

SCIENTIFIC OPINION

DHA and support of the cognitive development of the unborn child and breastfed infant

Scientific substantiation of a health claim related to DHA and support of the cognitive development of the unborn child and breastfed infant pursuant to Article 14 of Regulation (EC) No 1924/2006¹

Scientific Opinion of the Panel on Dietetic Products, Nutrition and Allergies

(Question No EFSA-Q-2008-773)

Adopted on 13 March 2009

PANEL MEMBERS

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SUMMARY

Following an application from Merck Selbstmedikation GmbH submitted pursuant to Article 14 of Regulation (EC) No 1924/2006 via the Competent Authority of Germany, the Panel on Dietetic Products, Nutrition and Allergies was asked to deliver an opinion on the scientific substantiation of a health claim related to DHA and support of the cognitive development of the unborn child and breastfed infant.

The scope of the application was proposed to fall under a health claim referring to children's development and health.

The food constituent that is the subject of the proposed claim is docosahexaenoic acid derived from tuna oil and presented in soft gel capsules which contain >200 mg DHA, >50 mg eicosapentaenoic acid (EPA) and between 11.4 and 14.4 mg d- α -tocopherol. The food supplement is intended for pregnant and lactating women.

DHA is a well characterised fatty acid the absorption of which is well documented. DHA can be quantified in foods by established methods. The Panel considers that the food constituent, DHA, for which the claim is made is sufficiently characterised.

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The claimed effect is that DHA provided via the mother contributes to the child's cognitive development. The target population for the claimed effect is unborn children and breastfed infants. The target population for the supplementation with DHA is pregnant and lactating women.

The Panel considers that normal cognitive development is beneficial for children's development and health.

The applicant identified a total of 48 publications to support the health claim (25 human intervention and observational studies, three meta-analyses of human intervention studies, five systematic reviews, four other review publications, three guidelines/consensus opinions and eight mechanistic human studies). Sixteen publications, including one unpublished follow-up study, on 15 randomised controlled trials (RCT), one non-randomised controlled trial and four observational studies were considered as pertinent by the applicant to substantiate the proposed claim.

The Panel considers that for the substantiation of the claim under consideration only human intervention or observational studies reporting effects on cognitive function development in offspring of mothers who were exposed to defined intakes of DHA either through supplementation or diet during pregnancy and/or lactation can provide the necessary evidence.

Five RCT of DHA supplementation in pregnant or lactating women which include endpoints related to cognitive function assessment and two observational cohort studies on the effects of maternal DHA status at birth or maternal oily fish consumption during pregnancy on children's intelligence, fine motor ability, communication and social development up to the age of seven years are considered as pertinent to the claim under consideration.

DHA supplementation during pregnancy

Two RCT have assessed the effect of supplementation of women with DHA during pregnancy. In the first study 29 pregnant women consumed either 200 mg DHA/day or a placebo. A two-step problem solving test was performed at the age of nine months in the infants of both groups of mothers as well as the Fagan Test of Infant Intelligence (FTII). No significant effect on performance in problem solving tasks but a significantly higher combined total intention score and total intentional solution score were found in infants of mothers supplemented during pregnancy compared to the placebo group. There were no significant differences between the groups in the five outcome variables of the FTII. The Panel notes the small sample size of this study and that the statistical significance in some outcome measurements appears only in regression analysis. In the second study 98 pregnant women received either fish-oil capsules (2.2 g DHA, 1.1 g EPA/day) or olive oil capsules. Their children were tested at the age of 2.5 years among others for development, receptive language, and behaviour. Compared to the olive oil group children from the fish-oil group attained a significantly higher score for eye hand coordination. There was no difference between the groups for other subscales of development, receptive language and for the different items of the Child Behaviour Checklist. There was a significant positive correlation between the eye and hand coordination score and n-3 PUFA composition of cord blood erythrocytes. The Panel considers this study not to be informative for the proposed claim under the proposed conditions, because of the high DHA dose applied. Further, the Panel notes that the high DHA dose in the mother did not promote cognitive development of their infants.

DHA supplementation during lactation

Two RCT have assessed the effect of supplementation of breastfeeding women with DHA. In the first study 52 mothers of term infants were randomised to either of five doses of a DHA-rich algal oil (0, 0.2 g, 0.4 g, 0.9 g, 1.3 g DHA) to be taken daily from day five after delivery

for 12 weeks. Infant red blood cell (RBC) DHA at 12 weeks and home stimulation were the only independent factors associated with Bayley's mental development index (MDI) at one year of age, whilst at two years gender and social score of the spouse were the only significant predictors of Bayley's MDI. In a second study 114 breastfeeding mothers were assigned to capsules with high-DHA algal oil (200 mg DHA/day) and 113 mothers to capsules with DHA-free vegetable oil for four months after delivery. There were no significant differences between groups in the Gesell Gross Motor Inventory, Clinical Adaptive Test (CAT) or Clinical Linguistic and Auditory Milestone Scale (CLAMS) developmental quotient at either 12 or 30 months and in the Bayley MDI at 30 months of age, but the Bayley Psychomotor Development Index (PDI) was higher in the children of the DHA group. No significant correlation could be found between infant plasma phospholipids DHA content at either four or eight months of age and any measure of neurodevelopment. Unpublished data on neuropsychological functions (gross and fine motor, executive, perceptual, visual, verbal) and a sustained attention subtest of the Leiter International Performance Scale at five years of age in 71 children from the DHA and 70 children from the control group showed better performance of children from the DHA group in one sustained attention subtest. The Panel considers that a positive association of one out of many neurodevelopmental indices with maternal DHA supplementation is insufficient to conclude on the overall effect on cognitive development. The significance of the results of the follow-up at the age of five years is questionable due to considerable attrition of both the DHA and the control group.

In another study 341 pregnant women consumed either 10 mL of cod liver oil (1183 mg DHA, 803 mg EPA) or corn oil (4747 mg linoleic acid, LA; 92 mg α -linolenic acid, ALA) from 18 weeks of gestation until three months after delivery. Children in the cod liver oil group had significantly higher scores on the Mental Processing Composite at age four years than children from the corn oil group. There was no correlation between umbilical plasma phospholipids n-3 LCPUFA and intelligence scores, but both docosapentaenoic acid (DPA) and DHA content of infants' plasma phospholipids at age four weeks and maternal EPA and DHA intake during pregnancy were positively correlated with individual intelligence scores. In a recent follow-up study 82 children from the cod liver oil group and 61 children from the corn oil group were tested with the Kaufman Assessment Battery for Children (K-ABC) at 7 years of age. No significant differences were found between children from the two different supplement groups. The Panel notes that the results obtained in too small groups of subjects at the age of 7 years did not establish a positive relationship between a high maternal DHA supplementation during both pregnancy and lactation and cognitive development.

In the Avon Longitudinal Study of Pregnancy and Childhood (ALSPAC) children were tested with an abbreviated form of the Wechsler Intelligence Scale for Children III at the age of eight years and the results were related to seafood consumption by the mothers during pregnancy. The odds ratio for a suboptimal outcome of the verbal IQ was 1.48 for no seafood consumption by the mother compared to high seafood consumption. Moreover, there was a significant trend for suboptimal results also for the fullscale IQ. The Panel considers that the available data do not permit an estimation of maternal DHA consumption and, therefore, cannot contribute to establish a relationship between maternal DHA supplementation and cognitive development of the child.

The Panel concludes that there is insufficient evidence to establish a cause and effect relationship between the consumption of supplementary DHA during pregnancy and lactation and cognitive development in unborn children or breastfed infants.

Key words: docosahexaenoic acid, fish oil, cognition, intelligence, development, children

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BACKGROUND

Regulation (EC) No 1924/2006² 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, Articles 14 to 17 of that Regulation lay down provisions for the authorisation and subsequent inclusion of reduction of disease risk claims and claims referring to children's development and health in a Community list of permitted claims.

According to Article 15 of that Regulation, an application for authorisation 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 01/12/08.
- The scope of the application was proposed to fall under a health claim referring to children's development and health.
- The scientific evaluation procedure started on 15/12/08.
- During the meeting on 13/03/2009, the NDA Panel, after having evaluated the overall data submitted, adopted an opinion on the scientific substantiation of a health claim related to DHA and support of the cognitive development of the unborn child and breastfed infant.

TERMS OF REFERENCE

EFSA is requested to evaluate the scientific data submitted by the applicant in accordance with Article 16 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 DHA and support of the cognitive development of the unborn child and breastfed infant.

EFSA DISCLAIMER

The present opinion does not constitute, and cannot be construed as, an authorisation to the marketing of DHA, a positive assessment of its safety, nor a decision on whether DHA 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 17 of Regulation (EC) No 1924/2006.

² 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.

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1. Information provided by the applicant

Applicant's name and address: Merck Selbstmedikation GmbH, Roesslerstrasse 96, 64293 Darmstadt, Germany

1.1. Food/constituent as stated by the applicant

DHA (docosahexaenoic acid; 22:6n-3)

1.2. Health relationship as claimed by the applicant

The applicant claims that DHA supports cognitive development of the foetus (unborn child) and infant.

1.3. Wording of the health claim as proposed by the applicant

DHA is important for early development of the brain in the foetus (unborn child) and infant. Maternal DHA supply contributes to the child's cognitive development.

1.4 Specific conditions of use as proposed by the applicant

Pregnant and lactating women should aim to achieve an average intake of 200 mg DHA per day.

2. Assessment

2.1. Characterisation of the food/constituent

The food constituent that is the subject of the proposed claim is docosahexaenoic acid derived from tuna oil which is concentrated and purified by transesterification, molecular distillation and chromatography and presented in soft gel capsules which contain >200 mg DHA, >50 mg eicosapentaenoic acid (EPA) and between 11.4 and 14.4 mg d- α -tocopherol. Complete specifications, manufacturing process, bioavailability and stability information have been provided. The food supplement is intended for pregnant and lactating women.

DHA is a well characterised fatty acid the absorption of which is well documented. DHA can be quantified in foods by established methods. The Panel considers that the food constituent, DHA, for which the claim is made is sufficiently characterised and that the present assessment applies to all products supplying a similar amount of DHA.

2.2. Relevance of the claimed effect to human health

The claimed effect is that DHA provided via the mother contributes to the child's cognitive development. The target population for the claimed effect is unborn children and breastfed infants. The target population for the supplementation with DHA is pregnant and lactating women.

The Panel considers that normal cognitive development is beneficial for children's development and health.

2.3. Scientific substantiation of the claimed effect

The applicant performed a literature search in MEDLINE (until November 2007) using the search terms “pregnancy, lactation, DHA, DHA supplementation, LCPUFA, fish oil, omega-3, cognitive, brain, breast milk, development, infant” in various combinations. In addition, reference lists of relevant publications and conference proceedings were searched. Inclusion criteria to identify pertinent publications were randomised trials which compared DHA supplementation during pregnancy and/or lactation with placebo and cohort studies in which maternal seafood consumption during pregnancy and/or lactation was related to measures of the claimed effect in the offspring. Studies which reported only on development of the eyes and of vision or which concerned only LCPUFA-enriched baby formula were excluded.

The applicant identified a total of 48 publications in support of the health claim (25 human intervention and observational studies, three meta-analyses of human intervention studies, five systematic reviews, four other review publications, three guidelines/consensus opinions and eight mechanistic human studies). Based on the exclusion criteria mentioned above 16 publications, including one unpublished follow-up study, on 15 randomised controlled trials (RCT), one non-randomised controlled trial and four observational studies were considered as pertinent by the applicant to substantiate the proposed claim.

Cognitive development in infants includes the development and maturation of different functions such as attention (concentration), memory, learning, intelligence and problem solving which can be estimated separately by a multitude of different psychometric tests validated for the relevant age group. Other indicators used are novelty preference, discrimination of native from foreign sounds, more mature sleep behaviour, and more mature electroencephalograms in infancy.

The Panel notes that the majority of the references considered pertinent by the applicant provide evidence that DHA and ARA are major structural and functional LCPUFA in the brain and retina and are readily incorporated into neural tissues during the brain growth spurt and throughout the first years of life. Consistent with early preferential accumulation of LCPUFA in certain tissues is the correlation between these fatty acids and brain function development. Whilst DHA can be synthesised in the human body from its precursor essential fatty acid alpha-linolenic acid (ALA) to a certain extent which may be determined by polymorphisms of the fatty acid desaturases, the human foetus appears to be largely dependent on placental transfer of DHA from the mother, derived either from her diet, from synthesis or from stores in adipose tissue. Placental transport specifically enriches DHA in foetal blood. After birth most DHA is provided to the infant via breast milk, in which the DHA concentration is dependent both on maternal dietary intake and on maternal DHA stores, whilst the contribution by synthesis is low (Koletzko *et al.*, 2007, 2008; IoM, 2007).

The Panel considers that for the substantiation of the claim under consideration only human intervention or observational studies reporting effects on cognitive function development in offspring of mothers who were exposed to defined intakes of DHA either through supplementation or diet during pregnancy and/or lactation can provide the necessary evidence.

Therefore, intervention studies which assessed cognitive development and quality of general movements in children who had been either breastfed or fed formula enriched with DHA are not regarded as pertinent for the substantiation of the proposed health claim, nor are RCT which describe the effects of DHA supplementation of pregnant women on the DHA concentrations in maternal and umbilical cord blood and in placenta and RCT conducted with DHA in lactating women which assess the effect on breast-milk DHA content.

Accordingly, the Panel considers two RCT as not pertinent: one an intervention study which compares IQ maturation at age four years in children who have been either breastfed or fed un-

enriched formula or formula enriched with DHA or both DHA and arachidonic acid (ARA) for the first 17 weeks of life (Birch *et al.*, 2007), and the other an intervention study in which the quality of general movements at three months of age was compared between breastfed infants, infants fed formula with either DHA plus ARA or no enrichment (Bouwstra *et al.*, 2003). A RCT in women of child-bearing age who were neither pregnant nor lactating which compared the effects on plasma fatty acid composition of a supplement consisting of a blend of DHA, EPA, ARA and γ -linolenic acid (GLA) to the effects of a placebo is also not considered as pertinent (Geppert *et al.*, 2008).

Also four RCT and one non-randomised controlled study describing the effects of DHA supplementation of pregnant women on the DHA concentrations in maternal and umbilical cord blood and in placenta (Sanjurjo *et al.*, 2004; Montgomery *et al.*, 2003; Larqué *et al.*, 2006; Krauss-Etschmann *et al.*, 2007; Connor *et al.*, 1996) are considered as not pertinent for the proposed health claim. The same holds true for two of five RCT conducted with DHA either in the form of the acid or as fish or fish oil or egg in lactating women starting from five days to two weeks postpartum (Jensen *et al.*, 2000; Fidler *et al.*, 2000), in which cognitive functions of the infants were not tested.

Five RCT of DHA supplementation in pregnant or lactating women which include endpoints related to cognitive function assessment and two observational studies on the effects of maternal DHA status at birth or maternal oily fish consumption during pregnancy on children's intelligence, fine motor ability, communication and social development up to the age of seven years are considered as pertinent to the claim under consideration (Dunstan *et al.*, 2006; Gibson *et al.*, 1997; Helland *et al.*, 2003; 2008; Jensen *et al.*, 2005; Jensen *et al.*, unpublished; Judge *et al.*, 2007; Columbo *et al.*, 2004; Hibbeln *et al.*, 2007).

DHA supplementation during pregnancy

Two RCT have assessed the effect of supplementation of women with DHA during pregnancy.

In a small prospective randomised double-blind placebo-controlled trial, in which 14 pregnant women consumed a low-EPA fish-oil containing cereal bar providing approximately 200 mg DHA/day and 15 other women consumed a placebo cereal bar from week 24 of pregnancy until term (total DHA intake was on average 313 and 99 mg/day). Women in the DHA-group had a significantly ($p=0.019$) longer gestational period than women in the placebo group (39.9 versus 39.0 weeks). A two-step problem solving test was performed at the age of nine months in the infants of both groups of mothers as well as the Fagan Test of Infant Intelligence (FTII) to assess recognition memory abilities. No significant effect on performance in problem solving tasks but a significantly higher combined total intention score ($p=0.017$) and total intentional solution score ($p=0.011$) were found in infants of mothers supplemented during pregnancy compared to the placebo group in a regression model adjusted for gestational age, maternal haematocrit, prepregnancy BMI, maternal education and infant feeding type. There were no significant differences between the groups in the five outcome variables of the FTII (Judge *et al.*, 2007). The Panel notes the small sample size of this study and that the statistical significance in some outcome measurements appears only in regression analysis.

In another double-blind randomised placebo-controlled trial 98 pregnant women received either fish-oil capsules (2.2 g DHA, 1.1 g EPA/day; $n=52$) or olive oil capsules ($n=46$) from week 20 until delivery. Thirty-three children from the fish-oil group and 39 children from the olive-oil group were tested at the age of 2.5 years among others for development (Griffiths Mental Development Scales, GMDS), receptive language (Peabody Picture Vocabulary Test), and behaviour (Child Behaviour Checklist). The phospholipid fatty acid analysis in cord blood red blood cells (RBC) showed significantly higher total n-3 poly-unsaturated fatty acids (PUFA), lower n-6 PUFA and higher total n-3 to n-6 ratio (all $p<0.001$) in the DHA- than in the

placebo-group. Children from the fish-oil group attained a significantly higher score for eye hand coordination ($p=0.021$) in the GMDS than children from the olive-oil group. This difference remained significant when adjusted for maternal age, maternal education and duration of breastfeeding. There was no difference between the groups for the mean general quotient or for mean quotients for other subscales of development. There was also no difference between the groups for receptive language and for the different items of the Child Behaviour Checklist. There was a significant positive correlation between the eye and hand coordination score and n-3 PUFA composition of cord blood erythrocytes (DHA $p=0.009$, EPA $p=0.007$), whilst there was an inverse correlation with cord blood ARA (Dunstan *et al.*, 2006). The Panel considers this study not to be informative for the proposed claim under the proposed conditions, because of the high DHA dose applied. Further, the Panel notes that the high DHA dose in the mother did not promote cognitive development of their infants.

DHA supplementation during lactation

Two RCT have assessed the effect of supplementation of breastfeeding women with DHA.

In a double blind, placebo-controlled trial 52 mothers of term infants who intended to breastfeed for at least three months were randomised to either of five doses of a DHA-rich algal oil (0, $n=12$; 0.2 g, $n=10$; 0.4 g, $n=12$; 0.9 g, $n=10$; 1.3 g DHA, $n=8$) to be taken daily from day five after delivery for 12 weeks. Breast milk DHA content ranged from 0.1 to 1.7% of total fatty acids and was related to infant plasma ($r=0.89$, $p<0.001$) and RBC ($r=0.88$, $p<0.001$) phospholipids in a saturable curvilinear manner so that milk DHA above 0.8% of fatty acids resulted in little further increase in infant plasma or RBC DHA levels. A stepwise multiple regression showed that infant RBC DHA at 12 weeks and home stimulation were the only independent factors associated with Bayley's MDI at one year of age (adjusted model $r^2=0.18$, $p<0.005$), whilst at two years gender and social score of the spouse were the only significant predictors of Bayley's MDI (adjusted model $r^2=0.22$, $p<0.005$) (Gibson *et al.*, 1997). The Panel notes that different DHA supplementation of lactating mothers did not have positive effects on the MDI of their infants up to the age of two years.

In another double-blind, placebo-controlled study 114 breastfeeding mothers were assigned to capsules with high-DHA algal oil (200 mg DHA/day) and 113 mothers to capsules with DHA-free vegetable oil for four months after delivery. Outcome measures were fatty acid patterns of maternal plasma phospholipids and milk lipids four months postpartum, the fatty acid pattern of infant plasma phospholipids and neurodevelopmental indices (Bayley Scales of Infant Development, Gesell Developmental Inventory, Clinical Linguistic and Auditory Milestone Scale (CLAMS), Clinical Adaptive Test (CAT)) of infants at 12 and 30 months of age. The DHA content of milk lipids was significantly greater in the DHA group than in the control group ($p<0.0001$) and the infant plasma phospholipid fatty acid pattern at four months of age mirrored that of milk lipid. There were no significant differences in the plasma phospholipid fatty acid pattern between groups at eight months of age. There were no significant differences between groups in the Gesell Gross Motor Inventory, CAT or CLAMS developmental quotient (DP) at either 12 or 30 months. The Bayley Mental Development Index (MDI) of the two groups did not differ significantly at 30 months of age, but the Bayley Psychomotor Development Index (PDI) was 8.4 points higher ($p=0.005$) in the children of the DHA group than in children of the control group. This difference remained significant after adjustment for gender, ethnicity, birth weight, duration of breastfeeding, weight and length at 30 months of age, maternal age, maternal education, maternal IQ, and the composite score of the Family Environment Scale. No significant correlation could be found between infant plasma phospholipids DHA content at either four or eight months of age and any measure of neurodevelopment (Jensen *et al.*, 2005). The applicant provided unpublished data on neuropsychological functions (gross and fine motor, executive, perceptual, visual, verbal) and a

sustained attention subtest of the Leiter International Performance Scale at five years of age in 71 children from the DHA and 70 children from the control group. Children from the DHA group performed better on the sustained attention subtest ($p < 0.008$) (Jensen *et al.*, unpublished). The Panel considers that because only one out of many neurodevelopmental indices showed a positive association with maternal DHA supplementation, no conclusion can be made on the overall effect on cognitive development. Similarly, the significance of the results of the follow-up at the age of five years is questionable due to considerable attrition of both the DHA and the control group.

DHA supplementation during both pregnancy and lactation

In a double-blind, placebo-controlled study 341 pregnant women were randomised to consume either 10 mL of cod liver oil (1183 mg DHA, 803 mg EPA) or corn oil (4747 mg linoleic acid, LA; 92 mg α -linolenic acid, ALA) from 18 weeks of gestation until three months after delivery. Of 135 invited children, 84 (48 from the cod liver oil and 36 from the corn oil group) could be tested for intelligence with the Kaufman Assessment Battery for Children (K-ABC) at the age of four years. The test battery comprised three scales: Sequential Processing, Simultaneous Processing and Nonverbal Abilities. The Scores from the two first scales are combined to form a Mental Processing Composite, which serves as the measure of intelligence. All children had been breastfed until at least three months of age. The DHA content of milk from mothers with cod liver oil both at four weeks and at three months contained significantly more DHA (1.41 and 1.26 weight% of total fatty acids) than the milk from mothers in the corn oil group (0.43 and 0.47). The DHA content in phospholipids from umbilical cord plasma and from infant plasma at four weeks and at three months was significantly higher ($p < 0.001$) in the cod liver oil group than in the corn oil group. Children in the cod liver oil group had significantly higher scores on the Mental Processing Composite at age four years (106.4 versus 102.3, $p = 0.049$) than children from the corn oil group, whilst the differences between the individual scales showed the same tendency but were not significant. There was no correlation between umbilical plasma phospholipids n-3 LCPUFA and intelligence scores, but both docosapentaenoic acid (DPA) and DHA content of infants' plasma phospholipids at age four weeks and maternal EPA and DHA intake during pregnancy were positively correlated with individual intelligence scores (Helland *et al.*, 2003). Recently a follow-up study at seven years of age was published (Helland *et al.*, 2008). 82 children from the cod liver oil group and 61 children from the corn oil group were tested with the K-ABC at 7 years of age. No significant differences in scores on the K-ABC were found between children from the two different supplement groups, although there was a non-significant tendency for higher sequential processing in children from the cod liver oil group. Maternal plasma phospholipids concentrations of ALA and DHA during pregnancy were found to be positively correlated to sequential processing ($p = 0.035$ and $p = 0.049$, respectively). To detect a difference in IQ scores of 4.1, 83 subjects in each group would have been required ($SD = 9.4$; $\alpha = 5\%$; $\beta = 20\%$). The Panel notes that the results obtained in too small groups of subjects at the age of 7 years did not establish a positive relationship between a high maternal DHA supplementation during both pregnancy and lactation and cognitive development.

Observational studies

A positive relationship between maternal DHA status (but not infant DHA status) as assessed by RBC DHA content and more mature visual attention and less distractibility was described by Colombo *et al.* (2004) in a follow-up at four, six, eight, 12 and 18 months of age of a cohort of 70 children born to mothers who had participated in a trial on the effects of DHA supplementation on duration of gestation. Attention, assessed as e.g. a decrease in looking duration which occurs typically between the age of four to eight months is associated with higher performance on the Bayley Scales of Mental Development (BSMD) at 18 months of age

(Colombo *et al.*, 1991). Early shorter peak look duration is interpreted as an indicator of faster processing of information, an early indicator related to later cognitive ability. Notably, maternal DHA status in this cohort was not influenced by DHA supplementation during the third trimester of pregnancy (Colombo *et al.*, 2004).

In the Avon Longitudinal Study of Pregnancy and Childhood (ALSPAC) 11,875 pregnant women provided a food frequency questionnaire at week 32 of gestation, which allowed to categorise them into groups without, with some (1-340 g/week) and with high (>340 g/week) seafood consumption. Approximately 5000 to 5400 of their children were tested with an abbreviated form of the Wechsler Intelligence Scale for Children III at the age of eight years and the results were related to seafood consumption by the mothers during pregnancy. The odds ratio for a suboptimal outcome of the verbal IQ was 1.48 (95% CI: 1.16-1.90) for no seafood consumption by the mother compared to high seafood consumption. Moreover, there was a significant trend for suboptimal results also for the fullscale IQ (Hibbeln *et al.*, 2007). The Panel considers that the available data do not permit an estimation of maternal DHA consumption and, therefore, cannot contribute to establish a relationship between maternal DHA supplementation and cognitive development of the child.

The Panel concludes that there is insufficient evidence to establish a cause and effect relationship between the consumption of supplementary DHA during pregnancy and lactation and cognitive development in unborn children or breastfed infants.

CONCLUSIONS

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

- The food constituent, DHA, for which the health claim is made is sufficiently characterised.
- The claimed effect is that maternal supplementation with DHA supports cognitive development of the unborn child and breastfed infant. The target population for the claimed effect is unborn children and breastfed infants. The target population for the supplementation with DHA is pregnant and lactating women. Normal cognitive development is beneficial for children's development and health.
- There is insufficient evidence to establish a cause and effect relationship between the consumption of supplementary DHA during pregnancy and lactation and cognitive development in unborn children or breastfed infants.

DOCUMENTATION PROVIDED TO EFSA

Health claim application on DHA and support of the cognitive development of the unborn child and breastfed infant pursuant to Article 14 of Regulation (EC) No 1924/2006 (Claim serial No: 0218b_DE). December 2008. Submitted by Merck Selbstmedikation GmbH.

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GLOSSARY / ABBREVIATIONS

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| ALA | Alpha-linolenic acid |
| ALSPAC | Avon Longitudinal Study on Parents and Children |
| ARA | Arachidonic acid |
| Bayley MDI | Bayley Mental Development Index |
| Bayley PDI | Bayley Psychomotor Development Index |
| BSMD | Bayley Scales of Mental Development |
| CAT | Clinical Adaptive Test |
| CBCL | Child Behaviour Checklist |
| CLAMS | Clinical Linguistic and Auditory Milestone Scale |
| EPA | Eicosapentaenoic acid |
| DHA | Docosahexaenoic acid |
| DPA | Docosapentaenoic acid |
| FTII | Fagan Test of Infant Intelligence |
| GLA | Gamma-linolenic acid |
| GMDS | Griffiths Mental Development Scale |
| Kaufmann ABC Test | Kaufmann Assessment Battery for Children Test |
| LCPUFA | Long chain polyunsaturated fatty acids |
| RBC | Red blood cells |
| RCT | Randomised controlled trial |