CODEX ALIMENTARIUS COMMISSION

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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 ADDITIONAL OR REVISED NUTRIENT REFERENCE VALUES FOR LABELLING PURPOSES IN THE GUIDELINEN ON NUTRITION LABELLING (VITAMIN A, D, E, MAGNESIUM, PHOSPHOROUS, CHROMIUM, COPPER, CHLORIDE AND IRON)

Comments of NHF

NHF – National Health Federation

Recommendation No. 1 – NRV-R for Vitamin A – The current NRV and that of IOM at 800 mcg are acceptable but not optimal. The NRV for Vitamin A should actually be set substantially higher – at a range of 1000 to 1400 micrograms.

Justification: NHF notes that the Helsinki Consultation in 1988 set an NRV for Vitamin A of 800 micrograms of retinol equivalent. In setting this figure, the Consultation took into consideration the relation between carotene and the prevention of cancer, and stated that although this subject had not yet been resolved from the scientific point of view, it considered that this aspect might lead to ***an increase*** in the international recommended daily intakes in the future when new scientific data was available. Since 1988, however, a large body of scientific evidence has clearly demonstrated that higher intakes of carotenes and/or pre-formed Vitamin A are protective against the development of a number of cancers.[i]

We also consider that the case for Vitamin A being linked to birth defects has been overstated in most cases. In one study, for example, no birth defects were reported among 120 infants exposed to maternal intakes of Vitamin A greater than 50,000 IU per day.[ii] In addition, compared to the infants that were not exposed to high maternal doses of Vitamin A, the infants in this study who were exposed to high doses actually experienced a 50% *decreased* risk for birth defects. In fact, excessive dietary intake of Vitamin A has been associated with birth defects in humans in fewer than 20 reported cases over the past 30 years.[iii] Other data suggests that 30,000 IU of Vitamin A per day should be considered safe for pregnant women.[iv]

In short, the most-recent and up-to-date data indicate that **the NRV for Vitamin A should actually be set substantially higher – at a range of 1000 to 1400 micrograms**.

Recommendation No. 2 – NRV-R for Vitamin D – None of the DIRVs proposed by the RASBs are adequate as they are all too low. Even the highest NRV figure of 15 mcg given (by IOM) is predicated upon a statistical mistake that grossly ***underestimates*** the need for Vitamin D. The other figures are so absurdly low as to constitute a joke on humanity or even an outright assault upon its well-being. They should be dismissed out of hand and not given any consideration whatsoever. **The correct NRV-R for Vitamin D should be 100-125 micrograms.**

Justification: The current recommended levels for Vitamin D are based upon incorrect calculations. As Dr. Robert P. Heaney, M.D. has pointed out in his article "The IOM Miscalculated Its RDA For Vitamin D,"[v] "two statisticians at the University of Edmonton in Canada (Paul Veugelers and JP Ekwaru) published a paper in the online journal *Nutrients* (6(10):4472-5) showing that the Institute of Medicine (IOM) had made a serious calculation error in its recommended dietary allowance (RDA) for vitamin D. Immediately, other statisticians checked the Canadians' analyses and found that, indeed, they were right. The true RDA for vitamin D was about 10 times higher than the IOM had said. Not a small error."

"An RDA is technically the amount of a nutrient every member of a population should ingest to ensure that 97.5% of its members would meet a specified criterion of nutritional adequacy. For vitamin D, the IOM panel determined that the criterion for adequacy was a serum concentration of a particular vitamin D derivative (25-hydroxyvitamin D) of 20 ng/mL or higher, and that for adults up to age 70, 600 IU of vitamin D per day was the RDA.

"The IOM panel identified a number of published studies showing the 25-hydroxyvitamin D response to various vitamin D doses. They plotted the average response in each of those studies against dose, thereby generating what is termed a 'dose response curve,' i.e., a way to estimate how much of a response would be predicted for any given vitamin D intake. But, to make a long story short, because it used average responses, that curve tells us nothing about the intake requirement for the individual members of a population, and particularly those whose response to a given dose falls in the bottom 2.5 percentiles. The IOM panel surely knew that the average intake required to meet or exceed 20 ng/mL was not the same as the RDA, as it would be inadequate for all those with below average responses (about half the population). So, to catch the 'weak' responders, they calculated the 95% probability range around their dose response curve, designating as the RDA the point where the bottom end of that probability range exceeded 20 ng/mL. While this might seem to have been the right approach, it was not. The panel appears to have overlooked the fact that the 95% probability range for their curve is for the average values that would be expected from similar studies at any particular dose. The dispersion of averages of several studies is, as every beginning student of statistics knows, much more narrow than dispersion of individual values within a study around its own average. And it's the 2.5 percentile individual values from those studies, not the study averages, that should have been used to create the relevant dose response curve.

"It's this latter approach that the Canadian statisticians used. They took precisely the same studies as the IOM had used and demonstrated that the requirement to ensure that 97.5% of the population would have a value of at least 20 ng/mL, ***was 8,895 IU per day***. Recall that the IOM figure was less than 1/10 that, i.e. 600 IU per day up to age 70 (and 800 IU per day thereafter). When my colleagues and I analyzed the large GrassrootsHealth dataset, we calculated a value closer to 7,000 IU per day, still a full order of magnitude higher than the estimate of the IOM, and not substantially different from the estimate of Veugelers and Ekwaru. … But, as the Edmonton statisticians noted, that number is woefully inadequate.

"There is almost no public awareness of this error or its implications in the United States, but that is not true for Canada. A large nutritional health foundation located in Calgary (Pure North S'Energy Foundation) has taken out a series of half page advertisements in Canada's national newspaper (*Globe and Mail*), alerting Canadians to the fact that the error was made and that they need more vitamin D than current policy indicates (http://www.purenorth.ca/?page_id=1356). The IOM, Health Canada, and the Canadian Ministry of Health have all been formally alerted to this problem. The Health Ministry has agreed to undertake an independent reanalysis of the calculation of the RDA, but the results are not yet available and the shape of the ministry's action is still uncertain.

"There may be a moral here. It is widely recognized that many of the panel members, before coming together to review the evidence, had already staked out a position to the effect that, while the previous (1997) recommendation for vitamin D (200 IU per day) was probably inadequate, the actual RDA was almost certainly below 1000 IU per day. Accordingly, when the statistical calculations produced a number that matched their own expectations, they may not have been inclined to question its derivation.

"There is a generally held belief that science is objective, data-driven. And to a substantial extent that is so. But science and scientists are not identical. Scientists often have strongly held opinions and, like people in general, find ways to construe the evidence to support their beliefs. When those beliefs are wrong, science, as a field, ultimately abandons them. I am confident that this IOM error will be corrected sooner or later. This is partly because it is demonstrably erroneous, and partly because the related set of IOM recommendations for vitamin D has not elicited a consensus in the field of vitamin D research. If the Dietary Reference Intakes produced by the IOM are important, then it is important that they be right. I can only hope that not too much human damage will occur as we wait for the needed correction to happen."

NHF Summary: The analyses in this paper shows that rather than 600 IU/day, it would take 8,895 IU/day to achieve 25(OH)D above 50 nmol/L in 97.5% of the population using data from 8/10 studies that the IOM considered (the other 2 studies did not report all necessary information). In other words, the RDA should be 8,895 IU/day.

The science supporting the human need for ***significantly*** higher levels of Vitamin D is increasing by leaps and bounds. In particular, the old and outdated concept that humans can get by on a daily intake of just 5 micrograms of Vitamin D is dead.

Instead, **adequate** levels of Vitamin D (i.e., from 25 micrograms up) are recognized as being necessary by such agencies as Health Canada and others. The scientific evidence supporting this position is extremely well-documented, but NHF will only footnote a small portion of such research here.[vi] To ignore this science by establishing below-minimum nutritional requirements for Vitamin D (such as an NRV-R of only 5 micrograms) borders on nutritional negligence.

Recommendation No. 3 – Footnote to NRV-R for Vitamin D – With respect to this recommendation, NHF agrees with and supports the comments of ELC in CX/NFSDU 15/37/4 Add. 1.

Recommendation No. 4 – NRV-R for Vitamin E – None of the DIRVs proposed by the RASBs are adequate as they are all too low, providing suboptimal levels of this nutrient. An adequate NRV would deliver 15-20 mgs (or approx. 400 IUs) of natural Vitamin E (preferably multi-tocopherol and not simply alpha-tocopherol) per day.

Justification: The World Health Organization currently attributes one-third of all global deaths annually (15.3 million) to cardiovascular disease,[vii] and patients with coronary artery disease have been shown to have significantly lower blood levels of Vitamin E than normal, healthy people.[viii]

Studies have demonstrated that Vitamin-E supplements are effective in the treatment of cardiovascular disease,[ix] and that the combination of Vitamin E and Vitamin C can slow the advancement of atherosclerosis.[x] Furthermore, a review of studies of Vitamins A, C, and E and cardiovascular disease found significant evidence to support the supplementation of these vitamins to lower the risk of death from this illness.[xi] As such, it is now clear that the progression of early stages of coronary calcifications can be stopped or limited by the synergistic effect of vitamins and essential nutrients,[xii] and that supplementing the diet with nutrients including Vitamins E, C, B6, and folate is conducive to the prevention of cardiovascular disease.[xiii] In this respect it is also interesting to note that some researchers particularly recommend dietary supplementation of Vitamin E and C in Northern Europe, where cardiovascular disease is most prevalent.[xiv]

Several observational studies have associated lower rates of heart disease with higher Vitamin-E intakes. One study of approximately 90,000 nurses found that the incidence of heart disease was 30% to 40% lower in those with the highest intakes of Vitamin E.[xv] Among a group of 5,133 Finnish men and women followed for a mean of 14 years, higher vitamin E intakes from food were associated with decreased mortality from CHD.[xvi]

Vitamin-E therapy has also been shown to reduce arterial blockage in patients suffering from intermittent claudication,[xvii] and recent research has indicated that it normalizes high blood pressure.[xviii] Vitamin E also promotes collateral circulation; consequently offering great benefits to diabetes patients.[xix]

A recent study looked at patients with colon cancer who received a daily dose of 750 mg of Vitamin E during a period of two weeks. The researchers found that supplementation with high doses of dietary Vitamin E produced a significant improvement in the immune functions of these patients, all of whom had advanced cancer. It is especially notable that this improvement was achieved in only two weeks.[xx] Other research suggests that Vitamin-E supplementation also improves immune function in healthy elderly people.[xxi]

Research has additionally shown that a high dietary intake of Vitamin E and Vitamin C may lower the risk of Alzheimer disease.[xxii] Other researchers have confirmed this, and have demonstrated that long-term supplement users of Vitamin E with Vitamin C have significantly better mental performance than do people

who have never used Vitamin E or Vitamin C supplements,[xxiii] and that Vitamins E and C may prevent dementia and improve cognitive functioning in later life.[xxiv] Similarly, a Columbia University study reported that the progression of Alzheimer's disease was significantly slowed in patients taking high daily doses (2,000 IU) of Vitamin E for two years.[xxv]

In another study, 400 IU of Vitamin E per day given to epileptic children for several months reduced the frequency of seizures in most of them by over 60 percent, while half of them had a 90 to 100 percent reduction in seizures. This study is also notable for the fact that the researchers specifically stated that the children suffered no adverse side effects from the Vitamin-E treatment.[xxvi] Similarly, preterm infants given 100 mg of Vitamin E per kilogram body weight (as a preventative treatment for incubator oxygen retina damage - a major cause of retrolental fibroplasia and subsequent blindness in premature infants) suffer no detrimental side effects from such therapy.[xxvii] It is also notable that a statistical analysis of published clinical results showed as early as 1940 that Vitamin E supplements reduce the rate of recurrent miscarriage.[xxviii]

An increased intake of Vitamins E and C has been found to reduce the risk of hip fractures,[xxix] and researchers have also demonstrated that a mixture of Vitamins E, C, and A dramatically reduces the postoperative complication rate.[xxx] Similarly, critically ill surgery patients have been shown to be significantly less likely to experience organ failure, spend less time using mechanical ventilation, and have shorter times in intensive care units when they are given supplements of Vitamin E and Vitamin C.[xxxi]

Research has shown that healthy centenarians have high levels of both Vitamin E and Vitamin A, and that this seems to be important in guaranteeing their extreme longevity.[xxxii]

Finally, we also note that the 2000 report by the Institute of Medicine of the National Academy of Sciences acknowledges that 1,000 mg (1,500 IU) Vitamin E is a "tolerable upper intake level . . . that is likely to pose no risk of adverse health effects for almost all individuals in the general population."

All of the above studies were conducted using daily intake levels for Vitamin E higher than those proposed by any of the RASBs, indicating that the RASBs are once again incorrectly fixated upon suboptimal levels of nutrient intake.

Recommendation No. 5 – NRV-R for Iron – NHF disagrees that the NRV-R for iron should be based solely on the absorption percentage. More important will be the establishment of separate NRVs for men and women. Aggregated or averaged NRVs for iron for use by both males and females will either leave females largely deficient in iron or males (and post-menopausal females) in great danger of iron overload. To have acceptable safe levels of iron and sufficient levels for iron for the two sexes, there is no alternative here but for the establishment of two separate NRVs, one for males and one for females.

There should be multiple NRVs-R for iron based upon age and gender, rather than upon percent dietary absorption. In the case of iron, the NRVs have been set for growing children and menstruating females, both of which groups require higher iron intake than males and menopausal women. The typical male at age 45 has three to four times the iron levels in his body as a woman of the same age and this is a significant factor in increased heart attacks and cancer rates in males versus females due to the pro-oxidant properties of iron. So, in this case, establishing young-female-friendly NRVs for pro-oxidant iron actually harms males and mature females.

Recommendation No. 8 – NRV-R for Magnesium – The DIRV of the IOM (365 mg/day) is closest to the proper intake level. However, since this Committee has unwisely already set an NRV for calcium at 1,000 mg/day, and since calcium and magnesium operate in the human body as twin minerals at least at a 2:1 ratio (or a 3:2 ratio), we are forced by the extremely high calcium NRV set by CCNFSDU to establish no less than a **500 mg/day** intake level for magnesium. Had the calcium NRV been set at a more reasonable 800 mg/day level, then the NRV for magnesium could be established at **400 mg/day** instead.

Justification: Research shows that dietary magnesium consumption has progressively declined over the past century from an average intake of 475-500mg in the period 1900-1908 to an average intake of 175-225mg in the period 1990-2002. [xxxiii]

As such it is hardly surprising that suboptimal intakes of magnesium and outright magnesium deficiencies are now commonplace in many population groups.[xxxiv] Indeed, a large segment of the U.S. population may have a chronic latent magnesium deficiency that has been linked to atherosclerosis, myocardial infarction, hypertension, cancer, kidney stones, premenstrual syndrome, and psychiatric disorders.[xxxv] In this respect, it has been shown that although serum levels are commonly used to assess magnesium deficiency, red cells and leucocytes can be still deficient despite normal serum values.[xxxvi]

Cell growth and metabolism are absolutely dependent upon the availability of magnesium, which can be compromised if excess calcium is present.[xxxvii] And soft tissue calcification can be a serious side effect of taking too much calcium and too little magnesium.[xxxviii]

Moreover, magnesium deficiency impairs Vitamin D metabolism, in that a lack of magnesium limits the conversion of Vitamin D to active, hormonal form.[xxxix] These nutrients – calcium, magnesium, and Vitamin D, as well as Vitamin K2 – are all tied together metabolically and, hence, appropriate NRVs must be set for each of them, taking into consideration the NRVs of the others.

Three parts calcium to two parts magnesium has been demonstrated as the most beneficial calcium-magnesium ratio, which means that given a 1000 mg/day NRV for calcium, the optimal amount of magnesium would be 600 mg/day.[xl]

Given that the World Health Organization currently attributes one-third of all global deaths annually (15.3 million) to cardiovascular disease,[xli] **NHF recommends an NRV-R for magnesium of 500-600 mg**.

Recommendation No. 9 – NRV-R for Phosphorus – The DIRV of the IOM (700 mg/day) is acceptable.

Justification: The recommended dietary allowance, 700 mg/day of phosphorus for healthy adults, is meant to sustain serum phosphorus concentrations within the physiologic range of 2.5 to 4.5 mg/dL. Therefore, the IOM DIRV for phosphorus is acceptable.

Recommendation No. 10 – NRV-R for Copper – The DIRV of the IOM (900 mcg/day) is acceptable.

Justification: Copper toxicity is rare in the general population. Acute copper poisoning has occurred through the contamination of beverages by storage in copper-containing containers, as well as from contaminated water supplies. Of more concern from a nutritional standpoint is the possibility of liver damage resulting from long-term exposure to lower doses of copper. In generally healthy individuals, doses of up to 10,000 mcg (10 mg) daily have not resulted in liver damage. For this reason, the U.S. Food and Nutrition Board set the tolerable upper intake level (UL) for copper at 10 mg/day from food and supplements. Individuals with genetic disorders affecting copper metabolism (e.g., Wilson's disease, Indian childhood cirrhosis, and idiopathic copper toxicosis) may be at risk for adverse effects of chronic copper toxicity at significantly lower intake levels. There is some concern that the UL of 10 mg/day might be too high. In particular, men in a research study consumed 7.8 mg/day of copper for 147 days. They accumulated copper during that time, and some indices of immune function and antioxidant status suggested that these functions were adversely affected by the high intakes of copper. However, another study did not report any adverse effects in individuals supplemented with 8 mg/day of copper for six months. Overall, the IOM DIRV, or even the Japanese DIRV, seem the most appropriate.

Recommendation No. 11 – NRV-R for Chromium – None of the DIRVs proposed are adequate. A more appropriate NRV would be 100-200 mcg/day.

Justification: In 1989, the National Academy of Sciences established an "estimated safe and adequate daily dietary intake" range for chromium of 50 to 200 mcg.[xlii] In 2001, DRIs for chromium were established. The research base was insufficient to establish RDAs, so AIs were developed based on average intakes of chromium from food as found in several studies.[xliii]

Due to the highly refined diet consumed in most of the developed world (which requires more chromium), as well as the rising rate of diabetes (which higher chromium levels help ameliorate), the NHF strongly suggests that the most appropriate NRV for chromium would be found in the **100-200 mcg/day range**.

Recommendation No. 12 – NRV-R for Chloride – NHF reserves its position on this nutrient at present, although the suggested NRV-R of 3000 mg seems appropriate.

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