MICHIGAN DEPARTMENT OF ENVIRONMENTAL QUALITY

INTEROFFICE COMMUNICATION

January 16, 1996

TO: File for 1-Amino-2-Methyl-1-Propanol (124-68-5)

FROM: Marco Bianchi

SUBJECT: Initial Threshold Screening Level

The initial threshold screening level (ITSL) for 1-amino-2-methyl-1-propanol (AMP) is 4 ug/m^3 based on an annual averaging time.

The following references or databases were searched to identify data to determine the ITSL: IRIS, HEAST, NTP Management Status Report, RTECS, EPB-CCD, EPB library, CAS-online, NLM-online, IARC, NIOSH Pocket Guide, and ACGIH Guide.

The only information available for AMP was a literature review by the American College of Toxicology, on the chemistry, use and toxicology of this compound. AMP is used in the cosmetics industry at concentrations up to 10%. AMP is an emulsifying agent for cosmetic creams and lotions, and used as pH adjusters. In hair sprays, it is used as neutralizing agents to regulate solubility, flexibility, and tackiness of the resin.

In clinical studies, AMP was neither a primary dermal irritant nor a contact sensitizer. Additionally, AMP is nonmutagenic, both with and without metabolic activation, in Salmonella typhimurium strains.

In a series of acute oral and inhalation studies, some of which included hair spray or cosmetic formulations, AMP was found to be nontoxic to rats and albino mice, but slightly toxic to deer mice. More specifically, a reported LD_{50} for AMP in fasted, young adult male rats was 2.90 g/kg. The oral LD_{50} values in Cox strain albino mice for AMP was estimated at 2.15 g/kg.

The literature review also included both oral and inhalation subchronic toxicity testing. A 13-week inhalation study was performed on Charles River albino rats for 4 hr/day, 5 days/week for 13 weeks. However, only one dose of an aerosolized form of hair spray containing 44% AMP (0.23 mg/m^3) was used. Statistically significant hematologic changes included increased packed cell volume and erythrocyte counts for males and females, and increased hemoglobin values for males. No treatment related microscopic changes were found in the evaluated tissues; frequency and severity of noted changes were equivalent for both the treated and control rats. Due to only one dose group use in this study and the uncertainties of additional hair spray components in the test solution, additional information was evaluated for ITSL derivation.

In an oral 90-day study, AMP was administered to rats by stomach tube at pHs of 11+ or 7. At each pH, the AMP solution was administered at doses of 0, 0.5, 0.75, 1.1 or 1.7 g/kg/day; the dosage groups consisted of 20 rats, divided equally by sex. The rats were observed daily, and body

weights and feed consumption were recorded weekly. All rats that died during and after the study were necropsied after samples were taken for hematologic, urologic, and clinical chemistry measurements. Results of the study indicated that mortality caused by AMP was due to AMP solutions with a pH of 11 or greater, however, no mention was made as to how many animals this included. In the pH 7 group rats, some occurrences of increased SGPT and OCT activities were noted, and males in the 1.7 g/kg group had significant decreases in packed cell volume and hemoglobin. Contrary to the results obtained in the 13-week inhalation study, the pH11+ group rats receiving doses of 0.5 and 0.75 g/kg had slight, though significant, *decreases* in erythrocyte counts. Although there was no interpretations from the authors as to why this occurred, AMP is known to effect the coupling and uncoupling of oxidative phosphorylation in rat liver mitochondria. No gross lesions were found at necropsy. Tissues were taken from dosed and control rats of both pH groups, however, no mention was made of the microscopic examination other than "the 1.7 g/kg oral dose of an AMP solution at pH 7 did not cause any significant changes in male or female rats under the conditions of the experiment." In the tissues of the pH 11+, 1.7 g/kg group female rat, the only abnormality noted was a few papillary protrusions of epithelium at the junction between the squamous and glandular portions of the stomach.

The 90-day oral study has serious limitations for its use in deriving an ITSL. No mention was made as to how many animals died during the study due to the high pH content of the compound, nor what vehicle was used to dissolve the AMP for dose administration. The unknown quantity and composition of this vehicle raises concern regarding the uncertainties of the outcome. The vehicle may have contributed to opposite effects in erthyrocyte count in the oral study as compared to the inhalation study. Therefore, it seems most appropriate to use the LD_{50} to derive an ITSL for AMP.

The ITSL was derived as follows:

LD_{50} mice = 2.15 g/kg

$$ITSL = \frac{1}{500} \times \frac{1}{40} \times \frac{1}{100} \times \frac{2{,}150 \text{ mg/kg}}{0.167 \times 1.685} = 0.0038 \text{ mg/m}^3$$

0.0038 g/kg x 1000 = 3.8 ug/m^3 based on annual averaging.

The ITSL for 1-Amino-2-Methyl-1-Propanol = 4 ug/m^3 based on annual averaging.

References:

Poudrier J.K. 1990. Final report on the safety assessment of aminomethylpropanol and aminomethylpropanediol. Journal of the American College of Toxicology. Vol. 9:2; 203-227.

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