CODEX ALIMENTARIUS COMMISSION E

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World Health Organization

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Agenda Item 4b **CX/NFSDU 16/38/5**

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

Thirty-eighth Session

Hamburg, Germany

5 – 9 December 2016

PROPOSED DRAFT ADDITIONAL OR REVISED NUTRIENT REFERENCE VALUES FOR LABELLING PURPOSES IN THE *GUIDELINES ON NUTRITION LABELLING* (VITAMIN D AND THE DIETARY EQUIVALENTS AND CONVERSION FACTOR FOR VITAMIN E)

COMMENTS AT STEP 3

Comments of Argentina, Brazil, Canada, Costa Rica, Cuba, United States of America, ELC and ISDI

ARGENTINA

Argentina considers it appropriate to postpone the review of the NRV-R for vitamin D until the next meeting when the conclusions of the EFSA are available.

With respect to the conversion factors for vitamin E, it accepts the proposal for equivalence with RRR-alpha tocopherol.

BRAZIL

SPECIFIC COMMENTS

Brazil reiterates its opinion expressed in CX/NFSDU 15/37/4 Add.1. We would prefer using the DIRV of 10µg based on the Nordic countries recommendations.

We also support adoption of a footnote to the NRV-R for vitamin D which would clarify that the value is based on minimal sunlight exposure. Therefore, it may not be applicable for all countries.

CANADA

GENERAL COMMENTS

In response to the 2015 decision of the Committee to postpone a recommendation for vitamin E dietary equivalents and conversion factors until the 38th session due to a lack of consensus, Canada appreciates the opportunity to provide the following input.

SPECIFIC COMMENTS

Canada re-iterates its position in supporting recommendation 14 from the NRV-R eWG report (CX/NFSDU 15/37/4) from the 37th session of CCNFSDU.

(A) Canada supports inserting an entry for vitamin E in the second table to paragraph 3.4.4.1 of the Guidelines.

(B) Canada supports including α-tocopherol as the active form of vitamin E occurring naturally in food rather than applying dietary equivalents.

(C) Canada supports limiting the information to key examples by only showing three common forms of vitamin E that are added.

Canada supports the position of the most recently published reports of RASBs (EFSA 2015, Nordic Council 2012, and Japanese NIHN 2012) and of the IOM (2000) that only natural *RRR*-α-tocopherol, just the 2*R*-stereoisomers of synthetic all-rac-α-tocopherol, and their esters have vitamin E activity and thus only these forms should be considered in setting an NRV-R for vitamin E.

Commercially available forms of α-tocopherol include natural 2*R*,4′*R*,8′*R*-α-tocopherol, the synthetic racemate all-rac-α-tocopherol that contains in equal proportions the eight stereoisomers of α-tocopherol (*RRR*-, *RRS*-, *RSR*-, *RSS*- and their enantiomers *SSS*-, *SSR*-, *SRS*-, *SRR*-), and their esterified forms.

Regarding α-tocopherol vs. β-, γ- and δ-tocopherols and the α-, β-, γ- and δ-tocotrienols, while they all have antioxidant bioactivities they are not qualitatively or quantitatively identical to α-tocopherol.

As explained in the EFSA (2015) Scientific Opinion on Dietary Reference Values for vitamin E as α-tocopherol, which supports the position established by IOM (2000), only the naturally occurring *RRR*-α-tocopherol is considered to be the physiologically active vitamer, as blood α-tocopherol concentrations are maintained by the preferential binding of α-tocopherol (compared to other tocopherols or tocotrienols) by the α-tocopherol transfer protein. Plasma vitamin E concentrations depend upon the secretion of vitamin E from the liver by hepatic α-tocopherol transfer protein, and thus, the liver, not the intestine, discriminates between tocopherols and is responsible for the preferential plasma enrichment with α-tocopherol.

With regard to the vitamin E activity of the stereoisomers of α-tocopherol, only the 2*R*-α-tocopherol stereoisomers (i.e., *RRR*-, *RRS*-, *RSR*-, *RSS*-) were found to meet human vitamin E requirements because the 2*S*-stereoisomers (i.e., *SSS*-, *SSR*-, *SRS*-, *SRR*-) present in all-rac-α-tocopherol possess low affinity to the hepatic α-tocopherol transfer protein and are rapidly metabolised in the liver. Since the 2*S*-stereoisomers of α-tocopherol that constitute the other half of all-rac-α-tocopherol are not maintained in human plasma or tissues for a physiologically significant period of time, they are not included in the definition of active components of vitamin E for humans.

The Nordic Council (2012) also recognized α-tocopherol as the only form that meets human requirements. For that reason, in the Nordic Nutrition Recommendations 2012 (NNR 2012), vitamin E activity is confined to α-tocopherol. They also recognized that while all of the stereoisomers have equal antioxidative activities, only those with the 2*R*-configuration have biologically relevant activities. Due to the lower affinity that α-tocopherol transport protein has for 2*S*-isomers, the relative bioavailability of the synthetic form of α-tocopherol is suggested to be only half that of the naturally occurring α-tocopherol. This means that only α-tocopherol in foods and 2*R*-α-tocopherols in vitamin E preparations contribute to vitamin E activity.

The same rationale was provided by the Japanese NIHN for their decision to consider only α-tocopherol when determining the current DRI for vitamin E (Tanaka et al. 2012).

WHO (2004) stated that to estimate the α-TE of a mixed diet containing natural forms of vitamin E, the number of milligrams of *d*-β-tocopherol should be multiplied by 0.5, *d*-γ-tocopherol by 0.1, *d*-δ-tocopherol by 0.030, *d*-α-tocotrienol by 0.3 and *d*-β-tocotrienol by 0.05 (*d*- is an outdated notation for *RRR*-). WHO (2004) recognized that the α- form predominates in blood and tissue due to the action of binding proteins that preferentially select the α- form over other forms. They noted that vitamin E homologues not preferentially selected by the hepatic binding proteins are eliminated during the process of nascent VLDL secretion in the liver and probably excreted via the bile. In cross-country correlations between coronary heart disease mortality in men and the supply of vitamin E homologues across 24 European countries, they noted that the correlation with d-α-tocopherol is highly significant ($P < 0.001$) whereas all other correlations do not achieve statistical significance. Thus, the WHO equivalence values were set for other tocopherols and tocotrienols despite both pharmacokinetic and efficacy evidence that they did not have significant vitamin E activity. It is notable that in WHO-FAO's 2006 publication, "Guidelines on food fortification with micronutrients", vitamin E is listed only as mg of α-tocopherol and no equivalencies for other forms of tocopherols or tocotrienols are provided.

In conclusion, in the publications of those RASBs where there is a discussion of the scientific evidence for absorption, distribution, metabolism and excretion of vitamin E, it is clearly recognized that the β-, γ- and δ-tocopherols and the α-, β-, γ- and δ-tocotrienols, despite having antioxidant activity in vitro, are not present in the blood in significant quantities or for a significant duration due to the action of a selective α-tocopherol transfer protein. All RASBs recognized that the 2*S*- isomers of α-tocopherol are inactive in the human body. This provides a strong scientific rationale for the exclusion of the β-, γ- and δ-tocopherols, the α-, β-, γ- and δ-tocotrienols, and the 2*S*- isomers of α-tocopherol from consideration in setting an NRV-R for vitamin E.

COSTA RICA

Costa Rica supports the value proposed for vitamin E of 9 mg, which is based on INL98 according to the Council of Ministers of Nordic countries. The value proposed by the IOM of 15 mg indicates that the vitamin E requirements in CX/NFSDU 15/37/4 from September 2015 were overestimated, so they are not supported despite being based on INL98.

Vitamin E dietary equivalents and conversion factors:

Costa Rica supports the proposal in CX/NFSDU 15/37/4.

Insert an entry for vitamin E in the second table of paragraph 3.4.4.1 of the Guidelines on Nutrition Labelling.

Include α-tocopherol as the active form of vitamin E occurring naturally in food.

Include the three common forms of vitamin E that are added to food, as supported by the majority of members of the 2015 eWG:

"Vitamin dietary equivalents, niacin etc.

…… Vitamin E is present in natural forms in food 1 mg of α-tocopherol = 1 mg of RRR-α-tocopherol (d-α-tocopherol) = Vitamin E added to food 1 mg of RRR-α-tocopherol = 1.10 mg of acetate of RRR-α-tocopheryl ** 1.23 mg of succinate of RRR-α-tocopheryl ** 2 mg of all-rac-α-tocopherol (dl-α-tocopherol)***

** Calculated using stoichiometry based on RRR-α-tocopherol *** Conversion factor for all of the all-rac-α-tocopherols based on the reduced activity in the RRR-α-tocopherol. It is therefore recommended that these forms all be added to the second chart in para. 3.4.4.1 of the Guidelines on Nutritional Labelling."

CUBA

In general, Cuba supports the proposal by Argentina with respect to the CL 2015/33, specifically point 4:

The NRV-R for Vitamin D and the dietary equivalents and conversion factor for Vitamin E (para. 52 b]; Appendix II, Part III).

UNITED STATES OF AMERICA

General Comments

The United States supports using a consistent scientific approach in which the same endpoint is used to derive NRV-Rs.

Specific Comments

Proposed NRV-R for Vitamin D

The United States supports an NRV-R for vitamin D of 15 µg based on the EFSA (2016 draft opinion) and IOM (2011) DIRVs of 15 µg. Both RASBs used the serum level of 25(OH)D, the biomarker of vitamin D status, of 50 nmol/L (or 20 ng/mL) that is associated with maintenance of musculoskeletal/bone health. Both RASBs based the DIRV on a regression curve of intake and serum levels and accounted for minimal sunlight exposure.

The Nordic countries (2013) also used a similar approach to set a DIRV of 10 ug derived from a regression curve of intake during winter months and considered body stores of vitamin D from previous summer sunlight exposure. The United States is not opposed to using the average of EFSA, IOM and Nordic DIRVs to set the NRV-R as the Nordic DIRV also was based on serum 25(OH)D associated with musculoskeletal or bone health outcomes and accounted for minimal sunlight exposure.

The United States notes that the 2004 FAO/WHO RNI of 5 µg was based on the 1997 IOM AI which has since been updated by the IOM in 2011 to 15 µg.

Vitamin E Dietary Equivalents and Conversion Factors

The United States supports the eWG recommendation to identify vitamin E as mg of α-tocopherol. Using mg α-tocopherol is consistent with the majority of RASBs (i.e., EFSA 2015, NIHN 2013, WHO/FAO 2006) upon which the proposed NRV-R of 9 mg is based. Other RASBs also identify mg α-tocopherol as the dietary equivalent of vitamin E (IOM 2000, Nordic Council 2012).

Among the naturally occurring forms of vitamin E (tocopherols and tocotrienols), only RRR-α-tocopherol (naturally occurring in food) and the 2R stereoisomers of α-tocopherol (forms added to food) are maintained in the human blood. Therefore, the United States views α-tocopherol as the only form of vitamin E that is biologically active in humans.

While other forms of vitamin E (β-, γ-, δ- tocopherols and tocotrienols) may be present in food, their biological activities remain to be proven in humans (IOM 2000, EFSA 2015, NIHN 2013, Nordic Council 2012). For this reason, the United States questions the use of α-tocopherol equivalents (α-TE) because it includes these forms of vitamin E. The United States also notes that the determination of α-TE is inconsistent among RASBs. α-TE calculations may or may not include tocotrienols and conversion factors for tocopherols and tocotrienols differ.

The United States supports the eWG recommendation shown below for vitamin E dietary equivalents occurring naturally in food and also suggests including the conversion factor for *all-rac*-α-tocopherol, the vitamin E form added to foods. Only half of the stereoisomers in *all-rac*-α-tocopherol have biological activity in humans thus a conversion factor would be needed to determine mg α-tocopherol added to food.

Vitamin	**Dietary equivalents**	
Vitamin E occurring naturally in food	1 mg α-tocopherol =	1 mg RRR-α-tocopherol (d-α-tocopherol)

Vitamin E added to food	1 mg α-tocopherol =	2.00 mg *all-rac*-α-tocopherol (dl-α-tocopherol)*

* conversion factor for all-*rac*-α-tocopherol is based on half the activity of α-tocopherol

ELC

ELC supports the increase of the NRV-R for vitamin D to 15 µg/D. Recent scientific evidence demonstrate that the key role of vitamin D is a number of metabolic pathways and its positive impact on health. Recent data shows that a vitamin D intake of 20 µg/ day reduces the risk of osteoporosis and decrease the risk of falling in relation to its role in muscle strength. EFSA gave a positive EFSA opinion on the role of vitamin D in reducing the risk of falling for a daily dose of 20 µg. This opinion has been translated into an EU authorized claim.

Even in sunny countries, it's important to get this intake from food due to the fact that endogenous vitamin D production is inhibited by several factors such as darker skin, limited skin exposure to sun (long sleeves etc.) and/ or use sun protection.

The RDA in the US has been revised in 2011 at 15 µg and some countries like Germany, Austria and Switzerland even chose a value of 20 µg (DACH recommendations, 2012).

EFSA, in its draft opinion published in March 2016 and subject to public consultation, sets an Adequate Intake at 15 µg/d for adults. This value is also valid for children 1 to 17, and for pregnant and lactating women.

References:

Institute of Medicine (2011). Dietary reference intakes for calcium and vitamin D. Washington, The National Academies Press.

Deutsche Gesellschaft für Ernährung (2012, 17. Jan. 2012). "Referenzwerte für die Nährstoffzufuhr- Vitamin D (Calciferole)." Retrieved 17. Jan. 2012, from http://www.dge.de/modules.php?name=Content&pa=showpage&pid=4&page=12.

***DRAFT** Scientific Opinion on Dietary Reference Values for vitamin D1. EFSA Panel on Dietetic Products, Nutrition, and Allergies (NDA) https://www.efsa.europa.eu/sites/default/files/consultation/160321.pdf*

ISDI

ISDI appreciates the on-going work of CCNFSDU to revise the NRV-R for Vitamin D and has reviewed the proposal to revise upward the existing NRV-R value from 5 µg to either 10 µg or 15 µg (CX/NFSDU 15/37/4).

ISDI supports an increase of the NRV-R for vitamin D from 5 to 15 µg. Recent scientific evidence demonstrate the key role of vitamin D in a number of metabolic pathways and its positive impact on health. The recommendation to increase the NRV-R to 15µg is based on recommendations of the IOM (INL_{98}) and the recent Draft Opinion from the European Food Safety Authority which recommends an AI of 15 µg/day for adults (including pregnant and lactating women) and children aged 1-17 years.