



Council for Responsible Nutrition

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VIA ELECTRONIC SUBMISSION

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Re: Comments on “Agenda Item 6 – Proposed Draft NRV-NCD for Eicosapentaenoic Acid (EPA) and Docosahexaenoic Acid (DHA) Long Chain Omega-3 Fatty Acids” in the November 7, 2017 “Draft U.S. Positions for the 39th Session of the Codex Committee on Nutrition and Foods for Special Dietary Uses (CCNFSDU); 4-8 December, 2017”

The Council for Responsible Nutrition (CRN)¹ is the leading trade association for the dietary supplement and nutritional products industry, representing manufacturers of dietary

¹ The Council for Responsible Nutrition (CRN), founded in 1973 and based in Washington, D.C., is the leading trade association representing dietary supplement and functional food manufacturers, marketers and ingredient suppliers. CRN companies produce a large portion of the functional food ingredients and dietary supplements marketed in the United States and globally. Our member companies manufacture popular national brands as well as the store brands marketed by major supermarkets, drug stores and discount chains. These products also include those marketed through natural food stores and mainstream direct selling companies. CRN represents more than

ingredients and of national brand name and private label dietary supplements, many of which are multinational and already actively selling ingredients, finished products and services globally.

World Health Organization (WHO) Nutrition Guidance Expert Advisory Group (NUGAG)

CRN appreciates the opportunity to review and comment on the U.S. position on “Agenda Item 6 – Proposed Draft NRV-NCD for Eicosapentaenoic Acid (EPA) and Docosahexaenoic Acid (DHA) Long Chain Omega-3 Fatty Acids” in the November 7, 2017 “Draft U.S. Positions for the 39th Session of the Codex Committee on Nutrition and Foods for Special Dietary Uses (CCNFSDU); 4-8 December, 2017”. CRN notes that the United States participated in the electronic Working Group (chaired by the Russian Federation and Chile), as did CRN.

The U.S. also considered the systematic reviews conducted by the Nutrition Guidance Expert Advisory Group (NUGAG) of the World Health Organization (WHO), as did CRN.

The U.S. considers that the reviewed evidence does not support establishing a quantitative NRV-NCD for EPA/DHA. Based on the systematic reviews provided by the eWG...” Further the U.S. notes that “the two systematic review, which follow systematic review reporting guidelines and include assessment of risk of bias, do not support a causal relationship between n-3 long chain polyunsaturated fatty acids (LC-PUFA) and changes in the risk of NCD events.” In conclusion, the U.S. states that “the United States does not support setting a NRV-NCD for EPA and DHA, at this time, as the totality of evidence does not meet the threshold of

150 companies that manufacture dietary ingredients, dietary supplements and/or functional foods, or supply services to those suppliers and manufacturers. Our member companies are expected to comply with a host of federal and state regulations governing dietary supplements and food in the areas of manufacturing, marketing, quality control and safety. Our supplier and manufacturer member companies also agree to adhere to additional voluntary guidelines as well as to CRN’s Code of Ethics. Learn more about us at www.crnusa.org.

“relevant convincing/generally accepted scientific evidence” required by the General Principles for the relationship between EPA and DHA and CHD mortality/fatal CHD.”

CRN evaluated the abridged versions of the systematic reviews of the randomized controlled trials (RCTs), hereafter also referred to as Document 1 and the prospective cohort studies, hereafter also referred to as Document 2 from the World Health Organization (WHO) Nutrition Guidance Expert Advisory Group (NUGAG) Subgroup on Diet and Health.

After an extensive review of the current body of scientific literature, plus discussions with and comments from eWG member, the Global Organization for EPA and DHA Omega-3s (GOED) dated September 25, 2017, CRN is submitting our comments and answers to the eWG questions posed in reference to the WHO NUGAG report.

Summary

Based on the breadth and global nature of research supporting the beneficial nature of regular intake of essential fatty acids, CRN supports the work of NUGAG in contributing to establishment of a NRV-NCD for EPA and DHA by providing their analyses of intake. Given the somewhat limited nature and method in reaching conclusions in Documents 1 and 2, there is a concern that inappropriate interpretation of the studies could hinder progress toward further focus on this important nutrient.

A study published in the journal, *Nutrition* documented that despite an increasing public understanding of the importance of regular intake of DHA and EPA, blood levels of omega-3 are significantly below optimum in both the U.S. and in Germany.²

² Thuppal SV, et al. (2017) Nutrients Discrepancy between Knowledge and Perceptions of Dietary Omega-3 Fatty Acid Intake Compared with the Omega-3 Index. *Nutrients* 9(9). pii: E930. doi: 10.3390/nu9090930. (<http://www.mdpi.com/2072-6643/9/9/930/htm>).

From the perspective of reaching overarching goals in making a substantive difference (improvement) in global public health initiatives, it is critical to focus on any (ANY) incremental steps that can avoid or decrease risk of serious disease/debility and add to healthy aging.

The global burden on non-communicable diseases, also termed chronic diseases, is overwhelming, and even risk decrements as inconsequential as one percent, can translate into millions of lives saved and millions of opportunities for a prolonged quality of life for those that would otherwise be afflicted.

Policy-makers and governmental / pan-national regulatory agencies must decide when sufficient scientific support has been developed to justify dietary and lifestyle public health recommendations. This principle was acknowledged by action on the part of the U.S. Institute of Medicine (now the National Academy of Medicine) when it published an adequate intake level for omega-3s even though all aspects of tolerance and upper limits value establishment were not fully implemented³.

CRN has been at the forefront of coalescing, moderating and publishing key scientific expertise in this arena. Last year in Hamburg, Germany, just prior to the Codex Committee on Nutrition and Foods for Special Dietary Uses (CCNFSDU), CRN (via CRN-International) held a scientific symposium on Optimal Nutrition, which has since been published in the *European Journal of Nutrition (EJoN)*⁴. The speakers and the conclusion made it clear that there are many dietary and lifestyle decisions that can and do affect one's quest for optimal nutrition, and that

³ Institute of Medicine, Food and Nutrition Board. Dietary reference intakes for energy, carbohydrate, fiber, fat, fatty acids, cholesterol, protein, and amino acids (macronutrients). Washington, DC: National Academy Press; 2005.

⁴ Shao AS, et al. (2017) Optimal nutrition and the ever-changing dietary landscape: a conference report. Eur J Nutr DOI 10.1007/s00394-017-1460-9.

it is short-sighted and contrary to public health policy to not give credence and make necessary changes...or at least necessary recommendations. This year, CRN/CRN-I will hold a similar scientific symposium in Berlin at the forefront of CCFNSDU on “Healthy Aging”.

As two prominent members of the U.S. National Academy of Medicine, Food and Nutrition Board (FNB) have stated from the podium during key scientific discussions on this topic, “do NOT let the perfect be the enemy of the good” (Voltaire)⁵. Better a diamond with a flaw than a pebble is another way to state the irrational pursuit of perfection and the sacrifice of current health opportunities in an age of ever-increasing chronic disease and debility.

Several years ago, the CRN/CRN-I scientific symposium focused on a process whereby a bioactive ingredient could and should be considered for NRV/DRI review and progression. All of the international speakers were in agreement and the subsequent *EJoN* publication⁶ put into the scientific literature, a well-discussed, well-vetted and well-accepted list of criteria that when met, were sufficient such that public policy could go forward in setting a NRV-NCD (or in the U.S., a DRI) for a bioactive ingredient. Those criteria have been met for EPA+DHA and there is NO scientific reason, much less common-sense reason to avoid making the appropriate recommendation for CCFNSDU to go forward.

⁵ *Le mieux est l'ennemi du bien*. Voltaire, Dictionnaire Philosophique.

⁶ Lupton J, et al. (2014) Exploring the benefits and challenges of establishing a DRI-like process for bioactives. *Eur J Nutr*. 2014 Apr;53 Suppl 1:1-9. doi: 10.1007/s00394-014-0666-3
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3991826/pdf/394_2014_Article_666.pdf.

Questions posed by the eWG

Document 1 - Systematic review and meta-analysis of RCTS

Q1.1 Do you believe that Document 1 represents/summarizes relevant convincing/generally accepted scientific evidence or the comparable level of evidence under the GRADE classification for the relationship between EPA/DHA and noncommunicable disease risk, as required for the selection of nutrients by 3.2.2.1 of General Principles for Establishing NRVs?

NO

Q1.2 Do you believe that Document 1 represents/summarizes relevant and peer-reviewed scientific evidence for quantitative reference values for daily intake that is required in order to determine an NRV-NCD that is applicable to the general population, according to 3.2.2.2 of General Principles for Establishing NRVs?

NO

Q1.3 Do you believe that Document 1 (section Coronary Heart Disease deaths, pages 48-54) presents evidence that sufficiently characterizes the relationship between EPA/DHA intake and the reduction of risk of CHD mortality/fatal CHD events, the health outcome selected for establishing the NRV-NCD?

NO

Q1.4 Authors of Document 1 have run sensitivity analysis excluding certain RCTs from the scope of the review. Do you find results of the sensitivity analysis which excluded RCTs reporting cardiac deaths only (figure 4.16 on page 50) relevant to establishing the NRV-NCD for EPA/DHA associated with CHD mortality?

NO

Q1.5 Figure 4.18 on page 52 depicts results of the sensitivity analysis which grouped studies based on the summary risk of bias. Do you find results of the sensitivity analysis which grouped RCT studies according to their summary risk of bias relevant to establishing the NRV-NCD for EPA/DHA associated with CHD mortality?

NO

Q1.6 Several RCT studies selected for review in the CHD mortality section of Document 1 were based on a comparison of EPA/DHA intake with intake of monounsaturated fatty acids (MUFA). Considering that there was convincing evidence that MUFA lowered levels of heart health biomarkers, comparing effects of EPA/DHA with MUFA intakes might not be entirely suitable for

establishing an NRV-NCD. Do you agree that for the purpose of establishing the NRV-NCD the sensitivity analysis may require exclusion of all studies that compared EPA/DHA intake with MUFA intake?

NO

Document 2 - Systematic review and meta-analysis of prospective cohort studies

Q2.1 Do you believe that Document 2 represents/summarizes relevant convincing/generally accepted scientific evidence or the comparable level of evidence under the GRADE classification for the relationship between EPA/DHA and noncommunicable disease risk relationship, as required for the selection of nutrients by 3.2.2.1 of General Principles for Establishing NRVs?

NO

Q2.2 Do you believe that Document 2 represents/summarizes relevant and peer-reviewed scientific evidence for quantitative reference values for daily intake that is required in order to determine an NRV-NCD that is applicable to the general population, according to 3.2.2.2 of General Principles for Establishing NRVs?

NO

Q2.3 Do you believe that Document 2 presents evidence that sufficiently characterizes the relationship between long chain n-3 PUFA intake and the reduction of risk of CHD mortality/fatal CHD events, the health outcome selected for establishing the NRV-NCD?

YES

Q2.4 Do you agree that results reviewed in Document 2 for total long chain n-3 PUFAs could be accepted as representative for associations of EPA/DHA with various health outcomes studied including the CHD mortality?

YES

Further, although not every omega 3 fatty acid study exhibits strong causal relationships, in fact a number of studies do suggest such a causal relationship. Please refer to Szolstak-Wegierek, et al. "The role of dietary fats for preventing cardiovascular disease, a

review⁷” or the 2015 *JCN* article titled “Replacement of saturated with unsaturated fats had no impact on vascular function but beneficial effects on lipid biomarkers, E-selectin, and blood pressure: Results from the randomized, controlled Dietary Intervention and Vascular Function (DIVAS) study⁸” where certain correlations exist, but it would be difficult to identify a specific level, or even range of levels, at which below, there is no influence and, at which above, there is a consistent significant influence. When you add in the additional risk of bias analysis, cited in the NUGAG report, some type of positive relationship between PUFAs and heart health exists, but the data may be less convincing when looking to set a specific NRV-NCD or establishing specific health outcomes, but that does not mean one should avoid making realistic public health policy decisions.

Nothing has been proposed in the scientific literature and/or amongst national regulatory bodies that in any way changes the conclusion of CRN, as echoed by the chairs of the electronic Working Group. In fact the current recommendations set by the European Food Safety Authority (EFSA) identify a 250 mg intake of EPA and DHA per day for the general adult population with a maximum tolerated dose of 5 g per day. CRN is in agreement with EFSA on their analysis, conclusion and recommendation.

⁷ Szostak-Wegierek, et al (2013). The role of dietary fats for preventing cardiovascular disease. A review *Rocz Panstw Zakl Hig.* 2013;64(4):263-9.

⁸ Vafeiadou K, et al. (2015). Replacement of saturated with unsaturated fats had no impact on vascular function but beneficial effects on lipid biomarkers, E-selectin, and blood pressure: results from the randomized, controlled Dietary Intervention and VAScular function (DIVAS) study. *Am J Clin Nutr.* 2015 Jul;102(1):40-8. doi: 10.3945/ajcn.114.097089. Epub 2015 May 27.

Should the U.S. Delegation to the Codex CCNFSDU have further questions that CRN could address, please do not hesitate contacting me at your earliest convenience. CRN awaits a substantive discussion at the 39th Session of the Codex Committee on Nutrition and Foods for Special Dietary Uses (CCNFSDU); 4-8 December, 2017 on this important issue.

Respectfully submitted,

A handwritten signature in black ink, appearing to be 'J. Griffiths', written in a cursive style.

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