European Food Safety Authority

Scientific Panel on Dietetic Products, Nutrition and Allergies Unit

Parma, 3 September 2009
Ref. JK/jj **out-4238006**

Mr. Basil Mathioudakis
European Commission
Head of Unit – Directorate E4
DG Health & Consumers
Rue de la Loi 200
B-1049 Brussels

Subject: **Response to comments with regard to the EFSA opinion on the scientific substantiation of a health claim related to *docosahexaenoic acid (DHA) and arachidonic acid (ARA)* and visual development pursuant to Article 14 of Regulation (EC) No 1924/2006 (EFSA-Q-2008-211).**

Dear Mr. Mathioudakis,

Thank you for informing EFSA about the various comments the European Commission received on above-mentioned EFSA opinion related to docosahexaenoic acid (DHA) and arachidonic acid (ARA) and visual development (EFSA-Q-2008-211)

I have discussed these comments with the chair of the NDA panel and the chair of the NDA standing working group on health claims and EFSA wishes to make the following comments:

1. Food constituent
Martek pointed out in its comments of 3 and 10 March 2009 that EFSA had wrongly stated in the opinion that the food constituents which were the subject of the health claim were DHA and ARA derived from single cell oils manufactured by the applicant (Mead & Johnson), rather than by Martek. EFSA would like to clarify that the information provided in application was not very clear in this respect but will now amend its opinion accordingly. However EFSA would also like to point out that the Panel decided not to limit the claim's evaluation to DHA and ARA from these specific sources but to extend the evaluation to DHA and ARA from all sources with appropriate bioavailability, given that the only active constituents identified in the oils for which the claim was requested were DHA and ARA which are well characterised nutrients.

2. Importance of ARA as component in infant and follow-on formulae
EFSA would like to note that the question addressed by EFSA in the context of the evaluation of the health claim was not whether ARA is needed in infant and follow-on formula, but rather whether ARA has an effect on the visual development of infants and young children. As stated in the EFSA opinion, the role of ARA on visual development could not be established on the basis of the data presented, and therefore, the presence of ARA in infant and follow-on formula is not a pre-condition to obtain the claimed effect.

3. Extension of the claim to weaning baby foods

The claimed effect could be extended to weaning baby foods (as for follow-on formula) provided that the target population is infants either breast-fed until weaning or having received a DHA-enriched infant formula containing 0.3% of fatty acids as DHA from birth until weaning. The evidence, however, does not establish that starting DHA supplementation at 4-6 months in infants who had received a control (DHA-free) formula in the first months of life would have an effect on the visual development of those children.

4. Studies on pre-term infants

The Panel did not consider studies in pre-term infants as pertinent for the substantiation of a claim on DHA and ARA and visual development in infants because the target population was interpreted as the "healthy/normal" infant population. Pre-term infants represent a population subgroup with special requirements, which may affect the rate of structural and functional maturation as compared to term-infants. Also, the evaluation of studies conducted in pre-term infants may need to be considered differently.

5. Review/recommendations from authoritative bodies to substantiate the claim

EFSA would like to note that these publications were considered by the Panel in the context of the background information providing biological plausibility for the claim. However, the narrative reviews and dietary recommendations by authoritative bodies presented did not address directly the specific scientific question raised in the application for authorisation, i.e., whether DHA and ARA supplemented formulas provide an advantage over (DHA and ARA) unsupplemented formulas on visual development in term infants under the specified conditions of use.

6. DHA supplementation only starting after the first (0-6) months of life

As stated in the opinion, there are no data from specific randomised control trials supporting a benefit of DHA supplementation starting at 6 months of life in infants fed a DHA-free formula in the first 6 months of life (see also opinion on DHA and ARA and development of the brain and eyes focusing on that target population, Claim serial No. 40-UK, EFSA-Q-2008-121). European legislation (Directive2006/141/EC[1]) allows supplementation of infant formulas with DHA, but such fortification is not mandatory.

7. Extension of the claim to young children

During the scientific evaluation of the application, the Panel considered whether a sustained effect of early DHA supplementation on visual development could be established, but found the evidence provided to be insufficient to substantiate that aspect of the claim. Only two out of the 9 randomised controlled studies considered as pertinent to the claim tested visual acuity after 12 months of life (Makrides *et al.*, 2000; Birch *et al.*, 2007[2]), and only one of these showed

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[1] Commission Directive 2006/141/EC of 22 December 2006 on infant formulae and follow-on formulae and amending Directive 1999/21/EC. Official Journal of the European Union OJ L 401, 30.12.2006, pp 1-32.

[2] Birch EE, Garfield S, Castaneda Y, Birch DG, Uauy R, Hoffman DR, 2007. Visual acuity and cognitive outcomes at 4 years of age in a double-blind, randomized trial of long-chain polyunsaturated fatty acid-supplemented infant formula. *Early Human Dev.* 83, 279-284; Makrides M, Neumann MS, Simmer K and Gibson RA, 2000. A critical appraisal of the role of dietary long-chain polyunsaturated fatty acids on neural indices of term infants: a randomized, controlled trial. *Pediatrics* 105, 32-38

significant differences between the DHA alone and the DHA plus ARA supplemented groups and the control formula group after 12 months (at 4 years) in a small sub-group of subjects.

8. Proposed conditions of use (at least 0.3% DHA of total fatty acids)
The Panel took into account the rules governing the composition of infant and follow-on formula in Europe. Directive EC 2006/141 states a mandatory content of ALA corresponding to 0.83% to 1.12% of total fatty acids from ALA. These levels are well below the 1.46% ALA contained in the control formula (non DHA supplemented) used in the Birch/Hoffman studies, which were taken into account by the panel for the substantiation of the claim.

We would like to point out that the Panel addressed the question whether infant and follow on formula, under the conditions of use proposed by the applicant, provided any benefit on visual development of infants as compared to standard (non DHA supplemented) formulas. The Panel did not address whether the conditions of use specified in the claim (0.3% DHA) could be modified by increasing the DHA precursor ALA levels to e.g. 2.6% of total fatty acid from ALA. The Panel also clearly indicated in the opinion that "a dose-response relationship (between DHA content and visual development) has not been directly tested".

I hope we addressed all scientific points raised during the commenting period on the EFSA opinion in question.

Yours sincerely,

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