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REFERENCES

Reply to VJ Drake et al

Dear Sir:

Thank you for the opportunity to respond to the letter of Drake et al. To err may be human, but the international unit (IU) calculations for provitamin A carotenoids in the US Department of Agriculture (USDA) National Nutrient Database for Standard Reference (SR) (1) are not in error. Drake et al allege, however, that a serious error exists in these calculations and state that the USDA thus should decrease by a factor of 6 the IU values listed for plant sources of β-carotene to take into account the relatively poor bioavailability of plant sources of vitamin A. Unfortunately, the authors have misunderstood both the definition and the appropriate use of this measure of vitamin A activity. The IU, used in the United States for vitamin A recommendations until 1974 (2), was defined by the World Health Organization many years ago (3). The IU values in the SR follow exactly this definition of an IU and thus are not in error.

As knowledge about vitamin A activity evolved, the IU was replaced by the retinol equivalent (RE), and later by the retinol activity equivalent (RAE) (4), as the preferred method of stating nutrient intake recommendations for vitamin A, because these directly include an estimate of bioavailability. Thus, researchers and others who wish to use vitamin A values in their studies should be using the RAE values from the SR, which reflect the most recent evaluation of the equivalency of provitamin A carotenoids to retinol (5). However, the Food and Drug Administration (FDA) continues to use vitamin A in IUs as the unit of measure for the daily value (DV) on nutrition and dietary supplement labels (5). This is the only valid use of vitamin A in IUs, and the only purpose for its inclusion in the SR is for comparison to the DV on the label. However outdated the IU measure may be, there would be no reason to redefine this measure in the SR, because the values would no longer be comparable to those mandated by the FDA.

Perhaps it requires more than 4 decades in nutrition to fully understand the evolving science that underpins the nutrition monitoring and food-composition program in the United States. The IU
equivalency defined by the WHO/FAO in 1967 (6) (in which 1 IU = 0.3 μg retinol or 0.6 μg β-carotene) addresses only bioconversion (the observation that it would take ≈2 μg β-carotene to form 1 μg of retinol within a human cell) (2). Thus, we agree with Drake et al that the IU by itself does not address factors such as the extent of absorption before bioconversion of carotenoids from differing plant sources, cooking processes, levels of nutritional status, or the presence of factors that enhance absorption (eg, lipids). However, the matter of bioavailability was included indirectly when recommended intakes were set in the United States on the basis of the assumption that half of the dietary vitamin A would come from animal sources and half from less bioavailable plant sources (7).

In the most recent review of vitamin A reference values from the Food and Nutrition Board (FNB) (4) as part of establishing dietary reference intakes (DRIs) for Canada and the United States, bioavailability factors were updated as RAEs. Whereas the current USDA database still includes entries for vitamin A in IU because IU is the unit used in nutrition labeling, the SR also includes vitamin A content for each food item in RAE and gives values in μg for retinol, β-carotene, α-carotene, and β-cryptoxanthin. These are the values that should be used for nutrition studies.

Today in the United States, we are faced with nutrition labeling regarding vitamin A that is essentially frozen in time via regulation by the FDA: the DV for vitamin A is 5000 IU. This value was the adult RDA (7) when voluntary nutrition labeling was initiated in 1973, and it became the US RDA. In 1993, with the implementation of mandatory nutrition labeling, the FDA opted to continue the use of the US RDA values for DVs. Because the USDA nutrient database is expected to support all federal programs, the FDA has relied on the inclusion of IU values in the database for foods for use by food manufacturers who must label their food products in IUs. In the documentation for the database (1) (available at http://www.nal.usda.gov/fnic/foodcomp/search), the IU equivalency is discussed; the documentation indicates that the IU equivalency is provided for nutrition labeling and includes a discussion of the RAE and the change from earlier values in RE.

It is unfortunate that the DV on the Nutrition and Dietary Supplement Facts Panels is still based on the 1968 RDA of 5000 IU, but the USDA cannot change the definition of the IU to directly take into account bioavailability, as Drake et al urge be done. The IU is defined by the WHO/FAO, not the USDA. Drake et al propose that it is scientifically appropriate to use the RAE equivalency to convert food values that are given in IUs to reduced-value IUs based on Table 4-3 in the DRIs report (4). However, the FNB did not redefine the IU. Instead, it established REs and then RAEs. The purpose of the footnote on Table 4–3 is to allow conversion from IUs to RAEs.

The good news in moving toward elimination of the IU is that the FDA has just published in the Federal Register a long-awaited notice requesting comments on updating the DV (8). The questions focus on how best to update the DVs with the DRIs or other standards, and they specifically ask whether IUs should be continued (not only for vitamin A, but for vitamin E as well). Thus, this is the right time for scientists and clinicians alike to bring up these issues of confusion and dated science by responding to the FDA’s request for comments, which we strongly urge Drake et al and others with concerns about nutrition labeling to do.

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**REFERENCES**


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**Homocysteine, vitamins, and vascular disease prevention: more negative results**

Dear Sir:

With much interest we read the article by McCully (1), which implies a potential role of homocysteine reduction in the primary prevention of cardiovascular disease (CVD). Although the author did note the negative results of the homocysteine reduction clinical trials, he further raised doubts about their conclusion because of the lack of statistical power, the length of the trials required, and the fortification of the North American food supply with folic acid. We believe that the evidence supporting any benefit of homocysteine reduction, whether in primary or secondary CVD prevention, is getting weaker and weaker.

In addition to the negative results of the 3 major studies mentioned in McCully’s article (VISP, NORVIT, and HOPE2), negative results from the HOST trial have also been published (2). The HOST trial (2)