NATIONAL ACADEMY OF SCIENCES
INSTITUTE OF MEDICINE
2101 Constitution Avenue, Washington, D. C. 20418

November 20, 1998

Albert W. Burgstahler, Ph.D. and others
Professor of Chemistry
The University of Kansas
4035 Malott Hall
Lawrence, Kansas 66045

Dear Dr. Burgstahler:

We apologize for the delay in responding to your letters of October 15, 1997 and February 4, 1998, to each of us individually. At the time we had a very large number of inquiries and comments, and while letters were prepared in response to your letter along with the others, for some reason they did not reach you. The letter that we found in our files is reprinted below.

We want to thank you and your co-signers for your October 15, 1997 letter to us concerning the Food and Nutrition Board's (FNB) recent report, *Dietary Reference Intakes for Calcium, Phosphorus, Magnesium, Vitamin D and Fluoride.* The publication of the report represents the initial report of a major new activity of the FNB: the development of a comprehensive set of reference values for nutrients and food components of possible benefit to health, that may not meet the traditional concept of a nutrient. If adequate scientific data exist that support a health benefit from the inclusion of these components in the diet, reference intakes will be established.

In replying to your letter, we have consulted with the Committee that produced the FNB report and asked them to review the important points that you raised concerning their report and the associated workshop, as well as to explain why they have reached the conclusions they reached despite the information you cite.

First, let us reassure you with regard to one concern. Nowhere in the report is it stated that fluoride is an essential nutrient. If any speaker or panel member at the September 23rd workshop referred to fluoride as such, they misspoke. As was stated in *Recommended Dietary Allowances 10th Edition*, which we published in 1989: "These contradictory results do not justify a classification of fluoride as an essential element, according to accepted standards. Nonetheless, because of its valuable effects on dental health, fluoride is a beneficial element for humans." Dr. Vernon Young, Chair of the Standing Committee on the Scientific Evaluation of Dietary Reference Intakes, stated this at the workshop's conclusion.

The adequate intake (AI) of fluoride for infants 0 to 6 months of age is set at 0.01 mg/day. As explained in Chapter 1 of the report, the average intake of a particular nutrient by full-term infants who are born to well-nourished mothers and exclusively fed human milk has

been adopted as the basis for deriving an AI for all nutrients and other food components during the first 6 months of life. Using the human milk-fed infant as the model supports the recommendation that exclusive breast feeding is the preferred method of feeding for normal full-term infants for the first 4 to 6 months of life -- a recommendation shared by the Canadian Paediatric Society (Health Canada, 1990), the American Academy of Pediatrics (1982), and the Food and Nutrition Board's report *Nutrition During Lactation* (IOM, 1991). (Infants who are exclusively breast fed for the first six months of life would have a low fluoride intake, and yet scientific evidence showing that these infants are at greater risk for dental caries than formula-fed infants is lacking.) During the second six months of life and thereafter, the AI for fluoride from all sources is set at 0.05 mg/kg/day because it confers a high level of protection against dental caries and is associated with no known unwanted health effects.

Although the report acknowledges that most of the anti-caries effect attributed to fluoride occurs by topical exposure, it does not matter whether that exposure is from food, water or dental products. As you state, the prevalence of caries in some countries around the world without water fluoridation has declined over the years. This has been attributed to national dental hygiene programs and the use of fluoride in school-based prevention programs (rinses or tablets), as well as to the use of fluoridated toothpaste. These programs provide both systemic and topical fluoride exposures.

In following the model for the development of Tolerable Upper Intake Levels (ULs), as explained in Chapter 3 of the report, moderate enamel fluorosis was considered as the critical adverse effect in children under 9 years of age. As noted by Dean and coworkers some 60 years ago, mild enamel fluorosis was present in some residents of areas where water contained < 2 mg/liter of fluoride. At that time the diet, particularly the water, was the only significant source of fluoride so that the daily intake of fluoride could be estimated with reasonable accuracy. The average intake by children at risk was 0.05 mg/kg/day. The prevalences of both dental caries and fluorosis in these communities was low and there is no reason to expect that level of intake (from all sources) to produce different results today. Compared with Dean's findings, recent studies have revealed a higher prevalence of dental fluorosis in the United States and Canada, including a few cases of moderate fluorosis. However, analytical epidemiological studies have repeatedly shown that the major risk factors are ingestion due to the early use of fluoride toothpaste and/or the use of dietary supplements. Thus, the total fluoride intake by some children whose water is fluoridated is now higher than in Dean's time. This is the reason that age-specific intakes for total fluoride, including that from dental products, are based on 0.05 mg/kg/day. To the extent that this intake level is followed, the prevalence of dental fluorosis can be expected to decline while a healthy dentition is maintained.

Three recent reviews of the literature, Kaminsky et al., 1990; NRC, 1993; USPHS, 1991, attempted to identify adverse functional effects of fluoride ingestion in adults. Fluoride exposures included those associated with drinking water containing as much as 8 mg/liter of

fluoride and the use of dental products. These reviews concluded that evidence linking chronic, high fluoride exposures with adverse effects such as cancer, including osteosarcoma, birth defects, genetic disorders, or bone fractures is either insufficient or highly contradictory. In addition, the majority of animal studies have shown no effect on cancer, birth defects, genetic disorders or bone strength of very high and long-term fluoride exposures. Thus, the primary adverse effects associated with chronic, excess fluoride intake are enamel fluorosis in children through 8 years of age and skeletal fluorosis in adolescents and adults over 8 years of age. In Hodge's 1979 article, he reported that evidence of crippling fluorosis "was not seen in communities in the United States where water supplies contained up to 20 ppm." In such communities daily fluoride intakes of 20 mg would not be uncommon.

Fluoride is continuously taken up by newly formed bone and released from older bone being resorbed. As long as intake remains constant, the concentration in bone tends to increase during life. It is not entirely clear why this happens but it may be due to the preferential resorption of bone crystallites that do not contain fluoride. In any event, in the United States and Canada, it is known that the development of skeletal fluorosis, even in earliest stages, has not occurred, even where the water fluoride concentrations have been in excess of 10 ppm.

In reviewing Raj Roholm's classic 1937 report of bone changes among Danish cryolite workers, it was noted that Roholm reported no intake data for fluoride, apparently because the researchers were not able to measure air-borne fluoride. On page 279, Roholm states: "It must be admitted that with respect to the important question of dose, that the observations available are sporadic and to some extent contradictory; in most of the spontaneous intoxications the intaken (his word) quantity of fluoride is not known at all." Later on page 319 Roholm states: "In man the disease (he is referring to crippling skeletal fluorosis) is probably caused by 0.20-0.35 mg fluoride daily per kg body weight." The reason for this estimate is not given. It is unfortunate that, in the absence of scientific data, these estimates were ever made. Although we are uncertain about the lower level of intake and time of exposure that causes clinically significant skeletal fluorosis, we do know that, at least for U.S. and Canadian citizens, intakes associated with water fluoride concentrations in excess of 10 ppm do not cause clinically significant skeletal fluorosis.

Our study was funded entirely by the governments of the United States and Canada. The funding agencies were the National Institute of Health's National Heart, Lung, and Blood Institute; the Agricultural Research Services of the U.S. Department of Agriculture; U.S. Food and Drug Administration; and Health Canada.

We thank you and your co-signers for your careful reading of the report and interest in assuring its accuracy and completeness. Given the complexities of the issues the report considers, we are confident that much room remains for further objective inquiry. We have tried to give you some of the reasons for the Committee's conclusions. However, we hope that the report will lead to additional research on which to base dietary reference intakes -- for both essential nutrients and other dietary constituents with documented health benefits.

Once again, we regret that this reply to your thoughtful letter did not reach you much earlier, when it was prepared.

Sincerely,

Bruce Alberts, Ph.D.
President
National Academy of Sciences

Kenneth Shine
President
Institute of Medicine