Appendix E

Martek's Oils Are Not Essential for Organic Handling

A material destined for 205.605 is either essential for handling, or not. Yet the Handling Committee answered "N/A" to the question, "Is the substance essential for handling of organically produced agricultural products?"

The "N/A" category is designed for questions that are not relevant to the material. For example, the question "Are there detrimental physiological effects on soil organisms, crops, or livestock?" would be "N/A" for a material like Martek's DHA, because the question is not relevant.

The question of essentiality would be irrelevant for a material under consideration by the Crops Committee, and therefore "N/A" would be an appropriate answer. But for a material under consideration by the Handling Committee, the question of essentiality needs to be answered.

By answering "N/A," the HC is simply avoiding the question, for which the only logical answer is "no."

Next to this unanswered question, the Handling Committee wrote: "Consumers, seeing products labeled as both Organic and containing DHA have chosen to purchase these products. DHA is essential for consumers to continue to have access to these organic products."

Consumers did indeed purchase these products, thinking they contained only organic or approved ingredients. According to a survey of nearly 1,500 organic consumers by PCC Natural Markets, organic consumers are interested in added DHA if the source is organic, or wild fish. Organic consumers who have "chosen to purchase these products" with DHA, did so under the assumption that the product they purchased contained only organic or approved ingredients.

The fact that organic consumers have been misled for years, because the USDA has failed to enforce the organic standards that require ingredients like these to be reviewed and approved before being added to organics, should not serve as justification for approving the petition.

In fact, the PCC survey suggests that many consumers likely believed that they were purchasing organic algal oil when purchasing organic products with Martek's oils. The PCC survey shows that 51.6% of organic consumers would be "more inclined to purchase" organic products with organic algae as a source of DHA. If they knew that Martek's oils are genetically modified, hexane-extracted and stabilized with

synthetic ingredients, the number of shoppers who would choose these products drops to 2.3% (GMO algae), 0.3% (hexane) and 0.4% (synthetic stabilizers).

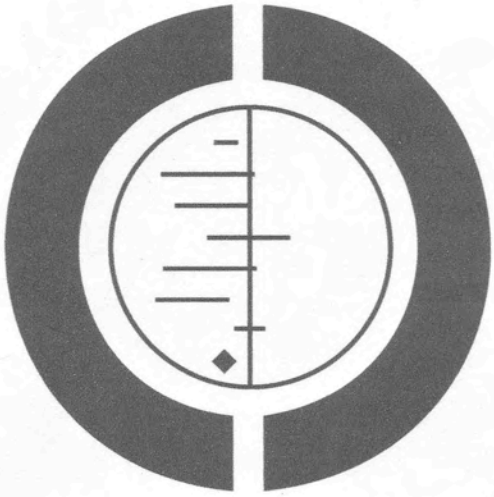
But perhaps the greatest oversight, by both the Technical Review and the Handling Committee, in answering the question of essentiality, is that the 0.4% of organic consumers who do wish to consume Martek's oils with synthetic ingredients, can buy supplements. Examples of such supplements are included in the Appendix. No consumer who wishes to ingest Martek's oils will be deprived from doing so if the NOSB votes to reject the petition.

In fact, question 9, which asks whether there are "alternatives to using the substance in terms of practices or other available materials"? should be answered "yes." Supplements are available for every segment of the population, from the general adult population (in the form of pills) to pregnant and nursing mothers (in the form of prenatal supplements) to children (in the form of "chewables") and infants (in the form of droppers that can be added to formula or milk).

Please note that arguments that organic infant formula will be nutritionally inferior if they cannot contain Martek's oils is not supported by sound science, as numerous meta-analysis studies have concluded that no benefits to infant development exist from DHA/ARA supplementation.

Longchain polyunsaturated fatty acid supplementation in infants born at term (Review)

Simmer K, Patole S, Rao SC



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[Intervention Review]

Longchain polyunsaturated fatty acid supplementation in infants born at term

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ABSTRACT

Background

The n-3 and n-6 fatty acids linolenic acid and linoleic acid are precursors of the n-3 and n-6 long chain fatty acids (LCPUFA). Infant formula has historically only contained the precursor fatty acids. Controversy exists over whether LCPUFA are also essential nutrients in infancy. Over the last few years, some manufacturers have added LCPUFA to formulae and marketed them as providing an advantage for the development of term infants.

Objectives

To assess whether supplementation of formula with LCPUFA is safe and of benefit to term infants.

Search strategy

Eligible studies were identified by searching MEDLINE (March 2007), EMBASE 1980 - 2007, Cochrane Central Register of Controlled Trials (CENTRAL, The Cochrane Library, Issue 1, 2007) and CINAHL (December 1982 - March 2007). Abstracts of the Society for Pediatric Research were hand searched from 1980 to 2006 inclusive. Reference lists of published narrative and systematic reviews were also reviewed. No language restrictions were applied.

Selection criteria

All randomised and quasi randomised trials comparing LCPUFA supplemented formula milk vs. non-supplemented formula milk and with clinical endpoints were reviewed.

Data collection and analysis

Methodological quality of eligible studies was assessed according to allocation concealment, blinding of intervention, blinding of outcome assessment and completeness of follow up. Data were sought regarding effects on visual acuity, neurodevelopmental outcomes and physical growth. When appropriate, meta-analysis was conducted to provide a pooled estimate of effect. Continuous data were analysed using weighted mean difference (WMD). There were no categorical outcomes in this review.

Main results

Twenty randomised studies were identified. Fourteen were included (n = 1719) and six excluded. Eleven included studies were of good quality. The main outcomes assessed were visual acuity, neurodevelopmental and physical growth.

Visual acuity was measured at various stages throughout the first three years of life by nine studies. Visual evoked potential was used to assess visual acuity in five studies. The remaining four used Teller visual acuity cards. The results were inconsistent. Three studies reported beneficial effect of LCPUFA supplementation on visual acuity while the remaining six did not.

Neurodevelopmental outcome was measured at different ages throughout the first two years by eleven studies. Bayley scales of infant development (BSID) was used in eight studies. Only one showed beneficial effect of LCPUFA supplementation on BSID scales. Pooled meta-analysis of the data also did not show any statistically significant benefit of LCPUFA supplementation on either mental or psychomotor developmental index of BSID. One study reported better novelty preference measured by Fagan Infant test at nine months in supplemented infants compared with controls. Another study reported better problem solving at 10 months with supplementation. One study used Brunet and Lezine developmental test to assess the developmental quotient and did not find beneficial effects of LCPUFA supplementation.

Physical growth was measured at various ages throughout first three years of life by twelve studies. Some studies reported the actual measurements while some reported the rate of growth over a time period. Some studies z scores. Irrespective of the type of LCPUFA supplementation, duration of supplementation and method of assessment, none of the individual studies found beneficial or harmful effects of LCPUFA supplementation. Meta-analysis of relevant studies also did not show any effect of LCPUFA supplementation on growth of term infants.

Authors' conclusions

The results of most of the well conducted RCTS have not shown beneficial effects of LCPUFA supplementation of formula milk on the physical, visual and neurodevelopmental outcomes of infants born at term. Only one group of researchers have shown some beneficial effects on VEP acuity. Two groups of researchers have shown some beneficial effect on mental development. Routine supplementation of milk formula with LCPUFA to improve the physical, neurodevelopmental or visual outcomes of infants born at term can not be recommended based on the current evidence. Further research is needed to see if the beneficial effects demonstrated by Dallas 2005 trial of Birch et al can be replicated in different settings.

PLAIN LANGUAGE SUMMARY

Longchain polyunsaturated fatty acid supplementation in infants born at term

It has been suggested that low levels of long chain polyunsaturated fatty acids (LCPUFA) found in formula milk may contribute to lower IQ levels and vision skills in term infants. Some milk formulas with added LCPUFA are commercially available. This review found that feeding term infants with milk formula enriched with LCPUFA had no proven benefit regarding vision, cognition or physical growth.

BACKGROUND

Dietary fat in infancy is fundamental for the provision of energy, fat soluble vitamins and essential fatty acids. Interest has recently focused on the importance of long chain polyunsaturated fatty acids (LCPUFA) such as docosahexaenoic acid (DHA) and arachidonic acid (AA) in infant nutrition. These fatty acids are found in high proportions in the structural lipids of cell membranes, particularly those of the central nervous system and retina (Fleith 2005). Their accretion primarily occurs during the last trimester of pregnancy and the first year of life (Clandinin 1980). LCPUFA are supplied during pregnancy via placental transfer and through breast milk after birth. Standard infant formulae contain only the precursor essential fatty acids (EFA), alpha-linolenic acid (ALA, the omega 3 precursor) and linoleic acid (LA, the omega 6 precursor) from which formula-fed infants must synthesise their own DHA and AA, respectively. The absence of LCPUFA in formula may be further exacerbated by inhibition of incorporation of endogenously produced LCPUFA by the high concentrations of LA in some formulae. Biochemical studies in both term and preterm infants indicate that infants fed formula unsupplemented with LCPUFA have significantly less DHA and AA in their erythrocytes relative to those fed breast milk (Clark 1992). Studies have also demonstrated that infants fed formula milk have lower levels

Infant Formula Supplementation With Long-chain Polyunsaturated Fatty Acids Has No Effect on Bayley Developmental Scores at 18 Months of Age—IPD Meta-analysis of 4 Large Clinical Trials

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ABSTRACT

Objectives: To find out whether supplementation of formula milk by long-chain polyunsaturated fatty acids (LCPUFA) affects neurodevelopment at 18 months of age in term or preterm infants by an individual patient data (IPD) meta-analysis.

Materials and Methods: Data of 870 children from 4 large randomised clinical trials for formula milk with and without LCPUFAs allowed for assessing the effect of LCPUFA with adjustment for potential confounders and extensive subgroup analysis on prematurity, LCPUFA source, and dosage. Any additional clinical trials examining the effect of LCPUFA supplementation on Bayley Scales of Infant Development at 18 months were regarded as relevant. Two relevant studies were identified by MEDLINE, but were not available to us. An IPD meta-analysis was performed with subgroup analyses by preterm delivery, very low birth weight (<1500 g), trials with higher amounts of docosahexaenoic acid (DHA) and arachidonic acid (AA), and specific sources of LCPUFA. The sample size of 870 children was sufficient to detect clinically relevant differences in Bayley Scales even in subgroups.

Results: There were no significant differences in mental or psychomotor developmental indexes between LCPUFA-supplemented and control groups for all children or in subgroups. This was confirmed with adjustment for the possible confounders: sex, gestational age, birth weight, maternal age, and maternal smoking. The adjusted mean differences in mental developmental index and psychomotor developmental index for all of the children were −0.8 (95% confidence interval −2.8 to 1.2) and −1.0 (−2.7 to 0.7), respectively.

Conclusions: These data based on considerable sample size provide substantial evidence that LCPUFA supplementation of infant formula does not have a clinically meaningful effect on the neurodevelopment as assessed by Bayley scores at 18 months. Inclusion of all relevant data should not have led to differing conclusions except, possibly, for very-low-birth-weight infants.

Key Words: Bayley scales, formula milk, IPD meta-analysis, LCPUFA, neurodevelopment

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Human milk contains long-chain polyunsaturated fatty acids (LCPUFA), most notably n-3 docosahexaenoic acid (DHA) and n-6 arachidonic acid (AA). Advantages in cognitive development of breast-fed in comparison with formula-fed infants have been attributed to the lack of these LCPUFAs in the past standard commercially available formulas (1).

Short-term beneficial effects of LCPUFAs such as DHA and AA on cognitive and visual development of the offspring were shown in several studies (2–4), but the long-term effect of these LCPUFAs on infant mental and psychomotor development at the age of 3 years, for example, is controversial (5,6). Guided by the short-term beneficial effects of LCPUFAs, Koletzko et al have recommended the use of formulas with a proportion of DHA between 0.2% and 0.5% of fatty acids and amounts of AA being at least equal to those of DHA (7).

In 1- to 2-year-old children, in particular, contradictory findings have been reported (8–21). It is unclear whether these differences may be attributed to whether term or preterm infants had been included in the study, to the LCPUFA amount, composition and source, population studied, and outcome measures used (22,23).

Systematic reviews on term and preterm children concluded that there is little evidence for benefits to LCPUFA-supplemented children in neurodevelopment, but small effects of LCPUFA supplementation may have escaped detection because of lack of

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The 4 trials are being followed up at school age in the Early Nutrition Programming Project. The long-term follow-up of the 4 intervention trials as well as the project on the IPD meta-analysis are funded under the Food Quality and Safety Priority of the Sixth Framework Programme for Research and Technical Development of the European Community (FOOD-CT-2005-007036, *www.metabolic-programming.org*).

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A.B. wrote the first draft, did the analysis, and is the guarantor. M.H.A. and H.B. were responsible for the Groningen trial, and M.F., K.K., A.S., and A.L. for the British trials. E.R. organized cooperation and data collection. M.H.A., M.F., K.K., B.K., and R.v.K. contributed to subsequent drafts of the article. A.B. and R.v.K. wrote the final draft together.

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power, the impossibility to adjust for confounders, and to perform subgroup analyses in the conventional meta-analysis approach (24–26).

These limitations may be overcome by an individual patient data (IPD) meta-analysis on the raw data of relevant original studies. Individual patient data meta-analyses are regarded as providing ''the least biased and most reliable means'' to combine results from different studies (27). However, this advantage may be challenged if data are not available from all relevant studies and if the assessment of relevant covariates differs substantially between the included studies.

We performed an IPD meta-analysis based on 4 independent large clinical trials (8–11) on LCPUFA supplementation in term or preterm infants, assessing neurodevelopment at 18 months using Bayley Scales of Infant Development II (BSID II) (28). The data were provided in the framework of the Early Nutrition Programming Project, a large European Union-funded research consortium exploring long-term consequences of nutrition during pregnancy and infancy on development and health (29). Unfortunately, we did not have access to data from 2 other relevant studies (13,18).

The question addressed was whether there is a global effect of LCPUFA supplementation on neurodevelopment, or a potential effect confined to subgroups of preterm infants, very-low-birthweight infants (VLBW), boys, girls, or regarding specific composition or sources of LCPUFA.

MATERIALS AND METHODS

Search for Other Relevant Studies

Because this IPD meta-analysis started with the data provided within the Early Nutrition Programming Project consortium, an effort was made to include all of the relevant data. We searched in MEDLINE (November 2007) for other randomised trials examining the effect of LCPUFA supplementation on neurodevelopment of infants measured by BSID II at 18 months of age. Search items were ''Bayley'' or ''development'' and ''LCPUFA.'' From 8 studies with adequate setting (12–19), only 2 proved to be relevant (13,18), because the others had assessed mental developmental index (MDI) and psychomotor development index (PDI) at time points other than 18 months of age; moreover, 2 of those had used BSID I (Table 1). Attempts to access the data from the relevant studies were not successful. We were not aware of other unpublished studies.

Data

The meta-analysis was based on individual patient data from randomised clinical trials from Groningen (8), Leicester, Nottingham (9,10), and Glasgow (11). Two of the British studies involved preterm infants (10,11). Here, the Leicester/Nottingham term and preterm studies will be called Leicester 1 and Leicester 2, respectively. The Leicester 2 children had a gestational age of <37 weeks and a birth weight <1750 g, the infants from the Glasgow study had a gestational age <35 weeks and a birth weight ≤ 2000 g.

In all of the trials, infants were randomised to receive either infant formulas with additional LCPUFA (LF) or a control unsupplemented infant formula (CF) in a double-blind design. The infants were not randomised to other interventions. The trial formulas were supplemented with n-3 DHA and n-6 AA and in the 2 preterm trials additionally with n-6 γ-linolenic acid (GLA). The control formulas were virtually free of DHA, AA, and GLA. The studies differed in formula composition, duration of formula feeding (Table 1), and formula sources: The LCPUFAs in the Groningen trial came from egg, fish oil (DHA), and single cell oil (AA), whereas the LCPUFAs in the UK trials contained mixtures of egg lipid/phospholipid, fish oil, and borage oil. The DHA content of formulas ranged from 0.17% to 0.5% of fatty acids, with varying DHA/AA ratios (Table 2). All 4 studies measured BSID II at 18 months corrected age as outcome variable. The Groningen trial used the Dutch version (BSID-II-NL).

In the term studies from Groningen and Leicester 1, data on MDI and PDI were available in 279 (132 LF + 147 CF) and 250 (125 LF +125 CF) cases, respectively. The preterm trial from Leicester 2 contained 147 (68 LF +79 CF) children, and the Glasgow study contained 194 (103 LF +91 CF). Therefore, the meta-analysis included 529 (257 LF +272 CF) term infants, 341 (171 LF +170 CF) preterm infants, and 870 (428 LF +442 CF) infants in total, with the numbers of LF and CF infants almost equal.

Subgroups

1. Term delivery
2. Preterm delivery as defined in the studies
3. Because different definitions for prematurity had been applied in the respective individual trials, we also generated the subgroup VLBW with children with birth weight of <1500 g ($n = 175 = 95$ LF + 80 CF), all of whom were born before the 35th week of gestation.
4. Because the level of DHA in the Leicester 2 trial was relatively low (Table 2), we investigated the subgroup ''higher DHA levels,'' including only the other 3 trials, which had used formulas with the recommended level of DHA between 0.2 and 0.5 (7).
5. Equivalently, we examined data from children supplemented with high AA levels (AA $\geq$ 0.2), leaving out the Glasgow study.

TABLE 1. Other randomised studies on the effect of LCPUFA supplementation on BSID indexed in MEDLINE

Study	Infants	BSID measured at (mo)	BSID version
Carlson (12)	Preterm	12	I
Birch et al (13)	Term	18	II
Makrides et al (14)	Term	12, 24	II
O'Connor et al (15)	Preterm	12	II
Van Wezel-Meijler et al (16)	Preterm	12, 24	I
Agostoni et al (17)	With phenylketonuria	5, 12	II
Clandinin et al (18)	Preterm	18	II
Fang et al (19)	Preterm	6, 12	II

BSID = Bayley Scales of Infant Development; LCPUFA = long-chain polyunsaturated fatty acids.

TABLE 2. Formula compositions of LCPUFA-supplemented formulas in grams per 100 g fat and duration of formula feeding in the 4 trials

	Groningen	Leicester 1	Leicester 2	Glasgow
DHA	0.30	0.32	0.17	0.50
AA	0.45	0.30	0.31	0.04
Other fatty acids	LA: 11.00*	LA: 15.90	GLA: 0.40	LA: 12.30
	GLA: 0.18	ALA: 1.10	EPA: 0.04	GLA: 0.90
	DGLA: 0.03	EPA: 0.01		ALA: 1.50
	ALA: 1.30*			EPA: 0.10
	EPA 0.23			
Duration	2 mo	6 mo	Until discharge (3 wk at minimum)	Until discharge, postdischarge formula

AA = arachidonic acid (n-6); ALA = α-linolenic acid (n-3); DGLA = dihomo-γ-linolenic acid (n-6); DHA = docosahexaenoic acid (n-3); EPA = eicosapentaenoic acid (n-3); GLA = γ-linolenic acid (n-6); LA = linoleic acid (n-6).
* The control group received similar amounts of LA (11.56) and ALA (1.27).

6. For the last subgroup we considered all 3 UK trials only because their LCPUFA sources in the formula differed from those in the Groningen study.
7. Boys
8. Girls

Statistical Methods

For all of the infants as well as for the 8 subgroups defined above, mean differences in Bayley MDI and PDI were calculated, adjusted for confounders, and tested by Student *t* test (2-sided hypothesis). This was done by applying multivariable linear models with BSIDs as outcome variables, LCPUFA supplementation as explanatory variable, and sex, gestational age, birth weight, maternal age, and maternal smoking during the third trimester as confounders. A significant mean difference between LF and CF groups in MDI and PDI was set at an α level of 0.05.

Although information on sociodemographics reported as maternal education (basic school at best vs certificate qualifying for university) was provided in all of the studies, we did not include this potential confounder in the main analyses because of missing data in 42% of the mothers in the Leicester 2 trial (7% in total); however, maternal education was considered in additional sensitivity analyses. Other sensitivity analyses looked for potential differences of the effects in boys and girls in subgroups 1 to 6.

We also examined a potential dose-response effect of DHA on MDI and PDI by calculating confounder-adjusted linear models replacing the explanatory variable LCPUFA supplementation with the variable amount of DHA given in the respective study (set to "0" for the CF group). From these analyses we excluded the data from the Groningen trial because the Bayley scores in this trial were higher than in the UK trials.

Power of the Study

For our power calculations, we assumed an α level of 0.05, a desired statistical power of 0.8, standard deviations of MDI and PDI of 15, and equal sizes of the number of LF and CF infants in every subgroup.

Data of 870 children permitted detection of a difference of 2.9 points in MDI or PDI, whereas 341 preterm children would be enough to find a score difference of 4.6. The subgroup of 175 VLBW infants would still allow detection of a difference of 6.4 score points in MDI or PDI.

RESULTS

As expected, the term children showed higher birth weight and gestational age and a smaller percentage of mothers smoking in the third trimester compared with the preterm children, whereas there were no significant differences in any of these variables for LCPUFA versus control infants (Table 3). Maternal age was

TABLE 3. Means (standard errors) and numbers of cases (%) of maternal and infant characteristics of term, preterm, and all children of all 4 included studies

	Term		Preterm		All	
	LCPUFA (n = 257)	Control (n = 272)	LCPUFA (n = 171)	Control (n = 170)	LCPUFA (n = 428)	Control (n = 442)
Males	139 (54%)	149 (55%)	79 (46%)	82 (48%)	218 (51%)	231 (52%)
Gestational age, wk	39.8 (1.3)	39.8 (1.2)	30.8 (2.2)	30.9 (2.2)	36.2 (4.7)	36.4 (4.7)
Birth weight, g	3595 (482)	3537 (438)	1426 (316)	1459 (307)	2725 (1145)	2731 (1087)
Maternal age, y	28.8 (4.7)	28.4 (4.7)	28.4 (4.7)	27.7 (5.5)	28.8 (4.7)	28.1 (5.0)
Higher maternal education*	45 (18%)	30 (11%)	41 (28%)	19 (15%)	86 (21%)	49 (12%)
Maternal smoking†	68 (27%)	85 (32%)	67 (40%)	70 (43%)	135 (32%)	155 (36%)

LCPUFA = long-chain polyunsaturated fatty acids.
* Missing values in UK 2 (42%).
† During third trimester; missing values in the Netherlands (6%) and UK 2 (6%).

TABLE 4. Mean values of MDI and PDI and unadjusted mean differences of LCPUFA vs control children in subgroups with term, preterm, and VLBW infants, high DHA and AA levels, children from the UK trials (receiving LCPUFAs from sources of egg lipid/phospholipid, fish oil and borage oil), boys, girls, and all infants

	MDI			PDI		
	LCPUFA	Control	Mean difference	LCPUFA	Control	Mean difference
All (n = 870)	93.9 (92.4–95.4)	94.5 (92.9–96.1)	−0.6 (−2.8 to 1.6)	93.3 (92.0–94.6)	94.4 (93.1–95.8)	−1.1 (−3.0 to 0.7)
Term (n = 529)	98.7 (96.9–100.5)	100.5 (98.7–102.4)	−1.8 (−4.4 to 0.7)	97.5 (96.1–99.0)	98.9 (97.5–100.4)	−1.4 (−3.4 to 0.6)
Preterm (n = 341)	86.8 (84.6–89.0)	84.9 (82.6–87.2)	1.9 (−1.3 to 5.0)	86.9 (84.9–88.9)	87.2 (85.0–89.4)	−0.2 (−3.2 to 2.7)
VLBW (n = 175)	85.7 (82.8–88.6)	83.6 (79.9–87.4)	2.0 (−2.7 to 6.8)	86.2 (83.4–89.0)	84.3 (80.7–87.8)	2.0 (−2.6 to 6.6)
DHA ≥ 0.2 (n = 733)	95.2 (93.6–96.8)	96.7 (95.0–98.5)	−1.6 (−3.9 to 0.8)	94.0 (92.7–95.4)	95.9 (94.4–97.3)	−1.8 (−3.8 to 0.2)
AA ≥ 0.2 (n = 676)	96.3 (94.6–98.0)	96.9 (95.1–98.6)	−0.6 (−3.0 to 1.8)	95.8 (94.5–97.2)	96.4 (95.0–97.9)	−0.6 (−2.6 to 1.4)
UK trials (n = 591)	89.9 (88.3–91.6)	89.1 (87.3–90.8)	0.8 (−1.6 to 3.2)	90.7 (89.2–92.1)	91.1 (89.5–92.6)	−0.4 (−2.5 to 1.7)
Boys (n = 449)	91.7 (89.7–93.7)	92.2 (90.1–94.3)	−0.5 (−3.4 to 2.4)	92.1 (90.2–93.9)	93.6 (91.7–95.5)	−1.5 (−4.1 to 1.1)
Girls (n = 421)	96.2 (94.1–98.4)	97.1 (94.7–99.5)	−0.9 (−4.1 to 2.4)	94.6 (92.8–96.4)	95.4 (93.5–97.3)	−0.8 (−3.4 to 1.8)

95% CIs in parentheses. AA = arachidonic acid (n-6); CI = confidence interval; DHA = docosahexaenoic acid (n-3); LCPUFA = long-chain polyunsaturated fatty acids; MDI = Mental Developmental Index; PDI = Psychomotor Developmental Index; VLBW = very-low-birth-weight infants.

comparable across all groups. However, the proportion of mothers with high levels of education was significantly higher in children randomised to LCPUFA supplementation.

Crude analyses are presented in Table 4. There were no significant differences between LF and CF groups in MDI and PDI overall and in any subgroups. Also, after adjustment for sex, gestational age, birth weight, maternal age, and maternal smoking, no significant mean differences were found between LCPUFA supplemented and control groups in MDI (difference −0.8 [95% confidence interval −2.8 to 1.2]) and PDI (−1.0 [−2.7 to 0.7]). Furthermore, there were no significant findings in any of the defined subgroups (Table 5).

Sensitivity analyses revealed identical findings in boys and girls overall, in all subcategories, and with inclusion of higher maternal education as a potential confounder (data not shown). The variable ''amount of DHA'' was no significant predictor in the dose response analyses.

TABLE 5. Mean differences in MDI and PDI of LCPUFA vs control children in subgroups with term, preterm; and VLBW infants, high DHA and AA levels, children from the UK trials (receiving LCPUFAs from sources of egg lipid/phospholipid, fish oil, and borage oil), boys, girls, and all infants

	MDI	PDI
All (n = 870)	−0.8 (−2.8 to 1.2)	−1.0 (−2.7 to 0.7)
Term (n = 529)	−2.2 (−4.8 to 0.4)	−1.2 (−3.3 to 0.9)
Preterm (n = 341)	2.1 (−1.2 to 5.4)	−0.3 (−3.3 to 2.7)
VLBW (n = 175)	1.2 (−3.7 to 6.1)	1.0 (−3.7 to 5.7)
DHA >0.2 (n = 733)	−1.5 (−3.7 to 0.7)	−1.3 (−3.1 to 0.5)
AA >0.2 (n = 676)	−1.2 (−3.5 to 1.1)	−0.7 (−2.6 to 1.2)
UK trials (n = 591)	0.6 (−1.7 to 2.9)	−0.6 (−2.6 to 1.4)
Boys (n = 449)	−1.0 (−3.7 to 1.7)	−1.8 (−4.3 to 0.7)
Girls (n = 421)	−0.1 (−3.1 to 2.9)	0.0 (−2.5 to 2.5)

95% CIs in parentheses. Adjusted for sex (as appropriate), gestational age, birth weight, maternal age, and maternal smoking. AA = arachidonic acid (n-6); CI = confidence interval; DHA = docosahexaenoic acid (n-3); LCPUFA = long-chain polyunsaturated fatty acids; MDI = Mental Developmental Index; PDI = Psychomotor Developmental Index; VLBW = very-low-birth-weight infants.

DISCUSSION

In contrast to classical meta-analyses based on aggregated data from different studies, this IPD meta-analysis on a large sample size allowed adjustment for confounders and to perform subgroup analyses. The absence of any detectable benefit or disadvantage in neurodevelopment assessed with BSID at the age of 18 months for all of the children or in any subgroup therefore provides evidence against beneficial effects of LCPUFA supplementation on BSID at 18 months under the conditions of the trials included here. The strength of the evidence depends substantially on the sample size of the data included and on the results of studies for which data were not available. In any case, our results do not exclude potential benefits under specific conditions, such as the reported improvement of BSID at 18 months in male preterm infants provided with a higher dosage of DHA of 0.5% of fatty acids (11).

The strength of our meta-analysis is its sample size with sufficient power to detect meaningful differences in Bayley scores, not only in the entire sample but also in subgroups. A difference of at least 5 points in the Bayley scores was considered as clinically relevant, taking account of the standard errors of measurement of MDI (4.27) and PDI (5.69) at 18 months given in the test manual (28). The sizes of the total sample and of the subgroups are large enough to find such a relevant difference, except for the subgroup of VLBW infants with a detectable difference of slightly above 5 points.

The only relevant data of term children not included in the IPD meta-analysis were those from the Birch et al (13) study, which had shown beneficial effects of LCPUFA supplementation on neurodevelopment; however, this trial included only 56 children. In our meta-analysis, supplemented term infants tended to have lower Bayley scores than controls. Therefore, inclusion of the Birch et al (13) data would be unlikely to change the results of our meta-analysis substantially (30).

The nonavailability of the data from the study of Clandinin et al (18), however, was a bigger concern. In the mentioned study, a control group (n = 54) was compared with 2 groups supplemented with different LCPUFAs (N = 104). All of the children included were born preterm, and almost all of them were born with VLBW (≤1500 g). In the control group, mean values of 77.2 in MDI and 83.0 in PDI were observed, in contrast to 85.1 (MDI) and 90.7 (PDI) in the combined group of supplemented children (26). Based on these results and the unadjusted mean differences from our study, weighted mean differences (95% confidence intervals) of preterm

children were 3.1 (0.3–6.0) in MDI and 2.1 (−0.8 to 5.1) in PDI and were therefore of no clinical relevance (as defined above). In respect of VLBW infants only, differences of 4.2 (0.5–7.9) and 4.7 (0.8–8.7) were detected in MDI and PDI, respectively. Although these appraisements did not consider possible confounding effects, they indicate that inclusion of the Clandinin et al (18) data would probably not have led to differing conclusions in other subgroups than the VLBW group.

These conclusions are in accordance with those from 2 recently published Cochrane reviews (24,25), which were based on the studies included in our IPD meta-analysis (8–11) and those from Birch et al (13) and Clandinin et al (18). These classical meta-analyses did not detect significant benefits in MDI and PDI of term and preterm children at 18 months of age. Another review on the effect of LCPUFA supplementation (26) on neurodevelopment included 2 additional studies that had assessed BSID II earlier than 18 months (15,19). This meta-analysis found a significant increase of MDI by 3.4 points, but no significant change in PDI. Again, it is disputable whether the observed change in MDI is of clinical relevance. Furthermore, the observed effects disappeared when the results of 2 studies with BSID I as outcome (12,16) were additionally considered.

Other possible weaknesses of this study may arise from limitations regarding the data provided. One of the trials lacked information on maternal education in about half of the mothers; however, including higher maternal education into multivariable analyses as an additional covariate where available had no considerable effects on the results. Furthermore, systematically higher MDI and PDI were reported in the Groningen trial. This may be because of different reference norms in the original and translated version of the Bayley test, but is unlikely to interfere with supplementation effects because of almost equal numbers of LF and CF groups in the Groningen trial.

Other studies detected benefits of LCPUFA supplementation on other neurological outcomes, such as general movements (2) or visual acuity (3,4) in children younger than 12 months during infancy. A previous trial in 18-month-old children detected effects of prenatal fatty acid status on neurologic optimality scores, but none on BSID (21). The reason may be that BSIDs, the most frequently used scores to assess neurodevelopment of infants (31), are a less subtle measurement than neurologic optimality scores and may have limitations in detecting differences in ''excellence.''

Measurements based on BSID at 18 months may miss subtle differences related to LCPUFA supplementation and may miss effects manifesting at later ages. For example, in a large double-blind randomised trial providing 200 mg DHA per day or placebo to breast-feeding women, Bayley scores at 18 months were not affected, but the supplemented group showed significantly better psychomotor development scores at $2^{1}/_{2}$ years (32). Similarly, randomised clinical trials providing oils with considerable amounts of DHA to women beginning in pregnancy found improved cognitive development at later ages of $2^{1}/_{2}$ years (33) and at 4 years (34), whereas another study showed no improvement of visual acuity and intelligence quotient for LCPUFA-supplemented children at 3 years of age (23). A dose-response effect between maternal n-3 LCPUFA intake from seafood and children's verbal intelligence quotient at the age of 8 years, after adjustment for 28 confounding factors, was reported in the Avon Longitudinal Study of Parents and Children (35).

This IPD meta-analysis provides substantial evidence that there are no clinically relevant effects of LCPUFA supplementation on neurodevelopment as assessed by BSID at 18 months in almost all subgroups except for VLBW children. For these, additional inclusion of data from all of the relevant studies in this field may have resulted in the detection of relevant beneficial effects. Possible effects of LCPUFA on other outcomes, including outcomes at later ages, deserve further study.

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World Health Organization

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In reply please refer to:

Your reference:

Ms Glenis Willmott MEP
ASP13G301
Brussels
BELGIUM

Geneva, 6th April 2011

Dear Ms. Willmott,

in response to your request for information, I would like to clarify that WHO does not have a recommendation about the addition of docosahexaenoic acid (DHA) to formula milk. The 2008 consultation on fats and fatty acids convened by FAO and WHO highlighted the importance of DHA as a component of human milk and its role in development of the brain and retina during foetal development and the first two years of life (Fats and fatty acids in human nutrition. Report of an expert consultation. FAO, 2010). The consultation did not provide any recommendations about supplementing synthesized DHA in infant formula, as to date no solid evidence exists to be able to say that adding DHA to infant formula will have important clinical benefits.

Were WHO to give such a recommendation, it would have to follow a strict guideline development process based on grading of all available evidence collected through systematic reviews by expert panels free from conflict of interest.

I take this opportunity to remind the European Parliament that WHO recommends exclusive breastfeeding for the first six months of life to achieve optimal growth, development and health and continued breastfeeding (with safe and appropriate complementary foods) for up to two years of age or beyond. The use of breastmilk substitutes is required in certain medical conditions (Acceptable medical reasons for use of breast-milk substitutes. WHO, 2009) and the final choice of whether to breastfeed rests with the mother.

The World Health Assembly Resolution WHA 39.28 states that "the practice being introduced in some countries of providing infants with specially formulated milks (so-called "follow-up milks") is not necessary" (WHA39.28, 1986). Those who are using (or need to use) infant formula can continue to do so after six months. Even when follow-up formula as a product in itself is not explicitly promoted as a breast-milk substitute, marketing techniques, e.g. packaging, slogans, and general promotion of such products may induce mothers to use infant formula or follow-up formula in the first 6 months of life and/or stop continued breastfeeding after this period.

Finally, on the issue of claims, the 58th World Health Assembly (2005) was "concerned that nutrition and health claims may be used to promote breastmilk substitutes as superior to breastfeeding" and thus called on Member States "to ensure that nutrition and health claims are not permitted for breastmilk substitutes, except where specifically provided for in national legislation" (WHA 58.32).

In 2010 the World Health Assembly adopted resolution WHA 63.23 calling on Member States "to end inappropriate promotion of food for infants and young children and to ensure that nutrition and health claims shall not be permitted for foods for infants and young children, except where specifically provided for, in relevant Codex Alimentarius standards or national legislation".

I hope this can help the discussion of resolution B7-0000/2011 that you have submitted to the European Parliament and I take the opportunity to send my best regards.

Yours sincerely,

Francesco Branca, MD PhD
Director
Department of Nutrition for
Health and Development

Archives of
DISEASE IN CHILDHOOD

Original article:
The 10-year follow-up of a randomised trial of long-chain polyunsaturated fatty acid supplementation in preterm infants: effects on growth and blood pressure
Kathy Kennedy, Sarah Ross, Elizabeth B Isaacs, Lawrence T Weaver, Atul Singhal, Alan Lucas, Mary S Fewtrell
Arch Dis Child 2010;**95**:588-595 Published Online First: 1 June 2010 doi:10.1136/adc.2009.167270
[Abstract] [Full text] [PDF]

Reply to letters from Dr J Hoffman and Dr A Lapillone

Katherine J Kennedy, Research scientist Alan Lucas, Mary Fewtrell

Institute of Child Health, UCL, London

Dear Sir

Response to letter from James P Hoffman of Martek Biosciences Corp.

We completely disagree with Dr Hoffman's statement that "caregivers of preterm infants are not well served by our report of a 10 year follow-up of LCPUFA supplementation in preterm infants". Our study (1) presents the results of the longest follow-up of a randomised trial LCPUFA supplementation during infancy to date. We have explicitly acknowledged the shortcomings of the study (mainly cohort attrition) to a much greater extent than is typical in a study of this type, and we have discussed the limitations of our data and the need for further research into these outcomes. Our responses to Dr Hoffman's specific points are detailed in the Appendix.

It is worth noting here that, although the vast majority of infant formulas now contain LCPUFA, the scientific evidence base for their addition is recognised by most investigators and Key Opinion Leaders in the field to be weak; the most recent update of the Cochrane systematic reviews on LCPUFA supplementation of formulas for both preterm and term infants (encompassing 29 trials) concluded that there is no evidence for outcome benefits of the intervention, at least up to 18 months of age (2,3). We contend this field of research has been driven to an extent by enthusiasm and vested interest. As one of the major groups to do outcomes research in this area, we do not hold a fixed position but are open to the scientific evidence, and we have published on both positive and negative effects of supplementation in different trials. Our experience of publishing in this field has consistently been that publications supporting the addition of LCPUFA to infant formula are more readily accepted and less criticised than those which do not support the intervention, or which raise potential concerns. Thus studies such as that of Birch et al (4), on a small number of subjects, with significant attrition even in infancy but showing apparent large beneficial effects of LCPUFA supplemented formula on cognitive development have been widely cited as supporting the addition of LCPUFA. Indeed, Birch's study, which may have been one of the most influential trials driving the addition of LCPUFA to US formulas, was based on an incomplete follow up where only 19 subjects remained in the relevant intervention group, providing inadequate power to provide any realistic estimation of the treatment effect. It is odd then that our much larger study with more complete longer-term follow-up and a range of outcomes not previously examined should attract such critical comment, as that from Dr Hoffman. We have previously received criticism for other trials where we found potentially unfavourable effects of LCPUFA supplementation. For example, in one preterm trial we found preterm infants supplemented with LCPUFA had a long term reduction in linear growth (5) - yet another group that found the same thing but appeared nevertheless to favour single cell oil supplementation, received no such adverse comment (6). In contrast, whenever we have generated positive results, these have been accepted with enthusiasm. If our contention that there may be some underlying bias in this area, is true, this would not "well serve the caregivers of preterm infants" - or term infants - who are best served by objective reporting of scientific data in the interests of child health.

We note that we also measured cognitive outcomes during the follow-up of our current study and will be interested to see whether publication of these findings, which suggest some long term beneficial effects of LCPUFA supplementation, but in the same cohort with the same attrition rate and limitations, will attract the same level of scrutiny and criticism, which we doubt.

We hope that Readers will appraise our current manuscript in a critical, but importantly, open-minded manner, considering the limitations we have highlighted; and that eventually these data can be considered alongside those from other similar studies examine the long-term health effects of LCPUFA supplementation of infants formulas, in order to strengthen the evidence-base for future products.

Kathy Kennedy, Mary Fewtrell, Alan Lucas

Appendix. Response to Dr Hoffman's specific comments and questions:

1. We have not claimed in the paper that LCPUFA supplementation has programmed preterm girls to later obesity and hypertension! This was deliberate, so as not to cause alarm or extrapolate beyond our findings. As stated in our discussion, the girls in our study all had blood pressure and BMI currently within the normal range, and we merely speculated on the potential longer-term significance of our findings, for example, given data showing tracking of BP. 2. We have noted the greater height of the LCPUFA supplemented girls at follow-up in our paper, along with higher weight, skinfold thicknesses and fat mass etc. Fat mass and fat free mass adjusted for height (FMI and FFMI) were indeed not significantly different between groups, as reported in the manuscript. The difference in stature (and potentially more advanced pubertal development, as we have discussed) could explain the greater skinfold thickness and weight of the supplemented girls; however, it is equally possible that LCPUFA supplementation has resulted in greater fatness, which is recognised to be associated with increased stature and earlier pubertal development. We consider it inappropriate to adjust for height (an outcome measure potentially influenced by the intervention) in our main analyses. 3. Dr Hoffman asks for the baseline and follow-up characteristics of the girls who were followed up and those who were not seen to be presented; in the interests of brevity these results were not presented in the paper. However, we can confirm that girls who were seen were more preterm (30.4 wk vs 31.6 wks, p = 0.001), had lower birth weights (1379g vs 1500g, p = 0.05), spent longer in hospital (46 days vs 36 days, p = 0.013), were more likely to have required ventilation (52% vs 29%, p = 0.009), and their mothers were less likely to have been educated to degree level (0% vs 8%, p = 0.04) compared to those who did not take part in the follow-up. This will affect the generalisability of our findings to the original cohort. However, of greater relevance to the preservation of randomisation for those seen at follow-up, there were no significant differences between supplemented and control girls studied for baseline or follow-up characteristics, with the exception of the number of days of ventilation (4.4 days vs 1.1 days, p = 0.013). We did not record details of the timing of the introduction of solids nor of subsequent diet or physical activity in this study. The randomisation procedure should mean that these factors are equal in the two groups, although we accept that with attrition at follow-up, this may be questioned to some extent. 4. We do not 'ignore the importance of LCPUFA in preterm infant nutrition'; rather we question the evidence that adding LCPUFA to infant formulas in the manner used for formulas tested in clinical trials to date produces clinical benefit. The ESPGHAN Committee on Nutrition paper cited here itself acknowledges that 'the long-term effects on visual and neural development are not fully known', and the Expert group providing advice during the recast of the EU Directive on the composition of infant formulas in Europe (EFSA) concluded that there was insufficient evidence on which to make the addition of LCPUFA to infant formulas compulsory; the addition of LCPUFA to infant formulas is currently optional under EU regulations. A significant number of Key Opinion Leaders in this field have this view.

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Reply to Dr Lapillone

We thank Dr Lapillone for his comments. We do not agree that our conclusions will confuse the readers of the Archives of Disease in Childhood, and this was certainly not our intention. The results are clearly presented (and summarised by Dr Lapillone). As he states, we assessed 'adiposity' in a number of ways - skinfold thicknesses, BMI, %fat and fat mass and fat free mass from deuterium dilution and normalised for height. We have clearly set out in the results and abstract which of these measures were significantly different between the supplemented and control groups; and in the abstract we do not claim that fat mass (or fat mass index) were significantly different.

Dr Lapillone is correct that our group has recommended using measures of fat and fat free mass normalised for height, rather than using % fat; however, this applies to whole body measurements. We have also advocated using skinfold thickness measurements as raw values to measure regional fat mass, and it is entirely plausible to have differences in regional adiposity not reflected in whole body measurements. Thus, we stand by our conclusion.

Kathy Kennedy, Mary Fewtrell, Alan Lucas

Conflict of Interest:

None declared

… less

Submit response

Published 24 August 2010

Long-term health consequences of LCPUFA supplementation of preterm girls

James P. Hoffman, Dir. Med. Svcs.

Martek Biosciences Corp.

Editor:

Caregivers of preterm infants and children are not well served by the report of Kennedy et al.,[1] "Girls who were born preterm and received LCPUFA supplemented formula showed increased weight,

More…

Submit response

Published 24 August 2010

Results of published, peer-reviewed clinical trials measuring the impact of DHA/ARA supplementation in infant formula on cognitive development

	Adelaide 1995	Adelaide 1996	China 2004	Dallas 1998	England 1999	Netherlands 2005	Portland 1997	Portland 2001
3 months, MDI			NO BENEFIT					
3 months, PDI			NO BENEFIT					
6 months, MDI			NO BENEFIT					
6 months, PDI			NO BENEFIT					
1 year, MDI	NO BENEFIT	NO BENEFIT					NO BENEFIT	NO BENEFIT
1 year, PDI	NO BENEFIT	NO BENEFIT					NO BENEFIT	NO BENEFIT
18 months, MDI				BENEFITS FOUND	NO BENEFIT	NO BENEFIT		
18 months, PDI				NO BENEFIT	NO BENEFIT	NO BENEFIT		
2 years, MDI		NO BENEFIT						
2 years, PDI		NO BENEFIT						

MDI: Bayley Scales of Infant Development; Mental Development Index
PDI: Bayley Scales of Infant Development; Psychomotor Development Index

Note: these clinical trials were determined by Simmer et al. 2008 to be of good quality, and included in their meta-analysis.

Results of published, peer-reviewed clinical trials measuring the impact of DHA/ARA supplementation in infant formula on visual development

	Adelaide 1995	Adelaide 1996	Dallas 1998	Dallas 2005	Portland 1997	Portland 2001	Memphis 1996
Test A, 4 months	DHA+ARA: NO BENEFITS FOUND DHA alone: BENEFITS FOUND	NO BENEFITS					
Test B, 4 months			BENEFITS FOUND	BENEFITS FOUND			
Test C, 4 months					NO BENEFITS FOUND		
Test D, 4 months					NO BENEFITS FOUND	NO BENEFITS FOUND	NO BENEFITS FOUND
Test C, 6 months					NO BENEFITS FOUND		
Test D, 6 months					NO BENEFITS FOUND	NO BENEFITS FOUND	NO BENEFITS FOUND
Test A, 7-8 months	DHA + ARA: NO BENEFITS FOUND DHA alone: BENEFITS FOUND	NO BENEFITS FOUND					
Test B, 12 months			BENEFITS FOUND	BENEFITS FOUND			
Test C, 12 months					NO BENEFITS FOUND		
Test D, 12 months					NO BENEFITS FOUND	NO BENEFITS FOUND	NO BENEFITS FOUND
Test D, 3 years					NO BENEFITS FOUND		

Test A: Steady
Test B: Sweep (logMar)
Test C: Sweep (cycles/degree)
Test D: Teller cards

Note: these clinical trials were determined by Simmer et al. 2008 to be of good quality, and included in their meta-analysis.

Appendix F

Organic Consumers Reject Martek's Oils

PCC Natural Market Consumer Survey – Excerpts

PCC Natural Markets surveyed nearly 1,500 organic shoppers to determine their awareness and concerns regarding the source and regulation of natural and synthetic nutrients added to organic foods. Below are excerpts of some of their findings:

A majority of PCC shoppers (52.9%) believe that most of the vitamins and minerals sold at PCC are made from natural ingredients. Only 4.9% say they believe that most vitamins and minerals PCC sells are made from synthetic ingredients. More than four out of ten shoppers (42.2%) say they don't know.

Although PCC shoppers are inclined to take dietary supplements on a regular basis, they tend ***not*** to shop purposefully for organic products that are labeled as containing added vitamins, minerals or other nutrients for enhanced nutritional value. This suggests that shoppers think of food and supplements differently.

Almost 8 out of 10 PCC shoppers (77.8%) **do not believe** that the FDA ensures all added nutrients, such as omega-3s, are effective and safe before allowing them on the market.

Shoppers who are **least confident** in the FDA's oversight of added nutrients are those whose food purchases are mostly (75-100%) organic. Conversely, shoppers whose grocery purchases are less than one-fourth organic tend either to have more confidence in the FDA (16.1%) or say they don't know (21.5%).

More than ninety percent of PCC shoppers (92.3%) purchase at least one common food source of natural omega-3s deliberately because of omega-3 content. Salmon or other fish is purchased by two-thirds of PCC shoppers. Close to half buy walnuts, flax or chia seeds/oil or grass-fed meat for their natural omega-3 content.

PCC shoppers who are less "organic" (referring to the portion of their grocery purchases that are certified organic) tend to have more interest in purchasing products labeled "added omega-3s."

PCC shoppers prefer, by an overwhelming margin, that added omega-3s be made from naturally occurring sources, compared to synthetically-derived omega-3s.

Six of 10 shoppers who are aware of how many certified organic foods they purchase would not purchase products to which omega-3s made from synthetic sources have been added. If responses of "less inclined" and "would not purchase" are combined, an obvious conclusion is that the majority of even "less organic" shoppers (those whose grocery purchases are less than 50% organic) **do not want** added, synthetically-derived omega-3s in their food.

Nutrient Additives

PCC Shopper Survey

August-September 2011

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Nutrient Additives

PCC Shopper Survey

Survey Background and Findings

SURVEY OBJECTIVE

- To determine the awareness and concerns of consumers – particularly those who prefer certified organic foods – regarding the source and regulation of natural and synthetic nutrients added to organic foods.

SURVEY BACKGROUND

The findings of this survey are intended to inform the National Organics Standard Board (NOSB) about the assumptions and expectations of organic consumers regarding nutrient additives in organic foods. PCC Natural Markets (PCC) developed this survey to determine the depth of shoppers' knowledge and opinions on nutrient additives.

This survey was prompted by the debate over how NOSB should address nutrient additives to organic foods. At the April 2011 NOSB meeting in Seattle, two NOSB members asked PCC's director of public affairs what NOSB "should do … in terms of the issue of moving forward on vitamins, nutrients and minerals ─ with open-endedness, or with citations" ─ and whether "PCC consumers know that most of the essential vitamins and minerals are synthetic?" She did not have adequate information or data to answer those questions with certitude but realized PCC could provide NOSB data to answer those questions and others related to nutrient additives by gathering data from shoppers in PCC's nine stores, the largest consumer-owned and -operated grocery retail business in the nation.

SURVEY METHODOLOGY

The survey questionnaire (addendum) was developed and pre-tested in-house at PCC. It was reviewed by industry experts from three organizations: two members of the NOSB, three staff at the Cornucopia Institute, and Consumers Union. The questionnaire was posted on PCC's website on July 28, 2011 and published in the August 2011 issue of PCC's newspaper, *Sound Consumer*. Potential respondents were invited to participate in the survey via PCC's electronic newsletters (12,169 subscribers) and an alert on the PCC website home page.

Responses submitted electronically (1,349) and in writing (171) were combined for analysis. A subset of responses from PCC shoppers was excerpted for analysis and reporting purposes. Included in this subset were survey participants who answered Q-9 (About what portion of your grocery purchases is certified organic?). Survey participants who reside beyond PCC's trade area (outside of King and Snohomish counties, Washington State) were excluded. The resulting respondent base totaled 1,432.

Q: About what portion of your grocery purchases is certified organic?

	Sample size	% of total sample
Less than 25%	93	6.5%
25 – 49 %	267	18.6%
50 – 74 %	426	29.8%
75 – 100%	622	43.4%
Don't know	24	1.7%
	1,432	100.0%

The response to this survey was, in itself, significant in that it demonstrates how sensitive consumers are to having nutrients – naturally or synthetically derived – added to food products. On the first day of the survey period, 312 questionnaires were completed online; by the second day 854 completed questionnaires were submitted. Some respondents felt compelled to respond by email as well:

> *Fascinating! I buy Omega-3 organic milk because we don't get enough from fish and my wife is pregnant. I'd never thought about where that Omega-3 comes from but I've assumed that if I bought it at PCC then they've done the research for me. That's why I'm willing to pay more.*
> *— Phil E.*

> *Invariably the "nutrients" added will be from the most cost effective source available which means they will more often than not be of very low quality and effectively worthless. Even if they were of the highest quality, the practice is contrary to the concept of organic foods and has no place whatsoever on the trusted shelves of PCC.*
> *— Todd H.*

SURVEY FINDINGS

Graphed responses to each question follow, preceded by highlights in four topic categories:

- **Dietary supplements**
- **Efficacy and safety of added nutrients**
- **Omega-3s**
- **Respondent characteristics**

Dietary supplements

- Dietary supplements (those listed in the survey) are taken by most (88.5%) of PCC shoppers.
- Vitamins, by far, are the most popular dietary supplement – taken by 82.1% of survey respondents. Omega-3s are taken by almost 6 out of 10 respondents.

Q: Which of the following dietary supplement do you take on a regular basis? Circle the numbers of all that apply.

		% of grocery purchases certified organic				
	Total	<25%	25-49%	50-74%	75-100%	Don't know
Vitamins	82.1%	84.9%	82.4%	84.0%	80.4%	79.2%
Omega-3s	59.2%	57.0%	60.3%	60.8%	58.8%	37.5%
Minerals	56.5%	57.0%	51.3%	57.3%	58.0%	58.3%
Herbal supplements	40.4%	29.0%	37.5%	40.4%	43.6%	37.5%
Digestive enzymes	29.7%	21.5%	24.0%	28.4%	34.7%	20.8%
None of the above	11.5%	11.8%	12.0%	10.8%	11.6%	16.7%

- A majority of PCC shoppers (52.9%) believe that most of the vitamins and minerals sold at PCC are made from natural ingredients. Only 4.9% say they believe that most vitamins and minerals PCC sells are made from synthetic ingredients. More than four out of ten shoppers (42.2%) say they don't know.

Q: Do you believe most vitamins and minerals sold at PCC are made from natural or synthetic ingredients?

		% of grocery purchases certified organic				
	Total	<25%	25-49%	50-74%	75-100%	Don't know
Natural (made from a Renewable resource found in nature)	52.9%	43.0%	47.1%	55.2%	56.2%	26.1%
Synthetic (man-made through chemical change)	4.9%	4.3%	2.3%	4.7%	6.5%	0.0%
Don't know	42.2%	52.7%	50.6%	40.1%	37.3%	73.9%

- Although PCC shoppers are inclined to take dietary supplements on a regular basis, they tend ***not*** to shop purposefully for organic products that are labeled as containing added vitamins, minerals or other nutrients for enhanced nutritional value. This suggests that shoppers think of food and supplements differently.

Q: When buying groceries, do you deliberately choose organic products because they're labeled as containing added vitamins, minerals or other nutrients for enhanced nutritional value?

Continued …

	% of grocery purchases certified organic					
	Total	<25%	25-49%	50-74%	75-100%	Don't know
"Yes" responses						
Milk & eggs	16.2%	20.4%	17.2%	17.7%	14.2%	12.5%
Bread & energy bars	14.7%	21.5%	16.2%	16.2%	11.6%	25.0%
Packaged cereal & pasta	9.7%	15.2%	12.8%	10.1%	7.0%	16.7%
Bottled juice, water & tea	9.3%	12.9%	12.1%	9.1%	7.5%	12.5%
General products	7.7%	12.0%	7.6%	7.7%	7.0%	8.3%

Efficacy and safety of added nutrients

- Almost 8 out of 10 PCC shoppers (77.8%) **do not believe** that the FDA ensures all added nutrients, such as omega-3s, are effective and safe before allowing them on the market.

- Shoppers who are **least confident** in the FDA's oversight of added nutrients are those whose food purchases are mostly (75-100%) organic. Conversely, shoppers whose grocery purchases are less than one-fourth organic tend either to have more confidence in the FDA (16.1%) or say they don't know (21.5%).

Q: Do you believe the U.S. Food and Drug Administration ensures all added nutrients, such as omega-3s, are effective and safe before allowing them on the market?

	% of grocery purchases certified organic					
	Total	<25%	25-49%	50-74%	75-100%	Don't know
Yes	6.6%	16.1%	6.7%	7.7%	4.3%	4.3%
No	**77.8%**	**62.4%**	**73.0%**	**77.5%**	**82.6%**	**73.9%**
Don't know	15.6%	21.5%	20.2%	14.8%	13.0%	21.7%

Omega-3s

- Close to 6 out of 10 PCC shoppers take omega-3 supplements on a regular basis, regardless of how much certified organic food they buy (with the exception of those shoppers who do not know what portion of certified organic they purchase).

Q: Which of the following dietary supplement do you take on a regular basis? Circle the numbers of all that apply.

	% of grocery purchases certified organic					
	Total	<25%	25-49%	50-74%	75-100%	Don't know
Omega-3s	**59.2%**	**57.0%**	**60.3%**	**60.8%**	**58.8%**	37.5%

- More than ninety percent of PCC shoppers (92.3%) purchase at least one common food source of natural omega-3s deliberately because of omega-3 content. Salmon or other fish is purchased by two-thirds of PCC shoppers. Close to half buy walnuts, flax or chia seeds/oil or grass-fed meat for their natural omega-3 content.

Q: Omega-3 fats occur naturally in fish, nuts, seeds, and meat and dairy from animals that graze. Which of the following do you purchase from PCC deliberately for their natural omega-3 content? Indicate all that apply.

		% of grocery purchases certified organic				
Rank order:	Total	<25%	25-49%	50-74%	75-100%	Don't know
Salmon or other fish	65.9%	65.6%	62.2%	70.9%	64.6%	50.6%
Walnuts	47.2%	33.3%	38.2%	45.8%	54.3%	41.7%
Flax or chia seeds/oil	46.1%	28.0%	38.6%	47.9%	51.6%	25.0%
Grass-fed meat	45.9%	32.3%	38.6%	46.9%	50.8%	37.5%
Omega-3 eggs	41.0%	28.0%	40.4%	45.1%	41.0%	25.0%
Pastured dairy	30.8%	17.2%	22.5%	30.5%	37.0%	20.8%
None of the above	7.7%	14.0%	11.2%	7.0%	5.0%	25.0%

- PCC shoppers who are less "organic" (referring to the portion of their grocery purchases that is certified organic) tend to have more interest in products labeled "*added* omega-3s." As a group they're also more likely (than more committed "organic" shoppers) to express "no opinion" on whether *added* omega-3s influence their purchasing decisions.

Q: Some manufacturers add omega-3s to foods that do not contain them naturally. When buying groceries other than those above (Salmon or other fish, Grass-fed meat, Omega-3 eggs, Pastured dairy, Flax or chia seeds/oil, Walnuts), are you more or less inclined to purchase organic products because they're labeled as containing added omega-3s?

		% of grocery purchases certified organic				
	Total	<25%	25-49%	50-74%	75-100%	Don't know
More inclined	14.9%	26.1%	15.1%	13.8%	13.5%	25.0%
Less inclined	35.0%	20.7%	32.5%	37.1%	37.1%	25.0%
Would not purchase	20.7%	12.0%	17.0%	17.4%	26.3%	8.3%
No opinion	29.5%	41.3%	35.5%	31.7%	23.1%	41.7%

- PCC shoppers prefer – by an overwhelming margin – that added omega-3s be made from naturally occurring sources, compared to synthetically-derived omega-3s.

- A significant proportion of shoppers (11.0% of total shoppers; 14.5% of shoppers whose food purchases are 75% organic or higher) would not purchase foods with *any* added omega-3s, even if the omega-3s are derived from natural sources.

Q: Are you more or less inclined to purchase foods is added omega-3s are made from naturally occurring sources or are synthetic?

Added omega-3s made from ***naturally occurring*** sources

		% of grocery purchases certified organic				
	Total	<25%	25-49%	50-74%	75-100%	Don't know
More inclined	**67.2%**	**77.2%**	**63.9%**	**71.8%**	**64.3%**	58.3%
Less inclined	10.8%	4.3%	11.7%	9.0%	12.5%	12.5%
Would not purchase	11.0%	2.2%	**10.2%**	9.0%	**14.5%**	4.2%
No opinion	11.0%	16.3%	14.3%	10.2%	8.7%	25.0%

- Six of 10 shoppers who are aware of how many certified organic foods they purchase would not purchase products to which omega-3s made from synthetic sources have been added. If responses of "Less inclined" and "Would not purchase" are combined, an obvious conclusion is that the majority of even "less organic" shoppers (those whose grocery purchases are less than 50% organic) **do not want** added, synthetically-derived omega-3s in their food.

Added omega-3s that are ***synthetic***

		% of grocery purchases certified organic				
	Total	<25%	25-49%	50-74%	75-100%	Don't know
More inclined	1.2%	2.4%	.8%	1.0%	1.2%	4.2%
Less inclined	30.3%	46.3%	36.0%	32.5%	22.8%	54.2%
Would not purchase	**60.8%**	**32.9%**	**50.2%**	**60.2%**	**71.7%**	20.8%
No opinion	7.7%	18.3%	13.0%	6.3%	4.2%	20.8%

- PCC shoppers' aversion to foods containing added omega-3s made from or with genetically engineered, chemically-derived or synthetic ingredients correlates directly with the portion of grocery purchases that are certified organic.

Q: A variety of ingredient sources and production methods are used to make the omega-3s that are added to foods. How likely are you to purchase organic foods with* added *omega-3s made from or with the following:

Added omega-3s from ***natural and/or organic sources***

		% of grocery purchases certified organic				
	Total	<25%	25-49%	50-74%	75-100%	Don't know
Flax seed, Organic						
More inclined	**64.3%**	**65.9%**	**61.6%**	**66.2%**	**64.7%**	45.8%
Would not purchase	14.4%	8.0%	15.6%	14.1%	15.3%	8.3%
No opinion	11.1%	17.0%	14.4%	9.8%	9.2%	25.0%

Continued …

Added omega-3s from ***natural and/or organic sources***

	% of grocery purchases certified organic				
	Total	<25%	25-49%	50-74%	75-100%	Don't know
Fish, Wild						
More inclined	**56.2%**	**70.0%**	**55.1%**	**57.0%**	**54.6%**	41.7%
Would not purchase	22.9%	7.8%	16.7%	23.3%	27.6%	20.8%
No opinion	9.3%	12.2%	15.2%	7.7%	6.7%	25.0%
Algae, Organic						
More inclined	**51.6%**	**44.0%**	**45.2%**	**55.2%**	**53.8%**	33.3%
Would not purchase	18.0%	12.1%	18.8%	17.3%	19.4%	8.3%
No opinion	17.6%	31.9%	26.4%	14.6%	12.7%	41.7%

Added omega-3s from ***other than natural and/or organic sources***

	% of grocery purchases certified organic				
	Total	<25%	25-49%	50-74%	75-100%	Don't know
Hexane						
More inclined	0.3%	0.0%	0.4%	0.5%	0.0%	4.2%
Would not purchase	**88.6%**	**75.3%**	**83.8%**	**89.5%**	**92.8%**	66.7%
No opinion	6.6%	15.7%	10.4%	4.8%	4.4%	20.8%
Glucose syrup solids						
More inclined	1.1%	11.2%	0.0%	0.7%	0.2%	4.2%
Would not purchase	**88.6%**	**68.5%**	**82.6%**	**90.5 %**	**93.6%**	66.7%
No opinion	4.4%	3.4%	8.9%	3.1%	3.1%	16.7%
Modified starch						
More inclined	0.4%	0.0%	0.4%	0.7%	0.0%	4.2%
Would not purchase	**87.9%**	**70.0%**	**81.6%**	**89.2%**	**93.6%**	58.3%
No opinion	5.4%	12.2%	10.7%	2.9%	3.3%	20.8%
Synthetic stabilizers						
More inclined	0.4%	0.0%	0.4%	0.7%	0.2%	4.2%
Would not purchase	**78.3%**	**58.9%**	**66.7%**	**80.2%**	**85.9%**	50.0%
No opinion	10.9%	22.2%	19.0%	8.1%	6.6%	37.5%
Algae, Genetically engineered						
More inclined	2.3%	1.1%	2.7%	2.4%	1.8%	12.5%
Would not purchase	**76.4%**	**50.6%**	**65.0%**	**76.2%**	**86.5%**	41.7%
No opinion	9.3%	23.0%	16.2%	7.2%	5.4%	20.8%

Continued …

Added omega-3s from ***other than natural and/or organic sources***

	% of grocery purchases certified organic					
	Total	<25%	25-49%	50-74%	75-100%	Don't know
Fish, Farmed						
More inclined	3.1%	4.5%	3.8%	2.9%	2.3%	12.5%
Would not purchase	**72.9%**	**58.4%**	**61.9%**	**73.8%**	**79.8%**	54.2%
No opinion	6.8%	10.1%	12.7%	4.1%	5.1%	20.8%
Mannitol						
More inclined	1.0%	1.1%	1.5%	1.0%	0.7%	4.2%
Would not purchase	**70.9%**	**50.0%**	**63.1%**	**71.7%**	**78.2%**	37.5%
No opinion	15.9%	26.7%	23.1%	13.4%	12.0%	37.5%
Sodium polyphosphate						
More inclined	0.4%	0.0%	0.4%	1.0%	0.0%	4.2%
Would not purchase	**68.7%**	**41.1%**	**58.8%**	**70.5%**	**77.4%**	29.2%
No opinion	22.9%	42.2%	31.9%	19.3%	17.0%	62.5%
Sunflower oil, Non-organic						
More inclined	4.7%	15.7%	6.2%	5.1%	2.0%	13.0%
Would not purchase	**57.3%**	**30.3%**	**41.3%**	**55.4%**	**71.1%**	8.7%
No opinion	13.1%	27.0%	22.4%	11.1%	7.4%	43.5%

- PCC shoppers' who have "no opinion" about what added omega-3s are made from or with tend to be those whose grocery purchases are **less than 50% certified organic**.

Q: A variety of ingredient sources and production methods are used to make the omega-3s that are added to foods. How likely are you to purchase organic foods with* added *omega-3s made from or with the following:

Added omega-3s from ***natural and/or organic*** sources

	% of grocery purchases certified organic					
	Total	<25%	25-49%	50-74%	75-100%	Don't know
Respondents with "No opinion"						
Algae, Organic	17.6%	31.9%	26.4%	14.6%	12.7%	41.7%
Fish, Wild	9.3%	12.2%	15.2%	7.7%	6.7%	25.0%
Flax seed, Organic	9.3%	12.2%	15.2%	7.7%	6.7%	25.0%

Continued …

Added omega-3s from *other than natural and/or organic* sources

Respondents with "No opinion"	Total	% of grocery purchases certified organic <25%	25-49%	50-74%	75-100%	Don't know
Algae, GMO	9.3%	23.0%	16.2%	7.2%	5.4%	20.8%
Fish, Farmed	6.8%	10.1%	12.7%	4.1%	5.1%	20.8%
Glucose syrup solids	4.4%	3.4%	8.9%	3.1%	3.1%	16.7%
Hexane	6.6%	15.7%	10.4%	4.8%	4.4%	20.8%
Mannitol	15.9%	26.7%	23.1%	13.4%	12.0%	37.5%
Modified starch	5.4%	12.2%	10.7%	2.9%	3.3%	20.8%
Sodium polyphosphate	22.9%	42.2%	31.9%	19.3%	17.0%	62.5%
Sunflower oil, non-organic	13.1%	27.0%	22.4%	11.1%	7.4%	43.5%
Synthetic stabilizers	10.9%	22.2%	19.0%	8.1%	6.6%	37.5%

Respondent Characteristics

- More than three-fourths (77.2%) of survey participants are the primary food shoppers for their household. A majority (85.9%) of shoppers are female and nine out of ten (92.7%) are PCC members.

- Age distribution is almost evenly spread among the 35-44, 45-54 and 54-64 age groups, (22.0%, 22.3% and 25.6%, respectively). The median ages of the more organic shoppers (50% and more), however, are somewhat less than those of less organic shoppers (less than 50%). Shoppers who claim not to know what percentage of their food purchases are certified organic comprise the youngest group, with a median age of 43.3 years old.

Q: About what portion of your grocery purchases is certified organic?
Q: Are you the primary food shopper in your household?
Q: Are you a member of PCC Natural Markets?
Q: What is you gender?
Q: How old are you?

	Total	% of grocery purchases certified organic <25%	25-49%	50-74%	75-100%	Don't know
Primary food shopper	77.2%	77.4%	70.4%	77.7%	81.2%	37.5%
Member of PCC	92.7%	87.9%	89.4%	92.7%	94.7%	95.8%
Female	85.9%	80.6%	85.0%	89.0%	85.5%	70.8%
Age 24 or less	1.5%	1.1%	1.1%	1.2%	1.6%	8.3%
Age 25 – 44	13.8%	9.7%	11.2%	15.7%	13.8%	20.8%
Age 35 – 44	22.0%	10.8%	23.6%	24.2%	21.4%	25.0%
Age 45 – 54	22.3%	20.4%	17.6%	23.9%	24.1%	8.3%
Age 55 – 64	25.6%	35.5%	25.5%	24.6%	25.4%	8.3%
Age 65+	14.9%	22.6%	21.0%	10.3%	13.7%	29.2%
Median age	50.7 yrs.	57.3 yrs.	53.0 yrs.	48.7 yrs.	50.5 yrs.	43.3 yrs.