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

July 19, 1988

OFFICE OF
THE ADMINISTRATOR
SAB-EHC-88-035

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

Subject: Science Advisory Board's review of the ACRYLAMIDE health criteria document

Dear Mr. Thomas:

The Drinking Water Subcommittee of the Science Advisory Board's Environmental Health Committee has completed its review of the Drinking Water Health Criteria Document for Acrylamide dated July 1987. The review was conducted February 4-5, 1988, at the Washington Circle Hotel in Washington, D.C.

The Subcommittee made the following conclusions and recommendations concerning this document on acrylamide:

- the Johnson study should be used in setting the standard since it was performed for the full two years;

- the final assessment of the carcinogenic potential should await the results of the current bioassay which should be useful in the quantitative risk analysis;

- because of the seriousness of the effects, the ability of acrylamide to produce heritable germ cell mutations should be given emphasis in the risk assessment process;

- the health implications of products formed from acrylamide as a result of chlorination and oxidation processes are potentially serious and must be considered in this document. They could alter the results significantly in either direction the results; and

- the potential effects of pH and metal ions in water are not addressed. If no data are available they need to be generated as they could alter significantly the results of the analysis presented in the document.

A more detailed discussion of these points and some minor ones are attached.

Additional chapter-specific comments have already been forwarded from individual members to the Office of Drinking Water.

We appreciate the opportunity to conduct this particular scientific review. We request that the Agency formally respond to the scientific advice provided here.

Sincerely,

Norton Nelson, Chairman
Executive Committee

Richard A. Griesemer, Chairman
Environmental Health Committee

Gary P. Carlson, Chairman
Drinking Water Subcommittee

SUBJECT: SCIENCE ADVISORY BOARD'S REVIEW OF THE ACRYLAMIDE HEALTH CRITERIA DOCUMENT

SCIENCE ADVISORY BOARD COMMITTEE: DRINKING WATER SUBCOMMITTEE OF THE ENVIRONMENTAL HEALTH COMMITTEE

DATE OF REVIEW: FEBRUARY 4-5, 1988

PLACE OF REVIEW: WASHINGTON CIRCLE HOTEL, WASHINGTON, D.C.

The toxicity of acrylamide is quite high and the adverse health effects of this substance are reflected in several ways. The neurotoxic effects have been studied, are well known, and are cited in the criteria document. The Burek study and Johnson study are representative of those dealing with neurotoxicity and both reveal similar dose response and dose-time-exposure relationships. Furthermore, each reflects toxic endpoints relevant to known human neurotoxicity. Since the Johnson study was performed for two years, its use to determine the NOAEL is rational and recommended by the Subcommittee. The Subcommittee views the Burek study as supportive. The extra 10-fold uncertainty factor built into the calculation, using the value from the Burek study, for the DWEL is not viewed by the Subcommittee as necessary. It was added sumply because a less than lifetime study was being used. However similar values for the drinking water equivalent level (DWEL) would otherwise result whether the Burek or Johnson study was used.

The carcinogenic potential of acrylamide in animals has been demonstrated in a number of bioassay studies cited in the criteria document. Significant increases in tumors (both benign and malignant) across two species (mice and rats) have been revealed in several studies. Tumors have been associated with numerous tissues in animals (skin, lung, oral cavity). However, the existing data are suspect due to the high dose levels used which may not be adequate to provide for good quantitative risk anlysis. There is an ongoing bioassay study with several dose levels currently underway, and this information should be included in the analysis. The Subcommittee recommends that the final quantitative analysis of acrylamide as a carcinogen await the results of this study. In vitro and in vivo studies on genetic interactions cited in the criteria document strengthen the evidence that acrylamide may be a human carcinogen.

Not cited in the document is recent evidence on the in vivo genetic activity of acrylamide. This raises considerable concern. Shelby et al (1986) have reported a substantive level of dominant-lethality in male mice following a 50 mg/kg (x5) dose of acrylamide. Further studies by this group (Shelby et al 1987) demonstrate that acrylamide produces heritable translocations in male mice. These studies establish that acrylamide is a mammalian germ cell mutagen. Further, the stages of spermatogenesis affected (late spermatid and early spermazoa) are

those that other monofunctional alkylating agents such as ethylmethanesulfonate, methylnitrosourea and ethylene oxide are known to cause, both for dominant lethal and heritable translocation events. The Subcommittee recommends that the ability of acrylamide to produce heritable germ cell mutations be given emphasis in the risk assessment process. Another reference that should be considered is that of Smith et al (1986) in which subchronic administration of acrylamide to male rats in drinking water produced a dose related increase in dominant lethality.

The criteria document notes the high reactivity of acrylamide. The addition reaction illustrated with bromine on page II-3 (1) is not as relevant as those with chlorine in water such as; CH_2=CHCONH$_2$ + HOCl ---> HOCH$_2$CHClCONH$_2$.Along with its rapid carbon-carbon additions, chlorine also reacts as a N-chlorinating and a deaminating agent. The health implications of the products resulting from these chlorination and oxidation processes have not been considered in the criteria document, and the Subcommittee recommends that they be analyzed and discussed.

Other potentially important reactions in water are also not addressed. The effects of pH and metal ions are likely to be important but are generally unstudied in dilute aqueous solutions. These reactions could have important health implications both positive and negative, and the Subcommittee recommends that they be studied and reported in the document.

There are uncertainties on the use, occurrence and environmental fate of acrylamide in water as discussed in Section IV. As noted in Table II-1, the vapor pressure is sufficiently low and the solublity in water high enough, that the Henry's Law equilibrium partitioning suggests low volatility from aqueous solution. This is contrary to the statement that... "volatilization is an important removal process for acrylamide from surface water ..." (page IV-2) as well as the statement on page IV-3 that "it is not expected to be a common contaminant in air". This apparent contradiction must be removed.

On page IV-4 the statement that ..."the maximum level of occurrence of acrylamide in water is 0.5 micrograms/L" needs elaboration and justification. It should be stated that this estimate is based on the maximum allowable quantity of acrylamide in the polymer used as coagulant at the maximum concentration of one ppm in drinking water. These conservative assumptions, coupled with the potential degradation of acrylamide suggest that actual levels of acrylamide could be considerably lower.

U.S. Environmental Protection Agency
Science Advisory Board
Drinking Water Subcommittee

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