

Appendix V.

**Bioavailability of HiDHA® tuna oil (2)**

Childhood Asthma Prevention Study, Children's Hospital at  
Westmead, NSW

12 JUL 2001



# Childhood Asthma Prevention Study

Northcott Children's Hospital  
Highett Rd, Northcott  
Sydney NSW 2116

Institute of Respiratory Medicine  
The University of Sydney  
NSW 2006

Liverpool Hospital  
Embrey St  
Liverpool NSW 2170

Westmead Hospital  
Darcy Road  
Westmead NSW 2145

Clover Corporation Limited  
PO Box 192 Caringbah NSW 2229  
Research & Development  
Attn: Mr Ortwin Bode  
June 20<sup>th</sup>, 2001

Childhood Asthma Prevention Study  
Childrens Hospital at Westmead  
Locked Bag 4001,  
Westmead NSW 2145 Australia  
phone: (02) 9845 1323

Dear Mr Bode

**RE: The use of tuna fish oil capsules in the Childhood Asthma Prevention Study.**

The Childhood Asthma Prevention Study (CAPS) is a primary prevention randomised control trial (RCT) that is being conducted to investigate whether we can prevent the development of asthma in young children. To date, a cohort of approximately 600 infants who are at high risk of developing asthma and who live in the western Sydney area have been enrolled in this trial. The youngest child is now 18 months old and the oldest is 3 years of age.

This study was conducted following the evidence that increases in the prevalence of asthma during the 1980's and 1990's has been significant with the result that asthma is now a common chronic illness in children. (1) The reasons for the increase must be environmental and there is evidence that the most important environmental factors that increase symptoms in children are related to diet and allergen exposure. (2) The research evidence suggests that a diet which is deficient in anti-oxidant nutrients may increase susceptibility to adverse exposures to allergens or industrial pollutants and lead to increased airway inflammation. However a healthy diet with a favourable balance of omega-3 and omega-6 fatty acids and adequate anti-oxidants together with house dust mite avoidance may protect against the development of asthma or symptoms of wheeze in children who are prone to this illness. (3)

The CAPS study has a factorial design in that all combinations of an active and placebo diet intervention and active and non-active house dust mite allergen avoidance interventions are being tested.(3)

A principal component of the dietary intervention involves the use of tuna fish oil soft gel capsules supplied by Clover Corporation. The capsules have been used by approximately half of the 600 infants who have been enrolled in the CAPS study.

Clover supplies CAPS with 600 capsules per day or, over five years with 1 056 000 individual capsules. To date Clover regularly test our capsules when they are near their use-by dates to ensure that they have not oxidised and are still safe for consumption.

The dose of tuna fish oil provided in the active capsules constitutes 33mg (6.7%) eicosapentaenoic acid (EPA) and 129mg (25%) docosahexaenoic Acid (DHA), 240mg total polyunsaturated fatty acids (PUFA), 7mg (1.4%) linoleic Acid and 2500ppm vitamin E. Thus the ratio DHA to EPA in the active capsules is about 4:1 . (3)

Because vitamin A, D and E in the fish oil are reduced in the refining process, a small amount of vitamin E is added to protect the oil from oxidation. Vitamin E is approved for use in edible oils and infant formula by the Australian New Zealand Food Authority and other authorities world wide. (3)

Recent studies show that the dietary supplementation of formula fed infants with DHA at 0.36% of total fatty acids maintains cellular fatty acid composition at a level equivalent to that of breastfeeding.(4)

There have been concerns about possible growth problems in infants supplemented with EPA due to interference of EPA and DHA with arachidonic acid metabolism. However, small doses of up to 500mg have been used safely in many trials of healthy term infants. (5)

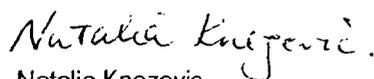
The plasma phospholipid levels of babies in the CAPS trial show that the tuna oil capsules have altered red cell plasma fatty acid membrane composition and are an effective measurable intervention for our purpose of investigating risk factors associated with the development of asthma.

The CAPS study is now in its 3<sup>rd</sup> year with parents being asked to continue to give their child one capsule per day. A minority of parents choose to give 2 capsules per day. To date, no children have had a negative effect from taking Clover manufactured tuna oil capsules.

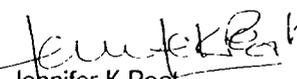
Frequent comments by parents include that the smell is pungent. The research team at CAPS have put together a fact sheet called "Are you cornered by capsules?" which suggests ways to add the capsule to foods with minimal fuss to the taste sensitive child. (see attached) This has helped many of our parents use the capsules everyday in creative ways.

Our working relationship with Clover has been a supportive, interested and satisfactory one. We look forward to ongoing research in the benefits of dietary interventions and to good industry relations with Clover Corporation in coming years.

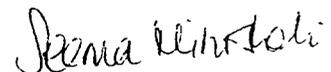
Yours sincerely



Natalia Knezevic  
Research Dietitian



Jennifer K Peat  
Principal Investigator



Seema Mhrshahi  
CAPS Coordinator

#### References

1. Peat JK, van den Berg RH, Green WF, Mellis CM, Leeder SR, Woolcock AJ. Changing prevalence of asthma in Australian children. *Br Med J* 1994; 308; 1591-1596.
2. Peat JK, Li J. Reversing the trend: reducing the prevalence of asthma. *J allergy Clin Immunol* 1999; 103; 1-10.
3. Peat J., Mirshahi S., Webb K. The Childhood Asthma Prevention Study (CAPS) Study Handbook. The Childrens Hospital at Westmead PO Box 3515 Parramatta NSW 2124.
4. Makrides M., Neumann MA., Simmer K., Gibson R. Erythrocyte fatty acids of term infants fed either breast milk, standard formula, or formula supplemented with long chain polyunsaturates. *Lipids* 1995; 30:941-948.
5. Makrides M., Neumann M, Simmer K., Pater J., Gibson R. Are long chain polyunsaturated fatty acids essential nutrients in infancy? *Lancet* 1995; 345:1463-1468.

# Are you cornered by Capsules??

As you know, the CAPS intervention for diet includes giving the daily oil capsule. Some children happily chew it like a lolly and others take it without noticing, but a few hate it! Because it is so important for the study for your children to take the capsules, we'd like to help you find ways to make capsule-giving, and feeding, in general, an easier daily experience..

Tips on how to address food refusal and CAPS capsules are listed below. Feel free to call the CAPS team if you have trouble with giving the capsule and need some assistance with more ideas.

## *Points to remember with food refusal and capsule intake;*

- By six months of age, a gradual change from milk to a variety of foods is necessary for good health and adequate growth. But children don't always accept these new foods with good humour! Often they refuse them the first few times.
- Infants and children who refuse to try a "new food" are either becoming "independent" or reacting to a 'learned caution' response. Research has shown with 2-5 year old children that as many as 8 or 10 exposures to a new food may be needed to reduce food refusal and increase acceptance.
- Just because they've never eaten a particular food before...don't be afraid of offering it again. Soon enough, they will try the food and usually, accept it.
- So, it is not always related to the study capsules that your child refuses to eat what you provide. Often the child is exerting their independence or they may be cautious about a new food.
- Try providing the capsule when the appetite is likely to be great; eg. with breakfast or dinner.

- Don't forget appetites ebb and flow like the tide each day. It is inevitable that some food will be wasted.
- Your child may dawdle and toy with food from time to time.. try to take it in your stride (as frustrating as it can be!) Try to develop a "take it or leave it" attitude towards the food being consumed. From the child's viewpoint, it takes off the pressure!
- Capsule refusal may happen when they see the bottle of capsules.  
Try to add it out of sight of the child.
- As children grow, their tastes also develop and they can become sensitive to some flavours . So, perhaps the best way to add a capsule to food is in a strongly flavoured food in small quantity. For eg; homemade pizza; where a combination of flavours disguise the taste and texture of the oil or an omelette that includes cheese and tomato. Alternatively, mix the oil in their BBQ or tomato sauce to go with the dinner or snack!

**A BIG THANK YOU FOR THE EFFORT YOU ARE PUTTING IN TO  
MAKE THE STUDY A SUCCESS.**