedure in Article 5 of Regulation (EC) No 258/97.

The applicant also states that food supplements containing the NI have been widely available on the European market since 2009 and on the markets of countries such as Canada, the USA and Japan since 2004. During this time, there have been no reports of any adverse effects on health.

In their opinion of 2007, the Finnish authorities noted that small quantities of shrimp-like crustaceans have been consumed in France, Japan, Russia and Ukraine since the 1970s.

This point did not give rise to any particular comments from the CES on human nutrition.

■ **Nutritional information on the NI**

The NI is basically composed of lipids and, as such, has a nutritional value of around 9 kcal/g.

With a content of over 30%, the NI constitutes a source of n-3 PUFA. As stated in the applicant's initial dossier from 2007, 100 g of the NI contains at least 12 g of MUFA, less than 30 g of SFA, between 0.8 g and 1.2 g of cholesterol and between 0.5 g and 3.5 g of proteins. The oil has a high phospholipid content, i.e. more than 40%. The fatty acids profile of the NI is similar to that of EPA- and DHA-rich fish oils.

The applicant points out that, during the assessment of the alleged health benefits, EFSA acknowledged that the NI can help to protect against cardiovascular disease.

The Finnish authorities refer to their initial assessment of the dossier of 2007 in which they underlined the similarity between the profiles of the fatty acids of the NI and oily fish. They stress that they have not assessed the health benefits of the NI because said assessment does not fall within the scope of the regulations on novel foods.

The CES on human nutrition wonders whether the NI is intended for use in the target foodstuff or if it will replace another fat (at least partially).

■ **Microbiological information about the NI**

The NI is the same product as that assessed by the Finnish authorities in 2007. The said authorities considered that the microbiological quality of the NI was controlled by an assessment of the critical points based on the HACCP method. Quality is ensured by monitoring the levels of aerobic bacteria and presence of coliforms, yeasts and moulds. The presence of pathogenic microbes is monitored by measuring *Salmonella, Escherichia coli, Staphylococcus aureus, Listeria monocytogenes* and *Pseudomonas aeruginosa* in the production batches. The applicant also gives the analysis results from three production batches.

The Finnish authorities highlight the fact that the European Union does not set out specific criteria for the microbiology of oils. The general obligations are laid out in Regulation (EC) No 852/2004 on the hygiene of foodstuffs applied to microbiological quality. The Finnish authorities state that the

HACCP method presented by the applicant and the microbiological tests performed are in line with both Canadian standards and the general recommendations of the EU.

***This point did not give rise to any particular comments from the CES on human nutrition**.*

■ **Toxicological information on the NI**

The Finnish authorities assessed the toxicological data on the NI in their previous opinion of 2007. They decided that the results presented by the applicant did not raise any doubts as to the safety of the NI. Fish oil may prolong bleeding time. According to the United States Food and Drug Administration (FDA), there should be no problems regarding clotting in doses of EPA+DHA of under 3 g per day. Furthermore, as krill has been consumed for many years, it is unlikely that any new problem regarding safety will arise.

In their 2007 opinion, the Finnish authorities noted that there was a possibility that individuals allergic to fish and crustaceans would have an allergic reaction to products containing the NI, although the amount of protein likely to be present in the NI is minimal. As a result of this, the Finish authorities decided that there should be a warning on the label of foodstuffs containing the NI indicating that the product contains crustacean oil in accordance with Directive 2000/13/EC on the labelling, presentation and advertising of foodstuffs. This point was taken into consideration in Commission Decision 2009/752/EC, which stated that the fact that the oil is an extract from crustaceans must be displayed on the labelling of the product.

The conclusion of the safety assessment carried out by the Finnish authorities in 2007 was confirmed by EFSA in its opinion of 2009.

The Finnish authorities state that the NI is the same as that which they assessed in 2007 and therefore they have issued a favourable opinion. The extension of uses of the NI has not affected their toxicological assessment and therefore the Finish authorities confirm their opinion of 2007, in which they deemed the toxicological results to be acceptable with regard to the use of krill as a foodstuff.

The CES on human nutrition agrees with the opinion of the Finnish authorities.

■ **Conclusions of the Finnish authorities**

The Finnish authorities feel that the application by the applicant for an extension of uses of the NI in bakery products, diet bars, non-alcoholic beverages and milk-based drinks and analogues fulfils the safety criteria of Article 3 of Regulation (EC) No 258/97 concerning novel foods and novel food ingredients. The Finnish authorities also feel that the increase in the maximum content of the NI in food supplements, bringing the sum of EPA and DHA to 250 mg per day, should fulfil the preconditions set out in the regulations on novel foods.

■ **Conclusions of the CES on human nutrition**

It is the opinion of the CES on human nutrition that:

- Despite the fact that no consideration was given to the basal level of DHA consumption, the estimated maximum consumption level of EPA and DHA in terms of the possible consumption levels of heavy consumers of seafood products is acceptable. The CES therefore feels that the maximum consumption level of EPA and DHA does not pose any serious public health problem. Nevertheless, it feels that any intake above the ANC[1] ~~RDA~~ is unnecessary;

[1] "Apports nutritionnels conseillés" (ANC) are the French equivalent of the Population Reference Intakes (PRI)

- the increase in the content of the NI in food supplements does not pose any serious public health problem;
- it is advisable to indicate the presence of the NI in the foodstuff on the label thereof;
- the rate of peroxidation of the novel ingredient and the enriched product must be checked regularly.

5. CONCLUSION AND RECOMMENDATIONS OF THE AGENCY

The French Agency for Food, Environmental and Occupational Health & Safety (ANSES) hereby adopts the conclusions of the CES on human nutrition.

Director General

Marc MORTUREUX

KEYWORDS

Krill oil, omega-3 fatty acids, novel food, EPA, DHA.

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