

30 August 2004

Laura M. Tarantino, Ph.D.  
Director, Office of Food Additive Safety (HFS-200)  
Center for Food Safety and Applied Nutrition  
Food and Drug Administration  
5100 Paint Branch Parkway  
College Park, Maryland 20740-3835

Dear Doctor Tarantino:

This letter is written with respect to the Food Additive Petition No. 4A4758, Kraft Foods Global, Inc., requesting that 21 C.F.R. 172.380 be amended to provide for the safe use of vitamin D as a nutrient supplement in various cheeses and cheese products.

I am a clinical endocrinologist by training, and my primary activity is clinical nutrition research, specifically on calcium, vitamin D, and the other bone-related nutrients. I have published extensively in that field, and in 2003–2004, was awarded E.V. McCollum International Lectureship by the American Society for Nutrition Sciences, in recognition of my work with vitamin D, and for the purpose of disseminating to international audiences the message of the importance of ensuring vitamin D adequacy. I served on the Panel for Calcium and Related Nutrients of the Food and Nutrition Board (IOM), involved in the publication of the DRIs for those nutrients in 1997, and in that capacity also served as a member of the Upper Limits Task Force (along with Dr. Michael Holick, Boston, the only other content expert on the Upper Limits Panel). I mention the latter point specifically because both Holick and I argued against the 2000 IU upper limit. The reason was that the single paper establishing the LOAEL was, in our judgement, seriously flawed, as well as because of many thousands of patient-years of experience of using vitamin D in larger doses without evidence of toxicity.

Subsequent to the deliberations of the Upper Limits Panel, a great deal of additional work has been published, some from my laboratory, showing that the body consumes in the neighborhood of 4000 IUs per day, simply to maintain an optimal concentration of serum 25OHD and that, if oral input were the only source, it would take about that amount to ensure adequacy. Furthermore, both Vieth of Toronto and I, in peer-reviewed journals, have explicitly stated that the TUIL is set too low and have shown that dosing in the range of 4000, 5000, and 10,000 IU/d for extended periods of time is quite safe (1–3).

Since most of us get most of our vitamin D from solar exposure to the skin, I am not arguing that most individuals need oral intakes in the range of even the current TUIL. My argument is simply that intakes at or even above the TUIL, being less than the body optimally needs and uses, would be quite safe.

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Specifically, in the above-referenced petition, Kraft Foods has asked for permission to fortify at a level of 81 IU per serving, a level which, by my reckoning, provides only about 5% of what the body uses every day under conditions of optimal health. Thus, in my judgement, a dietary exposure to vitamin D that would result from any plausible number of servings of cheese fortified at the requested level clearly presents a reasonable certainty of no harm.

The problem with setting the TUIL too low, as was done by the Food and Nutrition Board in 1997, is that the upper limit serves as a psychological barrier to addressing the issue of widespread vitamin D insufficiency. Growing recognition of this problem has prompted the NIH to hold two conferences on the vitamin D issue, one in the fall of 2003, and another one this November.

By way of background, it may be helpful to recall that the FNB set the serum 25OHD level as the functional indicator for vitamin D status, and that recent work has shown that values above 75 nmol/L are required for optimal health (4-7). Outdoor summer workers at mid latitudes commonly have values of 150 nmol/L or higher, absolutely without toxicity. By contrast, typical adults in North America have values in the range of 50 nmol/L or below. The upper level of serum 25OHD for safety is not known with certainty, but is probably above 250 nmol/L. (Available data indicate that it would take continuing inputs in excess of 10,000 IU/d to reach that level.) Raising blood 25OHD levels from 50 to 80 nmol/L improves calcium absorption efficiency by better than 65% (4), and reduces typical osteoporotic fractures by 33% (5). A very recent analysis of the NHANES-III database shows that lower extremity muscle function improves continuously up to values in the range of 120 nmol/L (6), and randomized controlled trials have shown that fall frequency in the elderly is reduced by 50% by as little as 12 weeks of therapy with vitamin D (7).

These effects on falls and on muscle function are the tip of the vitamin D iceberg. We had originally thought that vitamin D was important mainly for the calcium economy, and that in its absence we suffered rickets or osteomalacia. Recent syntheses have shown that, even for the skeletal system, osteomalacia is actually only the most extreme degree of vitamin D deficiency, and that lesser degrees vitamin D deficiency produce osteoporosis. Similarly, a large body of work has shown that many tissues use a vitamin D-based system for controlling cell replication, specialization, and programmed cell death, important as a first-line defense against many cancers. For these systems to function effectively, it is essential that the body maintain a high circulating level of 25OHD, well above the levels needed to prevent rickets or osteomalacia.

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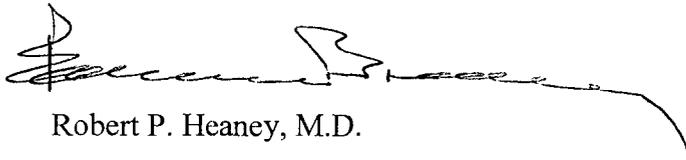
I realize that your office is concerned primarily with safety, but I thought it necessary to tell you not only that intakes in the range requested in the above-referenced petition are safe, but that it is probably necessary to use such food fortification stratagems to elevate vitamin D intake across a broad range of foods. To that same end, you may be aware of the fact that, in last month's issue of the American Journal of Clinical Nutrition, there was a paper which I co-authored with Harold Newmark and Paul LaChance of Rutgers (8), calling on the FDA to change the vitamin D fortification of cereal grain products from optional to mandatory status. The increase in vitamin D intake that would be produced by our recommendation is small, just as is the case with the Kraft petition, but it has seemed best to us to strive for widespread, low level fortification rather than massive supplementation of isolated food items.

One of the attractivenesses of adding vitamin D to cheese is that the consumer expects dairy products to have the nutrient profile of milk (which consumers generally recognize to be a source of vitamin D). Hence with very little education and no significant change in eating habits, the requested fortification would help improve a widespread deficiency problem in North America. Given the seriousness of the need, I hope that the FDA could act swiftly on this petition.

Finally, let me assure you that I am not an employee of Kraft, and receive no compensation from the company for my sending this letter to you. It is my goal and practice to support petitions such as this precisely for the reasons set forth in my article with Newmark and LaChance, as well as those set forth in our earlier citizens' petition to the FDA (Docket No. 92P-0064).

Thank you very much for your attention to this request.

Sincerely,

A handwritten signature in black ink, appearing to read "Robert P. Heaney", with a long, sweeping underline that extends to the right.

Robert P. Heaney, M.D.

Cc: Robert E. Brackett, Ph.D.  
Garfield N. Biddle, Ph.D.  
Ms. Judith L. Kidwell ✓

## References Cited

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