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

EPA-SAB-Ltr-90-004

OFFICE OF
THE ADMINISTRATOR

May 16, 1990

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

Subject: Science Advisory Board's review of issues relating to the health effects of ingested nitrate and nitrite.

Dear Mr. Reilly:

The Drinking Water Committee of the Science Advisory Board met February 1-2, 1990 in Washington, D.C. to review the issues being discussed in the Agency concerning the health effects of nitrate ion and its metabolite, the nitrite ion. Three major issues had been identified by EPA in a briefing document that represented areas of ongoing discussions within the Agency:

1) The relevance of new carcinogenicity studies
2) The degree to which the proposed standard is protective of toxic effects other than methemoglobinemia; e.g., developmental toxicity
3) The degree to which the proposed standard protects the most sensitive members of the population; cf., adequacy of the uncertainty factors used in estimated a reference dose (RfD).

It became quite clear during the Agency's presentations and subsequent discussion that different groups within EPA had different expectations about the consideration of these issues. As a result the Committee conducted an open discussion of the nitrate/nitrite issues, rather than an focused analysis of the Agency current position as impacted by the three areas above.

The Committee wishes to see a revised health criteria document that addresses the issues raised in our earlier review (May, 1987 copy attached), noting that a final regulation of nitrate/nitrite is scheduled for December 31, 1990. It is quite clear in our report of May 1987 and from other agency documents,

that a number of issues relating to nitrate/nitrite continue to be important to rulemaking. These include:

1. Carcinogenicity: The current Agency position appears to be that there is "inadequate evidence" that nitrate/nitrite present a potential cancer risk through drinking water. However, the Committee awaits an Agency position in the forthcoming criteria document.[1]

2. Developmental toxicity: Two new studies are available: one, a nitrite-feeding study in rats; the other, a human population study based in South Australia and New Brunswick, Canada. The Committee was informed that these and other studies are under discussion at the Agency, but that no position paper is yet available.[2]

3. Most sensitive population: The Agency informed the Committee that a 1977 study using several levels of sodium nitrite in drinking water is being considered as an appropriate basis on which to establish a standard. This study would replace the data on methemoglobin formation in infants with gastrointestinal disease. The Committee did not offer a position on this issue and awaits a revised Criteria Document.[3]

The Science Advisory Board, through the Drinking Water Committee, stands ready to assist your well-informed, conscientious staff in improving the scientific basis for rulemaking in this area. We wish to point out, however, that a part of the Agency seems to be proceeding with deliberate speed toward the promulgation of a MCL for nitrate in drinking water without the benefit of SAB comment on a revised criteria document for nitrate and its metabolic byproduct, nitrite. We understand that many of these issues are under discussion in the EPA RfD and CRAVE work groups. We look forward to reviewing the Agency's position on these issues in a timely manner prior to promulgation of the rule.

We look forward to your formal response to this report.

Sincerely,

Raymond C. Loehr

Dr. Raymond C. Loehr
Chair, Executive Committee

William H. Glaze

Dr. William H. Glaze
Chair, Drinking Water Committee

1. Conclusions of the Beresford (Is nitrate in the drinking water associated with the risk of cancer in the urban UK?, Int. J. Epi., 14:57-63, 1985) and Dutt et al (M. C. Dutt, H. Y. Lim and R. K. H. Chew, Nitrate consumption and the incidence of gastric cancer in Singapore, J. Chem. Toxic, 25:515-520, 1987) studies are still in a discussion phase. However, it appears that the Agency position is that there "is insufficient evidence" to conclude that nitrate/nitrite present a potential cancer risk through drinking water. The Beresford U.K. urban area study concluded that there was no evidence of a positive association between nitrate levels in drinking water and mortality from all cancers including stomach cancer. The Dutt et al study suggested an increase in gastric cancer in certain subpopulations in Singapore due to dietary nitrate consumption.

2. Two new studies were presented to the Committee in the area of developmental toxicity. In the drinking water study (Roth, A.C., Evaluation of developmental toxicity of sodium nitrite in Long-Evans rats, Fund. and App. Tox., 9:668-677, 1987) involving Long-Evans rats ingesting nitrite, a no observed effect level of 500 mg/L was determined. This level was calculated to be 50 times the exposure level that would result from the proposed nitrite standard. Results of the second report (Arbuckle, T.E. and Sherman, G., Corey, P.N., Walters, D. and Lo, B., Water nitrates and CNS birth defects: A population-based case-control study, Archives of Environmental Health, 43:162-167, 1988), based on a drinking water study in South Australia and another case-control study in New Brunswick, Canada were examined. Currently these and other studies are under discussion in the Agency, however, there appears to be insufficient evidence for the existence of developmental toxicity at the 10 mg/L (as nitrogen) drinking water standard level.

3. The Agency believes the standard of 10 mg/L nitrate contains an adequate margin of safety to protect infants with gastrointestinal disease. The Committee had previously concluded (May, 1987) that the Agency could set a proposed health advisory level on the basis of methemoglobin formation. It now appears that methemoglobin formation in infants with gastrointestinal disease is primarily the result of the infection rather than nitrate/nitrite levels in drinking water. However, a rat study (Shuval, H.I. and Greuner, N., Health effects of nitrites in water, Health Effects Research Laboratory, USEPA, Cincinnati, Ohio, 164 pp., 1977) using several levels of sodium nitrite in drinking water is being debated in the Agency as a more appropriate basis on which to establish a standard.

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NOVEMBER 1989

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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
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JUL 2 1987

THE ADMINISTRATOR

Norton Nelson, Ph.D.
Chairman, Executive Committee
Science Advisory Board
U.S. Environmental Protection Agency
401 M Street, SW
Washington, DC 20460

Dear Dr. Nelson:

Thank you for your letter of May 11, 1987, transmitting the recommendations of the Science Advisory Board (SAB) from their initial review of the draft Drinking Water Criteria Document on Nitrate and Nitrite. We are providing this initial response to your comments. As you know, since EPA will be preparing regulations for these substances, you will have another opportunity to review the completed documents.

We are incorporating many of SAB's editorial suggestions which should result in a more readable document. For example, a Foreword (enclosed) has been developed for use with Drinking Water Criteria Documents which more clearly presents the purpose and goals of a Criteria Document. This will be added to all such Criteria Documents.

Much of the Board's discussion has to do with the Walton report. While this report is the nominal "linchpin" of the proposed nitrate and nitrite standards, it is by no means the sole support of these standards. Rather, the proposed nitrate and nitrite standards are based on the Walton report in combination with other epidemiological information. This will be articulated more carefully in the revised documents.

A 10 mg/L (as N) guideline or standard for nitrate has been in effect successfully for more than 25 years. The margin of safety question is always considered whenever a health standard is developed. In this case the type of data that is available makes quantification of such a factor more difficult. We have recently proposed a 10 mg/L (as N) revised standard for nitrate and a 1 mg/L (as N) standard for nitrite, the proximate toxic agent for both nitrate and nitrite. We feel that there is a good basis for regulating both nitrate and nitrite since nitrite levels provide an indicator of oxidation-reduction conditions in water which could relate to other water quality factors as well as risks of methemoglobinemi

The discussion of alternate pathways of exposure beyond drinking water will be expanded somewhat, however, the document will still focus on drinking water as it relates to the risk of methemoglobinemia in infants. The Criteria Document will also briefly address endogenous nitrosamine formation and splenic sarcomas.

We agree that all significant topics including reproductive and developmental toxicity as well as the relationship with maternal toxicity should be addressed in EPA risk assessment documents whenever that information is available.

In the course of the rulemaking scheduled for proposal this fall, EPA will reexamine and review the issues raised in your report and provide the revised regulatory documents for your review according to the specifications of the Safe Drinking Water Act.

Again, thank you for your recommendations.

Sincerely,

Lee M. Thomas

Enclosure

FOREWORD

Section 1412 (b)(3)(A) of the Safe Drinking Water Act, as amended in 1986, requires the Administrator of the Environmental Protection Agency to publish maximum contaminant level goals (MCLGs) and promulgate National Primary Drinking Water Regulations for each contaminant, which, in the judgment of the Administrator, may have an adverse effect on public health and which is known or anticipated to occur in public water systems. The MCLG is non-enforceable and is set at a level at which no known or anticipated adverse health effects in humans occur and which allows for an adequate margin of safety. Factors considered in setting the MCLG include health effects data and sources of exposure other than drinking water.

This document provides the health effects basis to be considered in establishing the MCLG. To achieve this objective, data on pharmacokinetics, human exposure, acute and chronic toxicity to animals and humans, epidemiology and mechanisms of toxicity were evaluated. Specific emphasis is placed on literature data providing dose-response information. Thus, while the literature search and evaluation performed in support of this document was comprehensive, only the reports considered most pertinent in the derivation of the MCLG are cited in the document. The comprehensive literature data base in support of this document includes information published up to _____ ; however, more recent data may have been added during the review process.

When adequate health effects data exist, Health Advisory values for less than lifetime exposures (One-day, Ten-day and Longer-term, approximately 10% of an individual's lifetime) are included in this document. These values are not used in setting the MCLG, but serve as informal guidance to municipalities and other organizations when emergency spills or contamination situations occur.

Michael B. Cook
Director
Office of Drinking Water

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON D C 20460

SAB-EHC-87-029

May 11, 1987

OFFICE OF
THE ADMINISTRATOR

Honorable Lee M. Thomas
Administrator
U. S. Environmental Protection Agency
401 M Street, S. W.
Washington, D. C. 20460

Dear Mr. Thomas:

The Drinking Water Subcommittee of the Science Advisory Board's Environmental Health Committee has completed its review of the Drinking Water Criteria Document for Nitrate and Nitrite and is pleased to transmit its conclusions and recommendations to you.

The Subcommittee advises that further technical changes are warrented before finalizing the document. Specifically, the staff should clarify the use of the Walton study, including the limitations of the study and the weight assigned to its use for regulatory decision making. Second, a clearer scientific rationale should be presented on the selection of margins of safety. These and other issues are discussed in the attached report.

We appreciate the opportunity to conduct this scientific review and request a formal response to the Subcommittee's report.

Sincerely,

Richard Griesemer

Richard Griesemer, Chairman
Environmental Health Committee
Science Advisory Board

Norton Nelson

Norton Nelson, Chairman
Executive Committee
Science Advisory Board