CODEX ALIMENTARIUS COMMISSION E

Food and Agriculture Organization of the United Nations

World Health Organization

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Agenda Item 7 **CX/NFSDU 15/37/7 Add.1**

JOINT FAO/WHO FOOD STANDARDS PROGRAMME

CODEX COMMITTEE ON NUTRITION AND FOODS FOR SPECIAL DIETARY USES

37th Session
Bad Soden a.T. - Germany
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PROPOSED DRAFT NRV-NCD FOR EPA AND DHA LONG CHAIM OMEGA-3 FATTY ACIDS

Comments of Brazil, Canada, Egypt, Japan, New Zealand, Paraguay, Philippines, United States of America, ELC, FoodDrinkEurope, GOED, IADSA, ICGMA, IDF

BRAZIL

GENERAL COMMENTS

Initially, we would like to point out that Brazil did not receive the invitation to participate in the eWG. Considering that the subject is controversial, we understand that member countries should have more time to discuss it internally.

SPECIFIC COMMENTS

Given the body of scientific evidence presented in the report and several issues raised by some Codex Members Countries of the eWG, Brazil understands that **it is not possible to conclude** if the evidence is sufficient to meet the criterion in General Principles 3.2.2.1 at this time.

"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."

According to the text presented in Appendix I of CX/NFSDU 15/37/7, the proposed draft NRV-NCD for EPA and DHA (250mg) was based on convincing/generally accepted evidence for a relationship with NCD risk as reported in the Diet, Nutrition and the Prevention of Chronic Diseases. WHO Technical Report Series 916, WHO, 2003; and in the FAO/WHO Expert Consultations. Technical report Series 91 and 978, WHO, 2010.

Nevertheless, it is important to take into account that "*the evidence that is currently available from prospective cohort studies is largely based on the consumption of fish, not EPA + DHA in isolation*" (paragraph 17 of CX/NFSDU 15/37/7). The WHO Technical Report Series 916 states that most of the epidemiological evidence related to n-3 PUFAs is derived from studies of fish consumption in populations or interventions involving fish diets in clinical trials. According to the FAO Fisheries and Aquaculture Report n. 978 (2010), the evidence was found convincing for fish consumption. Consistent with the evidence, the WHO/FAO (2010) report recommends consumption of fish rich in n-3 PUFAs. It is not appropriate to extrapolate findings from the epidemiological studies based on the consumption of fish to solely EPA+DHA. The relationship between consumption of n-3 PUFAs from other sources and reduction of risk from coronary heart diseases (CHD) must be evaluated by further randomized controlled trials.

Moreover, studies published since 2010 counteract the benefit for EPA + DHA in patients with known CHD or with risk factors for heart disease. Chowdhury et al. (2010) concluded that the current evidence does not

[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.

clearly support cardiovascular guidelines that encourage high consumption of polyunsaturated fatty acids and low consumption of total saturated fats. The systematic review and meta-analysis of Rizos et al. (2012) concluded that overall, omega-3 PUFA supplementation was not associated with a lower risk of all-cause mortality, cardiac death, sudden death, myocardial infarction, or stroke based on relative and absolute measures of association. According to the review of Nestel et al. (2015), the summary of evidence published since 2007 concludes that dietary intake of fish was found to be mostly consistent with respect to protection from heart disease and stroke. Higher fish intake was associated with lower incident rates of heart failure in addition to lower sudden cardiac death, stroke and myocardial infarction. However, in relation to omega-3 LCPUFA supplementation, neither a beneficial nor adverse effect was demonstrated in primary or secondary prevention of coronary heart disease.

The Nutrient Reference Values for Australia and New Zealand document (NHMRC, 2006) reports that even though various expert groups may take account of the same body of published evidence regarding recommendations for consumption of ALA and/or the very long chain omega-3s, there is considerable variation between expert interpretations, consequent recommendations and their adoption by health authorities. It also mentions that there is a lack of dose-response data relating EPA and DHA consumption to chronic disease health benefit. According to the Australian Dietary Guidelines (NHMRC, 2013), the evidence that the consumption of at least two serves a week of fish is associated with reduced risk of mortality from cardiovascular disease, and with reduced incidence of cardiovascular disease is graded as C (suggestive association).

The Co-chairs point out that none scientific bodies represented by the authors of the meta-analyses identified in the literature search were qualified as RASB. Nevertheless, we understand that the findings from recent scientific references must be taken into account because they do not show consistent associations between consumption of EPA and DHA and reduction of death risk from CHD. According to FAO/WHO Technical Report Series 96 (2003), convincing evidence is defined as "*evidence based on epidemiological studies showing consistent associations between exposure and disease, with little or no evidence to the contrary. The available evidence is based on a substantial number of studies including prospective observational studies and where relevant, randomized controlled trials of sufficient size, duration and quality showing consistent effects. The association should be biologically plausible*".

Based on the results from recent studies, there is evidence to the contrary. Hence, Brazil considers that it is necessary to discuss thoroughly if the evidence is convincing to establish an NRV-NCD for DHA and EPA at this time. As suggested by New Zealand at the eWG, it may more appropriate to await further research and a more recent Guideline from the WHO/FAO NUGAG group prior to establishing an NRV-NCD for EPA and DHA.

References:

1. Chowdhury R, Warnakula S, Kunutsor S, Crowe F, Ward HA, Johnson L *et al.* Association of dietary, circulating and supplement fatty acids with coronary risk: a systematic review and meta-analysis. *Ann Intern Med* 2014;160(6):398-407.
2. Joint FAO/WHO Expert Consultation on the risks and benefits of fish consumption, 25–29 January 2010, Rome. FAO Fisheries and Aquaculture Report No. 978. FIPM/R978 (En), ISSN 2070-6987.
3. Nestel P, Clifton P, Colquhoun D, Noakes M, Mori TA, Sullivan D, Thomas B. Indications for omega-3 long chain polyunsaturated fatty acid in the prevention and treatment of cardiovascular disease. *Heart Lung Circ* 2015;24(8):769-779.
4. Rizos EC, Ntzani EE, Bika E, Kostapanos MS, Elisaf MS. Association between omega-3 fatty acid supplementation and risk of major cardiovascular disease events: a systematic review and meta-analysis. JAMA. 2012 Sep 12;308(10):1024-33.
5. World Health Organisation (2010) Fats and fatty acids in human nutrition Report of an expert consultation, (Geneva, Switzerland). Technical Report Series 91. Available at http://www.who.int/nutrition/publications/nutrientrequirements/fatsandfattyacids_humannutrition/en/
6. World Health Organisation (2003) Joint WHO/FAO Expert Consultation on Diet, Nutrition and the Prevention of Chronic Disease (Geneva, Switzerland). Technical Report Series 916.
7. National Health and Medical Research Council (NHMRC). Australian Dietary Guidelines. 2013. Available at https://www.nhmrc.gov.au/_files_nhmrc/publications/attachments/n55_australian_dietary_guidelines_130530.pdf
8. National Health and Medical Research Council (NHMRC). Nutrient Reference Values for Australia and New Zealand. 2003.

CANADA

GENERAL COMMENTS

At this time, Canada is not in a position to support the NRV-NCD proposed for EPA and DHA. Canada is of the opinion that further discussion is needed before a final recommendation can be made.

SPECIFIC COMMENTS

Paragraph 9: "The list of accepted RASBs is:

- European Food Safety Authority (EFSA)
- National Institute of Health and Nutrition, Japan
- Nordic Council of Ministers/Norwegian Scientific Committee

[…] Co-chairs proposed to focus their attention to RASBs already accepted by CCNFSDU and nominated by the eWG."

1) Canada notes that although a primary review of the evidence was conducted for the 2011 report by the Norwegian Scientific Committee[4], the recommended intake for EPA and DHA of 0.25 g/day seems to be based on EFSA's DIRV, rather than on their own primary evaluation of the scientific evidence. Therefore, Canada does not consider the Nordic Council of Ministers/Norwegian Scientific Committee EPA and DHA DIRV to be a suitable candidate for the NRV-NCD.

2) Canada suggests including the Australian National Health and Medical Research Council (NHMRC) as an accepted RASB. Specifically, conclusions from the following NHMRC report should be considered since a primary evaluation of the scientific evidence was conducted:

National Health and Medical Research Council (2011). A review of the evidence to address targeted questions to inform the revision of the Australian Dietary Guidelines.
https://www.nhmrc.gov.au/_files_nhmrc/file/publications/n55d_australian_dietary_guidelines_evidence_report.pdf

The 2011 NHMRC report concluded that the evidence suggests that consumption of at least two serves a week of fish is associated with reduced risk of mortality from cardiovascular disease, and with reduced incidence of cardiovascular disease. This association was rated as Grade C because it is suggestive. A convincing association is Grade A.

The different conclusion of the 2011 NHMRC report compared to the other RASB reports included might be due to the fact that NHMRC took into account evidence for primary prevention, but not for secondary prevention.

3) As suggested by another CMC in response to the first consultation paper, Canada supports including the 'Agence nationale de sécurité sanitaire de l'alimentation, de l'environnement et du travail' (ANSES) as a RASB. Specifically, recommendations from the following ANSES report should be considered for the purpose of establishing a NRV-NCD for EPA-DHA:

Agence nationale de sécurité sanitaire de l'alimentation, de l'environnement et du travail (2011). Actualisation des apports nutritionnels conseillés pour les acides gras. https://www.anses.fr/fr/system/files/NUT2006sa0359Ra.pdf

The conclusion from the 2011 ANSES report is as follows:

- Epidemiological studies and intervention trials show that the consumption of fish or EPA and DHA reduces cardiovascular mortality. These effects were observed for intakes between 0.4 g/d and 1.8 g/d of long chain n-3 PUFA (EPA-DHA) in patients with vascular history, but they are less well documented for primary prevention. Therefore, a daily intake of 500 mg of EPA and DHA (0.25% of energy intake) seems justified for the general population from the perspective of cardiovascular prevention.

4) Canada suggests including the Institute of Medicine (IOM) as a RASB. Specifically, recommendations from the following IOM report should be considered for the purpose of establishing a NRV-NCD for EPA-DHA:

Committee on Nutrient Relationships in Seafood: Selections to Balance Benefits and Risks, Food and Nutrition Board (2007). Benefits for prevention of adult chronic disease. Seafood choices: balancing benefits and risks. http://www.nap.edu/catalog/11762.html

The findings from the 2007 IOM report are as follows:

[4] Norwegian Scientific Committee for Food Safety (2011). Evaluation of negative and positive health effects of n-3 fatty acids as constituents of food supplements and fortified foods. Opinion of the Steering Committee of the Norwegian Scientific Committee for Food Safety. http://www.vkm.no/dav/c7a41adb79.pdf

- "Observational evidence suggests that increased seafood consumption is associated with a decreased risk of cardiovascular deaths and cardiovascular events in the general population. Evidence is insufficient to assess if this association is mediated through an increase in EPA and DHA consumption and/or a decrease in saturated fat consumption and/or other correlates of seafood consumption."
- "Experimental studies of the effect of EPA/DHA supplements on cardiovascular mortality or cardiovascular disease have not been conducted in the general population."
- "Evidence is inconsistent for protection against further cardiovascular events in individuals with a history of myocardial infarction from consumption of EPA/DHA-containing seafood or fish-oil supplements. The protection evidenced by population (observational) studies has not been consistently observed in randomized clinical trials."
- "Based on the three recent meta-analyses of observational studies […], there appears to be a linear association between seafood consumption and primary prevention of cardiovascular disease; the committee did not find strong scientific evidence to suggest a threshold of consumption, such as two servings per week, below which seafood consumption provides no benefit and above which increasing consumption provides no additional benefits."

Paragraph 10:	"In relation to primary and secondary prevention, one CMC noted that the NRV-NCD for potassium was accepted by the CCNFSDU on the basis of its positive effect only in those individuals with pre-existing hypertension, and that this disease was sufficiently prevalent to affect public health adversely. Therefore, consistent with this precedent, the Co-Chairs consider evidence of both primary and secondary prevention to be acceptable in the establishment of an NRV-NCD for EPA + DHA for the general population.

In Canada, the target population for recommendations about food and NCD risk reduction (e.g., food health claims) is typically the general adult population which is comprised of free-living, generally healthy adults. To ensure that the results are relevant to the general adult population, only primary prevention studies among free-living, generally healthy adults are used to establish such recommendations. One of the concerns with the use of secondary prevention studies is that there is often reason to think that the effect of the food might be different in medicated, hospitalized or diseased individuals. For example, the mechanism of action might be different in healthy vs. diseased individuals, or interactions between the food and medications could affect the efficacy of the food.

In this particular case, the Co-Chairs noted that "the pathophysiology of CVD is the same, whether for a first heart attack or a second (Nestel P, et al. 2015)." To help reach consensus, Canada will not oppose majority support for the use of evidence from both primary and secondary prevention studies.

Paragraph 13:	"The following outcome is proposed for this new work: Reduction of risk of coronary heart disease mortality/fatal CHD events"

This outcome was proposed by Canada following the first consultation paper. Canada continues to support this outcome. However, Canada notes that some of the recommendations from the included reports were not based specifically on this outcome, but on cardiovascular disease (CVD). CVD is more general than coronary heart disease (CHD) and it also includes stroke. If no relationship exists between stroke and EPA-DHA, but one exists between fatal CHD and EPA-DHA, reporting the effect of EPA-DHA on CVD could dilute the effect. Reporting on more specific outcomes is usually preferred unless the relationships are the same with all the specific outcomes.

Paragraph 17:	"Three CMCs suggested that the evidence that is currently available from prospective cohort studies is largely based on the consumption of fish, not EPA + DHA in isolation. As such, a guideline supporting consumption of fish rich in omega-3 PUFAs as reported by WHO/FAO in 2010 is consistent with the evidence. The extrapolation of this evidence base to solely EPA + DHA was considered as not being consistent with the available evidence."

Canada notes that in some cases RASBs have used evidence on fish consumption to support recommendations on daily intake of EPA+DHA (e.g. WHO/FAO 2010), and in some cases, fish consumption evidence was deemed insufficient (e.g. IOM 2007). Canada is comfortable with extrapolating evidence from fish consumption to EPA+DHA intake and it does not oppose using evidence on fish consumption to support a NRV-NCD for EPA-DHA.

Paragraph 41:	"Despite the drawbacks of the meta-analyses as described above, co-chairs recommend to take into account the quantitative results of the analyses as a strong evidence in support of the proposal to establish NRV-NCD for EPA and DHA in reducing risks of coronary heart disease mortality/fatal CHD events."

Canada does not support using the meta-analyses described in the report to establish a NRV-NCD for EPA-DHA because these meta-analyses have not been commissioned by RASBs for the purposes of providing advice on daily intake values as per general principle 3.1.2.

Canada notes that an analysis of recent systematic reviews conducted in March 2015 by EVIPNet (a network sponsored by the WHO) is available and was provided by the co-chairs along with the first consultation paper. The EVIPNet 2015 report is entitled "Evidence brief of benefits of fatty acids EPA and DHA to determine a recommended intake reference value". The relevant key messages of the report are that 1) EPA and DHA probably reduce cardiovascular mortality and coronary events, and 2) its effects on the rest of cardiovascular events are unclear.

Paragraph 46:	"To address the second criterion for GP 3.2.2.1, the eWG was asked if it agreed that EPA + DHA intake is sufficiently important for public health among Codex member countries."

Canada continues to agree that the relationship between increased intakes of EPA and DHA and a decreased risk of heart disease is of global public health importance.

Paragraph 60:	"No fatty acid apart from EPA+DHA should be a matter of discussion in this document."

Canada continues to agree that the NRV-NCD should be specific to EPA and DHA combined and not include alpha-linoleic acid (ALA) because ALA is outside the scope of this work.

Paragraph 64:	"It is recommended that CCNFSDU consider a harmonized NRV-NCD for EPA and DHA of 250 mg/day, for inclusion in paragraph 3.4.4.2 NRV-NCD of the *Guidelines on Nutrition Labelling* (CAC/GL 2-1985) as presented in Appendix I."

At this time, Canada is not in a position to support the NRV-NCD proposed for EPA and DHA. Considering the differing conclusions from the various RASB reports included, Canada is of the opinion that further discussion is needed before a final recommendation can be made.

Appendix I:	"The establishment of an NRV was based on convincing/generally accepted evidence for a relationship with NCD risk as reported in the Diet, Nutrition and the Prevention of Chronic diseases. WHO Technical Report Series 916, WHO, 2003; and in the FAO/WHO Expert Consultations. Technical report Series 91 and 978, WHO 2010."

It is unclear to Canada why the three WHO reports are cited as the basis for the NRV-NCD while only one of these reports is listed in the table following paragraph 11. Canada suggests citing only the most recent or most relevant report.

OTHER CONCERNS WITH THE REPORT

Appendix II:	Item 1. Summary of World Health Organisation (2003) Joint WHO/FAO Expert Consultation on Diet, Nutrition and the Prevention of Chronic Disease (2002: Geneva, Switzerland) Technical Report Series 916. "From these observations, it was considered likely that dietary EPA + DHA are beneficial for secondary prevention, i.e. for those with previous CHD."

Canada does not agree with the sentence reproduced above because it seems to be an interpretation that goes beyond the statements of the WHO report. Canada suggests removing this sentence because Appendix II is meant to summarize the information and authoritative statements from the various WHO reports.

Appendix III:	Norwegian Scientific Committee for Food Safety/Nordic Council of Minister Explanation of how the RASB "2) provides independent and transparent authoritative scientific advice through primary evaluation of the scientific evidence upon request": "[…] Although the mechanisms of actions are not fully understood and there is less evidence for primary prevention than secondary prevention […]"

Canada notes that the evidence and recommendations from the Norwegian report are discussed in the table in Appendix III. Item 2 of the table should instead be about how the RASB provides authoritative scientific

advice because the table is meant to describe how the nominated RASBs meet the components of the RASB definition.

Appendix III:	Norwegian Scientific Committee for Food Safety/Nordic Council of Minister RASB Publication: "Nordic Council of Ministers (2013). Nordic Nutrition Recommendations 2012 – Part 1 (5th ed). Nord 2013:009. [online] Available at http://norden.org/en/publications/publikationer/nord-2013-009" Recommendation: "At least 1 per cent of energy intake, 222 mg/day based on 2,000 kcal diet"

Canada notes that RASB publication and the recommendation cited in Appendix III for the Norwegian Scientific Committee for Food Safety/Nordic Council of Minister differs from the publication and recommendation in the table following paragraph 11. It is unclear which publication(s) has/have been used to support the relationship between EPA-DHA and fatal CHD events.

EGYPT

Egypt Supports proposed draft NRV-NCD for EPA and DHA of at least 250 mg EPA + DHA per day for inclusion to Section 3.4.4.2 of the *Guidelineson Nutrition Labeling*(CAC/GL 2-1985). Also supports the inclusion of the additional footnote, " The establishment of an NRV was based on convincing/generally accepted evidence for a relationship with NCD risk as reported in the Diet, Nutrition and Prevention of Chronic Diseases.

- Strong scientific evidence and support from Recognized Authoritative Scientific Bodies (RASBs), including the European Food Safety Authority (EFSA), THE National Institute of Health and Nutrition – Japan (NIHN), as well as two World Health Organization Technical Report Series (916 and 91) and the joint FAO/ WHO Expert Consultation on the risks and benefits of fish consumption (2010), support the establishment of a NRV for EPA and DHA

The proposal meets the conditions established in the Codex General Principles for Establishing NRVs.

JAPAN

We are pleased to submit the following general comments on Proposed Draft NRV-NCD for EPA and DHA Long Chain Omega-3 Fatty Acids for consideration at the forthcoming 37th Session of the Codex Committee on Nutrition and Foods for Special Dietary Uses.

General Comments

The report of the Joint FAO/WHO Expert Consultation (2010) stated that fish consumption lowers mortality from coronary heart disease; however, Japan considers that it is not appropriate to extrapolate into solely EPA + DHA on the basis of this evidence.

Also, Japan would like to note that it is unclear whether the GRADE classification for the determination of the evidence level has been done by qualified personnel. To review the strength and level of the available evidence accurately, Japan would like to propose that CCNFSDU request a third-party organization such as the joint FAO/WHO Expert Meetings on Nutrition (JEMNU).

After receiving the result from the third-party organizations, CCNFSDU should have discussion again to reach the consensus among members.

NEW ZEALAND

General Comments

New Zealand would like to thank Chile and Russia for chairing the electronic working group (eWG) and preparing the agenda paper on the draft NRV-NCD for EPA and DHA.

At this point in time New Zealand does not consider that the relationship between DHA and EPA and cardiac death is sufficiently characterized to establish an NRV-NCD.

Specific Comments

Paragraph 9: Recognised Authoritative Scientific Bodies

New Zealand notes that additional RASBs were identified by the eWG, namely the National Health and Medical Research Council (NHMRC). The NHMRC should be included in this list of accepted RASBs as it was supported by at least three CMCs, meets the criteria for a RASB, and has previously been accepted by the Committee as a RASB.

Paragraph 11: GP 3.2.2.1.

New Zealand does not consider that the evidence for the relationship between EPA and DHA and non-communicable disease risk meets the requirements of GP 3.2.2.1. To meet the requirements of GP 3.2.2.1 the relationship between the nutrient and non-communicable disease must be considered "convincing" as defined FAO/WHO report were used Diet, Nutrition and the Prevention of Chronic Diseases. WHO Technical Report Series 96. WHO, 2003:

The definition contained within the FAO/WHO report is as follows:

> Convincing evidence. Evidence based on epidemiological studies showing consistent associations between exposure and disease, with little or no evidence to the contrary. The available evidence is based on a substantial number of studies including prospective observational studies and where relevant, randomized controlled trials of sufficient size, duration and quality showing consistent effects. The association should be biologically plausible.

New Zealand does not support the view that the totality of evidence for DHA and EPA is consistent or as strong as indicated in the Agenda paper. Although prospective cohort studies have reported an association with lower risk of cardiovascular death this has been limited to studies reporting consumption of fatty fish.

The WHO/FAO guidelines are based on the evidence of consumption of fish rich in long chain omega-3 fatty acids. An NRV-NCD based on isolated fatty acids EPA and DHA is not warranted at this time as totality of evidence does not support the association between EPA and DHA in isolation with the reduction of cardiac death or other diet-related noncommunicable disease. We also support the questions raised to clarify whether health effects attributed to fish consumption can be also attributed to EPA and DHA consumption from any food source.

Of the identified RASBs, the NHMRC states that the relationship between omega-3 long chain polyunsaturated fats and cardiovascular benefits is "suggestive". This statement highlights the lack of consistency of effect in randomised controlled trials. Early high profile studies demonstrated significant reductions in cardiac death, yet these effects have not been replicated in several more recent high quality, large, well designed randomized controlled trials. The EVIPnet meta-analysis which was recently conducted also notes that the evidence regarding EPA and DHA and cardiovascular disease is "probable" but noting that the quality of evidence is variable, and that for the only high quality study conducted a neutral impact was shown.

For this NRV-NCD to proceed it must demonstrate that the effects across both prospective observational and randomized controlled trials show consistent effects with little or no evidence to the contrary. It is our view that there is significant evidence to the contrary and a lack of consistency in effect.

PARAGUAY

Bearing in mind that the definition of the NRV was based on convincing / generally accepted evidence that there is a relation with the risk of NCD, according to the "Diet, Nutrition and the Prevention of Chronic Diseases" report (WHO technical report series 916; WHO, 2003) and the joint FAO/WHO expert consultation on diet (WHO technical report series 91 and 978; WHO, 2010), **we present no objections to and approve the said value**.

PHILIPPINES

The Philippines supports the proposed Draft NRV-NCD for EPA and DHA Long Chain Omega-3 Fatty Acids at 250 mg based onconvincing/generally accepted evidence showing the beneficial relationship between the long chain omega-3 fatty acids EPA plus DHA in the diet as well as the reduction ofrisk ofcoronary heart disease (CHD) mortality/fatal CHD events.It was concluded that the totality of the evidence is convincing for a risk-reducing effect of EPA +DHA on CHD.

Rationale

Wesupport the proposed NRV-NCD for EPA and DHA Long Chain Omega-3 Fatty Acids at 250 mg based on consistent and recent scientific evidence. The Joint FAO WHO Expert Consultions in 2010 found convincing evidence that moderate consumption of oily fist lowers mortality from coronary heart disease (CHD) in general population. The beneficial effect in increasing the dietary intake of EPA and DHA Long Chain Omega 3 Fatty acids will have substantial global benefits in particular taking into account the gap between current consumption and recommendations.

The omega-3 index (O3I) or the sum of EPA+DHA content in red blood cell (RBC) membranes as a biomarker of n-3 FA status showed high correlation with myocardial EPA+DHA content. An O3I of ≥8% has been recommended as the cardio-protective level for reduced risk of primary cardiac arrest, sudden cardiac death, coronary atherosclerosis, and acute coronary syndrome. Numerous intervention trials indicated that higher intakes of DHA plus EPA can favorably influence several risk factors for CVD and fatal heart attacks

including reductions in blood pressure, fasting triglyceride levels in the circulation, lowering of the triglyceride: HDL-cholesterol ratio, lowering of blood viscosity, reduction in blood platelet reactivity and other thrombogenic risk factors. The meta-analysis evidence from several RCTs indicated that provision of EPA+DHA at 2g or more per day may reduce both SBP and DBP. The strongest benefits were noted in hypertensive individuals without antihypertensive medication. Randomized control trials (RCTs) in the context of secondary prevention also indicated that the consumption of EPA plus DHA is protective at doses <1 g/d. The therapeutic effect appears to be due to suppression of fatal arrhythmias rather than stabilization of atherosclerotic plaques. From a clinical and public health perspective, provision of EPA+DHA may lower BP & other risk factors which could ultimately reduce the incidence of CVD (Miller et al 2014; Flock et al, 2013, Breslow, 2006). Hence, the proposed draft NRV-NCD for EPA and DHA is acceptable since it is based on scientific judgement and consensus.

We are of the opinion that the evidence of both primary and secondary prevention is acceptable in the establishment of an NRV-NCD for EPA+DHA for the general population .

Thus, it is recommended that CCNFSDU consider a harmonised NRV-NCD for EPA and DHA of 250 mg/day, for inclusion in paragraph 3.4.4.2 NRV-NCD of the Guidelines on Nutrition Labelling (CAC/GL 2-1985).

As suggested during last consultations, NRVs-R should be considered as well for EPA + DHA for pregnant and lactating women. Consequently in addition to the amount of DHA and EPA provided with daily diet, specifically to pregnant and lactating women population, 100 to 200 mg of preformed docosahexaenoic acid should be added during pregnancy and lactation to compensate for oxidative losses of maternal dietary docosahexaenoic acid and accumulation of docosahexaenoic acid in body fat of the fetus/infant.

References

Flock MR, Skulas-Ray AC, Harris WS, Etherton TD, Fleming JA and Kris-Ehterton PM. Determinants of Erythrocyte Omega-3 Fatty Acid Content in Response to Fish Oil Supplementation: A Dose-Response Randomized Controlled Trial. Journal of the American Heart Association. 10 (1161):1-12.

Miller PE, Elswyk MV, Alexander DD. (2014).Long Chain Omega-3 Fatty Acids Eicosapentanoic and Docosahexanoic Acid and Blood Pressure: A Meta-Analysis of Randomized Controlled Trial. American Journal of Hypertension 27 (7): 885-893.

WHO Technical Report Series 916, WHO, 2003; and in the FAO/WHO Expert Consultations. Technical report Series 91 and 978, WHO, 2010.

UNITED STATES OF AMERICA

General Comments:

The United States believes that a final recommendation for a NRV-NCD for EPA and DHA is premature at this time and that further discussion is needed.

Specific Comments:

Paragraph 9. "The list of accepted Recognized Authoritative Scientific Bodies (RASB) is: European Safety Authority (EFSA), National Institute of Health and Nutrition, Japan, Nordic Council of Ministers/Norwegian Scientific Committee"

The United States agrees with the eWG Chairs' proposal "to focus their attention to RASBs already accepted by CCNFSDU and nominated by the eWG."

The United States notes that the National Health and Medical Research Council (NHMRC) was accepted by the eWG as a RASB and recommends that the 2011 NHMRC review of the evidence to address targeted questions to inform the revision of the Australian Dietary Guidelines be considered by the eWG. The *Agence Nationale de Sécurité Sanitaire de l'Alimentation, de l'Environnement et du Travail* (ANSES) was also nominated by members of the eWG and was not included in the list of accepted RASBs.

The U.S. supports consideration of the 2011 NHMRC and 2011 ANSES reports. A 2006 NHMRC report is cited in paragraph 19; however the more recent 2011 NHMRC report providing primary evaluation of literature is not included. The 2011 NHMRC report provided suggestive but not conclusive evidence for fish consumption and reduced risk of mortality from cardiovascular disease and reduced incidence of cardiovascular disease. The ANSES report may also provide primary evaluation but requires translation for evaluation by all eWG members.

The United States also suggests including the Institute of Medicine (IOM) as a RASB and considering the 2005 *IOM Dietary Reference Intakes for Energy, Carbohydrate, Fiber, Fat, Fatty Acids, Cholesterol, Protein, and Amino Acids (Macronutrients) and the 2007 IOM Seafood: Selections to Balance Benefits and Risks* reports. The 2005 IOM macronutrient report did not establish a dietary reference intake (DRI) for EPA and/or

DHA and the 2007 IOM seafood report found that evidence is insufficient to assess whether increased seafood consumption associated with decreased risk of cardiovascular deaths in the general population is attributable to EPA and DHA consumption.

The NHMRC and IOM reports' conclusions differ from the conclusions of the RASBs listed in paragraph 9. Consideration of these reports is necessary to evaluate the totality of evidence and meet the criteria in GP 3.2.2.1.

The references for the reports cited above are provided below:

National Health and Medical Research Council (2011). A review of the evidence to address targeted questions to inform the revision of the Australian Dietary Guidelines.
https://www.nhmrc.gov.au/_files_nhmrc/file/publications/n55d_australian_dietary_guidelines_evidence_report.pdf

Agence nationale de sécurité sanitaire de l'alimentation, de l'environnement et du travail (2011). Actualisation des apports nutritionnels conseillés pour les acides gras. https://www.anses.fr/fr/system/files/NUT2006sa0359Ra.pdf

IOM Dietary Reference Intakes for Energy, Carbohydrate, Fiber, Fat, Fatty Acids, Cholesterol, Protein, and Amino Acids (Macronutrients) (2005)

http://www.nap.edu/catalog/10490/dietary-reference-intakes-for-energy-carbohydrate-fiber-fat-fatty-acids-cholesterol-protein-and-amino-acids-macronutrients

IOM Seafood Choices: Balancing Benefits and Risks (2007)

http://www.nap.edu/catalog/11762/seafood-choices-balancing-benefits-and-risks

Paragraph 10. "…the Co-Chairs consider evidence of both primary and secondary prevention to be acceptable in the establishment of an NRV-NCD for EPA + DHA for the general population."

The United States notes that the outcome of primary reduction of death risk from coronary heart disease (CHD) initially proposed by the eWG chairs is no longer being considered as the outcome for this work (paragraph 13). The United States considers that intervention and observational studies in healthy populations (i.e., primary prevention) provide the most persuasive evidence for a relationship between EPA and DHA omega-3 fatty acids and reduced risk of CHD mortality/fatal CHD events for the general population.

The United States views evidence for EPA and DHA omega-3 fatty acids and reduced risk of CHD mortality in CHD patients (i.e., secondary prevention) applicable to the general population when: (1) the mechanism(s) for the reduction in risk measured in the diseased populations are the same as the mechanism(s) for risk reduction effects in non-diseased populations and (2) EPA and DHA omega-3 fatty acids affect these mechanisms in the same way in both diseased and healthy people.

Paragraph 11: Norwegian Scientific Committee for Foods Safety/Nordic Council of Ministers (NSCFS/NCM) 2011 recommendation "0.25 g to 0.5 g of EPA and DHA daily decreases the risk of mortality from coronary Heart disease and sudden cardiac death"

The United States notes that the NSCFS/NCM 2011 report cites the 2010 EFSA report in providing the Nordic recommendation "for adults on scientific evidence indicating that oily fish consumption (1-2 meals per week or dietary supplements containing EPA and DHA and equivalent to a range of 0.25 to 5.0 g/d of EPA and DHA daily) decrease the risk of mortality form CHD and sudden cardiac death." The citation suggests that the Norwegian daily EPA and DHA recommendation is based on EFSA's recommendation rather than their own primary evaluation of the scientific evidence, thus the U.S. suggests not considering this report.

Paragraph 13: "…based on the FAO/WHO 2010 reports and the EFSA 2010 scientific opinion, the following outcome is proposed for this new work: Reduction of risk of coronary heart disease mortality/fatal CHD events"

The United States does not oppose narrowing the proposed outcome to CHD mortality and fatal CHD events.

Paragraph 17: "Three CMC's suggested that the evidence that is currently available from prospective cohort studies is largely based on the consumption of fish, not EPA + DHA in isolation. As such, a guideline supporting consumption of fish rich in omega-3 PUFAs as reported by WHO/FAO in 2010 is consistent with the evidence. The extrapolation of this evidence base to solely EPA + DHA was considered as not being consistent with the available evidence."

Observational studies of fish consumption provide only an estimated intake of EPA and DHA omega-3 fatty acids from fish consumption rather than a direct measure and indicate only an association with disease risk, and not direct causality of disease risk. In addition, observational studies cannot separate the effect of EPA and DHA omega-3 fatty acids from the effects of other food components, and therefore it is not clear whether

any purported benefit is related to the EPA and DHA omega-3 fatty acids or to other dietary factors. Observational studies provide only supportive rather than direct evidence for a causal relationship.

The United States considers that intervention studies demonstrating that EPA and DHA omega-3 fatty acids reduced CHD mortality/fatal events of CHD in healthy populations provide the most persuasive evidence for a relationship between EPA and DHA omega-3 fatty acids and reduced risk of CHD mortality/fatal events of CHD. The Grades of Recommendation, Assessment, Development and Evaluation (GRADE) approach referenced in the *2012 WHO Handbook for Guideline Development* in the *Guidelines on Nutrition Labelling* for assessing the quality of evidence assigns a high quality rating when evidence is available from randomized controlled trials, and data from randomized controlled trials were included in the evidence for setting NRV-NCDs for saturated fat, sodium, and potassium.

Paragraph 41: "Despite the drawbacks of the meta-analyses as described above, co-chairs recommend to take into account the quantitative results of the analyses as strong evidence in support of the proposal to establish NRV-NCD for EPA and DHA in reducing risks of coronary heart disease mortality/fatal CHD events."

The United States supports the General Principles for establishing the NRV-NCDs based on the totality of evidence from reports from agreed upon RASBs, and thanks the Co-Chairs for their efforts in discussing the additional scientific articles and meta-analyses in paragraphs 30 – 40. We note, however, that these meta-analyses do not meet requirements of CP 3.1.2 and are not considered reports from RASBs.

Paragraph 46: "To address the second criterion for GP 3.2.2.1, the eWG was asked if it agreed that EPA + DHA intake is sufficiently important for public health among Codex member countries."

The United States agrees that supportive but not conclusive evidence suggests that EPA and DHA intakes are of global public health importance.

Paragraph 64: "It is recommended that CCNFSDU consider a harmonized NRV-NCD for EPA and DHA of 250 mg/day, for inclusion in paragraph 3.4.4.2 NRV-NCD of the *Guidelines on Nutrition Labelling* (CAC/GL 2-1985) as presented in Appendix I."

At this time, the United States does not support the NRV-NCD proposed for EPA and DHA based on the available information considered.

The United States supports the General Principles for establishing the NRV-NCDs based on the totality of evidence from reports from agreed upon RASBs. The United States considers that further discussion is needed to evaluate the totality of available evidence before issuing a final recommendation for a NRV-NCD for EPA and DHA.

The United States notes that footnote 11 in Appendix I cites three WHO reports while the Table in paragraph 11 cites only one. The United States suggests consistency in footnote 11 with the dietary intake(s) recommended in the Table in paragraph 11 to avoid confusion. There also should be clarification on whether the outcomes reported for each WHO report in footnote 11 match the outcome of "reduction of risk of coronary heart disease mortality/fatal CHD events" proposed in paragraph 13.

ELC - Federation of European Specialty Food Ingredients Industries

We share the fact that evidence of both primary and secondary prevention is acceptable in the establishment of an NRV-NCD for EPA+DHA for the general population.

We agree with the general comment on paragraph 44 and the fact that meta-analyses are rather consistent. We believe that a reduction of 9% in cardiac mortality rate (figure derived from the meta-analyses) is significant and demonstrate the key role of EPA+DHA in reduction of cardiac mortality.

As indicated in paragraph 47, we also firmly believe that increasing the dietary intake will have substantial global benefits in particular taking into account the gap between current consumption and recommendations.

The necessary intake could be subject of scientific discussion. We believe intakes between 250 and 500 mg/day will bring this benefit. The EU approved claim for maintenance of normal heart function is linked to a daily intake of 250 mg EPA+DHA. Therefore, choosing this value is consistent with a recent recommendation. EPA+DHA have additional benefits for higher levels.

We support the setting of a harmonized NRV-NCD for EPA+DHA of 250 mg/day for inclusion in paragraph 3.4.4.2. NRV-NCD as described in Appendix I.

FoodDrinkEurope

General comments

We share the fact that evidence of both primary and secondary prevention is acceptable in the establishment of an NRV-NCD for EPA+DHA for the general population and support the inclusion of an NRV-NCD for EPA and DHA of 250 mg per day in paragraph 3.4.4.2 as described in Appendix I of the document.

According to EFSA's Scientific Opinion on EPA and DHA, an intake of 250 mg per day of EPA plus DHA appears to be sufficient for primary prevention in healthy subjects. This value is as well supported by the FAO/WHO conclusions reported in this document, which stated that moderate consumption of fatty fish (one or two 100 g servings per week) would provide maximum benefit (two servings provide about 250 mg EPA + DHA); it was concluded that the totality of the evidence is convincing for a risk-reducing effect of EPA +DHA on CHD.

We agree with the general comment on paragraph 44 and the fact that meta-analyses are rather consistent. We believe that a reduction of 9% in cardiac mortality rate (figure derived from the meta-analyses) is significant and demonstrates the key role of EPA+DHA in reduction of cardiac mortality. As indicated in paragraph 47, we also firmly believe that increasing the dietary intake will have substantial global benefits in particular taking into account the gap between current consumption and recommendations.

Detailed comments

We would like to provide a few detailed comments on the summary document, which are important to be considered as the document will be kept as a reference for the discussion:

- Page 1, point 7: the second reference should be FAO instead of WHO;
- Page 2, point 9: some previously proposed RASBs have been omitted, despite their acceptance by most of the responders: Australia NHMRC, IOM, New Zealand. In addition, ANSES was proposed as well. We would like to request to add these back, and discuss and analyse them as well, for a complete analysis;
- Page 4, point 14: first sentence: this should be … *"accepted for the benefit described in bold in the paragraph **13**"* instead of 14;
- Page 5 point 24: the level of evidence for these observational study conclusions should be added;
- Page 5, point 25: the last sentence is not very clear, and should be rephrased;
- Page 7, point 41: the conclusion of this point (and the fact that quality of studies is not taken into account) seems is in contradiction to what is stated in point 42: *"Overall, a meta-analysis is only as good as the studies it pools together."* This should be clarified.

GOED – Global Organization for EPA and DHA Omega-3s

General Comments

GOED supports the proposed draft NRV-NCD of 250 mg/day for EPA+DHA for inclusion in the *Guidelines on Nutrition Labelling* (CAC/GL2-1985). GOED notes, however, that there are Codex Member Countries with reservations about the adoption of a NRV-NCD for EPA+DHA. GOED will be present at the upcoming CCNFSDU meeting and looks forward to an open dialogue with all Codex Member Countries and Observers.

There is one issue that GOED would like to address in advance of the November meeting and that concerns comment regarding whether the primary prevention of CHD is attributable to fish consumption versus EPA+DHA specifically. While the number of omega-3 primary prevention trials is extremely limited, with the most notable study being JELIS.[5], other evidence exists supporting the primary prevention benefits of EPA and DHA for the risk reduction of cardiovascular disease in the general, healthy population.

The proposed draft NRV-NCD mentioned that Chowdhury et al., 2014[6] reported no statistically significant effects of EPA+DHA supplementation on either cardiovascular mortality or major cardiovascular outcomes, but there is more to the story. Specifically, EPA+DHA is associated with a statistically significant, 25% risk reduction for coronary outcomes, based on circulating blood composition in prospective cohort studies.

[5] Yokoyama M Origasa H Matsuzaki M, et al. (2007). Effects of eicosapentaenoic acid on major coronary events in hypercholesterolaemic patients (JELIS): a randomised open-label, blinded endpoint analysis. Lancet. 369:1090-8.
[6] Chowdhury R, Warnakula S, Kunutsor S, et al. Association of dietary, circulating and supplement fatty acids with coronary risk: a systematic review and meta-analysis. *Ann Intern Med*. 2014;160:398-407.

Globally, in 2010, the attributable burden of a diet low in seafood (rich source of EPA+DHA) omega-3s was estimated to be 1.1% of global disability-adjusted life-years (DALYs).[7,8] It's important to note that this is a large number - 28.2 million DALYs. In addition, low seafood omega-3 intake accounted for a staggering 1.4 million deaths around the world in 2010, representing an almost 40% increase from 1990. A comparison of deaths from low seafood omega-3s in developing versus developed countries reveals that the number of deaths has increased in developing countries and decreased in developed countries. In the United States alone, low EPA+DHA intake accounts for 72,000-96,000 CVD deaths per year.[9] While this is specific to the United State, there's no reason to believe that the number of deaths wouldn't be similar in other countries with sub-optimal omega-3 intakes.

You, the co-chairs, have made it clear that evidence of both primary and secondary prevention is acceptable in the establishment of a NRV-NCD for EPA+DHA for the general population. This is based on the NRV-NCD for potassium which was accepted by the CCNFSDU on the basis of its positive effect only in those individuals with pre-existing hypertension and that this disease was sufficiently prevalent to affect public health adversely.

With this in mind, GOED brings to your attention two meta-analyses not mentioned in paragraphs 30-39 of the proposed draft NRV-NCD.

1) The first is a 2012 systematic review with random effects meta-analysis and mixed effects dose-response meta-regression.[10] Included were RCTs of EPA and DHA supplementation and large prospective cohorts quantifying EPA or DHA intake. This systematic review with meta-analysis was prepared for the Agency for Healthcare Research and Quality (AHRQ), a U.S. government funded agency. The results are as follows:

- In RCTs, the summary relative risks for all-cause mortality (17 trials, 51,264 patients) and cardiovascular mortality (14 trials, 48,500 patients) were 0.95 (95% confidence interval, CI: 0.89, 1.01) and 0.89 (95% CI, 0.83, 0.96), respectively, with no evidence for heterogeneity. Note: The results for all-cause mortality just missed statistical significance, while the results for cardiovascular mortality were statistically significant with an 11% risk reduction.
- In dose-response meta-regressions, mean EPA and DHA intake up to 0.20 grams daily was associated with a statistically significant decreased risk of cardiac, cardiovascular, or sudden cardiac death (odds ratio 0.64 per 0.20 grams average daily intake, 95% CI: 0.46, 0.89—data from 7 cohorts, 123,122 participants).

2) The second is a meta-analysis of 11 RCTs on omega-3 supplementation.11 Casula et al., 2013 reported statistically significant protective effects for cardiac death (RR, 0.68; 95% CI, 0.56 to 0.83), sudden death (RR, 0.67; 95% CI, 0.52 to 0.87), and myocardial infarction (RR, 0.75; 95% CI, 0.63 to 0.88).

IADSA – International Alliance of Dietary/ Food Supplement Associations

IADSA has considered the proposal of the eWG to establish NRV-NCD for EPA-DHA long chain fatty acids and we have reviewed the science to underpin it very carefully.

IADSA is of the view that there is consistent and convincing/generally accepted evidence to support the beneficial relationship between the long chain omega-3 fatty acids EPA+DHA and the reduction of risk of CHD mortality/fatal CHD events. IADSA also believes that the requirements to meet the Codex General Principles for the establishing of NRV-NCD for the general population have been fully fulfilled.

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[7] Engell RE, Sanman E, Lim SS, Mozaffarian D. Seafood omega-3 intake and risk of coronary heart disease death: an updated meta-analysis with implications for attributable burden. *Lancet*. 2013;381:S45. http://www.thelancet.com/journals/lancet/article/PIIS0140-6736(13)61299-4/fulltext

[8] Lim SS, Vos T, Flaxman AD, et al. A comparative risk assessment of burden of disease and injury attributable to 67 risk factors and risk factor clusters in 21 regions, 1990–2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet*. 2012;380:2224-60.

[9] Danaei G, Ding EL, Mozaffarian D, Taylor B, Rehm J, Murray CJ, Ezzati M. The preventable causes of death in the United States: Comparative risk assessment of dietary, lifestyle, and metabolic risk factors. *PLoS Med*. 2009;6:e1000058.

[10] Trikalinos TA, Lee J, Moorthy D, Yu WW, Lau J, Lichtenstein AH, Chung M. Effects of Eicosapentanoic Acid and Docosahexanoic Acid on Mortality Across Diverse Settings: Systematic Review and Meta-analysis of Randomized Trials and Prospective Cohorts. Technical Review 17, Vol. 4. (Prepared by the Tufts Medical Center Evidence-based Practice Center under Contract No. HHSA 290-2007-10055-1.) AHRQ Publication No. 12-EHC040-EF. Rockville, MD: Agency for Healthcare Research and Quality; February 2012.

[11] Casula M, Soranna D, Catapano AL, Corrao G. Long-term effect of high dose omega-3 fatty acid supplementation for secondary prevention of cardiovascular outcomes: A meta-analysis of randomized, placebo controlled trials. *Atheroscler Suppl*. 2013;14:243-51.

We therefore agree with the conclusions and recommendations of the report and specifically we support the recommendation to establish a harmonized NRV-NCD for EPA+DHA of 250 mg per day for the general population for inclusion in paragraph 3.4.4.2 of the Guidelines on Nutrition Labelling (CAC/GL 2-1985) as presented in Appendix I.

We would like to thank the Chairs for their extensive work and literature review and for addressing the issues raised by the members of the eWG over the consultation period. IADSA believes that this work is an important step forward in Codex and an important public health initiative consistent with the results of international expert consultations and dietary recommendations.

ICGMA – International Council of Grocery Manufacturer Associations

Proposed Draft NRV-NCD for EPA and DHA for inclusion in section 3.4.4.2 of the *Guidelines on Nutrition Labelling* (CAC/GL 2-1985) can be found in bold below. 3.4.4.2 NRVs - NCD <u>Intake levels not to exceed</u> Saturated fatty acids 20 g [8,9] Sodium 2000 mg [10] <u>Intake levels to achieve</u> Potassium 3500 mg [10] **Eicosapentaenoic acid (EPA)** **and Docosahexaenoic acid (DHA) 250 mg [11]** [8] This value is based on the reference energy intake of 8370 kilojoules/2000 kilocalories. [9] The selection of this nutrient for the establishment of an NRV was based on "convincing evidence" for a relationship with NCD risk as reported in the report Diet, Nutrition and the Prevention of Chronic Diseases. WHO Technical Report Series 916. WHO, 2003. [10] The section of these nutrients for the establishment of an NRV was based on "high quality" evidence for a relationship with a biomarker for NCD risk in adults as reported in the respective 2012 WHO Guidelines on sodium and potassium intake for adults and children. [11] **The establishment of an NRV was based on convincing/generally accepted evidence for a relationship with NCD risk as reported in the Diet, Nutrition and the Prevention of Chronic Diseases. WHO Technical Report Series 916, WHO, 2003; and in the FAO/WHO Expert Consultations.** Technical report Series 91 and 978, WHO, 2010.	ICGMA supports the proposed draft NRV-NCD for EPA and DHA of at least 250 mg EPA + DHA per day for inclusion to Section 3.4.4.2 of the *Guidelines on Nutrition Labelling* (CAC/GL 2-1985). ICGMA also supports the inclusion of the additional footnote, "The establishment of an NRV was based on convincing/generally accepted evidence for a relationship with NCD risk as reported in the Diet, Nutrition and Prevention of Chronic Diseases. WHO Technical Report Series 916, WHO, 2003; and in the FAO/WHO Expert Consultations. Technical Report Series 91 and 978, WHO, 2010." • Strong scientific evidence and support from Recognized Authoritative Scientific Bodies (RASBs), including the European Food Safety Authority (EFSA), the National Institute of Health and Nutrition – Japan (NIHN), the Norwegian Scientific Committee for Food Safety/Nordic Council of Ministers, as well as two World Health Organization Technical Report Series (916 and 91) and the Joint FAO/WHO Expert Consultation on the risks and benefits of fish consumption (2010), support the establishment of a NRV for EPA and DHA for the general population (ages 4+). • There is convincing and generally accepted evidence of the risk-reducing effect of EPA + DHA on Coronary Heart Disease (CHD) in the general population. • The risk of adverse effects in consuming EPA and DHA have not been seen, with many populations consuming minimal levels. EFSA concluded that intakes up to about 5 g/day do not cause adverse effects (2012). • The proposal meets the conditions established in the Codex General Principles for Establishing NRVs.

IDF – International Dairy Federation

IDF has made the following comments:

- It is difficult in practice to follow recommendations for a mix of nutrients i.e. a single figure for a combination of DHA and EPA. Can this be interpreted that 250mg of DHA alone would be sufficient, or 249g DHA plus 1g EPA, or should it be interpreted that this is 50:50? Taking this one step further, how would NIPs be labelled – EPA/DHA as a single figure?
- The proposed NRV will only be for the general population to reduce the risk of CVD. I.e., these are not recommendations specifically relating to other health benefits such as growth and development, cognition, etc. How do these specific recommendations for CVD relate to recommendations for DHA

for cognitive development in early life defined by other organisations such as EFSA, will CODEX cover this separately?

- The recommendation relating to EPA/DHA for primary prevention is mainly from observational studies looking at fish intake and CVD outcomes, and from secondary prevention RCTs using EPA/DHA supplements. A few codex member countries have raised their concerns that using observational data that link fish intake to CVD does not allow for conclusions to be made on EPA/DHA, but rather supports the beneficial effect of fish in the diet and that recommendations should relate to fish. We tend to agree with them, especially because more recent RCTs have found no benefit of EPA and DHA in secondary prevention trials, although possibly use of modern treatment for CVD may have not been sufficiently controlled for in these studies. This is raised in the document.
- Discussion around feasibility of the recommendations is missing, in particular in relation to sustainability of fish stocks. The experts of nutrition and health division examined suitability of the intake level of DHA and EPA described in Appendix I, considering Japanese intake level. It has been concluded to approve the intake level.
- There are no further comments to the draft.