CODEX ALIMENTARIUS COMMISSION

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Agenda Item 7 **CX/NFSDU 16/38/8-Add.2**

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JOINT FAO/WHO FOOD STANDARDS PROGRAMME
CODEX COMMITTEE ON NUTRITION AND FOODS FOR SPECIAL DIETARY USES

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PROPOSED DRAFT NRV-NCD FOR EPA AND DHA LONG CHAIN OMEGA-3 FATTY ACIDS

Comments of Brazil, Costa Rica, Japan and the United States of America

BRAZIL

SPECIFIC COMMENTS

According to the text presented in CX/NFSDU 16/38/8, the proposed draft NRV-NCD for EPA and DHA (250mg) was based on the data of systematic reviews and most recent scientific publications reviewed as described in the report and the recommendations from the FAO/WHO Expert Consultations and other nominated RASBs.

Nevertheless, Brazil understands that based on the body of scientific evidence, **it is not possible to conclude** that the evidence is convincing/generally accepted for the relationship between EPA and DHA intake and the reduction of risk of coronary heart disease mortality/fatal CHD events. Thus, the criterion in General Principles 3.2.2.1 has not been met.

"GP 3.2.2.1 states that the following criteria should be considered in the selection of nutrients for the establishment of NRVs-NCD:

Relevant convincing[1]/generally accepted[2] scientific evidence or the comparable level of evidence under the GRADE classification[3] for the relationship between a nutrient and non-communicable disease risk relationship, including validated biomarkers for disease risk, for at least one major segment of the population (e.g. adults).

Public health importance of the nutrient non-communicable disease risk relationship(s) among Codex member countries."

Initially, it is important to note that most of the scientific evidence presented in Table 2 of CX/NFSDU 16/38/8 was classified as moderate or low using the GRADE approach. Only 5 studies were classified as high.

With regard to the meta-analysis of Casula *et al* (2013), the authors concluded that the results supply evidence that long-term effect of high dose omega-3 fatty acid supplementation may be beneficial for the onset of cardiac death, sudden death and myocardial infarction among patients with a history of cardiovascular disease. However, subgroup analyses were not performed as previously intended by the authors, and the concomitant use of statins may have influenced the final result of the revision. Moreover, the dose of omega-3 supplement ranged from 1 to 6g/day, which is much higher than the proposed value of 250mg of EPA and DHA.

Delgado-Lista *et al* (2012) assessed clinical trials and randomized controlled trials of omega-3 fatty acids either in capsules or in dietary intake. Nevertheless, the studies with a dietary advice were not stratified in order to analyze the results, which can be considered a study limitation. Besides, the intervention dose ranged from 0.3 to 6.9 of EPA and DHA, which is above the proposed value of 250mg.

Although Kotwal (2012) concluded that omega-3 fatty acids may protect against vascular disease, it was highlighted that the evidence is not clear-cut, and any benefits are almost certainly not as great as previously believed.

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[1] At the time these guiding principles were drafted the definition and criteria for "convincing evidence" were taken from the FAO/WHO Report "Diet, Nutrition and the Prevention of Chronic Diseases" (WHO Technical Report Series 96, WHO, 2003).

[2] For these General Principles the terms convincing/generally accepted evidence are considered synonymous.

[3] WHO Guidelines Review Committee, WHO Handbook for Guideline Development. Geneva: WHO, 2012.

According to Chen (2011), there was no clear evidence that supplementation with omega-3 fatty acids, in addition to current guideline-adjusted therapy, improved the prognosis of patients for secondary prevention of cardiovascular disease.

The review of Marik (2009) concluded that the mortality benefits of dietary supplements of omega-3 fatty acids were only evident in people at higher risk. However, some methods were not well described and it was possible that studies were missed. Thus, it was highlighted that the conclusions may need to be treated with some caution.

We would also like to mention the meta-analysis of Khoueiry *et al* (2013)[4], which analyzed the effect of omega-3 PUFA on preventing potentially fatal ventricular arrhythmias and sudden cardiac death. The authors concluded that dietary supplementation with omega-3 PUFA does not affect the risk of sudden cardiac death or ventricular arrhythmias.

In relation to the RASBs selected by eWG (Table 3), it is important to note that the conclusions, health outcomes, and recommended doses of EPA + DHA vary among them. Some RASBs have not provided quantitative recommendations for EPA and DHA intake. Australia's NHMRC has reviewed the evidence on the EPA/DHA intake-health outcome relationship and found it inconclusive. While the recommended dose from the National Institute of Health and Nutrition (NIHN) is 1000 mg/day of EPA+DHA, the recommendation from Agence Nationale de sécurité sanitaire de l´alimentation de l´environnement et du travail (ANSES) is 500mg/day of EPA and DHA and the Health Council of the Netherlands recommends 450mg/day of omega-3 fatty acids from fish.

Therefore, we understand that the findings from recent scientific references do not show consistent associations between consumption of EPA and DHA and reduction of death risk from CHD. Besides, there is not a consensus among the selected RASBs.

Hence, Brazil **does not support** the proposed NRV-NCD for EPA and DHA of 250mg/day.

COSTA RICA

Costa Rica agradece a Chile y la Federación de Rusia, por el documento elaborado con los aportes del grupo de trabajo electrónico de 2016. Haciendo una revisión del mismo, apoya la inclusión de un VRN-ENT para el EPA y el DHA de 250 mg/día en el párrafo 3.4.4.2, VRN-ENT, de las Directrices sobre Etiquetado Nutricional (CAC/GL 2-1985), tal como se presenta en el apéndice I, en el entendido de que será colocado junto con el nivel para potasio entre los niveles de ingesta por alcanzar:

"3.4.4.2 VRN-ENT

EPA11 y DHA12 250 mg13

11 Ácido eicosapentaenoico

12 Ácido docosahexaenoico

13 El establecimiento de un VRN se basó en pruebas convincentes/generalmente reconocidas de que existe relación con el riesgo de ENT, según lo presentado en el informe Diet, Nutrition and the Prevention of Chronic Diseases (serie 916 de informes técnicos de la OMS; OMS, 2003) y en las consultas de expertos de la FAO/OMS (series 91 y 978 de informes técnicos de la OMS; OMS, 2010)."

Costa Rica apoya este valor principalmente porque los valores propuestos por otros Organismos Científicos Competentes Reconocidos (OCCR) que se analizaron, no han elaborado una recomendación cuantitativa sobre la ingesta de EPA y DHA para alcanzar el resultado seleccionado: LA REDUCCIÓN DEL RIESGO DE MORTALIDAD POR CARDIOPATÍA ISQUÉMICA O DE EPISODIOS DE CARDIOPATÍA ISQUÉMICA MORTALES, por lo que según los criterios previamente establecidos no deben ser considerados para establecer el VRN-ENT para EPA y DHA.

JAPAN

General Comments

At the previous session, the Committee considered the need to obtain additional scientific advice through JEMNU or NUGAG, and it was agreed that since NUGAG was already in the process of scoping a review, the Committee could evaluate the NUGAG work as it became available, continue work on the NRV and consider

[4] Khoueiry G. et al. Do omega-3 polyunsaturated fatty acids reduce risk of sudden cardiac death and ventricular arrhythmias? A meta-analysis of randomized trials. Heart Lung. 2013 Jul-Aug;42(4):251-6. doi: 10.1016/j.hrtlng.2013.03.006. Epub 2013 May 25.

whether any additional scientific advice would be needed in the future. Based on the acknowledgment, the Committee agreed to take into account the work of NUGAG in the discussion of the eWG. However, the NUGAG report has not been issued yet.

We would also note that, as described in the paragraph 14 and 15 of CX/NFSDU 16/38/8, researchers of different systematic reviews have drown different conclusions even though they studied almost the same set of RCTs. We believe that due consideration be given to the difference of interpretation in such a way that any qualified independent organizations objectively assess sufficient evidence to provide a basis for establishing NRV-NCDs.

We would therefore suggest requesting any qualified independent organizations to conduct review, and/or re-considering the establishment of NRV-NCDs for EPA+DHA as the NUGAG report becomes available.

UNITED STATES OF AMERICA

General Comments

The United States thanks Chile and Russian Federation for co-chairing the eWG referenced in CX/NFSDU 16/38/8.

The United States does not support setting a NRV-NCD for EPA and DHA at this time because the issues identified in para 3 of this CX paper remain unresolved.

Specific Comments

The United States suggests further discussion on the totality of evidence for setting a NRV-NCD for EPA and DHA and coronary heart disease (CHD) mortality/fatal CHD deaths. The United States considers that the totality of evidence does not meet the threshold of 'relevant convincing/generally accepted scientific evidence' for the relationship between EPA and DHA and the risk of CHD mortality/fatal death. RASBs that have not set daily intake reference values (DIRV) for EPA and DHA based on the totality of the evidence should also be considered in setting a NRV-NCD for EPA and DHA.

The United States recognizes the recognized authoritative scientific bodies (RASBs) identified by the eWG (EFSA, NCM, ANSES), and we note that some of the RASB reports discussed by the eWG establish DIRVs based, in part, on evidence for fish consumption and reduced risk for CHD mortality/fatal CHD events (EFSA 2010, NNR 2012, NIHN 2013, ANSES 2011, GNS 2015); other RASB reports (NHMRC 2011, Health Council of Netherlands 2006, IOM 2007, SACN 2004) provide food based dietary recommendations only.

The United States would like to clarify that, under item 4 of Table 3 in CX/NFSDU 16/38/8, the Authority listed should be the U.S. Department of Agriculture (USDA) and Department of Health and Human Services (DHHS) and the correct citation for the publication should be the 2010 Dietary Guidelines for Americans instead of the 2010 Scientific Report of the Dietary Guidelines Advisory Committee (DGAC). The United States does not consider the Scientific Report from the DGAC to be a consensus report or policy document, and the Dietary Guidelines for Americans report does not provide a recommendation for a quantitative amount for EPA and DHA that could be used as a DIRV because the guidelines and key recommendations pertain to seafood only. While the 2010 Dietary Guidelines for Americans report discusses the evidence for seafood and health outcomes, the Departments' conclusion on seafood is reflected in its key recommendations for seafood, not for EPA and DHA. Notably, the key recommendations are to "increase the amount and variety of seafood consumed" and for women who are pregnant or breastfeeding to "consume 8 to 12 oz. of seafood from a variety of seafood types." The report text also emphasizes that "the recommendation is to consume seafood for the total package of benefits that seafood provides, including its EPA and DHA content."

The United States also would like to clarify that the U.S. Food and Drug Administration, not the Agency for Healthcare Research and Quality (AHRQ), conducted the scientific evaluation for the 2004 Omega-3 Fatty Acids and Reduced Risk of Coronary Heart Disease. While the AHRQ also conducts systematic reviews for the DHHS, the United States does not consider those evidence reports as policy documents or an official position of AHRQ, sponsoring government agency, or the DHHS.

The United States appreciates the efforts of the co-chairs in presenting the scientific evidence and suggests further discussion of PICO (patient-intervention-comparison-outcome) parameters presented. The United States notes that the establishment of the NRV-NCD for Potassium was supported by the WHO NUGAG report that provided both the strength of evidence (section 3.2.2.1) and a DIRV (section 3.2.2.2) from the same scientific evaluation of evidence. As consensus among RASBs on the strength of evidence for the relationship between EPA and DHA and CHD mortality/fatal CHD events is lacking and not all RASBs have set reference values for EPA and DHA, the United States suggests further discussion of external input to the Committee to evaluate the totality of evidence for a NRV-NCD for EPA and DHA and CHD mortality/fatal CHD events.