CODEX ALIMENTARIUS COMMISSION

Food and Agriculture Organization of the United Nations

World Health Organization

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Agenda Items 3, 5 **CAC/40 CRD/27**

JOINT FAO/WHO FOOD STANDARDS PROGRAMME

CODEX ALIMENTARIUS COMMISSION

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Comments of National Health Federation (NHF)

GENERAL COMMENT

The National Health Federation (NHF), a non-profit international organization of consumers, appreciates the opportunity to comment on the following Agenda items.

Agenda Item 3 Reports of the FAO/WHO Coordinating Committee REP/17/EURO

NHF Comment: Given the negative health effects upon animals and humans of growth promoters in animal feed, NHF agrees with and supports CCEURO's near-unanimous position against the use of any such growth promoters, especially zilpaterol. Any work on Codex standards for growth promoters should be discontinued.

Agenda Item 5 (CX/CAC 17/40/3) Final adoption of Codex Texts

Part 1 – Standards and related texts submitted for adoption Draft standards and related texts submitted at Steps 5/8 and 8.

NHF Comments:

CCRVDF (Lasalocid sodium) – The NHF agrees with the position taken by the EU (and other delegations), wherein the EU states that lasalocid sodium is a risk to consumers that "cannot be ruled out, as in the absence of a methodology for derivation of a microbiological acute reference dose, there is no health-based guidance value with which to satisfactorily compare the acute exposure." Therefore, NHF opposes the adoption of the proposed draft MRLs for lasalocid sodium at Step 5/8.

CCPR (Malathion (49)) – The NHF also opposes the adoption of the proposed draft MRLs for Malathion at Step 8 because it has been proven to be carcinogenic and toxic to humans and animals. In particular, "WHO reported it "probably causes cancer....causes tumors in rats and DNA and chromosomal damage and disrupted hormone pathways." (*See, e.g.*, http://www.winnipegsun.com/2015/03/21/malathion-probably-causes-cancer) "Malathion, WHO found, could cause non-Hodgkin lymphoma and prostate cancer. In California, Malathion use has decreased by more than 40 percent from 2003 to 2012. Much of the Malathion applied in California goes to strawberry and alfalfa crops." (*See* https://www.revealnews.org/article/use-of-monsanto-pesticide-linked-to-cancer-has-boomed-in-california/) NHF has been long known for its stance against this carcinogen. Codex work in establishing an MRL for this pesticide should be discontinued.

CCPR (Chloropyrifos-methyl (90)) – The NHF also opposes the adoption of the proposed draft MRLs for Chloropyrifos-methyl at Step 8 because it has been proven to be a potent neurotoxin that particularly adversely affects children and pregnant women. Codex work in establishing an MRL for this pesticide should be discontinued.

CCPR (Buprofezin (173)) – The NHF also opposes the adoption of the proposed draft MRLs for Buprofezin at Step 5/8 because it gives rise to toxic aniline under high-temperature processing conditions. The U.S. EPA has classified **aniline** as a Group B2, probable human **carcinogen** that should be avoided. (*See* https://www.epa.gov/sites/production/files/2016-08/documents/aniline.pdf) Therefore, Codex work in establishing an MRL for this pesticide should be discontinued.

CCPR (Teflubenzuron (190)) – The NHF also opposes the adoption of the proposed draft MRLs for Teflubenzuron at Step 5/8 because it has been shown to be ecotoxic. Codex work in establishing an MRL for this pesticide should be discontinued.

CCPR (Saflufenacil (251)) – The NHF also opposes the adoption of the proposed draft MRLs for Saflufenacil at Step 5/8 because it has been shown to be ecotoxic. Further, NHF notes the reservations of the EU, which commented at the 2017 CCPR meeting that "an ARfD had been established in the EU and that they have identified potential acute dietary exposure concerns" with respect to certain commodities. Accordingly, Codex work in establishing an MRL for this pesticide should be discontinued.

CCPR (Fluazifop-P-Butyl (283)) – The NHF also opposes the adoption of the proposed draft MRLs for Fluazifop-p-butyl at Step 5/8 because it has been shown to be ecotoxic. Codex work in establishing an MRL for this pesticide should be discontinued.

CCPR (Flupyradifurone (285)) – The NHF also opposes the adoption of the proposed draft MRLs for Flupyradifurone at Step 5/8 because it has been shown to be extremely toxic to bees. Codex work in establishing an MRL for this pesticide should be discontinued.

CCPR (Glyphosate (158)) – The NHF absolutely opposes the establishment of any MRL for glyphosate as it is a proven carcinogen, endocrine disrupter, and destroys beneficial bacteria in the human and animal intestinal tracts, leading to chronic diseases in both.

Unfortunately, the Joint WHO-FAO Meeting on Pesticide Residues (JMPR) - the body that determines and sets the so-called "safe" level of pesticide residues allowed in our food, water, and the like - has declared that glyphosate/Roundup is unlikely to cause cancer in humans through consumption of glyphosate/Roundup residues in our food. The summary report from the JMPR is available at this link: http://www.who.int/foodsafety/jmprsummary2016.pdf?ua=1

Source: http://www.reuters.com/…/us-health-who-glyphosate-idUSKCN0Y…

Monsanto and regulatory agencies in the U.S. (EPA), EU (EFSA), and in Canada (Health Canada) are attempting to discredit and to dismiss the recent WHO/International Agency for Research on Cancer (IARC), as well as the California regulatory agency responsible for classifying potential carcinogens, credible and alarming classification of glyphosate as a "probable human carcinogen" by arguing that a health hazard is not a health risk, because – they (erroneously) argue – a health risk is based on the level of human exposure and consumption of glyphosate/Roundup.

However, toxicology research has alarmingly found that glyphosate/Roundup® has an inverse dose-toxicity relationship (i.e., a low dose = high toxicity). Moreover, Professor Gilles Eric Séralini and his team of researchers have recently and alarmingly found glyphosate, Roundup®, and each one of its co-formulants to be Endocrine Disrupting Chemicals (EDCs). As stated by Séralini, "A new study shows that the acceptable daily intake (ADI), the supposedly safe level, for glyphosate is unreliable in terms of assessing the risks of the complete commercial formulations that we are actually exposed to. The co-formulants were shown in the new study to have a far more powerful endocrine-disrupting effect at lower doses than the isolated active ingredient, glyphosate. The complete formulations (i.e., Roundup®) were also found to have much greater endocrine disrupting effects at lower doses than glyphosate alone.

"The research shows that the ADI should be calculated from toxicity tests on the commercial formulations as sold and used. The new study is the first ever demonstration that the endocrine-disrupting effects of glyphosate-based herbicides are not only attributable to glyphosate, the declared active ingredient, but above all to the co-formulants." (Link to the study: http://www.gmoseralini.org/new-research-shows-regulatory-s…/)

The Endocrine Society has also recently published an alarming (2nd) Scientific Statement on the toxicity and human health hazards of EDCs. The Society states,

"This Executive Summary to the Endocrine Society's second Scientific Statement on environmental endocrine-disrupting chemicals (EDCs) provides a synthesis of the key points of the complete statement. The full Scientific Statement represents a comprehensive review of the literature (1300 studies) on seven topics for which there is strong mechanistic, experimental, animal, and epidemiological evidence for endocrine disruption, namely: obesity and diabetes, female reproduction, male reproduction, hormone-sensitive cancers in females, prostate cancer, thyroid, and neurodevelopment and neuroendocrine systems.

Scientific advances over the past 5 years (encompassing 1300 studies) reveal numerous EDC effects on obesity, diabetes, male and female reproduction (including cancer), the prostate and thyroid glands, and neurodevelopment. The past 5 years represent a leap forward in our understanding of EDC actions on endocrine health and disease." (Link to the complete Scientific Statement: http://www.healthandenvironment.org/partnership_calls/18015)

Furthermore, the following research paper alarmingly found and explains:

"The endocrine disrupting effect of glyphosate and its commercial formulations (i.e. Roundup) is their most insidious and worrying toxic effect. This is because EDC's do not function like normal poisons, where a higher dose gives greater toxicity. Often, endocrine disruptive effects are seen at lower doses but not at higher doses. The studies conducted by industry for regulatory purposes use relatively high doses and are not able to detect these effects. Endocrine disruption in humans is thought to contribute to some cancers, birth defects, reproductive problems such as infertility, and developmental problems in foetuses, babies, and children.

Under European law, pesticides that disrupt hormones ("endocrine disrupting chemicals" or EDCs) are not allowed to be marketed. Governments recognize the threat posed by endocrine disruption, which are believed to be implicated in serious diseases, such as cancer, reproductive and developmental problems, and birth defects. These effects are thought to result from very low doses over a long period of exposure or from exposures in critical windows of development, such as foetal development in the womb." (See http://detoxproject.org/glyphosate/hormone-hacking/)

Alarmingly, several other studies have also found both glyphosate and Roundup® to be EDCs: http://www.endocrinedisruption.org/…/tedx-l…/chemicalsearch…

Moreover, the October 1, 2016 issue of *Environmental Science and Pollution Research International* includes a study in which Australian researchers report,

"In 2005, the Food and Agriculture Organization (FAO) reported that glyphosate and its major metabolite, aminomethylphosphonic acid (AMPA), are of potential toxicological concern, mainly as a result of accumulation of residues in the food chain...Research has now established that glyphosate can persist in the environment. On the same date (October 1, 2016) the journal *Aquatic Technology* included a study in which fresh water fish were carefully monitored for glyphosate exposure, reporting:

"The study suggests that glyphosate is a likely mediator of aquatic metal toxicity, and that videotracking provides an opportunity for quantitative studies of sub lethal effects of pesticide complexes"

Glyphosate Risk Assessment: Health *Hazard* vs Health *Risk*

Furthermore, the risk assessment of glyphosate/Roundup® carried out by regulatory agencies worldwide is scientifically flawed for the reasons briefly explained below.

(1) "The dose makes the poison"

The health hazards vs health risks assessment used by all regulatory agencies is scientifically flawed and invalid because regulators erroneously believe and argue that the "dose makes the poison." However, toxicology peer-reviewed and published scientific research has shown that this belief is in many cases inaccurate and quite often the opposite is true (i.e. linear vs nonmonotonic dose-response curves) Study link: http://www.ncbi.nlm.nih.gov/pubmed/22419778

(2) Active Principle (glyphosate) vs Formulation/product (Roundup®)

Regulatory agencies only review the toxicity of the Active Principle alone (i.e. glyphosate) and not the whole product formulation (i.e., Roundup®), which contains other highly toxic and synergistic "secret" adjuvants. However, a recent landmark peer-reviewed and published study has alarmingly found Roundup® and other pesticide formulations to be 125-1000 times more toxic than their declared Active Principle. The authors of the study alarmingly found and write:

"We tested the toxicity of 9 pesticides, comparing active principles and their formulations, on three human cell lines [...] Despite its relatively benign reputation, Roundup was among the most toxic herbicides and insecticides tested. Most importantly, 8 formulations out of 9 were up to one thousand times more toxic than their active principles. Our results challenge the relevance of the acceptable daily intake for pesticides because this norm is calculated from the toxicity of the active principle alone. Chronic tests on pesticides may not reflect relevant environmental exposures if only one ingredient of these mixtures is tested alone."

Study Link: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3955666/

(3) Acceptable Daily Intake (ADI)

The Joint WHO-FAO Meeting on Pesticide Residues determines and sets the Acceptable Daily Intake (ADI) of glyphosate/Roundup based exclusively on the Active Principle alone (AP) (i.e., glyphosate) and not on the product formulation (i.e., Roundup.) However, the actual product that is approved by regulatory agencies and copiously sprayed on our food crops, soil, water, air and environment is not only glyphosate (AP) but the whole-product formulation (i.e., Roundup.)

Therefore, it is fair to conclude that both the Risk Assessment and the ADI for glyphosate/Roundup® are scientifically flawed and extremely hazardous to both our health and our lives since they expose us to extremely high doses of endocrine disrupting chemicals (EDC) and to cocktails of other extremely toxic-chemical formulations present in the form of extremely high pesticide residues in our food, water, soil, air, etc., all of which seriously endanger both our health and our lives.

CCNFSDU (NRV-R for Vitamins D and E) –

1. Vitamin D. Unfortunately, none of the DIRVs proposed by the RASBs are adequate as they are all too low. Even the highest NRV figure given (15 micrograms, by IOM) is predicated upon a statistical mistake that grossly ***underestimates*** the human intake need for Vitamin D. (*See* NHF's CRD 6 from CNFSDU meeting in 2016.)

The science supporting the human need for ***significantly*** higher levels of Vitamin D is rapidly increasing.[1] In particular, the old and outdated concept that humans can exist in good health on a daily intake of just 5 micrograms of Vitamin D is dead. As the United States noted in its recent comments to CCNFSDU, "the 2004 FAO/WHO RNI of 5 mcg was based on the 1997 IOM AI which has since been updated by the IOM in 2011 to 15 mcg." And recently, EFSA came out with its opinion that 15 mcg was the appropriate daily intake level for Vitamin D. So, there is no justification for leaving the Vitamin-D NRV at an unhealthy 5 mcg.

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 endnote a small portion of such research here.

To ignore this current science by establishing below-minimum nutritional requirements for Vitamin D (such as an NRV of only 5 micrograms) is racially discriminatory, scientifically negligent, and dangerous to public health.

NHF does not expect this Commission to break with a traditional and long-accepted view held on Vitamin-D NRVs and accept values of 100-125 mcg, no matter how demonstrably wrong the suggested values of 5 mcg, 10 mcg, and even 15 mcg might be. However, the above scientific discussions and new evidence do reveal how dangerously off-target the values suggested at this Committee are. Not only do these low values ***racially discriminate*** against various First Nations and other such darker-skinned groups living above the 33rd-degree Latitude, but they also adversely affect the health of ***all peoples***, regardless of race, age group, or gender.

Because Committee members will most probably not accept at this time the greater daily values of 100-125 micrograms necessary to ensure optimal health, the NHF proposes and advocates for setting the NRV for Vitamin D ***at 20 micrograms***, which is in alignment with the DACH values recommended in 2012 and accepted by Germany, Switzerland, and Austria. Although an NRV of 20 mcg is still low, it is probably the highest value that this Committee could accept at this time and will provide some nutritional hope for all humans and especially for racial groups previously unrepresented and otherwise discriminated against at the higher latitudes.

2. Vitamin E. None of the DIRVs proposed by the RASBs, and therefore to this Commission, particularly that of 9 mg/day, are adequate as they are all too low. An adequate level would deliver no less than 400 IUs of natural Vitamin E (preferably in the multi-tocopherol form and not simply alpha-tocopherol form) per day.[2] This equates to 268 milligrams per day.

Optimal Vitamin-E Levels Preserve Health

The World Health Organization currently attributes one-third of all global deaths annually (15.3 million) to cardiovascular disease,[3] and patients with coronary artery disease have been shown to have significantly lower blood levels of Vitamin E than normal healthy people.[4]

Studies have demonstrated that Vitamin-E supplements are effective in the treatment of cardiovascular disease,[5] and that the combination of Vitamin E and Vitamin C can slow the advancement of atherosclerosis.[6] 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.[7] 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,[8] and that supplementing the diet with nutrients including Vitamins E, C, B6, and folate is conducive to the prevention of cardiovascular disease.[9] 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.[10]

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, primarily from supplements.[11] 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.[12]

Vitamin-E therapy has also been shown to reduce arterial blockage in patients suffering from intermittent claudication,[13] and recent research has indicated that it normalizes high blood pressure.[14] Vitamin E also promotes collateral circulation; consequently offering great benefits to diabetes patients.[15]

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.[16]

Other research suggests that Vitamin-E supplementation also improves immune function in healthy elderly people.[17]

A high dietary intake of Vitamin E and Vitamin C may lower the risk of Alzheimer disease.[18] 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,[19] and that Vitamins E and C may prevent dementia and improve cognitive functioning in later life.[20] 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.[21]

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.[22] 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.[23] 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.[24]

An increased intake of Vitamins E and C has been found to reduce the risk of hip fractures,[25] and researchers have also demonstrated that a mixture of Vitamins E, C, and A dramatically reduces the postoperative complication rate.[26] 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.[27]

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.[28]

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 exacerbated by the error of employing only one fraction of Vitamin E when it possesses eight functioning as a complex.

Current Vitamin-E Intake Levels are Too Low

Very importantly, a recent study (2015) showed that “Using a criterion of adequacy of 30 μmol/L, 87% of persons 20-30 y and 43% of those 51+y had inadequate vitamin E status ($p<0.01$).”[29] This is a significant level of Vitamin-E deficiency within a population that is supposedly well nourished. It demonstrates that current NRV levels are woefully inadequate at addressing this deficiency and must be raised.

Another recent study (2016) systematically reviewed the published literature on Vitamin-E intake levels and serum concentrations in order to obtain a global overview of α-tocopherol status. Articles published between 2000 and 2012 were considered; 176 articles referring to 132 single studies were included. In applying an RDA of 15 mg/day and EAR (estimated average requirement) of 12 mg/day to all populations with a minimum age of 14 years, 82% and 61% of mean and median data points were below the RDA and the EAR, respectively. Regarding serum concentrations, globally 13% of the included data points were below the functional deficiency threshold concentration of 12 μmol/L, mostly for newborns and children. Several prospective observational studies suggest that a serum α-tocopherol concentration of ≥30 μmol/L has beneficial effects on human health. Of the reported study populations and subpopulations, only 21%

reached this threshold globally. This systematic review suggests that the α-tocopherol status is inadequate in a substantial part of the studied populations.[30]

Conclusion

The current proposal to establish an NRV for Vitamin E of 9 mg/day is not supported by the science. Such a daily level would condemn the vast majority of the human population to inadequate levels of this key nutrient with all the attendant health consequences. The absolute minimum NRV that should be established is 15 mg a day; but even this level, as demonstrated above, is not adequate to avoid widespread Vitamin-E deficiencies. A truly optimal nutrient intake would dictate daily levels of 200 mg and more, but NHF acknowledges that this Committee may not yet be prepared to stretch that far.

Agenda Item 5 (CX/CAC 17/40/3) Final adoption of Codex Texts

Part 2 – Standards and related texts held at Step 8 by the Commission.

Draft MRLs for Bovine Somatotropin (ALINORM 95/31, App II) –

For all of the reasons raised by NHF over the years of discussion on this MRL, the NHF opposes the adoption of any MRLs for Bovine Somatotropin and instead urges the Commission to discontinue all work on this matter.

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[1] Mezquita Raya P, Munoz Torres M, Lopez Rodriguez F, Martinez Martin N, Conde Valero A, *et al*., "Prevalence of vitamin D deficiency in populations at risk for osteoporosis: impact on bone integrity," *Med Clin (Barc)*, 2002 Jun 22;119(3):85-9; Rodriguez-Martinez MA, Garcia-Cohen EC, "Role of Ca(2+) and vitamin D in the prevention and treatment of osteoporosis," *Pharmacol Ther*. 2002 Jan;93(1):37-49; Lilliu H, Pamphile R, Chapuy MC, Schulten J, Arlot M, Meunier PJ, "Calcium-vitamin D3 supplementation is cost-effective in hip fractures prevention," *Maturitas*, 2003 Apr 25;44(4):299-305; Pfeiffer, *J Bone Min Res*. 2000, 15:1113-6; Trivedi DP, Doll R, Khaw KT, "Effect of four monthly oral vitamin D3 (cholecalciferol) supplementation on fractures and mortality in men and women living in the community: randomised double blind controlled trial," *BMJ* 2003;326:469-72; Chapuy MC, Arlot ME, Duboeuf F, Brun J, Crouzet B, Arnaud S, Delmas PD, Meunier PJ, "Vitamin D3 and calcium to prevent hip fractures in the elderly women," *N Engl J Med*, 1992; 327:1637-1642; Dawson-Hughes B., Harris S. S., Krall E. A., Dallal G. E, "Effect of Calcium and Vitamin D Supplementation on Bone Density in Men and Women 65 Years of Age or Older," *N Engl J Med*, 1997; 337:670-676; Fardellone P, Sebert JL, Garabedian M, Bellony R, Maamer M, Agbomson F, Brazie RM, "Prevalence and biological consequences of vitamin D deficiency in elderly institutionalized subjects," *Rev Rhum Engl Ed*. 1995 Oct;62(9):576-81; Markestad T, "Effect of season and vitamin D supplementation on plasma concentrations of 25-hydroxyvitamin D in Norwegian infants," *Acta Paediatr Scand*, 1983 Nov;72(6):817-21; Zamora SA, Rizzoli R, Belli DC, Slosman DO, Bonjour JP, "Vitamin D supplementation during infancy is associated with higher bone mineral mass in prepubertal girls," *J Clin Endocrinol Metab*. 1999 Dec; 84(12):4541-4; Garland CF, Garland FC, Gorham ED, "Calcium and vitamin D. Their potential roles in colon and breast cancer prevention," *Ann N Y Acad Sci*. 1999;889:107-19; Peehl DM, "Vitamin D and prostate cancer risk," *Eur Urol*. 1999;35(5-6):392-4; Hypponen E, Laara E, Reunanen A, Jarvelin MR, Virtanen SM, "Intake of vitamin D and risk of type 1 diabetes: a birth-cohort study," *Lancet*, 2001 Nov 3;358(9292):1500-3; Munger KL, Zhang SM, O'Reilly E, Hernan MA, Olek MJ, Willet WC, Ascherio A, "Vitamin D intake and incidence of multiple sclerosis," *Neurology*, 2004 Jan 13;62(1):60-65; Goldberg P, Fleming MC, Picard EH, "Multiple sclerosis: decreased relapse rate through dietary supplementation with calcium, magnesium and vitamin D," *Med Hypotheses*, 1986 Oct;21(2):193-200; Sasidharan PK, Rajeev E, Vijayakumari V, "Tuberculosis and vitamin D deficiency," *J Assoc Physicians India*, 2002 Apr;50:554-8; Bicknel F, Prescott F, The Vitamins in Medicine, third edition. Milwaukee, WI: Lee Foundation. 1953, p.544, 584-591; Vieth, R. (1999), "Vitamin D supplementation, 25-hydroxyvitamin D concentrations, and safety," *American Journal of Clinical Nutrition*, Vol. 69, No. 5, 842-856, May 1999; Marya RK, Rathee S, Lata V, Mudgil S, "Effects of vitamin D supplementation in pregnancy," *Gynecol Obstet Invest*. 1981;12(3):155-61.

[2] Because Vitamin E is a complex and not simply a single vitamin, all of its components must be considered: alpha tocopherol, beta tocopherol, delta tocopherol, gamma tocopherol, and the tocotrienol components. To only consider alpha tocopherol and to ignore all of the other Vitamin-E components would be like considering only the tires on an automobile and ignoring the engine, transmission, and other components that make a car a car.

[3] Diet, Nutrition and the Prevention of Chronic Diseases, WHO Technical Report Series, Report of a Joint WHO/FAO Expert Consultation, Geneva 2003, p. 81.

[4] Delport R, Ubbink JB, Human JA, Becker PJ, Myburgh DP, Vermaak WJ, "Antioxidant vitamins and coronary artery disease risk in South African males," *Clin Chim Acta*. 1998 Nov;278(1):55-60.
[5] Azen SP, Qian D, Mack WJ, *et al*., "Effect of supplementary antioxidant vitamin intake on carotid arterial wall intima-media thickness in a controlled clinical trial of cholesterol lowering," *Circulation*, 1996;94(10):2369-2372; Stephens NG, Parsons A, Schofield PM, Kelly F, Cheeseman K, Mitchinson MJ, "Randomised controlled trial of vitamin E in patients with coronary disease: Cambridge Heart Antioxidant Study (CHAOS)," *Lancet*, 1996;347(9004):781-786; Boaz M, Smetana S, Weinstein T, *et al.*, "Secondary prevention with antioxidants of cardiovascular disease in end stage renal disease (SPACE): randomised placebo-controlled trial," *Lancet,* 2000;356(9237):1213-1218.

[6] Salonen JT, Nyyssonen K, Salonen R, Lakka HM, Kaikkonen J, Porkkala-Sarataho E, Voutilainen S, Lakka TA, Rissanen T, Leskinen L, Tuomainen TP, Valkonen VP, Ristonmaa U, Poulsen HE, "Antioxidant Supplementation in Atherosclerosis Prevention (ASAP) study: a randomized trial of the effect of vitamins E and C on 3-year progression of carotid atherosclerosis," *J Intern Med*, 2000 Nov;248(5):377-86.
[7] Brown DJ, Goodman J, "A review of vitamins A, C, and E and their relationship to cardiovascular disease," *Clin Excell Nurse Pract.* 1998 Jan;2(1):10-22.
[8] Rath M, Niedzwiecki A, "Progression of early stages of coronary calcifications can be stopped by the synergistic effect of vitamins and essential nutrients," *Atherosclerosis*, 1997; 134:333; Sinatra ST, DeMarco J, "Free radicals, oxidative stress, oxidized low density lipoprotein (LDL), and the heart: antioxidants and other strategies to limit cardiovascular damage," *Conn Med*. 1995 Oct; 59(10):579-88.
[9] Kendler BS, "Nutritional strategies in cardiovascular disease control: an update on vitamins and conditionally essential nutrients," *Prog Cardiovasc Nurs*, 1999 Autumn;14(4):124-9.
[10] Gey KF, Stahelin HB, Ballmer PE, "Essential antioxidants in cardiovascular diseases--lessons for Europe*," Ther Umsch*, 1994 Jul; 51(7):475-82.
[11] Stampfer MJ, Hennekens CH, Manson JE, Colditz GA, Rosner B, Willett WC, "Vitamin E consumption and the risk of coronary disease in women," *N Engl J Med*, 1993;328:1444-9.
[12] Knekt P, Reunanen A, Jarvinen R, Seppanen R, Heliovaara M, Aromaa A, "Antioxidant vitamin intake and coronary mortality in a longitudinal population study," *Am J Epidemiol,* 1994;139:1180-9.
[13] Williams SR, *Nutrition and Diet Therapy, Seventh Edition*, St. Louis: Mosby, 1993. (p 186). Sixth edition, 1989. (p 225); Williams HTG, Fenna D, MacBeth RA, "Alpha Tocopherol in the Treatment of Intermittent Claudication," Surgery, Gynecology and Obstetrics 132:#4, 662-666, April 1971.
[14] Vasdev S, Gill V, Parai S, Longerich L, Gadag V, "Dietary vitamin E supplementation lowers blood pressure in spontaneously hypertensive rats," *Mol Cell Biochem*, 2002 Sep; 238(1-2):111-7; Vaziri ND, Ni Z, Oveisi F, Liang K, Pandian R, "Enhanced nitric oxide inactivation and protein nitration by reactive oxygen species in renal insufficiency," *Hypertension*, 2002 Jan; 39(1):135-41; Galley HF, Thornton J, Howdle PD, Walker BE, Webster NR, "Combination oral antioxidant supplementation reduces blood pressure," *Clin Sci (Lond)*, 1997 Apr;92(4):361-5.

[15] Shute, Vogelsang, Skelton and Shute, *Surg., Gyn. and Obst*. 86:1. 1948.
[16] Malmberg KJ, Lenkei R, Petersson M, Ohlum T, *et al*., "A short-term dietary supplementation of high doses of vitamin E increases T helper 1 cytokine production in patients with advanced colorectal cancer," *Clin Cancer Res*, 2002 Jun; 8(6):1772-8.
[17] Cheraskin E, "Antioxidants in health and disease: the big picture," *Journal of Orthomolecular Medicine* 10: #2, 89-96, Second Quarter, 1995, citing Meydani, S.N., Barklund, M.P., Liu, S., Meydani, M., Miller, R.A., Cannon, J.G., Morrow, F.D., Rocklin, R., Blumberg, J.B, "Effect of Vitamin E Supplementation on Immune Responsiveness of Healthy Elderly Subjects," *FASEB Journal* 3: A1057, 1989; Meydani, S.N., Barkiund, M.P., Liu, S., Meydani, M., Miller, R.A., Cannon, J.G., Morrow, F.D., Rocklin, R., Blumberg, JB, "Vitamin E supplementation enhances cell-mediated immunity in healthy elderly subjects," *American Journal of Clinical Nutrition* 52:#3, 557-563, September 1990.
[18] Engelhart MJ, Geerlings MI, Ruitenberg A, van Swieten JC, Hofman A, Witteman JC, Breteler MM, "Dietary intake of antioxidants and risk of Alzheimer disease," *JAMA*, 2002 Jun 26;287(24):3223-9.
[19] Grodstein F, Chen J, Willett WC, "High-dose antioxidant supplements and cognitive function in community-dwelling elderly women," *Am J Clin Nutr*, 2003 Apr;77(4):975-84.
[20] Masaki KH, Losonczy KG, Izmirlian G, Foley DJ, Ross GW, Petrovitch H, Havlik R, White LR, "Association of vitamin E and C supplement use with cognitive function and dementia in elderly men," *Neurology*, 2000 Mar 28;54(6):1265-72.
[21] Sano M, Ernesto C, Thomas RG, Klauber MR, Schafer K, Grundman M, *et al.*, "A controlled trial of selegiline, alpha-tocopherol, or both as treatment for Alzheimer's disease, The Alzheimer's Disease Cooperative Study," *N Engl J Med*, Apr 24; 336(17):1216-22. 1997.
[22] Ogunmekan AO, Hwang PA, "A randomized, double-blind, placebo-controlled, clinical trial of D-alpha-tocopheryl acetate (vitamin E), as add-on therapy, for epilepsy in children," *Epilepsia*. 1989 Jan-Feb; 30(1):84-9.

[23] Hittner HM, Godio LB, Rudolph AJ, Adams JM, Garcia-Prats JA, Friedman Z, Kautz JA, Monaco WA, "Retrolental fibroplasia: efficacy of vitamin E in a double-blind clinical study of preterm infants," *N Engl J Med*, 1981 Dec 3; 305(23):1365-71.
[24] *British Medical Journal*, 890, 1940 (cited in Bicknell & Prescott. *The vitamins in medicine*. Milwaukee: Lee Foundation, 1953, p 632).
[25] Melhus H, Michaelsson K, Holmberg L, Wolk A, Ljunghall S, "Smoking, antioxidant vitamins, and the risk of hip fracture," *J Bone Miner Res*, 1999 Jan;14(1):129-35).
[26] Sukolinskii VN, Morozkina TS, "Prevention of postoperative complications in patients with stomach cancer using an antioxidant complex," *Vopr Onkol*, 1989;35(10):1242-5.
[27] Nathens AB, Neff MJ, Jurkovich GJ, Klotz P, Farver K, Ruzinski JT, Radella F, et al., "Randomized, prospective trial of antioxidant supplementation in critically ill surgical patients," *Ann Surg*, 2002 Dec;236(6):814-22.
[28] Mecocci P, Polidori MC, Troiano L, Cherubini A, Cecchetti R, Pini G, Straatman M, Monti D, Stahl W, Sies H, Franceschi C, Senin U, "Plasma antioxidants and longevity: a study on healthy centenarians," *Free Radic Biol Med*, 2000 Apr 15;28(8):1243-8.
[29] McBurney MI, Yu EA, Ciappio ED, Bird JK, *et al.*, "Suboptimal Serum α-Tocopherol Concentrations Observed among Younger Adults and Those Depending Exclusively upon Food Sources, NHANES 2003-20061-3," PLoS One. 2015 Aug 19;10(8):e0135510; doi: 10.1371/journal.pone.0135510. eCollection 2015.
[30] Péter S, Friedel A, Roos FF, Wyss A*, et al*., "A Systematic Review of Global Alpha-Tocopherol Status as Assessed by Nutritional Intake Levels and Blood Serum Concentrations," *Int J Vitam Nutr Res*, 2016 Jul 14:1-21. [Epub ahead of print]. FULL TEXT: http://econtent.hogrefe.com/doi/pdf/10.1024/0300-9831/a000281.