The National Health Federation's Proposals for Nutrient Reference Values

Written by Paul Anthony Taylor and Scott Tips
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Subject: CCNFSDU: NRV's Electronic Working Group

Dear Working Group Member,

At the recent CCNFSDU meeting in Bonn (November 2003), an electronic Working Group was established under the leadership of South Africa to update the Nutrient Reference values [Codex Guidelines on Nutrition Labeling - CAC/GL 2-1985 (Rev.1 - 1993)]. Interested members are now invited to forward proposals for additional or revised NRV's for labeling purposes to the following e-mail address before or on 31 March 2004:
E-mail: booyza@health.gov.za

Regards,

Antoinette Booyzen
South Africa

Dear Antoinette,

I enclose (as a Microsoft Word attachment) the National Health Federation's proposals for additional/revised NRVs. I would also be grateful if you could confirm to me that the document has been safely received and that you have been able to open it successfully.

Hope all is well with you.

Kind regards,

Paul Anthony Taylor
on behalf of the National Health Federation (NHF)

Proposals of the National Health Federation for additional/revised Codex NRVs for labeling purposes

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Introduction

The World Health Organization currently attributes one-third of all global deaths annually (15.3 million) to cardiovascular disease (332), and in 2000 over 6 million deaths occurred globally from cancer (333). Moreover, estimates predict that by 2020 the total number of cases of cancer will have increased by 73% in the developing world and by 29% in the developed world. (333). By 2020 it is estimated that chronic diseases will account for almost three-quarters of all deaths worldwide (561).

Faced with these statistics we are forced to question the wisdom of assuming that populations are healthy merely because they don't suffer from classical nutritional deficiency diseases such as scurvy, rickets, beri-beri or pellagra.

Current estimates of nutritional sufficiency, be they RDAs, AIs, EARs or NRVs, do not set nutritional intakes with the concept of optimum health in mind. They are simply estimates of the amounts of nutrients that healthy populations would require to maintain normal function and health and to avoid nutritional deficiency diseases. This approach, in our opinion, is highly flawed.

Given the increasing prevalence in our societies of conditions such as cardiovascular disease, cancer, obesity, diabetes, asthma, eczema, psoriasis, allergies, arthritis, high blood pressure, osteoporosis and depression, we believe that by definition our current system of nutritional values is no longer applicable.

Moreover, the consistency of evidence in the scientific literature clearly demonstrates that individuals who consume nutritional supplements have a lower risk of contracting serious disease - a position that has now been taken by two of the world's leading medical journals.

The Journal of the American Medical Association, for example, recently reversed its historical anti-vitamin policy by acknowledging that "it appears prudent for all adults to take vitamin supplements" (562). The article, authored by Robert H. Fletcher and Kathleen M. Fairfield from the Harvard School of Medicine, examined English-language articles about vitamins in relation to chronic diseases published between 1966 and 2002, and concluded that inadequate intake of several vitamins has been linked to the development of diseases including coronary heart disease, cancer, and osteoporosis.

Similarly, the April 9, 1998 issue of the New England Journal of Medicine featured an article entitled "Eat Right and Take a Multivitamin" that was based on a succession of positive studies showing the disease-prevention benefits resulting from the consumption of nutritional supplements (563).

We therefore consider that it would be a major step forward for global public health if the CCNFSDU were to finally accept and support the growing medical evidence that vitamin and mineral supplements prevent disease, promote optimum health and prolong lifespan.

Research has shown that there appears to be little-to-no risk to supplement users of experiencing adverse side effects due to excessive intakes of micronutrients (564).

We therefore propose the NRVs contained in this document as the minimum preventative intakes necessary to prevent disease, promote optimum health and prolong lifespan in the majority of people.

We also strongly believe that it is the duty of the CCNFSDU to make recommendations that advance nutritional welfare, prevent disease, promote optimum health and prolong lifespan and that as such a general recommendation supporting the use of nutritional supplements would admirably fulfill all of these criteria.

Paul Anthony Taylor

NHF Board Member & Codex Delegate

29th March 2004

Vitamin A

Note: Includes provitamin A carotenoids that are dietary precursors of retinol. Given as retinol activity equivalents (RAEs). 1 RAE = 1 *µ*g retinol, 12 *µ*g beta-carotene.

Infants
0-6 mo 400*µ*g
7-12 mo 500*µ*g
Children
1-3 y 500*µ*g
4-8 y 650*µ*g
Males
9-13 y 1050*µ*g
14-18 y 1680*µ*g
19-30 y 1800*µ*g
31-50 y 1800*µ*g
50-70 y 1800*µ*g
> 70 y 1800*µ*g
Females
9-13 y 880*µ*g
14-18 y 1350*µ*g
19-30 y 1400*µ*g
31-50 y 1400*µ*g
50-70 y 1400*µ*g

> 70 y 1400μg
Pregnancy
≤ 18 y 1550μg
19-30y 1600μg
31-50 y 1600μg
Lactation
≤ 18 y 1750μg
19-30y 1800μg
31-50 y 1800μg

Justification: The Helsinki Consultation in 1988 set a 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 preformed vitamin A are protective against the development of a number of cancers. (1-23).

Although some research exists to suggest that large doses of beta-carotene may possibly be capable of increasing the risk of lung cancer in smokers, we consider that in view of the many important health benefits to be obtained from higher intakes of carotenes it would be irresponsible for the CCNFSDU to recommend lower intakes for the entire population, as a means of protecting smokers, when official WHO policy is to substantially reduce the incidence of tobacco use. Tobacco, not carotene, is the main cause of lung cancer in smokers.

We also consider that the case for vitamin A being linked to birth defects has been overstated in some 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. (24). In addition, compared to the infants that were not exposed to high maternal doses of vitamin A the infants in this study that 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. (25). Other data suggests that 30,000 IU of vitamin A per day should be considered safe for pregnant women. (26).

Vitamin B1

Infants
0-6 mo 3mg
7-12 mo 6mg
Children
1-3 y 8mg
4-8 y 13mg
Males

9-13 y 23mg
14-18 y 37mg
19-30 y 40mg
31-50 y 40mg
50-70 y 40mg
> 70 y 40mg
Females
9-13 y 23mg
14-18 y 37mg
19-30 y 40mg
31-50 y 40mg
50-70 y 40mg
> 70 y 40mg
Pregnancy
≤ 18 y 38mg
19-30y 41mg
31-50 y 41mg
Lactation
≤ 18 y 39mg
19-30y 42mg
31-50 y 42mg

Justification: There is now a wealth of research demonstrating that higher intakes of thiamin can improve general health and prevent disease. (27-49). This research also includes evidence that currently used assays may not be adequate to assess thiamin status, and that thiamin deficiency is under diagnosed in life, in part because the classical clinical presentations are uncommon.

Furthermore, given that some of this research has shown that alcohol use, even moderate, interferes with thiamin metabolism (more so than with any other nutrient), we consider this increase in the NRV for thiamin to be both appropriate and essential.

No adverse effects associated with thiamin from food or supplements have ever been reported.

Vitamin B2

Infants
0-6 mo 3mg
7-12 mo 6mg
Children
1-3 y 8mg
4-8 y 13mg
Males
9-13 y 23mg
14-18 y 37mg
19-30 y 40mg

31-50 y 40mg
50-70 y 40mg
> 70 y 40mg
Females
9-13 y 23mg
14-18 y 37mg
19-30 y 40mg
31-50 y 40mg
50-70 y 40mg
> 70 y 40mg
Pregnancy
≤ 18 y 38mg
19-30y 41mg
31-50 y 41mg
Lactation
≤ 18 y 39mg
19-30y 42mg
31-50 y 42mg

Justification: Riboflavin has been shown to be protective against the development of degenerative diseases (62, 68), and studies have repeatedly demonstrated that worldwide intakes of riboflavin are below recommended values (50, 51, 52, 55, 59, 65).

Research has also shown that supplementation of riboflavin can improve health and wellbeing; either taken with other nutrients (53, 54, 60, 63, 69), or alone (56, 58); and that early detection of vitamin deficiency is difficult to diagnose due to the fact that it often occurs without any of the clinical signs of vitamin deficiency being present. (53).

Given that riboflavin intake has additionally been found to be inversely associated with coronary heart and vascular disease deaths and hospitalizations, as well as being a contributory factor in a number of other disease conditions when intake is insufficient (61, 64, 67), we consider this increase in the NRV for riboflavin to be entirely appropriate. (57).

Finally, we also note that a supplement of 15mg riboflavin has been shown to be insufficient to achieve normal biochemical indices in pregnancy (66), and that no adverse effects associated with riboflavin from food or supplements have been reported.

Niacin

Includes nicotinic acid amide, nicotinic acid (pyridine-3-carboxylic acid), and derivatives that exhibit the biological activity of nicotinamide.

Infants
0-6 mo 15mg
7-12 mo 30mg
Children

1-3 y 40mg
4-8 y 60mg
Males
9-13 y 120mg
14-18 y 190mg
19-30 y 200mg
31-50 y 200mg
50-70 y 200mg
> 70 y 200mg
Females
9-13 y 120mg
14-18 y 190mg
19-30 y 200mg
31-50 y 200mg
50-70 y 200mg
> 70 y 200mg
Pregnancy
≤ 18 y 200mg
19-30y 210mg
31-50 y 210mg
Lactation
≤ 18 y 205mg
19-30y 215mg
31-50 y 215mg

Justification: Increased consumption of niacin has been shown to prevent a range of diseases, illnesses and adverse health events; including heart attacks (70), migraine headaches (71), and cancer (72, 73). It has also been found to be effective in the treatment of schizophrenia (74-80), arthritis and joint disorders (81, 82), insulin-dependent diabetes (83), and hypoglycemia (84), and has repeatedly been shown to lower blood levels of cholesterol and triglycerides (85-93).

Pantothenic Acid

Infants
0-6 mo 15mg
7-12 mo 30mg
Children
1-3 y 40mg
4-8 y 60mg
Males
9-13 y 120mg
14-18 y 190mg
19-30 y 200mg
31-50 y 200mg
50-70 y 200mg
> 70 y 200mg

Females
9-13 y 120mg
14-18 y 190mg
19-30 y 200mg
31-50 y 200mg
50-70 y 200mg
> 70 y 200mg
Pregnancy
≤ 18 y 200mg
19-30y 210mg
31-50 y 210mg
Lactation
≤ 18 y 205mg
19-30y 215mg
31-50 y 215mg

Justification: Pantothenic acid and its natural derivatives have been shown to prevent and alleviate arthritis (94, 95); lower levels of cholesterol and other lipids (96-100); boost energy and athletic ability (101); and improve immune response (102).

Vitamin B6

Infants
0-6 mo 3mg
7-12 mo 7mg
Children
1-3 y 10mg
4-8 y 16mg
Males
9-13 y 29mg
14-18 y 47mg
19-30 y 50mg
31-50 y 50mg
50-70 y 50mg
> 70 y 50mg
Females
9-13 y 29mg
14-18 y 47mg
19-30 y 50mg
31-50 y 50mg
50-70 y 50mg
> 70 y 50mg
Pregnancy
≤ 18 y 49mg
19-30y 52mg
31-50 y 52mg
Lactation

≤ 18 y 50mg
19-30y 53mg
31-50 y 53mg

Justification: Studies in the elderly have repeatedly shown prevalence's of B6 deficiency of around 25% (103). The prevalence of B6 deficiency, demonstrated biochemically, in population studies in developed countries, generally ranges from 9% in pre-school children (104), to 68% in pregnant women on low incomes (105). Studies in adults repeatedly show prevalence's of B6 deficiency of around 25% (106).

Oral contraceptives have been shown to deplete levels of vitamin B6 (110-114). Not surprisingly then, vitamin B6 supplements can restore normal biochemical values (115, 116) and protect against metabolic imbalances in women taking these drugs (117).

Vitamin B6 supplements have also been shown to boost immunity in the elderly (107), reduce the risk of developing kidney stones in women (108), and relieve symptoms of pre-menstrual tension (109); as well as being effective in the treatment of autism (118), asthma (119), sickle cell anaemia (120), and morning sickness (121, 122). It has additionally been shown that patients with carpal tunnel syndrome are deficient in vitamin B6 (123), and that vitamin B6 is an effective treatment for this disorder (124, 125). Researchers have also demonstrated that levels of homocysteine, a risk factor for heart disease and stroke, can be reduced by supplements of vitamin B6, vitamin B12 and folic acid (126-129), and that levels of vitamins B6 are inversely related to homocysteine levels (126, 130). Levels of vitamin B6 are also inversely related to risk of lung cancer in men. (131).

Finally, we note that vitamin B6 is considered safe during pregnancy, and that it has been used in pregnant women without any evidence of foetal harm (132). Furthermore, it has also been found to have a positive effect upon pregnancy outcome (133), and to prevent certain types of seizures in infants (134).

Given all of the above evidence therefore, we consider this increase in the NRV for pyridoxine to be entirely appropriate.

Vitamin B12

Infants
0-6 mo 7*μ*g
7-12 mo 15*μ*g
Children
1-3 y 20*μ*g
4-8 y 30*μ*g
Males
9-13 y 60*μ*g
14-18 y 90*μ*g
19-30 y 100*μ*g
31-50 y 100*μ*g

50-70 y 100μg
> 70 y 100μg
Females
9-13 y 60μg
14-18 y 90μg
19-30 y 100μg
31-50 y 100μg
50-70 y 100μg
> 70 y 100μg
Pregnancy
≤ 18 y 94μg
19-30y 104μg
31-50 y 104μg
Lactation
≤ 18 y 97μg
19-30y 107μg
31-50 y 107μg

Justification: A number of population groups have been shown to have dietary intakes below the RDA for vitamin B12 (135-137), and vitamin B12 deficiency is estimated to affect 10%-15% of individuals over the age of 60 (138). Vitamin B12 deficiency becomes increasingly common with advancing age (139), and current findings in the scientific literature suggest that even subtle B12 deficiency is clinically significant (140). Frank deficiencies carry many health risks, and low serum levels of vitamin B12 are known to increase the risk of breast cancer in women (141), as well as being associated with a doubling of the risk of developing Alzheimer's disease (142).

Vitamin B12, when taken with folic acid, has been shown to be effective in the treatment of osteoarthritic hands (143), and has been found to reduce the incidence of bronchial squamous metaplasia, a precancerous change - even in heavy smokers (144-145). It has also been demonstrated to be capable of curing sciatica (146), reversing some of the effects of chronic nitrous oxide exposure (147), and when taken with the amino acid carnitine, has been shown to be effective in the treatment of anorexia nervosa (148).

There is now abundant evidence that high levels of homocysteine are associated with an increased risk of developing cardiovascular disease (149-161), and that serum levels of vitamin B12 are inversely related to homocysteine levels (162-163). It has also been shown that a deficiency of vitamin B12 can raise levels of homocysteine (164), and that supplementation with combinations of folic acid, vitamin B6 and vitamin B12 is an effective means to reduce elevated levels of homocysteine (165-168). Raised levels of homocysteine have also been shown to increase the risk of developing Alzheimer's disease (169).

Observational studies have found that as many as 30% of patients hospitalized for depression are deficient in vitamin B12 (170), and that vitamin B12 deficient women over the age of 65 are twice as likely to be severely depressed as non-deficient women

(171). Indeed, there is also epidemiological evidence that even a moderate deficiency of vitamin B12 may lead to mental illness (172).

Supplementation of vitamin B12 has been shown to have a significant positive effect upon memory (173), and to improve emotional state, even in the absence of deficiency (174). Studies have additionally shown that vitamin supplements that include vitamin B12 are associated with better performance on difficult visuospatial and abstraction tests (175), and that regular use of such supplements confers some degree of protection against vitamin B12 deficiency in older adults (176).

Finally, researchers have also shown that vitamin B-12 dependency disorders are common and that they are neglected by the medical profession (174), and that the cut-off point of serum concentration should be raised, because many elderly people with "normal" serum vitamin B12 concentrations are metabolically deficient in cobalamin (177).

We therefore have no hesitation in recommending the above increase in the NRV for vitamin B12.

Folate

Infants
0-6 mo 65*μ*g
7-12 mo 120*μ*g
Children
1-3 y 155*μ*g
4-8 y 260*μ*g
Males
9-13 y 465*μ*g
14-18 y 750*μ*g
19-30 y 800*μ*g
31-50 y 800*μ*g
50-70 y 800*μ*g
> 70 y 800*μ*g
Females
9-13 y 465*μ*g
14-18 y 750*μ*g
19-30 y 800*μ*g
31-50 y 800*μ*g
50-70 y 800*μ*g
> 70 y 800*μ*g
Pregnancy
≤ 18 y 780*μ*g
19-30y 830*μ*g
31-50 y 830*μ*g
Lactation
≤ 18 y 815*μ*g

19-30y 865μg
31-50 y 865μg

Justification: Many studies have shown that an inadequate intake of folate is relatively common (178-187), and research over the past 30 years has demonstrated a relationship between folic acid deficiency and psychopathology (188). Neuropsychiatric diseases secondary to folate deficiency may include dementia, schizophrenia-like syndromes, insomnia, irritability, forgetfulness, endogenous depression, organic psychosis, peripheral neuropathy, myelopathy, and restless legs syndrome (189). Low serum folate levels are also known to be associated with a doubling of the risk of developing Alzheimer's disease (142).

Higher levels of folate however have been shown to be related to a lower incidence of nuclear lens opacities, which are associated with the development of cataracts (193).

Data from the Nurses' Health Study conducted at the Harvard Medical School found that long-term supplementation with folic acid reduces the risk of colon cancer in women by 75% (190). Indeed, there is an inverse relationship between the intake of folate and the risk of developing various esophageal and gastric cancers (191), and folic acid is known to be effective in the treatment of atrophic gastritis, where it prevents or reverses precancerous lesions (192). Furthermore, folic acid taken with vitamin B12 has been found to be effective in the treatment of osteoarthritic hands (143), and in the reduction of the incidence of bronchial squamous metaplasia (a precancerous change) - even in heavy smokers (144-145).

Folic acid supplements have also been shown to reduce blood pressure in smokers (194), and research has established that supplementing the diet with vitamins C, E, B6 and folate is conducive to the prevention of cardiovascular disease (195). In this respect there is now abundant evidence that high levels of homocysteine are associated with an increased risk of developing conditions such as cardiovascular disease (149-161) and Alzheimer's disease (169), and studies have shown that supplementation with combinations of folic acid, vitamin B6 and vitamin B12 is an effective means to reduce elevated levels of homocysteine (165-168).

High levels of homocysteine accompanied by low levels of folate are also known to be risk factors for heart attack (197). This link has been further established through research showing that folic acid supplements can reduce levels of homocysteine (198) and hence protect against heart attacks (199). As such it is noteworthy that children with a family history of CVD have been found to have lower intakes of folate, lower serum folate levels, and higher levels of homocysteine (196), and that supplements of folic acid, vitamin B6 and vitamin B12 have even been shown to reduce the progression of atherosclerosis in hyperhomocysteinemic renal-transplant recipients (200).

Scientific evidence has now clearly demonstrated that women given folic acid supplements during pregnancy have a lower incidence of delivering babies with neural tube birth defects (201-203), and researchers have therefore emphasised the importance of all fertile women, regardless or not of whether they are intending to

become pregnant, taking daily multivitamins that contain 400μg (0.4 mg) of folic acid (204). Folic acid-containing multivitamins have additionally been shown to reduce the risk of gestational hypertension (205).

It is now known that in the elderly even moderate folate depletion will only respond to an intake of folate in excess of the RDA (206). Researchers have also shown that folic acid supplements are more effective than increased dietary folate intake in elevating serum folate levels (207). Indeed, the use of nutritional supplements is particularly beneficial in promoting adequate intakes of folate in women aged 18-50 years (208), and research has made it clear that people who do not take folic acid supplements are at increased risk for functional folate deficiency (209).

Given that research has already shown that the current RDA for folate is insufficient to attain optimal homocysteine levels (210), and that micronutrients both prevent cancer and delay aging (211), there can now be little doubt that the Helsinki Consultation's recommendation to reduce the NRV for folate from 400μg to 200μg was a step in the wrong direction.

Biotin

Infants
0-6 mo 60μg
7-12 mo 120μg
Children
1-3 y 155μg
4-8 y 260μg
Males
9-13 y 465μg
14-18 y 750μg
19-30 y 800μg
31-50 y 800μg
50-70 y 800μg
> 70 y 800μg
Females
9-13 y 465μg
14-18 y 750μg
19-30 y 800μg
31-50 y 800μg
50-70 y 800μg
> 70 y 800μg
Pregnancy
≤ 18 y 780μg
19-30y 830μg
31-50 y 830μg
Lactation
≤ 18 y 810μg

19-30y 860μg
31-50 y 860μg

Justification: There is good evidence that biotin deficiency is by no means uncommon (212-216). Biotin is essential for numerous biochemical, dermatological and neurological processes, and long-term auditory and visual complications can result from a deficiency in this nutrient (217, 218). Biotin deficiency has also been found to cause mitochondrial decay with oxidant leakage leading to accelerated aging and neural decay (219). Biotin has furthermore been shown to improve glucose metabolism (220-223), and research suggests that biotin supplements may be particularly useful in the prevention of diabetes (224). High doses of biotin may also synergize with chromium picolinate to enable a definitive nutritional therapy for type II diabetes, and may likewise be useful in the prevention and management of gestational diabetes, as well as being an aid to glycemic control in type I patients. (225). Indeed, drugs such as metformin and troglitazone, which are expensive and require regular physician monitoring to avoid potentially dangerous side effects, would appear to be less practical options from cost-effectiveness, convenience and safety standpoints, given the fact that the population at risk for diabetes is huge. (226). Finally, biotin supplements have also been found to effect a marked improvement in patients suffering from severe diabetic peripheral neuropathy (227), and have been shown to significantly increase the growth rate and strength of hair in children (228). Worldwide, the number of cases of diabetes is estimated to be around 150 million, and is expected to double by 2025 (229). Because of the wealth of research demonstrating the ability of biotin supplements to both prevent diabetes and improve glucose metabolism we have no hesitation in recommending the above NRVs.

Vitamin C

Infants

0-6 mo 200mg

7-12 mo 400mg

Children

1-3 y 600mg

4-8 y 1000mg

Males

9-13 y 1750mg

14-18 y 2800mg

19-30 y 3000mg

31-50 y 3000mg

50-70 y 3000mg

> 70 y 3000mg

Females

9-13 y 1750mg

14-18 y 2800mg

19-30 y 3000mg

31-50 y 3000mg

50-70 y 3000mg

> 70 y 3000mg

Pregnancy

≤ 18 y 2900mg

19-30y 3100mg

31-50 y 3100mg

Lactation

≤ 18 y 3000mg

19-30y 3200mg

31-50 y 3200mg

Justification: Studies have shown that several population groups have an inadequate intake of vitamin C, and that deficiencies of ascorbic acid are far more prevalent than is commonly believed (230-241). Moreover, patients suffering from dementia (242), epilepsy (243), preeclampsia (244, 245), gallbladder disease (246), schizophrenia (247, 248), coronary artery disease (249-253), cerebral vascular disease (254), esophageal, stomach and colorectal cancers (255, 256) and gastric cancer (257), have all been found to have significantly lower levels of vitamin C than are found in normal healthy people.

Similarly, the risk of stroke has been shown to increase significantly with a decreased intake of vitamin C (258), and low levels of ascorbic acid are implicated in the development of gastric cancer (259-261), periodontal disease (262), and

cardiovascular disease (263). A high intake of ascorbic acid, on the other hand, has been found to be protective against the development of gastric cancer (264-269, 292-296), as well as cancers of the esophagus (270), uterus (290), oral cavity, stomach, pancreas, cervix, rectum, lung (291), breast (291, 298, 299), ovaries (310), and others (271). In this respect it is interesting to note that megadoses of vitamin C and other nutrients have been shown to significantly reduce the recurrence of tumors in patients with bladder cancer (297), and that male smokers with a high intake of vitamin C have been shown to have a lower risk of cancer than male smokers with a lower intake of vitamin C (300).

Hospital patients with low levels of ascorbic acid have a greater frequency of postoperative complications, and administering ascorbic acid until blood levels returned to normal has been proven to prevent postoperative complications (327). Other researchers have demonstrated that a mixture of vitamins C, E and A also dramatically reduces the postoperative complication rate (328).

People with the highest levels of vitamin C have also been found to have a significantly lower incidence of nuclear opacities. In fact, it has been found that the longer the duration that vitamin C supplements are taken for the lower is the prevalence of nuclear opacities. This has led researchers to conclude that vitamin C plays a strong role in preventing nuclear opacities (272). Other studies recommend the use of vitamin C and other antioxidant supplements in the prevention of age-related cataract and macular degeneration (273), and research also shows that that ascorbic acid can protect the cornea from ultraviolet radiation (274).

Research has shown that a high dietary intake of vitamin C and vitamin E may lower the risk of Alzheimer disease (329). 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 (331), and that vitamins C and E may prevent dementia and improve cognitive functioning in later life (330).

Studies have also confirmed that vitamin C has a protective effect against the development of coronary heart disease (275, 276), and that vitamin C is beneficial in preventing the advancement of arteriosclerosis in heart transplant patients (277). Indeed, researchers have shown that human cardiovascular disease is the direct consequence of the inability of man to synthesize ascorbate in combination with insufficient intake of ascorbate in the modern diet. Since ascorbate deficiency is the common cause of human CVD, ascorbate resupplementation is the universal treatment for this disease (278). As such, the therapeutic use of vitamin C and other nutrients may well pave the way towards a new therapeutic goal, namely, the noninvasive reversal of existing cardiovascular disease with nutritional supplements (279). In that respect it is now increasingly clear that vitamin C should be used in the treatment of coronary arterial disease patients, and those with heart attacks, strokes, or hypertension (301).

A daily dose of 2700 mg of Vitamin C, when taken with other nutrients, has been shown to halt the progression of early coronary atherosclerosis (280), and other

researchers have similarly found that the combination of vitamin C and vitamin E can slow the advancement of atherosclerosis (281). 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, and concluded that diabetics, smokers and those with hypertension would all benefit from taking supplemental vitamin C (282). 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 (283, 289), and that supplementing the diet with nutrients including vitamins C, E, B6 and folate is conducive to the prevention of cardiovascular disease (284). In this respect it is also interesting to note that some researchers particularly recommend dietary supplementation of vitamin C and E in Northern Europe, where cardiovascular disease is most prevalent (285).

Deaths from stomach cancer and cardiovascular disease and cerebrovascular disease are all associated with low levels of vitamin C (286); in fact it has been demonstrated that mortality for all causes of death decreases strongly with an increased intake of supplemental vitamin C (287). A study of 8,453 Americans' serum ascorbic acid (SAA) levels and mortality rates from disease, for example, found that those with a normal to high level of SAA had a 21%-25% lower risk of dying from cardiovascular disease, and that they had a 25%-29% decrease in risk of mortality from all causes compared to those with low levels of SAA (288).

Vitamin C supplements have also been shown to improve the body's ability to metabolize glucose and lipids and as such are seen as being beneficial to those with Type II diabetes (302). Similarly, people with higher levels of vitamin C have been found to have a lower incidence and risk of hyperglycemia (303).

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 C and vitamin E (304).

Vitamin C supplements have been shown to be an effective treatment for hypertension, both in non-diabetics (305-308), and in diabetics (309), and have been found to reduce muscle soreness and improve muscle function after exercise (317, 318).

Research has also demonstrated the ability of higher doses of vitamin C to delay bone loss (311), and to increase bone density (312). Similarly, an increased intake of vitamins C and E has been shown to reduce the risk of hip fractures (313).

Studies have also found that the duration and severity of colds can be decreased by an increased intake of vitamin C (314, 315), and that doses of vitamin C between 500-2000mg improve antioxidant protection (316).

Some researchers have argued for higher intakes of vitamin C to be recommended for populations chronically exposed to air pollutants (such as ozone),

cigarette smoking, or those doing vigorous exercise (319). Other studies have made similar recommendations for people who are exposed to passive smoking (320, 321). Indeed, it has been shown that high doses of vitamin C can reduce or eliminate the negative effect that smoking has on blood flow (322), and that vitamin C supplements can protect against the cardiovascular problems caused by cigarette smoke inhalation (323). In this respect it is also interesting to note that vitamin C supplements have been shown to significantly reduce cholesterol, LDL-C and triglycerides, as well as increase serum HDL (324).

Researchers also recommend that people who are smokers, diabetics, pregnant, users of antibiotics, people who ingest alcohol, and users of contraceptives all need to supplement with vitamin C. (325). Indeed, vitamin C is depleted in women who use oral contraceptives, which may result in cardiac problems and thrombosis. (326). Since vitamin supplements are routine for pregnancy, they should also be routine for the pseudo pregnancy of oral contraception (326).

Finally, we note that the World Health Organization currently attributes one-third of all global deaths annually (15.3 million) to cardiovascular disease (332), and that in 2000 over 6 million deaths occurred from cancer (333). Moreover, estimates predict that by 2020 the total number of cases of cancer will have increased by 73% in the developing world and by 29% in the developed world. (333). Given therefore the proven safety and efficacy of ascorbic acid in the prevention and treatment of both cardiovascular disease and cancer, we have no hesitation in recommending the above NRVs for this nutrient.

Vitamin D

Note: 1μg calciferol = 40 IU vitamin D.

Infants

0-6 mo 5μg

7-12 mo 5μg

Children 1-3 y 5μg

4-8 y 6.5μg

Males 9-13 y 12μg

14-18 y 18μg

19-30 y 20μg

31-50 y 20μg

50-70 y 20*μ*g

> 70 y 20*μ*g

Females

9-13 y 12*μ*g

14-18 y 18*μ*g

19-30 y 20*μ*g

31-50 y 20*μ*g

50-70 y 20*μ*g

> 70 y 20*μ*g

Pregnancy

≤ 18 y 20*μ*g

19-30y 20*μ*g

31-50 y 20*μ*g

Lactation

≤ 18 y 20*μ*g

19-30y 20*μ*g

31-50 y 20*μ*g

Justification: Nowadays, severe deficiency of vitamin D is not a common finding in most developed countries. However, the prevalence of vitamin D insufficiency is relatively high and it can contribute to the lowering of bone mass in osteoporosis risk populations (334). In this respect it is important to note that Vitamin D deficiency can occur without any symptoms, and that if symptoms are present it indicates severe deficiency (349). Moreover, serum calcium and phosphorus values do not often predict the existence of deficiency (349).

A decrease in bone mineral density is the most important cause of fracture (335). Among other factors, Calcium and vitamin D deficiencies are important risk factors for a decrease in bone mineral density, and can consequently induce osteoporosis (335). In this respect it is interesting to note that the high prevalence of vitamin D deficiency in healthy elderly people in southern European countries increases the risk of osteoporotic

fractures in these populations to levels above those anticipated for the general elderly population of the European community (335). As such, the ageing of the European population will double the number of osteoporotic fractures over the next 50 years unless adequate preventative measures are undertaken (335).

Research assessing the cost implications for a preventive treatment strategy for institutionalized elderly women found that the incidence of hip and other fractures was reduced by vitamin D and calcium supplements, and concluded that such strategies are cost saving (336). The doses given in this study were 1200 mg/day calcium and 20*μ*g (800 IU) daily of vitamin D, and the data used in the research was collected from studies conduced in seven European countries (336).

Other research concurs that a daily dose of 20*μ*g (800 IU) of vitamin D (or the equivalent 2500*μ*g/100,000 IU given three times per year) reduces the frequency of both falls (337) and fractures (338-340). Moreover, research has shown that severe vitamin D deficiency is present in virtually all elderly institutionalized subjects, and that as such, routine vitamin D supplementation is warranted for such people (341).

Studies also suggest that a daily supplement of 10*μ*g (400 IU) is helpful in maintaining an adequate concentration of vitamin D in infants (342), and that vitamin D supplementation during infancy is associated with higher bone mineral mass in prepubertal girls (343).

Research has also shown that most cases of colon cancer may be prevented with an intake of vitamin D in the range of 20*μ*g (800 IU) per day, and epidemiological data suggest that such an intake may additionally be associated with enhanced survival rates among breast cancer cases (344). Other evidence from diverse areas of study - epidemiologic, molecular, genetic, cellular, animal models, and clinical trials - suggests that vitamin D may be an effective preventive agent against prostate cancer (345).

Dietary supplementation of vitamin D is also associated with reduced risk of Type-1 diabetes, and children who take a 20*μ*g (2000 IU) dose of vitamin D daily have been shown to have a lower risk of developing the disease than children who do not (346).

Women with the highest vitamin D intake from supplements (10*μ*g/400 IU or more per day) have been shown to be 40 percent less likely to develop multiple sclerosis than those women who do not use supplements (347). Similarly, women who consume vitamin D in both supplement and food form have also been shown to have a lower risk of developing multiple sclerosis; whereas women who derive their intake of this vitamin from food only do not experience a reduced risk of developing the disease (347). In addition, patients already suffering from multiple sclerosis who are given supplements of vitamin D, calcium and magnesium have been shown to have a decreased rate of relapse (348).

Research has also shown that vitamin D deficiency exists in patients with tuberculosis, and that it is possibly a cause rather than an effect of this disease (349).

Given the fact therefore that the incidence of this disease is currently increasing in many countries, there exists an urgent need for effective, affordable preventative measures to be instigated at the earliest opportunity.

Finally, we are of the opinion that the alleged dangers of vitamin D supplements have been exaggerated in many cases, as single doses ranging from 200,000 units to over 500,000 units have been given to infants both orally and by injection without any ill effects. (350). Moreover, the weight of evidence shows that the currently accepted, no observed adverse effect limit of 2,000 IU per day is too low by at least 5-fold (351). One hour of total-body sun exposure easily provides the equivalent of 10,000 IU of vitamin D, for example (351); clearly, many people get this on a regular basis without experiencing toxicity symptoms. Doses of 15000μg (600,000 IU) of vitamin D have also been given to pregnant women in the 7th and 8th months of pregnancy without evidence of harm (352).

Vitamin E

Infants

0-6 mo 30 IU

7-12 mo 60 IU

Children

1-3 y 80 IU

4-8 y 130 IU

Males

9-13 y 230 IU

14-18 y 370 IU

19-30 y 400 IU

31-50 y 400 IU

50-70 y 400 IU

> 70 y 400 IU

Females

9-13 y 230 IU

14-18 y 370 IU

19-30 y 400 IU

31-50 y 400 IU

50-70 y 400 IU

> 70 y 400 IU

Pregnancy

≤ 18 y 385 IU

19-30y 415 IU

31-50 y 415 IU

Lactation

≤ 18 y 400 IU

19-30y 430 IU

31-50 y 430 IU

Justification: The World Health Organization currently attributes one-third of all global deaths annually (15.3 million) to cardiovascular disease (332), and patients with coronary artery disease have been shown to have significantly lower blood levels of vitamin E than normal healthy people. (249).

Studies have demonstrated that vitamin E supplements are effective in the treatment of cardiovascular disease (353-355), and that the combination of vitamin E and vitamin C can slow the advancement of atherosclerosis (281). 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 (282). 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 (283, 289), and that supplementing the diet with nutrients including vitamins E, C, B6 and folate is conducive to the prevention of cardiovascular disease (284). 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 (285).

Vitamin E therapy has also been shown to reduce arterial blockage in patients suffering from intermittent claudication (356, 357), and recent research has indicated

that it normalizes high blood pressure (358-360). Vitamin E also promotes collateral circulation; consequently offering great benefits to diabetes patients (361).

A recent study looked at patients with colon cancer who received a daily dose of 750 mg of vitamin E during a period of 2 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 (362).

Other research suggests that vitamin E supplementation also improves immune function in healthy elderly people (366, 367).

Research has additionally shown that a high dietary intake of vitamin E and vitamin C may lower the risk of Alzheimer disease (329). 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 (331), and that vitamins E and C may prevent dementia and improve cognitive functioning in later life (330). 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 (363).

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, whilst 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 (364). 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. (365).

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 (368).

An increased intake of vitamins E and C has been found to reduce the risk of hip fractures (313), and researchers have also demonstrated that a mixture of vitamins E, C and A dramatically reduces the postoperative complication rate (328). 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 (304).

Finally, 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 (369).

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."

Vitamin K

Infants

0-6 mo 45*μ*g

7-12 mo 90*μ*g

Children

1-3 y 120*μ*g

4-8 y 190*μ*g

Males

9-13 y 350*μ*g

14-18 y 560*μ*g

19-30 y 600*μ*g

31-50 y 600*μ*g

50-70 y 600*μ*g

> 70 y 600*μ*g

Females

9-13 y 350*μ*g

14-18 y 560*μ*g

19-30 y 600*μ*g

31-50 y 600*μ*g

50-70 y 600*μ*g

> 70 y 600*μ*g

Pregnancy

14-18 y 580μg

19-30 y 620μg

31-50 y 620μg

Lactation

14-18 y 605μg

19-30 y 645μg

31-50 y 645μg

Justification: Research using healthy adults aged 19-36 years who were given vitamin K supplements has shown that a daily phylloquinone intake of approximately 1000μg is required to maximally gamma-carboxylate circulating osteocalcin (370), and that a diet low in vitamin K1 can result in a functional subclinical deficiency of vitamin K (decreased urinary gamma-carboxyglutamic acid excretion) without affecting blood coagulation (371). Current estimates suggest that the dietary intake of vitamin K is in the range 124-375 μg /d in a European population (372).

Studies have repeatedly shown that higher intakes of vitamin K reduce the risk of hip fracture (373, 374) and that low intakes may increase the risk of hip fracture in women (375). This data supports the case for a reassessment of the vitamin K requirements that are based on both blood coagulation and bone health (375).

Low dietary vitamin K intake is also associated with low bone mineral density in women (376), and evidence from observational studies and first intervention trials indicate that vitamin K intakes much higher than the current recommendations improve both biochemical markers of bone formation and bone density (377). In deed, the mechanistic data as well as the observational data and the results of the first controlled clinical trials in humans point to a beneficial effect of additional intakes of vitamin K in bone health (377).

Supplements of vitamin K (containing 45mg of menatetrenone) have been shown to promote bone formation in postmenopausal women when taken for a period of 48 weeks (378), and therapy combining vitamin K(2) and D(3) has been shown to be useful for increasing vertebral bone mass in postmenopausal women (379). Similarly, research findings indicate that the combined administration of vitamin D3 and vitamin K2 appears to be useful in increasing the bone mineral density of the lumbar spine in postmenopausal women with osteoporosis (380), and that vitamin K (as menatetrenone) may be beneficial in the prevention of bone loss in patients with anorexia nervosa (381).

Vitamin K (as menatetrenone) has also been shown to reduce the risk of hip fracture in elderly female Parkinson's disease patients (382). Significant reduction in

bone mineral density occurs in patients with Parkinson's disease, resulting in an increasing risk of hip fracture, especially in elderly women. (382).

Research also suggests that it would be prudent to consider routine vitamin K supplementation in patients with cystic fibrosis, severe noncholestatic and cholestatic liver disease, major small-bowel resection, and pancreatic insufficiency or lung disease necessitating frequent use of antibiotics (383). Patients with Crohn's disease have also been found to have low serum levels of vitamin K, and as such are at particular risk of osteoporosis (384).

Studies have demonstrated that oral vitamin K is as effective as injectable Vitamin K in newborns, and researchers are now recommending its usage to reduce the complications and costs of parenteral therapy (385). Other data has confirmed the effectiveness of oral vitamin K given to newborns in reducing infant mortality and morbidity from bleeding disorders such as intracranial hemorrhage (386). Indeed, additional research suggests that supplementation of infants with vitamin K is highly advisable, and that increments of vitamin K during pregnancy and lactation should also be recommended (387). In this respect it is interesting to note that maternal vitamin K supplementation can maintain the vitamin K status of infants throughout the late neonatal period and prevent an onset of vitamin K-deficient hemorrhage (388).

Finally, research has also shown that low dietary vitamin K intake is associated with an increased risk of aortic calcification (389), and that vitamin K may play an important role in the acute insulin response in glucose tolerance (390).

Boron

Based upon the knowledge that we have at this time, we consider that the science suggests an optimal intake of 1.5-3mg for men and women aged 18 years and above, and that dietary boron is sufficiently important to be considered essential in human beings.

Justification: The daily intake of boron in humans has been estimated to range from 0.3-41 mg. The wide range is due to the variation of the analytical methods used and differences in the soil content of boron (464).

Dietary boron influences the activity of many metabolic enzymes, as well as the metabolism of steroid hormones and several micronutrients, including calcium, magnesium, and vitamin D (465).

Research shows that a boron supplement of 3 mg/day markedly reduces the urinary excretion of calcium and magnesium in post-menopausal women (466).

Because boron deprivation causes changes similar to those seen in women with postmenopausal osteoporosis, this element is apparently needed for optimal calcium metabolism and is thus needed to prevent the excessive bone loss which often occurs in postmenopausal women and older men (467).

The elevation of endogenous estrogen as a result of supplementation suggests a protective role for boron in atherosclerosis (468).

When contrasted with the high boron intake, low dietary boron results in significantly poorer performance on tasks emphasizing manual dexterity; eye-hand coordination; attention; perception; encoding and short-term memory; and long-term memory. Data indicates that boron may play a role in human brain function and cognitive performance, and provides additional evidence that boron is an essential nutrient for humans (469).

Evidence suggests boron is a safe and effective treatment for some forms of arthritis. Epidemiologic evidence shows that in areas of the world where boron intakes usually are 1.0 mg or less/day the estimated incidence of arthritis ranges from 20 to 70%, whereas in areas of the world where boron intakes are usually 3 to 10 mg, the estimated incidence of arthritis ranges from 0 to 10%. Experimental evidence from a double-blind placebo-boron supplementation trial with 20 subjects with osteoarthritis showed a significant favorable response to a 6mg boron/day supplement, in that 50% of subjects receiving the supplement improved compared to only 10% receiving the placebo. This data indicates that boron is an essential nutrient for healthy bones and joints (470).

Finally, men who ingest the greatest amount of boron have been shown to be 64% less likely to develop prostate cancer compared to men who consumed the least amount of boron (471).

Calcium

Infants
0-6 mo 210mg
7-12 mo 270mg
Children
1-3 y 500mg
4-8 y 800mg
Males
9-13 y 1300mg
14-18 y 1300mg
19-30 y 1000mg
31-50 y 1000mg
50-70 y 1200mg
> 70 y 1200mg
Females
9-13 y 1300mg
14-18 y 1300mg
19-30 y 1000mg
31-50 y 1000mg
50-70 y 1200mg
> 70 y 1200mg

Pregnancy
≤ 18 y 1300mg
19-30y 1000mg
31-50 y 1000mg
Lactation
≤ 18 y 1300mg
19-30y 1000mg
31-50 y 1000mg

Justification: The above figures are the current US NRVs for calcium (391), and we broadly concur with both the US supporting data and with other research which suggests that the daily consumption of calcium in the diet should, optimally, be at least 1200 mg/day (392).

Copper

Infants

0-6 mo 200*μ*g

7-12 mo 290*μ*g

Children

1-3 y 390*μ*g

4-8 y 645*μ*g

Males

9-13 y 1160*μ*g

14-18 y 1870*μ*g

19-30 y 2000*μ*g

31-50 y 2000*μ*g

50-70 y 2000*μ*g

> 70 y 2000*μ*g

Females

9-13 y 970*μ*g

14-18 y 1570*μ*g

19-30 y 1680μg

31-50 y 1680μg

50-70 y 1680μg

> 70 y 1680μg

Pregnancy

≤ 18 y 1670μg

19-30y 1780μg

31-50 y 1780μg

Lactation

≤ 18 y 1770μg

19-30y 1880μg

31-50 y 1880μg

Justification: Several national food surveys in the United States have revealed marginally to moderately low contents of copper in the typical American diet (393), and the dietary intake of copper has been shown to be below the recommended daily allowance in several different population groups. (394-396).

Metabolic balance studies have demonstrated that daily copper losses are approximately 1.3mg/day (397). In order to remain in copper balance, the average adult male must consume a diet that contains at least 2mg copper/day. (397). However, some research suggests that up to eighty-one per cent of people consume less than 2mg of copper in their daily diets (398), and that a marginal deficiency of this trace element exists in up to 62% of people suffering from hypertension (399). In this respect it is interesting to note that supplementation with 5mg of copper per day has been shown to decrease both systolic and diastolic blood pressure in patients with mild stable hypertension (399).

Research has shown that the recovery from mild copper depletion may require more aggressive intervention than 2mg per day of copper taken for 35 days (400), and a review of studies of experimental copper deprivation conducted in adult humans indicated that 2.6mg of copper per day taken for periods of up to 42 days is similarly sufficient for recovery from copper deprivation (401). Studies from animal models and in human volunteers have permitted to construct a provisional continuum of acceptable intakes of copper that would avoid copper deficiency and/or toxicity: acceptable intakes may vary between 10 and 50μg/kg body weight (402).

Men and women fed diets close to 1mg of copper per day, amounts quite frequent in the United States, responded with reversible, potentially harmful changes in blood pressure control, cholesterol and glucose metabolism, and electrocardiograms (403). Copper deficiency is also known to impair cell-mediated immunity (408).

Numerous anatomical, chemical and physiological similarities between animals deficient in copper and people with ischemic heart disease have been noticed (403, 406), and a correlation has been established between low intake of copper and prevalence of ischemic heart disease, dyslipoproteinemia, arterial hypertension and excessive body mass (404). Dietary copper deficiency may also impair cardiovascular health by contributing to enhancement of inflammation, anemia and reduced blood clotting (405).

Indeed, some researchers believe that more features of the etiology, pathogenesis, and pathophysiology of ischemic heart disease can be explained in terms of copper deficiency than can be explained by any other environmental insult (406). It is interesting to note therefore that people with ischemic heart disease have been shown to have decreased cardiac and leucocyte copper and decreased activities of some copper-dependent enzymes (407).

Chromium

Infants
0-6 mo 15*μ*g
7-12 mo 30*μ*g
Children
1-3 y 40*μ*g
4-8 y 65*μ*g
Males
9-13 y 115*μ*g
14-18 y 190*μ*g
19-30 y 200*μ*g
31-50 y 200*μ*g
50-70 y 200*μ*g
> 70 y 200*μ*g
Females
9-13 y 115*μ*g
14-18 y 190*μ*g
19-30 y 200*μ*g
31-50 y 200*μ*g
50-70 y 200*μ*g
> 70 y 200*μ*g
Pregnancy
≤ 18 y 210*μ*g
19-30y 210*μ*g
31-50 y 210*μ*g

Lactation
≤ 18 y 215μg
19-30y 215μg
31-50 y 215μg

Justification: Normal dietary intake of chromium for humans is suboptimal, and most diets contain less than 60% of the minimum suggested intake of 50μg (409).

Suboptimal dietary intake of chromium is associated with an increase in risk factors associated with diabetes and cardiovascular diseases (410), and produces signs and symptoms similar to those seen in these diseases (411).

Supplemental chromium is associated with a reduction in the risk factors for maturity-onset diabetes and cardiovascular diseases (412). Supplemental chromium given to people with impaired glucose tolerance or diabetes leads to improved blood glucose, insulin, and lipid variables (409).

Diabetics are frequently found to be low in chromium (413). Research has also demonstrated that plasma chromium levels are significantly lower in patients with coronary artery disease (423), and rheumatoid arthritis (424).

A daily supplement containing 200μg has been shown in some patients to be capable of reducing their requirements for insulin, sulfonylurea or metformin (414). Other research similarly confirms the beneficial effects of chromium supplements in individuals with diabetes (415-418). However, it is important to note that the beneficial effects of chromium in individuals with diabetes are generally only observed at levels higher than the upper limit of the Estimated Safe and Adequate Daily Dietary Intake (419). 200μg per day of supplemental chromium is adequate to improve glucose variables of those who are mildly glucose intolerant, whereas people with more overt impairments in glucose tolerance and diabetes usually require more than 200μg per day (420).

Chromium supplementation of normal adult men, as well as diabetics, has been reported to increase high density lipoprotein cholesterol and decrease triglycerides and total cholesterol (421). Indeed, some researchers consider that the beneficial effects of chromium repletion are now so well established and the trivalent form is so free of toxicity that it should now be used in clinical medicine for the benefit of those with some forms of diabetes and its complications and those suffering from atherosclerosis (422).

Chromium has also been shown to have antidepressant effects in patients with atypical depression (425), and has been found to be capable of increasing lean body mass in obese patients (426). Niacin-bound chromium supplements at a daily dose of 600μg have been demonstrated to cause overweight women on a modest dietary and exercise regimen to lose a significant amount of fat compared to placebo (427).

Finally, most recent evidence strongly supports the conclusion that there is little fear of toxic reactions from chromium consumption, and that supplementation may be

useful to ameliorate many of the manifestations of ageing (411). In this respect, we note that the 350-fold difference between the acceptable daily intake and the calculated reference dose for humans of 70μg per day seems without precedent with respect to other nutritional minerals, and that the beneficial effects of chromium on serum glucose and lipids and insulin resistance occur even in the healthy (428).

Iodine

Infants
0-6 mo 110μg
7-12 mo 130μg
Children
1-3 y 90μg
4-8 y 90μg
Males
9-13 y 120μg
14-18 y 150μg
19-30 y 150μg
31-50 y 150μg
50-70 y 150μg
> 70 y 150μg
Females
9-13 y 120μg
14-18 y 150μg
19-30 y 150μg
31-50 y 150μg
50-70 y 150μg
> 70 y 150μg
Pregnancy
≤ 18 y 220μg
19-30y 220μg
31-50 y 220μg
Lactation
≤ 18 y 290μg
19-30y 290μg
31-50 y 290μg

Justification: The above figures are the current US NRVs for iodine (429), and the FAO/WHO Helsinki Consultation similarly set a figure of 150μg for Iodine when it met in 1988. We currently see no reason to alter these figures.

Iron

Infants
0-6 mo 0.27mg
7-12 mo 11mg
Children

1-3 y 7mg
4-8 y 10mg
Males
9-13 y 8mg
14-18 y 11mg
19-30 y 8mg
31-50 y 8mg
50-70 y 8mg
> 70 y 8mg
Females
9-13 y 8mg
14-18 y 15mg
19-30 y 18mg
31-50 y 18mg
50-70 y 8mg
> 70 y 8mg
Pregnancy
≤ 18 y 27mg
19-30y 27mg
31-50 y 27mg
Lactation
≤ 18 y 10mg
19-30y 9mg
31-50 y 9mg

Justification: The above figures are the current US NRVs for iron (430), and we broadly concur with the US supporting data.

Magnesium

Infants
0-6 mo 40mg
7-12 mo 75mg
Children
1-3 y 95mg
4-8 y 160mg
Males
9-13 y 290mg
14-18 y 480mg
19-30 y 500mg
31-50 y 500mg
50-70 y 500mg
> 70 y 500mg
Females
9-13 y 290mg
14-18 y 480mg
19-30 y 500mg

31-50 y 500mg
50-70 y 500mg
> 70 y 500mg
Pregnancy
≤ 18 y 500mg
19-30y 520mg
31-50 y 520mg
Lactation
≤ 18 y 520mg
19-30y 540mg
31-50 y 540mg

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 (431).

As such it is hardly surprising that suboptimal intakes of magnesium and outright magnesium deficiencies are now commonplace in many population groups (435-452). 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 (453). In this respect it should be noted that although serum levels are commonly used to assess magnesium deficiency, red cells and leucocytes can be still deficient despite normal serum values (454).

Magnesium deficiency produces abnormal cardiac rhythms that can cause sudden death from a heart attack (432, 433), and optimal levels of magnesium are strongly related to a lower risk of heart disease (434). Moreover, magnesium deficiency is commonplace in patients suffering from congestive heart failure (438), and a correlation between low magnesium consumption and the prevalence of the ischemic heart disease has been observed (451, 449). Further supporting evidence for the role of magnesium in protecting the heart can be drawn from the fact that magnesium infusions in patients with acute myocardial infarction have been shown to reduce the incidences of arrhythmias, death and the size of infarction (444).

In addition, serum magnesium levels are also known to be inversely associated with the risk of hypertension (448), and research has demonstrated that hypomagnesemia detected at the time of admission to hospital of acutely ill medical patients is associated with an increased mortality rate for both ward and intensive care unit patients (455).

Erythrocyte magnesium levels in patients with premenstrual tension syndrome have been shown to be significantly lower than those of the normal population (456), and as such it is believed that magnesium deficiency may also play a role in the etiology of this syndrome (457). Similarly, the biochemical signs of chronic magnesium deficiency are also known to be present in patients suffering from osteoporosis (459-461) and diabetes (462, 463).

Finally, we note that a 100 mg/day higher magnesium intake has been shown to be associated with better lung function and a reduced risk of airway hyper-reactivity and wheezing (458), and that a number of age-related neurodegenerative diseases have also been linked with various types of magnesium depletion (446).

Given that the World Health Organization currently attributes one-third of all global deaths annually (15.3 million) to cardiovascular disease (332) we have no hesitation in recommending the above NRVs for magnesium.

Manganese

Infants

0-6 mo 0.4mg

7-12 mo 0.9mg

Children

1-3 y 1.2mg

4-8 y 1.9mg

Males

9-13 y 3.5mg

14-18 y 5.6mg

19-30 y 6.0mg

31-50 y 6.0mg

50-70 y 6.0mg

> 70 y 6.0mg

Females

9-13 y 2.9mg

14-18 y 4.7mg

19-30 y 5.0mg

31-50 y 5.0mg

50-70 y 5.0mg

> 70 y 5.0mg

Pregnancy

≤ 18 y 4.9mg

19-30y 5.2mg

31-50 y 5.2mg

Lactation

≤ 18 y 5.1mg

19-30y 5.4mg

31-50 y 5.4mg

Justification: Patients suffering from osteoporosis have been found to have low blood levels of manganese (472, 473), and studies suggest that manganese supplements, either alone or in combination with other minerals, may both prevent fractures and halt bone loss (474, 475).

People with diabetes may also have low blood levels of manganese (476), and research suggests that manganese deficiency can contribute to glucose intolerance and that this may be reversed by supplementation (477).

Similarly, manganese deficiency may also aggravate Meniere's disease (481).

Research has also demonstrated that manganese supplements can both prevent and reverse the development of Tardive Dyskinesia (478-480).

Manganese is often low in refined and processed foods (482, 483). As such therefore, people whose diets consist primarily of these types of foods may consequently have a low manganese intake.

Finally, an increased manganese intake may be especially important whenever iron is supplemented, because iron can reduce the absorption of manganese and cause lower body levels of it (484).

Molybdenum

Infants
0-6 mo 10μg
7-12 mo 20μg
Children
1-3 y 30μg

4-8 y 50μg
Males
9-13 y 90μg
14-18 y 140μg
19-30 y 150μg
31-50 y 150μg
50-70 y 150μg
> 70 y 150μg
Females
9-13 y 70μg
14-18 y 100μg
19-30 y 125μg
31-50 y 125μg
50-70 y 125μg
> 70 y 125μg
Pregnancy
≤ 18 y 105μg
19-30y 130μg
31-50 y 130μg
Lactation
≤ 18 y 110μg
19-30y 135μg
31-50 y 135μg

Justification: The average diet in Western countries contains up to 500μg of molybdenum daily (485, 486).

Molybdenum levels in soil have been shown to be substantially lower in areas with the highest incidence of esophageal cancer (486, 487), and research suggests that molybdenum deficiency is associated with oesophageal cancer (486, 488).

Moreover, molybdenum also has an inhibitory effect upon gastrointestinal carcinogenesis, and research has demonstrated inverse correlations between molybdenum levels and female mortality from cancers of the esophagus and rectum (489).

Asthma symptoms are known to be triggered in some people by ingestion of sulfites, and molybdenum has been shown to aid in the detoxification of sulfites (490). Trials have used molybdenum supplements in amounts of 500μg per day in the treatment of such conditions (491).

Molybdenum has also been shown to be useful in the treatment of children whose teeth have become stained through the ingestion of fluorine (492).

Finally, we note that molybdenum is accepted as an essential element and that it has a relatively low toxicity (485).

Selenium

Infants
0-6 mo 15*μ*g
7-12 mo 30*μ*g
Children
1-3 y 40*μ*g
4-8 y 65*μ*g
Males
9-13 y 115*μ*g
14-18 y 190*μ*g
19-30 y 200*μ*g
31-50 y 200*μ*g
50-70 y 200*μ*g
> 70 y 200*μ*g
Females
9-13 y 115*μ*g
14-18 y 190*μ*g
19-30 y 200*μ*g
31-50 y 200*μ*g
50-70 y 200*μ*g
> 70 y 200*μ*g
Pregnancy
≤ 18 y 210*μ*g
19-30y 210*μ*g
31-50 y 210*μ*g
Lactation
≤ 18 y 215*μ*g
19-30y 215*μ*g
31-50 y 215*μ*g

Justification: Selenium intake has been shown to be inadequate in many countries, and selenium deficiency is now relatively commonplace (493-501).

Research has demonstrated an inverse relationship between serum selenium levels and the incidence of cancer (502), and mounting evidence reveals that selenium has both anticarcinogenic and antitumorigenic properties (503).

Studies have also shown that the lower the soil levels of selenium are in a region the higher will be the prevalence of cancer in that region (504-506). In this respect it is interesting to note that researchers have measured the selenium content of the soil across the whole of the United States and found that it varies widely; the highest levels being found in the soil of South Dakota, and the lowest levels being found in Ohio. Analysis of this research showed that Rapid City, South Dakota, had the lowest overall cancer mortality rate in the whole of the United States, whilst the death rate from cancer in Ohio was almost twice that of South Dakota (507-510). Additional research has confirmed these results and extended them to almost thirty countries; definitively

showing that the lower the intake of selenium the higher was the incidence of leukaemia and cancers of the large intestine, rectum, prostate, breast, ovary, lung, pancreas, skin and bladder (511). As such, the mythical “healthy diet” is clearly insufficient to prevent the development of cancer in areas where selenium is deficient in the soil.

Selenium supplements have been shown to reduce both the incidence of cancer and mortality resulting from it (512-516). Research has clearly shown, for example, that 200μg of supplemental selenium a day can reduce overall cancer mortality by 50% in humans compared to a placebo group not receiving supplemental selenium (517).

Research has also demonstrated an inverse relationship between serum selenium levels and the incidence of cardiovascular disease (502). Similarly, there is a significant, inverse correlation between plasma levels of selenium and severity of coronary atherosclerosis (518), and the serum selenium concentration of patients with acute myocardial infarction has been shown to be significantly lower than that of healthy people (519, 520). Indeed, low serum levels of selenium are associated with an increased risk of death from acute coronary heart disease and a higher risk of both fatal and nonfatal myocardial infarction (521). These findings are corroborated by separate research which shows a lower life expectancy and an elevated mortality from endemic and chronic diseases for people living in areas where the soil is deficient in selenium (534).

It has also been demonstrated that in the United States there is an inverse relationship between the quantity of selenium in the soil and mortality from AIDS (522). In this respect it is interesting to note that a selenium supplement of 200μg has been shown to markedly decrease the hospital admission rates of patients infected with HIV, decreasing the cost for hospitalization by 58% (523).

Patients with systemic inflammatory response syndrome (SIRS) have been found to have low selenium levels (524), as have patients suffering from chronic pancreatitis (525), and muscular dystrophy (526). Research also suggests that the incidence of goiter is related to low serum levels of selenium (529).

Selenium supplements have been found to improve immune function in corticoid-dependent asthmatics (527), and in patients on haemodialysis (528). When taken with supplements of vitamin E, selenium supplements, have also been shown to produce an improvement of sperm motility and semen quality (530, 531).

Finally, it has been shown that the lower the level of selenium in the diet the more subjects report feelings of anxiety, depression, and tiredness. A 100μg supplement of selenium however has been shown to elevate mood and in particular, decrease anxiety (532, 533).

Zinc

Infants
0-6 mo 2mg

7-12 mo 4mg
Children
1-3 y 6mg
4-8 y 10mg
Males
9-13 y 17mg
14-18 y 28mg
19-30 y 30mg
31-50 y 30mg
50-70 y 30mg
> 70 y 30mg
Females
9-13 y 14mg
14-18 y 23mg
19-30 y 25mg
31-50 y 25mg
50-70 y 25mg
> 70 y 25mg
Pregnancy
≤ 18 y 24mg
19-30y 26mg
31-50 y 26mg
Lactation
≤ 18 y 25mg
19-30y 27mg
31-50 y 27mg

Justification: An insufficient intake of zinc and/or zinc deficiency has been shown to be relatively common (393-395, 535-540), and a high serum copper concentration in the presence of low serum zinc is known to be associated with an increased mortality from all cardiovascular diseases and from coronary heart disease in particular (548).

Similarly, children who suffer from allergies are at risk of zinc deficiency (553), and patients suffering from Parkinson's disease have been found to be functionally deficient in this nutrient (550).

Levels of zinc have also been shown to be significantly reduced in type-2 diabetes mellitus (541) and it has been established that zinc supplementation is helpful in achieving better glycemic control and improvement in the severity of peripheral neuropathy in diabetic patients (542).

Researchers have also demonstrated inverse correlations between blood pressure and serum levels of zinc (545), and that inadequate intakes of zinc are associated with an increased risk of bone fractures in middle-aged and elderly men (549).

Serum levels of zinc are frequently diminished in human immunodeficiency virus (HIV) infection, (543, 544), and research has shown that low levels of plasma zinc predict a 3-fold increase in HIV-related mortality, whereas normalization has been associated with significantly slower disease progression and a decrease in the rate of opportunistic infections (544).

It has also been shown that in patients with chronic liver disease the hepatic zinc concentration decreases as the severity of liver damage increases. Researchers have therefore suggested that zinc supplementation may improve hepatic encephalopathy by increasing the efficiency of the urea cycle (546). Indeed, zinc supplementation has also been found to improve glucose disposal in patients with cirrhosis (547).

Zinc supplements can have beneficial effects on the immune response in elderly people (556), and can decrease the incidence of infection and increase the survival rate following infection (557). Similarly, treatment of the common cold with zinc gluconate lozenges has been shown to result in a significant reduction in duration of symptoms (560).

In patients suffering from macular degeneration zinc supplements can reduce the visual loss associated with this disease (558).

Research also suggests that zinc inhibits human prostatic carcinoma cell growth (559).

People suffering from tinnitus have been shown to have lower levels of zinc than people who do not have tinnitus, and zinc supplements are known to be effective in decreasing the severity of this condition (551, 552).

Finally, we note that boys suffering from acne have been shown to have significantly lower serum levels of zinc than healthy subjects of the same age (554), and that researchers have demonstrated that zinc supplements are an effective treatment for this common adolescent condition (555).

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