



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

EPA-SAB-LTR-91-003

March 26, 1991

OFFICE OF
THE ADMINISTRATOR

Honorable William K. Reilly
Administrator
U.S. Environmental Protection Agency
401 M Street, S.W.
Washington, D.C. 20460

Subject: Science Advisory Board's review of the Calculation of RfDs for Minerals Which Are Nutritionally Essential

Dear Mr. Reilly:

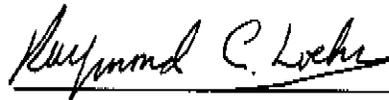
The Metals Subcommittee of the Science Advisory Board met in Bethesda, Maryland, on August 7 to consider the calculation of RfDs for minerals which are nutritionally essential but retain the possibility of toxicity. A roster of the Subcommittee members is attached.

Chromium, selenium, and zinc are examples of minerals that serve essential biological functions at low dietary levels but that can elicit toxic responses at high levels. Such a dual role poses difficulties for EPA's attempts to set RfDs and to translate them into exposure standards. The Subcommittee noted that at least part of the problem stems from current Agency practices, which rely upon arbitrary effect levels, such as NOAELs, to calculate RfDs. These practices assume a monotonic dose-response function. For the three elements above, however, the function is biphasic, or U-shaped. Such a function could be a combination of two dose-response curves, one reflecting increasing toxicity with increasing dose, the other reflecting the dose-essentiality relationship. Two dose-response functions allow two different endpoints to be determined and modeled.

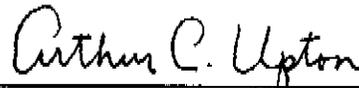
Inadequate and excessive intakes both incur health risks. Consequently, a different method of calculating exposure standards than that currently practiced by the agency is required to deal with this unique condition. In particular, a method is required that uses the complete dose-response function in calculating allowable levels. As noted above, the Subcommittee has recommended such a change in EPA policy in an earlier

Executive Committee letter to you ("Comments on The Use of Uncertainty and Modifying Factors in Establishing Reference Dose Levels", EPA-SAB-EC-005). In addition, it recommended that the Agency develop and maintain liaisons with the Food and Nutrition Board of the National Academy of Sciences, which establishes Recommended Daily Allowances, and the Food and Drug Administration, to coordinate the roles and interests of the three organizations in proposing dietary intake standards. The Subcommittee also recommends that EPA sponsor a workshop devoted to the scientific and regulatory issues presented by the dual possibilities discussed above.

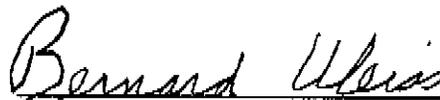
We appreciate the opportunity to review this issue, and look forward to your response regarding the future use of complete dose-response functions (as opposed to identifying LOAEL/NOAEL points) for standard setting.



Dr. Raymond Loehr, Chairman
Science Advisory Board



Dr. Arthur Upton, Chairman
Environmental Health Committee



Dr. Bernard Weiss, Chairman
Metals Subcommittee

ATTACHMENT

Attachment I.

U.S. ENVIRONMENTAL PROTECTION AGENCY
SCIENCE ADVISORY BOARD
METALS SUBCOMMITTEE MEETING

AUGUST 6-7, 1990

CHAIRMAN

Dr. Bernard Weiss
Division of Toxicology
P.O. Box RBB
University of Rochester
School of Medicine
Rochester, New York 14642

VICE CHAIRMAN

- Dr. Ronald Wyzga *
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Palo Alto, California 94303
- Dr. Thomas Clarkson *
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- Dr. Robert Goyer
The University of Western Ontario
Department of Pathology
Health Science Center
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- Dr. Marvin Kuschner
Professor of Pathology
Department of Pathology
School of Medicine
Health Science Center
Stony Brook, New York 11794
- Dr. Brooke T. Mossman *
Department of Pathology
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Neurotoxicology Laboratory
College of Pharmacy
Rutgers University
Busch Campus
Piscataway, New Jersey 08855-0789

Dr. F. William Sunderman
Department of Laboratory Medicine
University of Connecticut
Health Center, Room C 2021
Farmington, Connecticut 06032

Executive Secretary

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Science Advisory Board
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Washington, D.C. 20460

Staff Secretary

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U.S. Environmental Protection Agency
Science Advisory Board (A101F)
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Washington, D. C. 20460

Director, Science Advisory Board

Dr. Donald G. Barnes
U.S. Environmental Protection Agency
Science Advisory Board
401 M Street, S. W., Room 1145W
Washington, D. C. 20460

* Dr.'s Wyzga, Clarkson, and Mossman were unable to attend this meeting. Dr. Edward Bender will be sitting in for Mr. Rondberg.



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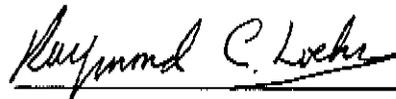
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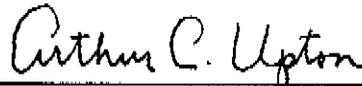
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