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Lisa Brines
USDA - AMS - National Organic Program
Agricultural Marketing Specialist
1400 Independence Ave SW
Room 2646 South Building
Washington, DC 20250-0268

Re: DHA Algal Oil and ARA Single-Cell Oil Petitions

Dear Ms. Brines,

Attached please find a short summary of relevant references to the scientific literature and regulatory recognitions regarding the referenced Petitions. The references are provided solely to update and refresh the existing record. We wanted to be sure these were timely submitted in order that they may be made available to the technical review team. We look forward to addressing the merits of the Petitions at the National Organic Standards Board meeting in November 2011.

Please do not hesitate to contact me if you require any additional information or have any questions.

Best Regards,

Susan Cheney

Susan Cheney
Director Regulatory Affairs
Martek Biosciences Corporation

DHA Algal Oil

New DHA Approvals/Recommendations

Support for the specific role of DHA in neurologic development and function throughout life continues to grow. Since our original petition several expert bodies and competent authorities have issued conclusions and regulations reflecting the importance of preformed DHA in the diet for neurologic health. They are as follows:

- The U.S. Dietary Guidelines Advisory Committee (DGAC) concludes that moderate evidence supports an association between increased maternal dietary intake of DHA and increased DHA levels in breast milk and improved infant health outcomes, such as visual acuity and cognitive development. (DGAC, 2010)

- The 2010 Dietary Guidelines for Americans note that "moderate evidence indicates that intake of omega-3 fatty acids, in particular DHA, from *at least* 8 ounces of seafood per week for women who are pregnant or breastfeeding is associated with improved infant health outcomes, such as visual and cognitive development." (USDA and DHHS, 2010)

- Due to the preponderance of scientific evidence, health claims regarding the role of maternal DHA intake and improved fetal/infant neural development are now approved for use in the European Union. The European Commission (2011) has authorized the use of the following claims on labels of foods providing a daily intake of 200 mg DHA:

    - *Docosahexaenoic acid (DHA) maternal intake contributes to the normal development of the eye of the foetus and breastfed infants*

    - *Docosahexaenoic acid (DHA) maternal intake contributes to the normal brain development of the foetus and breastfed infants*

- Due to the preponderance of scientific evidence, predominately from studies conducted with Martek's algal DHA, health claims regarding the role of infant DHA intake and improved visual development are now approved for use in the European Union. The European Commission (2011) has authorized the use of the following claim on labels of foods supporting a daily intake of 100 mg DHA or, if used on follow-on formula, containing 0.3% of fatty acids as DHA:

    - *Docosahexaenoic acid (DHA) intake contributes to the normal visual development of infants up to 12 months of age*

- Following an evidence-based review of the data, the European Food Safety Authority (EFSA) has concluded that there is a cause and effect relationship between DHA intake and maintenance of normal brain function for the general population. EFSA recommends adults consume 250 mg of DHA daily to maintain normal brain function (EFSA, 2010). Related claims for use on food labels are pending authorization by the European Commission.

- Similarly, EFSA has concluded that sufficient evidence exists to confirm a cause and effect relationship between DHA intake and maintenance of normal visual function for the general population. EFSA recommends adults consume 250 mg of DHA daily to maintain normal visual function (EFSA, 2010). Related claims for use on food labels are pending authorization by the European Commission.

- The FAO expert panel on fats and fatty acids concludes "there can be little doubt about the essentiality of DHA and AA for the brain." (FAO, 2010)

- The competent authority of France (AFSSA, 2010) recommends 250 mg DHA per day for adults to support normal neurologic function noting that DHA "...is a major constituent of cerebral and visual structure and function. The new data, specifically those related to the very low conversion of alpha-linolenic acid into DHA, now clearly demonstrated, has led to the minimum physiological requirement being set at 250 mg/day for an adult (or 0.113% of energy), a value twice as high as that suggested in 2001."

Safety of DHA

DHA Algal Oil (and ARA Single-Cell Oil) has a history of safe consumption. FDA has completed favorable reviews of GRAS notifications and New Dietary Ingredient Notifications. DHA Algal Oils have also received numerous global regulatory approvals and clinical trials indicate excellent tolerability and safety.

Since our original submissions, a Chemical Abstract Number (CAS) has been assigned to DHA Algal Oil derived from *Crypthecodinium Cohnii*, that CAS # is 1258273-84-5.

Essentiality of DHA

DHA is recognized as an essential fatty acid necessary to ensure proper function of the body, particularly the brain and eyes (AFFSA, 2010). Although DHA can be made by the body, in very limited amounts, from its metabolic precursor alpha-linolenic acid (ALA) experts and competent authorities consistently agree that conversion of dietary ALA to DHA is too limited, unreliable, and variable to expect that ALA intake is sufficient to meet DHA needs.

As noted most recently by the U.S. Dietary Guidelines Advisory Committee (2010), "ALA is poorly converted to long-chain *n*-3 PUFA, primarily docosahexaenoic acid (DHA), so increased intake of ALA does not substantially improve levels of DHA."

The evidence regarding the insufficiency of ALA as a substitute for DHA can be summarized as follows:

- The average ALA to DHA conversion rate, as calculated from numerous studies, is estimated to be less than 0.5% and varies dependent upon age, health status, gender, and background diet (Plourde and Cunnane, 2007; Brenna et al., 2009). At least one study suggests the conversion rate of ALA to DHA may be 10 times lower than the average equaling only 0.05% (Pawlosky et al., 2001).

- Based on the estimated intake of ALA by Americans (1.6 g/day; IOM, 2005) metabolic conversion of ALA to DHA likely contributes a maximum of 8 mg of DHA/day toward maintaining DHA status

- Supplementing up to 10x the amount of ALA normally found in the U.S. diet, fails to alter DHA status in adults, pregnant and nursing women, and infants (Barcelo-Coblijn et al., 2008; Francois et al., 2003; Hoffman et al., 2006).

- Due to the insufficient conversion of ALA to DHA and DHA's important role in brain and eye function DHA has recently been recognized as an essential fatty acid for the general population. (AFFSA, 2010)

The specificity of recent conclusions regarding DHA intake confirms the essential nature of preformed DHA, independent of other long-chain n-3 fatty acids such as EPA, for neurologic health and development. This concept is further supported by an EFSA recommended dietary reference values for pregnant and nursing women requiring a total of 450 mg EPA+DHA of which *at least 200 mg must be DHA* (EFSA, 2009). The FAO recommends at least 300 mg EPA+DHA of which *at least 200 mg* must be DHA (FAO, 2010). A minimum of *200 mg DHA* during pregnancy and nursing has also been endorsed by the U.S. March of Dimes (MOD, 2009). In fact, the American Dietetic Association Position on Breastfeeding recognizes that *only DHA from algal oil* has been sufficiently characterized to confirm a dose response relationship between maternal DHA intake and breast milk DHA content (ADA, 2009).

Recent research indicates, however, that U.S. women do not likely meet the MOD recommended DHA intake during pregnancy. Donahue and co-workers (2011) report only 12.1% of U.S. women achieved ≥200 mg DHA per day during mid-pregnancy and that this number declined to only 2.7% the month prior to delivery this despite the fact that their fish intake remained the same. These data suggest that due, at least in part, to concerns regarding methyl-mercury and other contaminants in large, fatty fish women shift their intake of fish away from DHA-rich species in the time leading up to delivery thus further limiting an already insufficient DHA intake. Organic foods enriched with DHA from marine micro-algae provide pregnant and nursing women with healthful, sustainable, vegan and allergen-free alternatives to fish to achieve DHA intake goals during this critical period.

For women with limited DHA intake during pregnancy or for those who abbreviate breastfeeding, organic infant formulas containing DHA are useful alternatives to supply much needed DHA to the developing infant. As noted above, research consistently supports a role for DHA in the visual development of infants and young children, particularly when at least 0.3% of fatty acids in infant formula are supplied as DHA. Most recently, results from the DIAMOND study indicate that extended

feeding of DHA/ARA infant formula up to 12 months of age results in enhanced cognitive development at 18 months as measured by the Bayley's Mental Development Index (Drover et al., 2011).

Recent research suggests that the importance of algal DHA during early life extends beyond neurologic development and function. Ramakrishnan and co-workers (2010) have reported that supplementation of 400 mg DHA from Martek's algal oil daily from mid-pregnancy to low to middle socioeconomic status women giving birth to their first child, supports sustained linear growth from birth to at least 18 months of age (Stein et al., 2011) with most of this growth impact occurring during gestation. The authors also note that, due to lower socioeconomic status, many infants in their study exhibited postnatal growth failure. Infants born of women consuming supplemental DHA, however, "avoided much of the postnatal growth failure observed" in their cohort (Stein et al., 2011). Regarding their findings the authors indicate the following in support of the importance of DHA, independent of EPA, in the maternal diet, *"We provided algal DHA to our study participants. Other studies investigating this question have supplied fish oil (which contains EPA as well as DHA) or have been observational and hence could not completely control for potential confounding. It is possible that isolated DHA acts differently from fish oil and EPA may hamper the efficacy of DHA."* (Stein et al., 2011)

Finally, a recent U.S. study found that providing toddlers with 10x their estimated normal intake of DHA (13 mg DHA vs. 130 mg) from Martek's algal DHA for 60 days resulted in a significantly lower incidence of respiratory illness (Minns et al., 2010). Specifically, only 5% of toddlers supplemented with 130 mg DHA daily were subject to respiratory complications (upper respiratory infection, cough, bronchitis, etc.) while 13% of un-supplemented children developed respiratory illnesses during the study.

While fish oils may appear as a likely alternative to algal sourced DHA, fish oil has disadvantages, such as non-sustainability and contribution to over-fishing, environmental contaminants, allergen concerns, and non-vegan status. DHA Algal Oil supports the organic philosophy because it is obtained from naturally occurring, non-genetically modified, sustainable, microalgal sources. Algal sourced DHA is made from the same marine microalgae (i.e., phytoplankton) that fish consume, which are the original source of omega-3 fatty acids in the food chain. This approach ensures environmental sustainability and purity. Furthermore, the availability of a renewable source of DHA is increasingly important as additional food products are fortified with DHA.

References

AFSSA 2010. Opinion from the French Food Safety Agency Regarding the update of the Recommended Dietary Intake for Fatty Acids. Hearing no. 2006-SA-0359.

American Dietetic Association, 2009. Position of the American Dietetic Association: Promoting and Supporting Breastfeeding. J Am Diet Assoc., 2009; 109:1926-1942.

Barcelo-Coblijn G et al., 2008. Flaxseed oil and fish-oil capsule consumption alters human red blood cell n-3 fatty acid composition: a multiple-dosing trial comparing 2 sources of n-3 fatty acid. Am J Clin Nutr 88:801-9.

Brenna JT et al. for the International Society for the Study of Fatty Acids and Lipids, ISSFAL, 2009. α-linolenic acid supplementation and conversion to n-3 long-chain polyunsaturated fatty acids in humans. Prostaglandins, Leukotrienes, and Essential Fatty Acids 80:85-91.

DGAC, 2010. USDA Center for Nutrition Policy and Promotion. Report of the Dietary Guidelines Advisory Committee on the Dietary Guidelines for Americans, Part D. Section 3: Fatty Acids and Cholesterol. 2010 http://www.cnpp.usda.gov/Publications/DietaryGuidelines/2010/DGAC/Report/D-3-FattyAcidsCholesterol.pdf, accessed 3/14/11

Donahue SMA, et al. 2011. Prenatal fatty acid status and child adiposity at age 3 y: results from a US pregnancy cohort. Am J Clin Nutr doi: 10.3945/ajcn.110.005801.

Drover JR, et al. 2011. Cognitive function in 18-month-old term infants of the DIAMOND study: a randomized, controlled clinical trial with multiple dietary levels of docosahexaenoic acid. Early Hum Dev 87:223-30.

European Commission, 2011. Commission Regulation (EU) No 440/2011 on the authorization and refusal of authorization of certain health claims made on foods and referring to children's development and health, 7.5.2011 L119/4-9.

EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA), 2010. Scientific Opinion the substantiation of a health claim related to docosahexaenoic acid (DHA) and maintenance of normal (fasting) blood concentrations of triglycerides... maintenance of normal brain function (ID 565, 626, 631, 689, 690, 704, 742, 3148, 3151), maintenance of normal vision (ID 627, 632, 743, 3149) and maintenance of normal spermatozoa motility (ID 628) pursuant to Article 13(3) of Regulation (EC) No 1924/2006. The EFSA Journal; 8(10):1734. [27 pp.]. doi:10.2903/j.efsa.2010.1734. Available online: www.efsa.europa.eu/efsajournal.htm

Francois CA et al., 2003. Supplementing lactating women with flaxseed oil does not increase docosahexaenoic acid in their milk. Am J Clin Nutr 77:226-33.

Hoffman DR et al., 2006. Docosahexanoic acid in red blood cells of term infants receiving two levels of long-chain polyunsaturated fatty acids. JPGN 42:287-92.

Institute of Medicine, 2005. Dietary reference intakes for energy, carbohydrate, fiber, fat, fatty acids,

cholesterol, protein, and amino acids (Macronutrients). The National Academy of Sciences Press, Washington DC, Chapter 8.

March of Dimes, 2009. Omega-3 Fatty Acids During Pregnancy
http://www.marchofdimes.com/pnhec/159_55030.asp

Minns et al., 2010. Toddler formula supplemented with docosahexaenoic acid (DHA) improves DHA status and respiratory health in a randomized, double-blind, controlled trial of US children less than 3 years of age. Prost Leuko Essential Fatty Acids, doi:10.1016/j.plefa.2010.02.009.

Pawlosky RJ, et al. 2001. Physiological compartmental analysis of α-linolenic acid metabolism in adult humans. J Lipid Res 42:1257-1265.

Plourde M and Cunnane SC. 2007. Extremely limited synthesis of long-chain polyunsaturates in adults: implications for their dietary essentiality and use as supplements. Appl Physiol Nutr Metabl 32:619-634.

Ramakrishnan U, Stein AD, Parra-Cabrera S, Wang M, Imhoff-Kunsch B, Juárez-Márquez S, Rivera J, Martorell R, 2010. Effects of docosahexaenoic acid supplementation during pregnancy on gestational age and size at birth: Randomized, double-blind, placebo-controlled trial in Mexico. Food Nutr Bull 31(2 Suppl):S108-16.

Stein AD, Wang M, Martorell R, Neufeld LM, Flores-Ayala R, Rivera JA, Ramakrishnan U., 201. Growth to age 18 months following prenatal supplementation with docosahexaenoic acid differs by maternal gravidity in Mexico. J Nutr 141 (2):316-20.

USDA and DHHS, 2010. *Dietary Guidelines for Americans, 2010.* 7th Edition, Washington, DC: U.S. Government Printing Office, December 2010