Attention: Ms S Janse van Rensburg, Dr C Albrecht,
CANSA.

19 March 2013.

Thank you for this "response" received at 23h58 on 7 March 2013.

I will comment in blue font below. This is once again in my personal capacity and is my honest opinion, based on my scientific background, medical training, experience and personal research.

CANSA RESPONSE TO LETTER FROM PROFESSOR M.ROY JOBSON DATED 27 February, 2013 CONCERNING OMEGA CARO-E "NUTRITIONAL SUPPLEMENT"

7th March, 2013.

Response No.1:

Question:

Why is Omega Caro E not regarded as a medicine?

Answer:

In order to be called a medicine, a product must be registered by the Medicines Control Council (MCC). The MCC looks at safety, efficacy and chemical integrity of the product. In order for a product to be registered by the MCC it must be subjected to stringent tests and it is estimated that it now costs a billion dollars[1,2]to develop a new drug from scratch. It is important to realise that there are about 10 000 registered drugs in the world of which not a single one was developed in South Africa. CANSA adheres to evidenced-based medicine and accepts the important role of the MCC but has never intended Omega Caro-E to be regarded as a medicine in order to treat cancer or any other illness. Although this product is not formally registered it is regarded as a nutritional supplement by CANSA which may lower the risk of cancer.

References:

1. "***The $800 million Pill – the truth behind the cost of new drugs***", Merrill Goozner, University of California Press, Berkeley, Los Angeles, London, 2004, ISBN 0-520-23945-8.

2. ***"Drug development cost estimates hard to swallow",*** CMAJ (News), 2009, 180(3), 279-280

Jobson comment: The question: 'Why is Omega Caro E not regarded as a medicine?' did not appear in my letter of 27 February 2013. This is a red herring. Omega Caro E can also not be compared to a new chemical entity (NCE) and neither can the development costs be compared to those of a NCE. It must be noted that the Collier article referred to raises many questions and concerns about these estimated costs.

The statement that "[i]n order to be called a medicine, a product must be registered by the Medicines Control Council (MCC)" (my emphasis) is false. A medicine is a medicine because it is used or purported to be suitable for use, or manufactured or sold for use, in particular situations (including prevention – not just "treatment" of conditions). [Medicines and Related Substances Act, 1965.] This is clarified by Judge Zondi in the TAC vs Matthias Rath judgment. Quotations from this judgment were provided to Dr Albrecht in my email of 19 February, 2013, and a copy of the whole judgment was attached to the email. A registered medicine, by definition, is one for which the manufacturer (or other applicant) is in possession of a certificate of registration.

Response No.2

Question:

If Omega Caro-E is not a medicine, what is it?

Answer:

CANSA defines Omega Caro-E as a "Food Supplement". This is product is constituted from food and can increase the tissue concentrations of certain important molecules that could reduce the risk of cancer. The food referred to here is a mixture of fish oil and a palm oil concentrate. A plate of Fish and Chips could contain the molecules found in Omega Caro-E. In oily fish such as Snoek there are omega-3 fatty acids such as DHA and EPA which have been found to correlate inversely with a decrease in the risk of certain cancers. Likewise the palm oil in which the fish and chips are fried could contain the carotenes, vitamin E (alpha tocopherol) and tocotrienols which are concentrated in Omega Caro-E and have also been found to correlate inversely with the risk reduction of certain cancers as reported in Pubmed (As discussed elsewhere in this document). The carotenes can also be obtained from fresh vegetables and fruit. However recent studies have shown that most people do not eat enough fish or plant material every day[1,2]. CANSA believes there is a vast amount of

research linking cancer risk to diet and that Omega Caro-E can play an important role supplementing important molecules to the existing diet[3]. [highlighting in original, underlining added]

References:

1. "***Fruit and vegetable intake and associated factors in older adults in South Africa***", Peltzer K, Phaswana-Mafuya N., Glob Health Action. 2012 Nov 29;5:1-8.

2. "***The food and meal pattern in the urban African population of the Cape Peninsula, South Africa: the BRISK Study",***Bourne LT, Langenhoven ML, Steyn K, Jooste PL, Nesamvuni AE, Laubscher JA, Cent Afr J Med. 1994 Jun;40(6):140-8.

3. "***Plants, Diet, and Health***", Martin C, Zhang Y, Tonelli C, Petroni K., Annu Rev Plant Biol. 2013 Feb 28. [Epub ahead of print]

Jobson comment: It is stated that: "This is (sic) product [Omega Caro-E] . . . *can increase the tissue concentrations* of certain important molecules that could reduce the risk of cancer." (my emphasis) However – there is no evidence yet that Omega Caro-E can indeed increase the tissue concentrations of any molecules that could reduce the risk of cancer. Until this has in fact been demonstrated, all claims of benefit are unproven.

[The comparison to a plate of fish and chips is surely a logical fallacy – would CANSA give its Smart Choice Seal of Recognition to fish and chips because they could reduce the risk of cancer?]

Response No.3

Question:

What is CANSA,s stand on the registration of Omega Caro-E?

Answer

CANSA is very much in favour of evidenced based products that require certain standards in order to be registered. We believe the 155 000 products which are not formally registered and are in the market place in South Africa should be grouped according to corresponding characteristics, i.e. there should be categories that include Food Supplements; African Traditional Medicines; Vitamins; Herbal preparations; Naturapathic products; Homeopathic products and so on. In order to be registered a dossier would need to be prepared for the product. This would contain reference chromatographic data showing a chemical "Fingerprint" of the product; a list of important ingredients and concentrations; proof of microbiological safety; all relevant Pubmed articles concerning mode of action; safety; and efficacy of *the product* as well as manufacturing details and some other criteria. A dossier with all of this information exists for Omega Caro-E but unfortunately there is no agency interested in receiving the document. A product called *Phyo Nova Sutherlandia* was developed as an African Traditional Medicine in 2001 and an extensive dossier and R2000 inspection fee was submitted to the MCC for consideration. As yet, 12 years later, the product has not received any registration - but it has been on the market for years. [emphases and highlighting added]

Jobson comment: Has CANSA made a formal submission to the MCC about its belief about how the "tsunami" of unregistered products on the market should be "grouped"? Did CANSA make a submission to the MCC concerning the Draft 2011 Regulations to the Medicines Act dealing with exactly these issues?

I can find no published articles for Omega Caro-E as a complete *product*. I would be very interested in seeing what evidence has been incorporated into the Omega Caro-E dossier for Omega Caro-E (i.e. the "product as a whole") in terms of its claimed "efficacy" – e.g. reduction in the risk of cancer. From all the information I have been provided by CANSA, it would appear that no evidence specific to the complete product Omega Caro-E exists.

[The Sutherlandia issue is a total red herring and of no relevance here. Submission of a product in 2001 as an African Traditional Medicine when there was not even a statutory definition of African Traditional Medicine seems quite bizarre if not devious. In the absence of any such definition or classification – if the product "purported to be suitable for use" in any condition – it would have to be considered by the MCC in exactly the same way as any other medicine. The fact that the product is being sold is a reflection on the unfortunate dysfunctional status of the MCC and its secretariat as well as the Department of Health's Inspectorate and Law Enforcement. It also sadly reflects on unscrupulous individuals and organisations whose primary interest appears to be to extract disposable income from possibly vulnerable persons.]

Response No.4

Question:

If Omega Caro-E is a Food Supplement -is it registered with the MCC?

Answer:

No. Omega Caro-E, like any other food supplement on the market, is not registered with any formal institution in South Africa because there is no legislation covering products such as food supplements that are not licenced. In other words there is only one category of medicine legislation in South Africa and that is formal registration through the Medicines Control Council (MCC). (emphasis added)

Jobson comment: This is false. The Bill of Rights in the Constitution ensures that everyone has the right to bodily and psychological integrity. Being convinced that a particular product can reduce the risk of cancer when there is no evidence that that particular product can in fact do so, potentially contravenes this. Furthermore Sections 24 and 41 of the Consumer Protection Act provide the necessary legislation should one be of the view that neither the Medicines Act (Medicines and Related Substances Act, 1965) nor the Foodstuffs Act (Foodstuffs, Cosmetics and Disinfects Act, 1972) apply. [Note however, in this context, CANSA's response 28 below and my comment.] In essence, no-one is allowed to mislead consumers. Misrepresentation is also dealt with under other aspects of the law. The question is: Does the claim that Omega Caro-E can reduce the risk of cancer, mislead consumers?

Health claims for "food supplements" may well be incorporated into phase 2 of the Foodstuffs Labelling and advertising Regulations.

It should be noted that Responses 1 to 4 above do not address issues as I raised them in my letter of 27 February 2013.

Response No.5

(See 2nd last comment on page 1 of Jobson's letter).

Question

Scientists have found that different individuals absorb different amounts of carotenoids. How does this affect Omega Caro-E?

Answer

There is no information available on the uptake of carotenes into human tissue and blood from Omega Caro-E because there are no local commercial analytical companies that can do these determinations. CANSA found out that in order to have the uptake of carotenes measured in 30 individuals over 3 months would cost R500 000 at a company registered by the MCC to conduct clinical trials. Nevertheless, a sophisticated pharmacokinetic clinical study is being planned by CPUT and CANSA to measure uptake of individual carotenes, omega-3 fatty acids and the vitamin E family including the four tocotrienols. When this has been done, it will become clear to what extent there indeed is interindividual carotene uptake and to what extent this is correlated with existing carotene blood levels, i.e. those who have high blood values may absorb less than those with low blood levels. (CANSA has committed R100 000 to this study because CANSA wishes to empower products selected to carry the Smart Choice Seal with State of the Art research.) [My emphases and highlighting]

Jobson comment: This acknowledgment of no information about the uptake of individual carotenes, omega-3 fatty acids and the Vitamin E family from Omega Caro-E being available, is accepted. I look forward to publication of the results.

Response No.6

(See 2nd last paragraph on page 1 of Jobson's letter).

Question

Is Omega Caro-E a supplement?

Answer

Omega Caro E is a specific supplement - a food supplement.

Many food supplements available on the market consist of one or more synthetic molecules, especially vitamins. CANSA does not recognise synthetic molecules as being a Smart Choice and no synthetic products have ever received the Smart Choice emblem. The reason for not choosing man-made molecules is because of concerns of purity and chemical integrity. Furthermore more and

more studies are showing that families of natural molecules , such as the carotene range or family can help to reduce the risk of cancer, while synthetic molecules such as beta carotene were used in two clinical trials where smokers receiving the synthetics molecules developed about 20 percent more lung cancer[1]. There is a possibility that the synthetic isomer of beta carotene used in this clinical trial actually stimulated carcinogenesis.

References:

[1] ***"Alpha-Tocopherol and beta-carotene supplements and lungcancer incidence in the alpha-tocopherol, beta-carotenecancer prevention study: effects of base-line characteristics and study compliance."*** Albanes D, Heinonen OP, Taylor PR, Virtamo J, Edwards BK, Rautalahti M, Hartman AM, Palmgren J, Freedman LS, Haapakoski J, Barrett MJ, Pietinen P, Malila N, Tala E, Liippo K, Salomaa ER, Tangrea JA, Teppo L, Askin FB, Taskinen E, Erozan Y, Greenwald P, Huttunen JK., J NatlCancer Inst. 1996 Nov 6;88(21):1560-70.

Jobson comment: This does not answer the statement made by the authors of the article I referred to: i.e. "population studies of health outcomes do not support the use of dietary [food] supplements." This article was referred to by the CEO of CANSA in her letter to me dated 22 February 2013, as part of the information that had been considered in awarding Omega Caro-E the Smart Choice Seal of Recognition. I find it disturbing that CANSA used an article which explicitly does not support the use of dietary supplements, to justify endorsing a food [dietary] supplement as a "smart choice."

Response No. 7

(See 2nd paragraph top of page 2 of Jobson's letter)

Question

Should pharmacokinetic studies of Omega Caro-E be mandatory

Answer

Yes. However there is no law in South Africa stating this. We believe such studies are important to do and are planning to do so at present. However if this became mandatory for all forms of non-registered so-called medicines, this would probably exclude hundreds of existing products because of the cost, expertise and technical constraints that could inhibit the measurement of the relevant molecules - which is required. It is also problematical when the nature of the pharmacologically active molecules is not known. It could require a major research project to make a pharmacokinetic study worth the expense of time and funds. Up to now this has not been a requirement for selling product and CANSA considers it unrealistic to expect pharmacokinetic studies on products which are not to be registered. (Nevertheless CANSA and CPUT are planning a sophisticated pharmacokinetic study of Omega Car-E).

Jobson comment: It is good to hear that CANSA considers that pharmacokinetic studies should be mandatory – and indeed that CANSA would prefer full pharmacokinetic studies beyond just the bioavailability component that I suggested. It would appear that CANSA does not appreciate that, unlike Omega Caro-E, thousands (not hundreds) of existing products have not even had any analyses

of quality performed. These myriad products could contain “anything” or “nothing.” Should they not, in the interests of public health, be “excluded” from being available to consumers? Following validation of the quality of a product (medicine or “supplement”), I would agree that full pharmacokinetic studies would be the next logical and mandatory step.

Response No.8

(See paragraph 6 in the middle of page 2 of Jobson’s letter).

Question

Is it not better to eat food rather than molecules in a capsule?

Answer

Yes - it is but unfortunately it is a fact that the diets of majority of South Africans is very low in the ingredients of Omega Caro-E, such as long chain omega-3 fatty acids (DHA and EPA), which are only found in oily fish, carotenes and tocotrienols. It is considered more efficient, affordable and relevant to make food supplements like Omega Caro-E available for use by the general public at the cost of three cigarettes a day. Health promotion campaigns to eat "Five-a-Day" over decades haveapparently not worked. An intervention raised consumption from 2.49 to 3.45 fruits and vegetables per day in Germany.[1]

References:

1.***Increasing fruit and vegetable intake. "Five a day" versus "just one more"***Ungar N, Sieverding M, Stadnitski T., Appetite.2013 Feb 13.pii: S0195-6663(13)00065-2. doi: 10.1016/j.appet.2013.02.007. [Epub ahead of print]

Jobson comment: Again my concern is only partially answered. As the article to which I was referred by the CANSA CEO recommended as its “main message” eating a variety of antioxidant-rich and carotenoid-rich fruit and vegetables, there is a dissonance in CANSA's use of it to support “awarding” the Smart Choice Seal of Recognition to Omega Caro-E. There is no evidence that in the majority of South African citizens it would not be better to spend R97 (up from CPUT's R65) a month on a variety of fruit and vegetables, than on Omega Caro-E or 3 cigarettes a day. (The latter comparison is surely a most bizarre one for a Cancer-support organisation!) Furthermore a variety of fruit and vegetables will provide phytochemicals and fibre not present in Omega Caro-E.

The article referred to in the above answer is taken completely out of context – the intervention was to see if the “just one more” approach was better than the “5 a day” approach. The conclusion of the abstract states: “Results of our study support the rationale of the “5 a day” campaign, at least in the short term.”

If there is no evidence that the ingredients in Omega Caro-E are in fact adequately absorbed, there is no valid basis for stating that it is “more efficient, affordable and relevant to make food supplements like Omega Caro-E available for use by the general public.” It may in fact be more efficient, affordable and relevant for members of the general public who have R97 a month to spare, to spend it on food. At this time, we just don't know.

Response 9

(See last sentences of paragraph 6 on page 2 of Jobson's letter.)

Question:

Is it true that by definition Omega Caro-E is not a food?

Answer:

Yes that is correct. This product is not sold as a food and is not ordinarily not eaten or drunk. However this is simply because it is in a capsule for convenience and also to protect the important molecules against sunlight and oxygen. In a sense the product is food in a capsule. Absolutely nothing has been added to the natural oils from oily fish and the palm tree. There is absolutely nothing artificial or man-made about the product.

Jobson comment: Surely the gelatine capsule is "man-made"? However the intention of my statement has again been bypassed. It was the CEO who stated, with reference to Omega Caro-E that "[w]e also see it as a natural right of consumers to know what is in their food and what the health consequences of this knowledge are." My understanding was that she was referring to Omega Caro-E. [But see also contradictory Response 18; and Response 28.]

Response 10

Question:

Is the concentration of beta carotene in Omega Caro-E safe for smokers?

Answer

Yes. The daily dose of the whole carotene family in Omega Caro-E is 6 mg. The average daily intake of β-carotene is in the range 2–7 mg, as estimated from a pooled analysis of 500,000 women living in the USA, Canada and some European countries[1].It is far less than the 20 mg per day of synthetic beta carotene taken in clinical trials where smokers who took this beta carotene developed 20 present (sic) more lung cancer[2]. There is no evidence whatsoever that natural, non- synthetic , carotenes as a family or range of molecules pose any lung cancer threat for smokers. (highlighting in original)

References:

1. "***Intake of the major carotenoids and the risk of epithelial ovarian cancer in a pooled analysis of 10 cohort studies".***Koushik, A.; Hunter DJ, Spiegelman D, Anderson KE, Buring JE, Freudenheim JL, Goldbohm RA, Hankinson SE, Larsson SC, Leitzmann M, Marshall JR, McCullough ML, Miller AB, Rodriguez C, Rohan TE, Ross JA, Schatzkin A, Schouten LJ, Willett WC, Wolk A, Zhang SM, Smith-Warner SA. (2006). *Int J Cancer***119** (9): 2148–54.

2. ***"Alpha-Tocopherol and beta-carotene supplements and lungcancer incidence in the alpha-tocopherol, beta-carotenecancer prevention study: effects of base-line characteristics and study***

compliance."Albanes D, Heinonen OP, Taylor PR, Virtamo J, Edwards BK, Rautalahti M, Hartman AM, Palmgren J, Freedman LS, Haapakoski J, Barrett MJ, Pietinen P, Malila N, Tala E, Liippo K, Salomaa ER, Tangrea JA, Teppo L, Askin FB, Taskinen E, Erozan Y, Greenwald P, Huttunen JK., J NatlCancer Inst. 1996 Nov 6;88(21):1560-70.

Jobson comment: At the time of writing my letter of 27 February 2013 the concentrations of the individual ingredients had not been generally made public. However this response (in the form of a question I did not ask) again sidesteps my real concern. My real concern is related to the fact that, according to the CEO, CANSA had ostensibly supported the awarding of its Smart Choice Seal of Recognition to Omega Caro-E in part based on this article which explicitly stated that there was "very little scientific support for the use of dietary [food] supplements of carotenoids to improve health outcomes." Again I am disturbed by the extent of the apparent cognitive dissonance.

I would very much like to see the evidence as to what the perceived differences between the effects of "natural" and "synthetic" carotenes are. Otherwise it would appear that CANSA is merely adopting an uncritical unproven general mythology about "natural" vs "synthetic" substances. Can one really still refer to a product which contains an ingredient that has undergone "molecular distillation" (Response 18) as "natural"?

Response 11:

(See 2nd paragraph page 4 of Jobson's letter)

Question:

Should one be wary of epidemiological results linking a nutrient such as the carotene family with a reduction in risk for breast cancer?

Answer:

Yes. One should always be wary but when over one million participants are involved and the work was done in the Department of Nutrition of Harvard School of Public Health and the claim is not inordinate, i.e. only about 13 percent reduction in breast cancer (non-HER positive)[1] the indications are that carotenes could in some way help to reduce the risk of breast cancer. A13percent reduction in risk could translate into 100 000 less women getter breast cancer per year.

Reference:
1. ***Carotenoid intakes and risk of breast cancer defined by estrogen receptor and progesterone receptor status: a pooled analysis of 18 prospective cohort studies***, Zang X et al., Am J ClinNutr, 2012, 95, 713-725

Jobson comment: The authors of this study themselves state that "it is unclear whether the observed association is real or due to other constituents in the same food sources." Futhermore, the "usual dietary intake of daily consumption of each of the major carotenoids (α-carotene, β-carotene, β-cryptoxanthin, lutein/zeaxanthin, and lycopene; food sources only)" in the studies included in the analysis, was determined by self-administered Food Frequency Questionnaires (FFQs). The authors themselves point to this as a limitation of the study. I would call it a major limitation. Their statement is more subdued: "Measurement error occurred as a result of assessing

intake of the specific carotenoids with the use of FFQs. Most [of the 18] studies did not collect information on cooking methods for the specific fruit and vegetables consumed, and how fruit and vegetables are prepared and consumed may influence the bioavailability of carotenoids." They also concede that "[t]he use of a single questionnaire will . . . also contribute to error in the estimation of longer term intake, which is likely to be important in the etiology of breast cancer."

The authors state that "the observed associations with dietary carotenoids may have been due to their correlation with other bioactive constituents of fruit or vegetables" and "the associations with specific carotenoids should be interpreted with caution because they may still be due to other unmeasured or unadjusted constituents of fruit and vegetables." In this regard it is worth noting that the studies analysed included b-cryptoxanthin and lutein/zeaxanthin, and it is not clear whether Omega Caro-E contains these latter substances.

A major confounding factor in the relevance to South Africans of this analysis, is that the "study populations are mainly of European origin, which limited our ability to examine the potential effect of carotenoid intakes on breast cancer risk in other ethnic groups, such as African American and Asian populations." Does CANSA keep the demographics of South African citizens in mind when using scientific references in justifying the awarding of its Smart Choice Seal of Recognition? Is there a particular protocol that is followed that incorporates these issues?

Response 12:

(See paragraph 5 on page 4 of Jobson's letter)

Question

Assuming that the carotene family could reduce the risk of cancer, is it possible that interactions between the carotenes and other molecules may be responsible for reducing the risk?

Answer

Yes it is quite possible and would argue against using a single synthetic beta carotene in a supplement. Omega Caro E contains three families of molecules namely, long chain omega-3 fatty acids; carotenes and tocotrienols. Advanced research is required to find out if any of these molecules interact with other molecules to inhibit carcinogenesis and reduce the risk of cancer.

It is not reasonable for such research to be a pre-requisite of CANSA awarding Omega Caro-E the "Smart Choice Supplement" status, especially if such an effort were not rewarded by some form of official recognition and registration.

Jobson comment: The concern about interactions was raised by the researchers and authors of the study quoted. My own as yet unanswered question was how CANSA could use a study about breast cancer only, to help support the claim that Omega Caro-E could reduce the risk of [any] cancer – and then awarding the Smart Choice Seal of Recognition to Omega Caro-E by using this study as part of its rationale for doing so.

How research efforts are “rewarded” raises a multitude of moral and ethical issues. There is an abundance of research done to improve people's lives with no expectation of reward. It would be interesting to understand what ethical standpoint CANSA is adopting or adhering to in awarding its Smart Choice Seal of Recognition to Omega Caro-E while at the same time being the major distributor of the product.

Response 13:

(See last comment on page 4 of Robson’s letter).

Question

Is there any evidence for the effects of each of the carotenes to reduce the risk of cancer?

Answer

Yes there is evidence in the reference cited in the previous answer (Response 10). Here it was found that alpha carotene reduced the risk of breast cancer by 13 percent; 16 percent bybeta carotene and 13 percent by lutein/zeaxanthin. Lycopene is also a carotene and has been linked to cancer risk reduction extensively. There are 408 Pubmed abstracts on "Lycopene and cancer prevention”. (emphasis added)

Jobson comment: I assume that this refers to Response 11 as the references for Response 10 had to do with i) epithelial ovarian cancer and ii) lung cancer. Response 11 refers to breast cancer. Please see my comment on Response 11. As for lycopene, the 408 references would need to be “deconstructed” to determine how many of these were studies in human beings; and of those done in human beings whether the concentration of lycopene is similar (if not equivalent) to that in Omega Caro-E. My suspicion is that the majority of these studies would been in laboratory cancer cell-lines and not have involved living humans and measured the development of cancer clinically.

As no evidence for adequate / sufficient absorption of any of the carotenes in Omega Caro-E is presently available, the limitation raised by the authors in yet another article stated by the CANSA CEO to have been used to support the awarding of the Smart Choice Seal of Recognition, is of concern.

Response No.14

(See3rd paragraph on page 5 of Jobson’s letter)

Question

Could specific carotenoid supplements be harmful to smokers?

Answer

There is no evidence at all that natural carotenes as found in food pose any health threat to anyone.

If this were the case, there would be warning signs on packets of carrots. However, it is a fact that clinical trials were conducted in the 90's where participants were elderly male smokers and the aim of the study was to find out if synthetic beta carotene at 20 mg day could reduce the incidence of lung cancers in the smokers. Paradoxically it was found that the synthetic beta carotene caused about 20 percent more lung cancers in the smokers compared to controls. A logical explanation of this outcome is that while relatively high concentrations of synthetic beta carotene as a single molecular structure does increase the risk of cancer. On the other hand CANSA believes that it is quite reasonable to postulate that natural, non-synthetic beta carotenes as a family or range of molecules, at normal food concentrations, can reduce the risk of cancer. The molecular explanation of this paradox remains to be elucidated. (emphases and highlighting added)

Jobson comment: This was not the question I asked – but is a statement contained in an article (for which the reference was sent to me by the CANSA CEO) which was said to have been used to support the awarding of the Smart Choice Seal of Recognition to Omega Caro-E. My question was how such a reference which advised against carotenoid supplements and raised the possibility of harm to smokers could have been used for the purpose of awarding the Smart Choice Seal of Recognition.

I find the comment above about warning signs on packets of carrots inane and fatuous. [Overconsumption of carrots (and other sources of carotenoids) can however cause a recognised condition of carotenaemia leading to carotenosis.]

Again the distinction between "synthetic" and "natural" made by CANSA is a spurious one. The misinterpretation in the response above is to state that the *aim* of the study referred to related to "synthetic" beta carotene. The statement is false. To quote from the "methods" of the Alpha-Tocopherol, Beta Carotene Cancer Prevention (ATBC) Study Group's 1994 report in the New England Journal of Medicine:[1][footnote] "We performed a randomized, double-blind, placebo-controlled primary-prevention trial to determine whether daily supplementation with alpha-tocopherol, beta carotene, or both would reduce the incidence of lung cancer and other cancers." I do not see the word "synthetic" in this statement!

Response 15:

(See 8th paragraph on page 5 of Robson's letter)

Question

What is the best evidence that fish oil could help to reduce the risk of cancer?

Answer

There is growing evidence that the short- and long- chain omega-3 fatty acids which are present in canola and fish oil respectively can help protect cells against cancer. This is especially the case if the ratio between omega-6 and omega-3 fatty acids is not much greater than two to one. In many Western countries with high cancer incidences, the omega-6 to omega-3 ratio is higher than ten to one. It has been recommended in a recent review article that a moderate intake of plant and marine omega-3 could reduce the risk of especially breast cancer[1][NB: the reference below, not the

1 http://www.nejm.org/doi/full/10.1056/NEJM199404143301501

footnote.] There are at least ten studies in Pubmed that show a correlation between a low omega-6 to omega-3 ratio and a lower incidence of breast cancer.

References:

1. ***New insights into the health effects of dietary saturated and omega-6 and omega-3 polyunsaturated fatty acids***, De Lorgeril, M and Patricia Salen, BMC Medicine, 2012, 10:50)

Jobson comment: Again this is not quite the question I asked. What I asked was how CANSA could use a highly flawed study (in my view – as previously explained in my letter of 27 February 2013) in Korean women with breast cancer to support the awarding of the Smart Choice Seal of Recognition to Omega Caro-E for use in South Africans.

The concluding statement of the abstract from the article referred to above is: "A moderate intake of plant and marine omega-3 in the context of the traditional Mediterranean diet (low in saturated and omega-6 fatty acids but high in plant monounsaturated fat) appears to be the best approach to reduce the risk of both cardiovascular diseases and cancers, in particular breast cancer." (highlighting and emphasis added) This is not the same statement as was made in the answer above.

The authors did not study omega fatty acids as would be provided by supplements. In fact they stated: "To simplify the dietary advice aimed at protecting health – and help consumers to understand it – the best approach is probably the traditional Mediterranean diet model. No dietary pattern has been so extensively studied, and no other has been shown to provide so many benefits without any adverse effects." (highlighting and emphasis added) Quite clearly this reference can also not be used to justify the awarding of the Smart Choice Seal of Recognition to Omega Caro-E. Of course it remains unknown whether or not the omega fatty acids contained in the particular formulation of Omega Caro-E, are adequately absorbed.

Response 16:

Question

Is Omega Caro-E a food - subject to rules and regulations governing food and foodstuffs in South Africa?

Answer

No. Omega Caro-E is not a food but rather a "Food Supplement"

Jobson comment: This answer would seem to contradict Response 18; and Response 28 in which CANSA uses the EFSA definition of food supplement. Please see my comments to these.

It is interesting however that most of the arguments defending the use of Omega Caro-E are based on foods "per se" and not food supplements. It appears that CANSA, in its justification for Omega Caro-E by using studies of food components, regards the product as "equivalent to" food. The question remains – how is a food legally differentiated from a food supplement in South Africa? And when is it legitimate for a food supplement to make health claims such as "can assist to reduce the risk of cancer"?

Response 17:

(See last sentence on page 7 of Jobson's letter)

Question

It is stated by Jobson that "CANSA is not doing what is right"

What is CANSA doing that is wrong?

Answer

CANSA has endorsed a food supplement for the first time. This is done because CANSA agrees with world literature that states that the risk of at least 30 present (sic) of cancers is due to the diet, This is about 4 million cancer cases world-wide per annum. The hypothesis is that if that which is wrong in the diet could be corrected this could reduce the risk of cancer substantially. Two of the main dietary problems related to cancer are the high omega-6 to omega-3 ratio and the lack of a variety of vegetables. In order to address the Omega problem CANSA has endorsed canola oil and canola margarine. Long chain omega-3 fatty acids are a problem because they are only in fatty fish oil. CANSA would like to endorse such fish as a 'Smart Choice' food but unfortunately this fish is most often sold in cans which contain BPA. Hake, the most popular fish in South Africa, unfortunately does not contain sufficient DHA and EPA long chain fatty acids. It is also extremely unfortunate that human enzymes cannot produce sufficient long chain omega-3 fatty acids from short chain ALA. There is evidence that elongation of omega-3 fatty acids in human tissue is blocked by an excess of omega-6 which is ubiquitous in sun flower seed oil –the cheapest plant oil in South Africa. Taking these constraints into consideration as well as the quality, academic foundation, composition, source, manufacturing and cost of Omega Caro-E it was decided after lengthy consultations and investigations of 64 existing fish oil products, to endorse Omega Caro-E as a "Smart Choice Supplement" in order to help the public reduce the risk of cancer. CANSA also believes that the public should be able to make informed choices and that standards should be set for food supplements and that CANSA wishes to play a role doing so. CANSA makes no apology for doing this and considers this to be the right thing. (highlighting and emphases added)

Jobson comment: In my view, what CANSA is doing wrong, is to imply that by taking Omega Caro-E a person's blood levels of the ingredients will be increased. This has not yet been demonstrated. In the absence of demonstrated absorption to blood levels which have shown to be advantageous, it is also wrong (indeed "*more* wrong") to state that endorsing Omega Caro-E with the Smart Choice Seal of Recognition, CANSA will help the public "reduce the risk of cancer." This is surely, at this time, a misrepresentation, and a premature and misleading statement.

In my view, what is also wrong is that citizens may end up being "experimented on" without having full information about the product. This is not "informed consent" and would surely be in contravention of the country's Constitution. (Section 12(2)(c): Everyone has the right to bodily and psychological integrity which includes the right – not to be subjected to medical or scientific experiments without their informed consent.)

It seems, in the context of the awarding of the Smart Choice Seal of Recognition to Omega Caro-E, antithetical for CANSA to consider playing a role in helping the public to make informed choices or help set standards for food supplements – because CANSA is distributing and selling a product for

which no determination has been made as to the extent to which the ingredients are absorbed and / or increase blood levels. It is of concern that CANSA considers it to be "the right thing" to promote a product where such basic information has not yet been confirmed.

I would want to know if CANSA actually submitted any responses to the various draft regulations published by the Department of Health for, amongst others, the foodstuffs regulations: labelling and advertising. I would expect no less from an advocacy organisation.

Response 18

Question

What is known about the pharmacokinetics of the palm oil used?

Answer

No such studies were done simply because this type of study is usually not done on food components. Palm oil is the number one cooking oil in Malaysia. The component that is under discussion is not palm oil as such, but red palm oil containing a spectrum of phytonutrients. During the conventional refining of crude palm oil, all the carotenes are lost and probably around twenty percent of the vitamin E. Red palm oil is obtained by a patented process involving molecular distillation and the concentrate we use in our Omega Caro –E is also obtained by molecular distillation of red palm oil. The concentrate is used in the food industry as an anti-oxidant and coloring agent. (highlighting and emphases added)

Jobson comment: The author of this response would therefore seem to consider the red palm oil component of Omega Caro-E to be a food component (i.e. foodstuff), in contradiction to Responses 9 and 27; and in agreement with my interpretation of Response 28.

Response 19

(See paragraph 6 on page 1 of Jobson's letter)

Question

Comment on Inter -individual pharmacokinetics of carotenoids in Omega Caro-E

Answer

Individuals do not react in the same manner- whether food, fats or medicines. To find differences between individuals is not uncommon. Inter- individual differences are usually reflected by the standard deviations calculated for the various end-point measurements. To establish the effect of

treatment, therefore requires a comparison with a placebo group and a comparison of changes between the groups. This is standard practice in all our studies. (emphases added)

Jobson comment: This question was raised and answered slightly differently in Response 5. However this author's response about the "effect of *treatment*" categorises Omega Caro-E as a medicine considering that the answer is to a question about inter-individual pharmacokinetics of carotenoids in Omega Caro-E. It is a pity that the author does not clearly state (in contrast to Response 5) that nothing is known about inter-individual pharmacokinetics of carotenoids in the formulation Omega Caro-E.

Response 20

(See last paragraph on page 2 of Jobson's letter)

Question.

Is there very little support for carotenoid supplements?

Answer

This is a general statement and is evident of Prof Jobson's total lack of knowledge with regards to studies that have been done over many years. We would like to refer him to the various studies carried out by ourselves and others on the effect of red palm oil supplementation on serum retinol concentration of learners.(Nutrition Division, MRC and Functional Foods Unit, CPUT) This is especially true in populations where subclinical vitamin A deficiency exists.

References:

Me van Stuijvenberg and AJS Benade. Food and Nutrition Bulletin 21: 212-214, 2000.

Canfield LM, Kaminsky RG . Eur J Nutr 40: 30-38, 2001.

Jobson comment: Thank you for the ad hominem attack. The statement objected to was in fact made by "Donaldson" in an article referred to by the CEO of CANSA as having been used to support the awarding of the CANSA Smart Choice Seal of Recognition to Omega Caro-E. It would appear that Donaldson and CANSA are therefore the ones who have a total lack of knowledge concerning the studies done at MRC and the FFU of CPUT.

However the problem remains that, at this time, the extent of the absorption of the carotenoids from Omega Caro-E is unknown (and no evidence for a reduction in the risk of cancer as a result of taking Omega Caro-E can therefore be provided or even extrapolated).

The other comment made by Donaldson, which remains unanswered, is that "responsible scientists and food producers need to emphasize the use of foods and whole food products to improve plasma

carotenoid concentrations" and not supplements. This again raises an apparent cognitive dissonance within CANSA in ignoring recommendations stated in the very articles it purported to have used to support the awarding of the CANSA Smart Choice Seal of Recognition to Omega Caro-E.

Response 21

(See paragraph 2 on page 3 of Jobson's letter)

Question

Could Omega Caro-E disturb carotenoid concentrations in vivo?

Answer

Omega Caro-E contains 3mg carotenes per capsule of which alpha- carotene and beta- carotene make up 35% and 56% respectively and lycopene 1-2%. Intake of red palm oil does increase carotene levels as indicated by several studies. Whether the ratios of the different carotenes will be altered remains to be established. As Omega Caro-E is a supplement and has to be taken during a meal, it can be assumed that the biggest contribution will come from alpha and beta carotene and lycopene. (emphasis added)

Jobson comment: The question asked does not reflect any concern of mine in paragraph 2 on page 3 of my letter of 27 February 2013.

Omega Caro-E is a new formulation in a gelatine capsule. The carotene blood levels may not be increased as anticipated. This still needs to be determined. My main concern is that according to the CEO of CANSA, the article being referred to was used to support the awarding of the Smart Choice Seal of Recognition to Omega Caro-E – despite its recommendations against the use of carotenoids in dietary supplements. This concern remains unanswered.

Response 22

(See last sentence of paragraph 2 on page 6 of Jobson's letter) (underlining in original)

Question

Is there evidence for absorption to be of any benefit

Answer

Our studies in KZN, as well as the studies of Canfield, Manorama(Manorama et al. Asia Pacific Journal of Clinical Nutrition 6: 56-59, 1997)showed that absorption has definite benefits in terms of subclinical vitamin A deficiency. Researchers from the Institute of Nutrition and Food Science,

University of Dhaka reported a decrease in the prevalence of acute respiratory infection from 38% to 17% in school children aged 13-15 years (Shah et al. Chest and Heart Journal27: 70-76, 2003). Our studies in KZN showed that children supplemented with a biscuit fortified with beta-carotene missed fewer school days than children in the control group because of respiratory- and diarrhea related illness (van Stuijvenberg et al. Am J ClinNutr 69: 497-503,1999).

Jobson comment: Yet again this was not the question I asked. I asked if there was any evidence that the "high quality fish oil from Iceland and a palm oil fraction from Malaysia in a gelatine capsule" [i.e. Omega Caro-E] is sufficiently absorbed to be of *any* benefit? As the "answer" above, does not address the question I asked, I must reject this. It has also been made clear in Response 5 that the studies on absorption of the components of Omega Caro-E have not yet been done.

Response 23

Question

Is it correct to say that animal studies must be disregarded

Answer

Animal studies can be helpful developing models for evidence based nutrition. In our case we used the sub-human primate model to study the metabolism of Omega-3 fatty acids. This model clearly showed that Omega-3 long chain fatty acids are absorbed and metabolized in this model. It also showed that the metabolism of Omega-3 fatty acids is slower in animals consuming a western atherogenic diet (van Rooyen et al. Prostaglandins, Leucotrienes and Essential Fatty Acids 59:27-38,1998).(emphasis added)

We subsequently established that the metabolism of Omega-3 fatty acids in humans are similar to that observed in sub-human primates and that Omega-3 fatty acid absorption in both species are comparable. (Abstract ISSFAL Congress Vancouver, 2012) Animal studies can therefore be of value determining research direction.

Jobson comment: Animal studies are certainly acceptable as models (see my comment to Response 26 for examples) and may help delineate metabolic pathways and other responses and reactions. But when it comes to supporting the use of substances in public, making claims for humans, and promoting a product to the general public – animal studies cannot be used as evidence. I note that none of the primate studies referred to above used Omega Caro-E.

Response 24

(See paragraph 6 on page 6 of Jobson's letter)

Question

What is the composition of Omega Caro-E?

Answer

Refer to "Frequently asked questions of Omega caro-E" on CANSA website (www.cansa.org.za)

Jobson comment: Thank you for this information. It had not been made available at the time of writing my letter of 27 February 2013.

Response 25

(See paragraph 6 on page 6 of Jobson's letter)

Question

Is there any evidence concerning the uptake of Vitamin E?

Answer

Evidence of uptake of Vitamin E is provided by a bio-availability study conducted by Yap et al J Pharm Pharmacol 53: 67-71, 2001.

Jobson comment: Again this is not quite the question I asked. My question was about saturation of carrier transport systems for tocotrienols.

In a more recent review (than the Yap article) by Sylvester et al in a Supplement to the Journal of the American College of Nutrition, 2010, Vol. 29, No. 3, 324S–333S (and the basis of my concern in paragraphs 7 and 8 on page 6 of my letter of 27 February 2013) the following statements are made:

"Bile excretion [needed for the emulsification of fat soluble vitamins] is dependent on the level and type of dietary fat consumed, and studies have shown that tocotrienol absorption is reduced in fasted versus full-fed individuals [20–22]." [NOTE: Reference 21 is Yap et al, 2001 referred to in the "answer" above.]

"Although food enhances γ-tocotrienol absorption by stimulating excretion of bile and pancreatic enzymes that enhance the formation of mixed micelles, γ-tocotrienol absorption remains limited and far from complete [21,22]." (emphasis added) [NB Yap again]

"These data also indicate that the carrier-mediating intestinal absorption becomes saturated and apparently undergoes down-regulation after exposure to increasingly higher doses of tocotrienols in the intestinal lumen [25]. [animal study] This hypothesis would explain why it is difficult to obtain elevated levels of tocotrienols in the blood and target tissue following oral administration and also why increasing the oral dose does not result in a corresponding increase in bioavailability [21,22,24]." [Another Yap reference.] (emphasis added)

"It is now clearly evident that it is very difficult to obtain and/or sustain therapeutic levels of γ-tocotrienol in the blood and target tissues by simple oral administration because absorption and transport mechanisms within the body are extremely limiting and display significant preference for alpha-tocopherol, the more common form of vitamin E. Although various tocotrienol-containing products are already commercially available, these products are simply capsules filled with a blend of various tocopherols and tocotrienol oils and sold as nutritional supplements for oral consumption. Data presented in the previous section [of the article] demonstrate that this type of formulation or delivery system displays poor solubility in the fluids of the intestine and that high oral doses of tocotrienols inhibit its own absorption from the gut. Consequently, only relatively low levels of tocotrienol will reach the blood when simply formulated as an oil-filled capsule delivery system." (emphases added)

". . . tocotrienol absorption in the small intestine is primarily dependent on a carrier-mediated transporter mechanism that not only displays saturation but also appears to undergo down-regulation when exposed to high concentrations of tocotrienol in the gut. Since high oral doses of tocotrienols inhibit its own absorption from the gut, oral consumption of high doses of tocotrienol in oil-filled capsules ultimately results in only relatively low levels of tocotrienol reaching the circulation."

These statements all support the need for bioavailability testing to assess just how much of the tocotrienol component of Omega Caro-E is absorbed and/or makes any advantageous changes to blood (or tissue) concentrations in living humans.

Response 26

Question

Is it correct to say that - No proof of any absorption-no proof of any benefit

Answer

Evidence is provided by the scientific literature of absorption of Omega-3 fatty acids, carotenes and Vitamin E.

Jobson comment: There is no evidence in any scientific literature available concerning the absorption of omega-3 fatty acids, carotenes and Vitamin E from the formulation: "Omega Caro-E." See Response 5. If there is no evidence of absorption, how can any benefit from taking the product be assumed? However it is possible that even with evidence of absorption, no benefit is proven. In the context of cardiovascular disease, there was no proof of benefit with tocotrienol

supplementation despite proof of absorption. (See Annexure 1: reference 5 on page 32 of 35 of this document.)

Response 27

Question

Is Omega Caro-E a food?

Answer

Omega Caro-E is not a food

Omega Caro-E comprises of food grade fish oil as well as a food grade carotenoid and vitamin E concentrate. The fish oil, carotenoid and vitamin E content in Omega Caro-E are similar to those found in food. No pharmaceutical amount of any of the compounds is present in Omega Caro-E. All compounds are enclosed in a soft gel gelatine capsule to ease consumption. Soft gel capsules are used to encapsulate edible oils in order to mask the taste of the oil (in this case fish oil), to prevent oxidation of the oil and to protect carotenes against direct light. Omega Caro-E is therefore not a food product as such but provides additional nutrients in a soft gel capsule form to supplement a diet low in fatty fish, fruit and vegetables. (emphases added)

Jobson comment: This is a repetition with a different answer to Response 9 and Response 18. It contradicts the definition of a food supplement used in Response 28. This response makes an assumption that the "additional nutrients" provided are adequately absorbed in order to actually "supplement" the diet. This has not yet been demonstrated (Response 5).

Response 28

Question

Is it problematic to call Omega Caro-E a nutritional supplement

Answer

In South Africa there is currently no legal definition for nutritional/dietary/food supplements, however it is not illegal either to use the term nutritional/dietary/food supplement. Because of a lack of legislation for nutritional/dietary/food supplements the definition of the European Food Safety Association (EFSA) was used as guideline.

*EFSA defines food supplments as: 'food supplements' means **foodstuffs** the purpose of which is to **supplement the normal diet** and which are **concentrated sources of nutrients** or other substances with a **nutritional** or physiological effect, **alone or in combination**, marketed in **dose form**, namely forms such as **capsules**, pastilles, tablets, pills and other similar forms, sachets of powder, ampoules of liquids, drop dispensing bottles, and other similar forms of liquids and powders designed to be taken in **measured small unit quantities**.* (highlighting added; emphases not added)

Omega Caro-E is therefore a food supplement since it provides additional nutrients in the form of essential fatty acids, carotenes and vitamin E to a diet deficient in these compounds. Hence Omega Caro-E is supplemental to the diet and not intended to replace any nutrient or whole food in the diet. [But to what extent are these additional nutrients absorbed?]

It is not always possible to consume adequate amounts of omega-3 fatty acids through the diet, because very few individuals consume fatty fish every day of the week. Nutritional supplements are especially useful in individuals who struggle to meet their nutrient needs because of inadequate dietary intakes. At risk groups for poor dietary intakes may include infants and pre-school children, pregnant women, the aged, individuals with compromised nutritional status and those with a limited variety in food selection. Recently conducted clinical trials indicated that South Africans experience limited dietary omega-3 fatty acid intakes. In three separate clinical trials conducted by the FFRU, baseline omega-3 blood values of healthy individuals between the ages of 20-55 years were about 3-5% (Oppermane*t al.,* 2012; Benade*et al.*, 2012). According to von Schacky (2011) these levels increase the risk for developing cardiovascular disease (CVD) while levels above 8% are recommended to reduce the risk for CVD. In the clinical trials conducted by the FFRU supplementation with fish oil over a period of 8 weeks increased the omega-3 blood level of participants to 13-14%. [Surely similar studies should have been done using Omega Caro-E before advertising it or placing it on the market?]

The International Society for the Study of Fatty Acids and Lipids (ISSFAL) recommends a daily dietary intake of 500 mg EPA+DHA per day. For the average consumer, meeting these dietary recommendations for omega-3 fatty acids will be difficult to achieve without adequate supplementation. In order to reach a 500 mg/day EPA+DHA intake by using supplements an intake of approximately 2 000 mg fish oil with a 180mg:120mg (EPA:DHA) content ratio would be required. To consume these amounts of EPA+DHA through diet/non-supplementation, approximately 79 g/day of tuna or 60 g/day of pilchards or 52 g/day of salmon should be consumed. Omega Caro-E provides 500 mg EPA+DHA with the daily intake of two capsules. [But to what extent is it absorbed?]

Research has indicated that South Africans consume too few fruit and vegetables on a daily basis. According to Schneider *et al.* (2007) South Africans consume about 200g fruit and vegetables per day, while 400g is recommended by the World Health Organisation. Five portions of fruit and vegetables supply about 6 mg of carotenes. Two capsules of Omega Caro-E provide 6 mg of carotenes as recommended by the American Heart Association. [But to what extent is it absorbed?]

Jobson comment: The definition provided unambiguously states that *" 'food supplements' means* ***foodstuffs*** *. . ."* This is the definition from Article 2 of Directive 2002/46/EC of the European Parliament and of the Council of the European Union of 10 June 2002. It should therefore be an acceptable definition for legal purposes in South Africa.

By using this definition which defines food supplements as foodstuffs, CANSA is itself clearly acknowledging that the product Omega Caro-E falls squarely under the legislative framework of the *Foodstuffs*, Cosmetics and Disinfectants Act, 1972 (Act 54 of 1972). The question then arises as to whether or not it is indeed legal to advertise or promote or sell Omega Caro-E with its claim that it is a "smart choice," or that it can assist in "reducing the risk of cancer."

Response 29

Question

Does Omega Caro-E contravene regulation 13(d)?

Answer

Notwithstanding the fact that no labeling legislation exist for food supplements, no such words have been used anywhere on the Omega Caro-E label or on any of the promotion material. Information

provided in the promotion material such as “may reduce the risk of…” is presented in combination with comprehensive evidence based scientific nutrition research available on Medline as well as scientific peer-reviewed publications by the inventors of the Omega Caro-E product.

Jobson comment: Regulation 13(d) of Notice R.146 of 1 March 2010 states:
13. The following information or declarations shall not be reflected on a label or advertisement of a foodstuff:
(d) the words "health" or "healthy" or other words or symbols implying that the foodstuff in and of itself or a substance of the foodstuff has health-giving properties in any manner including the name or trade name, except in the case of the fortification logo for food vehicles as determined by regulations made under the Act and regulation 51(2); (emphases added)

I would argue that the claim of “assists to reduce the risk of cancer” implies that Omega Caro-E (which in terms of the EU definition is a foodstuff) has “health giving properties.” Unfortunately as has already been ascertained from Response 5, it has not yet been determined to what extent the substances in Omega Caro-E are absorbed (or not).

Please see Annexure 2 for examples of promotional claims made for Omega Caro-E – clearly, in my view, in contravention of Regulation 13(d).

Response 30

Question

What is Regulation 13(a)(ii) of Notice R.146 of 1 March 2010 - looks like it concerns making health claims

Answer

Again, this regulation is applicable to foods and should not be extrapolated to food supplements. Nevertheless, if it was decided to enforce this legislation on food supplements, there is an abundance of evidence-based nutrition research which Cansa can utilize to motivate the endorsement of Omega Caro-E as a “Smart Choice Supplement”

References:

Opperman, M., Marais, C.D. and Benadé, A.J.S. 2012. Washout kinetics of eicosapentaenoic and docosahexaenoic acid from human plasma after supplementation with salmon oil. 10th Conference of the International Society for the Study of Fatty Acids and Lipids, Vancouver, Canada 26-30 May, 2012. *Prostaglandins, Leukotrines and Essential Fatty Acids.* (This does not appear to have used Omega Caro-E.)

Benadé, S., Opperman, M. and Marais, C.D. 2012. Disappearance of long chain omega-3 fatty acids from human red blood cells (RBC) *in vivo* after supplementation with salmon oil. 10th Conference of the International Society for the Study of Fatty Acids and Lipids, Vancouver, Canada 26-30 May, 2012. *Prostaglandins, Leukotrines and Essential Fatty Acids.* (This does not appear to have used Omega Caro-E.)

Von Schacky, C. 2011. The omega-3 index as risk factor for cardiovascular disease. *Prostaglandins and other Lipid Mediators,* 96:94-98. (There is no evidence that the omega-3 index - defined as eicosapentaenoic plus docosahexaenoic acids in erythrocytes – has been determined for Omega Caro-E).

Schneider, M., Norman, R., Steyn, N.and Bradshaw, D. 2007. South African Comparative Risk Assessment Collaborating Group.Estimating the burden of disease attributable to low fruit and vegetable intake in South Africa in 2000.*South African Medical Journal,*97(8 Pt 2):717-23. (This could help motivate for the rationale for a product such as Omega Caro-E – but cannot be used to motivate for awarding it CANSA's Smart Choice Seal of Recognition.)

Jobson comment: Regulation 13(a)(ii) of Notice R.146 of 1 March 2010 states:

13. The following information or declarations shall not be reflected on a label or advertisement of a foodstuff:

(a) words, pictorial representations, marks, logos or descriptions which create an impression that such a foodstuff is supported, endorsed, complies with or has been manufactured in accordance with recommendations by

(ii) organisations, associations, foundations and other entities (excluding religious certifying organisations or any Fauna and Flora related certifying and endorsing bodies), unless approved by the Director-General and which can provide proof of the fact that they are involved in generic health promotion which is supported by evidence-based nutrition, and that the directions of the

organisation, association or foundation do not contradict the requirements of these regulations in terms of nutrition claims and the criteria thereof; (emphasis added)

It seems clear to me (according to Response 28) that CANSA indeed regards Omega Caro-E as a "foodstuff." As no evidence for the absorption of the ingredients or their resulting blood concentrations has been provided, surely the requirements of the regulations in terms of nutrition claims is being contravened.

The references above do not apply – as annotated by myself.

In summary: Many of my direct concerns were not addressed. Questions that I had not asked were posed as if I had asked them. There was a high level of repetition of responses / "questions." The concession in response 5 that no studies of the absorption of the ingredients of Omega Caro-E had been performed was the primary question which effectively "negated" many of the other responses. My concerns that CANSA sent me references to articles which recommended against dietary / food supplements, or preferred dietary options, as evidence of the support for the awarding of the CANSA Smart Choice Seal of Recognition to Omega Caro-E, has not been addressed at all.

Yours sincerely,

M. R. JOBSON

Annexure 1 – Additional information from the literature.

1.

Cochrane Database Syst Rev. 2012 Oct 17;10:CD002141. doi: 10.1002/14651858.CD002141.pub2.

Drugs for preventing lung cancer in healthy people.

Cortés-Jofré M, Rueda JR, Corsini-Muñoz G, Fonseca-Cortés C, Caraballoso M, Bonfill Cosp X.

Source

Facultad de Medicina, Universidad Católica de la SS. Concepción, Programa Doctorado en Ciencias Médicas, Universidad de LaFrontera, Concepción, Chile. tutor.mimbe@cochrane.es

Abstract

BACKGROUND:

This is an updated version of the original review published in Issue 2, 2003. Some studies have suggested a protective effect of antioxidant nutrients on lung cancer. Observational epidemiological studies suggest an association between higher dietary levels of fruits and vegetables containing beta-carotene and a lower risk of lung cancer.

OBJECTIVES:

To determine whether vitamins, minerals and other potential agents, alone or in combination, reduce incidence and mortality from lung cancer in healthy people.

SEARCH METHODS:

For this update we have used a search strategy adapted from the design in the original review. The following electronic databases have been searched up to December 2011: MEDLINE, EMBASE and the Cochrane Central Register of Controlled Trials (CENTRAL). References included in published studies and reviews were also screened.

SELECTION CRITERIA:

Included studies were randomised controlled clinical trials comparing different vitamins, mineral supplements or supplements with placebo, administered to healthy people with the aim of preventing lung cancer.

DATA COLLECTION AND ANALYSIS:

Two authors independently selected the trials to be included in the review, assessed the methodological quality of each trial and extracted data using a standardised form. For each study, relative risk and 95% confidence limits were calculated for dichotomous outcomes and pooled results were calculated using the random-effect model.

MAIN RESULTS:

In the first version of this review four studies were included; in this review update, an additional five studies have been included. Four studies included only males and two only females; two studies included only participants considered at high risk, namely smokers or exposed to asbestos, and one

study included people deficient in many micronutrients. Six studies analysed vitamin A, three vitamin C, four vitamin E, one selenium supplements, and six studied combinations of two or more products. All the RCTs included in this review were classified as being of low risk of bias.For people not at high risk of lung cancer and compared to placebo, none of the supplements of vitamins or minerals or their combinations resulted in a statistically significant difference in lung cancer incidence or mortality, except for a single study that included 7627 women and found a higher risk of lung cancer incidence for those taking vitamin C but not for total cancer incidence, but that effect was not seen in males or when the results for males and females were pooled.For people at high risk of lung cancer, such as smokers and those exposed to asbestos and compared to placebo, beta-carotene intake showed a small but statistically significant higher risk of lung cancer incidence, lung cancer mortality and for all-causes mortality.

AUTHORS' CONCLUSIONS:

There is no evidence for recommending supplements of vitamins A, C, E, selenium, either alone or in different combinations, for the prevention of lung cancer and lung cancer mortality in healthy people. There is some evidence that the use of beta-carotene supplements could be associated with a small increase in lung cancer incidence and mortality in smokers or persons exposed to asbestos. (emphasis added)

Update of

Cochrane Database Syst Rev. 2003;(2):CD002141.

PMID: 23076895 [PubMed - indexed for MEDLINE]

2.

Am J Clin Nutr. 2012 Aug;96(2):356-73. doi: 10.3945/ajcn.112.034165. Epub 2012 Jul 3.

Dietary compared with blood concentrations of carotenoids and breast cancer risk: a systematic review and meta-analysis of prospective studies.

Aune D, Chan DS, Vieira AR, Navarro Rosenblatt DA, Vieira R, Greenwood DC, Norat T.

Source

Department of Epidemiology and Biostatistics, School of Public Health, Imperial College, London, United Kingdom. d.aune@imperial.ac.uk

Abstract

BACKGROUND:

Measurement errors in the dietary assessment of fruit and vegetable intake may attenuate associations with breast cancer risk and might explain the weak associations observed in epidemiologic studies. Carotenoid concentrations in blood are biomarkers of fruit and vegetable intake; however, no systematic assessment has compared dietary intake with blood concentrations of carotenoids and breast cancer risk.

OBJECTIVE:

We conducted a systematic review and meta-analysis of prospective studies of dietary intake and blood concentrations of carotenoids and breast cancer risk.

DESIGN:

We searched PubMed and several other databases for relevant studies up to 31 August 2011. Random-effects models were used to estimate summary estimates.

RESULTS:

Of the 6 dietary carotenoids assessed, only intake of β-carotene was significantly associated with a reduced breast cancer risk (summary RR: 0.95; 95% CI: 0.91, 0.99; I(2): 0%) per 5000 μg/d (n = 10). In contrast, the summary RR for blood concentrations of carotenoids was 0.78 (95% CI: 0.61, 0.99; I(2): 53%) per 100 μg total carotenoids/dL (n = 7), 0.74 (95% CI: 0.57, 0.97; I(2): 43%) per 50 μg β-carotene/dL (n = 13), 0.82 (95% CI: 0.73, 0.92, I(2): 3%) per 10 μg α-carotene/dL (n = 12), and 0.68 (95% CI: 0.52, 0.89; I(2): 0%) per 25 μg lutein/dL (n = 6).

CONCLUSIONS:

Blood concentrations of carotenoids are more strongly associated with reduced breast cancer risk than are carotenoids assessed by dietary questionnaires. Our results suggest that the use of certain biomarkers may clarify inconsistent and weak results between dietary intake and breast cancer risk.

PMID: 22760559 [PubMed - indexed for MEDLINE] (emphasis added)[Note – the studies sent by CANSA's CEO did not use blood concentrations of carotenoids.]

3.

Eur J Nutr. 2012 Oct;51(7):769-81. Epub 2012 Jun 9.

Antioxidant vitamins and mineral supplementation, life span expansion and cancer incidence: a critical commentary.

Dolara P, Bigagli E, Collins A.

Source

Department of Preclinical and Clinical Pharmacology, Viale Pieraccini 6, 50139, Florence, Italy. piero.dolara@unifi.it

Abstract

PURPOSE:

Experimental evidence indicates a strong connection between oxidative damage, cancer, and aging. Epidemiological observations suggest that a diet rich in fruits and vegetables is associated with lower incidence of some cancers and longer life expectancy; since fruits and vegetables contain natural antioxidants, a considerable effort has been dedicated to understanding their effects in experimental studies and in human trials.

RESULTS:

A: Effects of antioxidant-containing food and supplements on oxidation damage in humans.

Intervention trials employing a variety of biomarkers have shown either a slight decrease in oxidation damage or no effect.

B: Effects of selected antioxidants on mortality and cancer incidence.

β-carotene and α-tocopherol, alone or in combination, increase cardiovascular and all-cause mortality or have no effect. In some studies, β-carotene and retinyl palmitate significantly increase the progression of lung cancer and aggressive prostate cancer. Protection against cardiovascular mortality or no effect of vitamin E has been reported, with an increase of all-cause mortality at dosages greater than 150 IU/day. [Omega Caro-E is said to provide 20 mg (30 IU) of Vitamin E per day.] Selenium showed beneficial effects on gastrointestinal cancer and reduced the risk of lung cancer in populations with lower selenium status. For multivitamin and mineral supplementation, no significant reduction of mortality or cancer incidence was observed, but some reports indicate a possible preventive effect in cervical cancer. (emphases added)

CONCLUSIONS:

The majority of supplementation studies indicate no variation of general mortality and of cancer incidence or a detrimental effect on both. Antioxidant supplements so far tested seem to offer no improvement over a well-balanced diet, possibly because of the choice of the substances tested or of an excessive dosage. However, new natural or synthetic compounds effective in vitro and in experimental studies might still be worth investigating in human trials. (emphasis added)

PMID: 22684632 [PubMed - indexed for MEDLINE]

4.

Cochrane Database Syst Rev. 2012 Mar 14;3:CD007176. doi: 10.1002/14651858.CD007176.pub2.

Antioxidant supplements for prevention of mortality in healthy participants and patients with various diseases.

Bjelakovic G, Nikolova D, Gluud LL, Simonetti RG, Gluud C.

Source

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Abstract

BACKGROUND:

Our systematic review has demonstrated that antioxidant supplements may increase mortality. We have now updated this review.

OBJECTIVES:

To assess the beneficial and harmful effects of antioxidant supplements for prevention of mortality in adults.

SEARCH METHODS:

We searched The Cochrane Library, MEDLINE, EMBASE, LILACS, the Science Citation Index Expanded, and Conference Proceedings Citation Index-Science to February 2011. We scanned bibliographies of relevant publications and asked pharmaceutical companies for additional trials.

SELECTION CRITERIA:

We included all primary and secondary prevention randomised clinical trials on antioxidant supplements (beta-carotene, vitamin A, vitamin C, vitamin E, and selenium) versus placebo or no intervention.

DATA COLLECTION AND ANALYSIS:

Three authors extracted data. Random-effects and fixed-effect model meta-analyses were conducted. Risk of bias was considered in order to minimise the risk of systematic errors. Trial sequential analyses were conducted to minimise the risk of random errors. Random-effects model meta-regression analyses were performed to assess sources of intertrial heterogeneity.

MAIN RESULTS:

Seventy-eight randomised trials with 296,707 participants were included. Fifty-six trials including 244,056 participants had low risk of bias. Twenty-six trials included 215,900 healthy participants. Fifty-two trials included 80,807 participants with various diseases in a stable phase. The mean age was 63 years (range 18 to 103 years). The mean proportion of women was 46%. Of the 78 trials, 46 used the parallel-group design, 30 the factorial design, and 2 the cross-over design. All antioxidants were administered orally, either alone or in combination with vitamins, minerals, or other interventions. The duration of supplementation varied from 28 days to 12 years (mean duration 3 years; median duration 2 years). Overall, the antioxidant supplements had no significant effect on mortality in a random-effects model meta-analysis (21,484 dead/183,749 (11.7%) versus 11,479 dead/112,958 (10.2%); 78 trials, relative risk (RR) 1.02, 95% confidence interval (CI) 0.98 to 1.05) but significantly increased mortality in a fixed-effect model (RR 1.03, 95% CI 1.01 to 1.05). Heterogeneity was low with an I(2)- of 12%. In meta-regression analysis, the risk of bias and type of antioxidant supplement were the only significant predictors of intertrial heterogeneity. Meta-regression analysis did not find a significant difference in the estimated intervention effect in the primary prevention and the secondary prevention trials. In the 56 trials with a low risk of bias, the antioxidant supplements significantly increased mortality (18,833 dead/146,320 (12.9%) versus 10,320 dead/97,736 (10.6%); RR 1.04, 95% CI 1.01 to 1.07). This effect was confirmed by trial sequential analysis. Excluding factorial trials with potential confounding showed that 38 trials with low risk of bias demonstrated a significant increase in mortality (2822 dead/26,903 (10.5%) versus 2473 dead/26,052 (9.5%); RR 1.10, 95% CI 1.05 to 1.15). In trials with low risk of bias, beta-carotene (13,202 dead/96,003 (13.8%) versus 8556 dead/77,003 (11.1%); 26 trials, RR 1.05, 95% CI 1.01 to 1.09) and vitamin E (11,689 dead/97,523 (12.0%) versus 7561 dead/73,721 (10.3%); 46 trials, RR 1.03, 95% CI 1.00 to 1.05) significantly increased mortality, whereas vitamin A (3444 dead/24,596 (14.0%) versus 2249 dead/16,548 (13.6%); 12 trials, RR 1.07, 95% CI 0.97 to 1.18), vitamin C (3637 dead/36,659 (9.9%) versus 2717 dead/29,283 (9.3%); 29 trials, RR 1.02, 95% CI 0.98 to 1.07), and selenium (2670 dead/39,779 (6.7%) versus 1468 dead/22,961 (6.4%); 17 trials, RR 0.97, 95% CI 0.91

to 1.03) did not significantly affect mortality. In univariate meta-regression analysis, the dose of vitamin A was significantly associated with increased mortality (RR 1.0006, 95% CI 1.0002 to 1.001, P = 0.002). (emphases added)

AUTHORS' CONCLUSIONS:

We found no evidence to support antioxidant supplements for primary or secondary prevention. Beta-carotene and vitamin E seem to increase mortality, and so may higher doses of vitamin A. Antioxidant supplements need to be considered as medicinal products and should undergo sufficient evaluation before marketing. (emphases and highlighting added) [Note: This conclusion mirrors my concerns initially expressed to the CANSA CEO in my letter of 19 February 2013. At that stage I did not know that the absorption and resulting blood concentrations of the constituents had not been determined.]

Update of

Cochrane Database Syst Rev. 2008;(2):CD007176.

PMID: 22419320 [PubMed - indexed for MEDLINE]

5.

Vikkie A Mustad, Carla A Smith, Peter P Ruey, Neile K Edens, and Stephen J DeMichele. Supplementation with 3 compositionally different tocotrienol supplements does not improve cardiovascular disease risk factors in men and women with hypercholesterolemia. Am J Clin Nutr December 2002 vol. 76 no. 6:1237-1243.

http://ajcn.nutrition.org/content/76/6/1237.full

Conclusion:

Supplementation with 200 mg tocotrienols/d from 3 commercially available sources has no beneficial effect on key cardiovascular disease risk factors in highly compliant adults with elevated blood lipid concentrations.

[Note – although this “old” study showed adequate absorption and increased serum levels of tocotrienols, no benefit in cardiovascular disease was shown in the study population. See also Response 26 above.]

Annexure 2 – Omega Caro-E Promotional material

1. CPUT Bulletin May 2012 page 5

Note the claims made for Omega Caro-E:

Advantages – lowers your risk of chronic ailments like heart disease, arthritis and cancer; improves your skin and hair; assists in combating Alzheimers, muscle degeneration and depression.

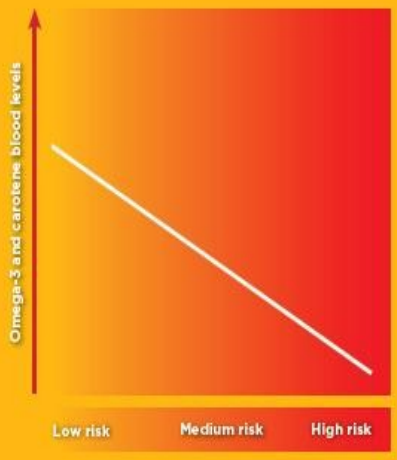
2. CANSA-CPUT Omega Caro-E brochure (front) – underlining added

This promotion implies that Omega Caro-3 is the product containing omega-3 fatty acids which will increase their dietary intake. However their absorption from the Omega Caro-3 formulation in a gelatine soft capsule has not been demonstrated. The promotion also implies that 500 mg omega-3 fatty acids, 6.0 mg carotenes, 16.2 mg tocotrienol and 3.8 mg tocopherol would be absorbed ("provides") from taking two capsules of Omega Caro-E daily.

2. CANSA-CPUT Omega Caro-E brochure (back) – underlining added

Carotenes are plant derived colour pigments. In humans, carotenes such as beta-carotene are precursors for vitamin A, which is essential for good vision. Carotenes may act as antioxidants and display anti-inflammatory properties. Research suggests that diets rich in carotenes from fruit and vegetables may protect against heart disease and certain types of cancer. Carotenes also assist in the maintenance of skin, hair and nails. Food sources of carotenes include the yellow fruit and vegetables such as carrots, pumpkin, orange fleshed sweet potatoes, apricots and mangoes.

Vitamin E is the collective name for tocopherols and tocotrienols, which are fat soluble vitamins with antioxidant properties. Tocopherols protect cell membranes from oxidation while tocotrienols may protect against stroke, decrease platelet aggregation and demonstrate anti-inflammatory and anti-cancer activities. Green leafy vegetables such as spinach, broccoli and Brussels sprouts are examples of food sources for tocopherols while oils such as avocado oil, canola oil, wheat germ oil and soybean oil also contain tocopherols but only minute amounts of tocotrienols.



Increased **blood omega-3 levels** are associated with a decreased risk for degenerative diseases such as heart disease, type 2 diabetes, cancer, depression, arthritis and Alzheimer's disease. Research indicates that the blood omega-3 fatty acid levels of most Americans and many Europeans are very low. There is no reason to believe that South Africans' levels are any better. Supplementation with omega-3 fatty acid has been proven to increase your blood omega-3 levels hence lowering your risk to develop degenerative diseases.

Current research pointed out that the lower your **blood carotene levels** the higher your risk for developing cancer and certain other non-communicable diseases. Science indicates that South Africans consume less than half the recommended amount of fruit and vegetables per day. Carotenes are abundant in fresh fruits and vegetables and may play a fundamental role in reducing the risk of disease. It has been shown that blood carotene levels can be increased via supplementation with a spectrum of natural carotenes.

Note that the promotion explicitly links Omega Caro-E with the statements "Supplementation with omega-3 fatty acid has been proven to increase your blood omega-3 levels hence lowering your risk to develop degenerative diseases"; and also "supplementation with a spectrum of natural carotenes" causing an increase in blood carotene levels. However the studies to show that Omega Caro-E increases omega-3 levels or blood carotene levels, have not been done.