MICHIGAN DEPARTMENT OF NATURAL RESOURCES

INTEROFFICE COMMUNICATION

January 4, 1993

TO: FILE

FROM: Cathy Simon

SUBJECT: Amyl Alcohol (Cas No. 71-41-0)

The ITSL for amyl alcohol is 120 ug/m3 based on an annual averaging time.

The following references or databases were searched for information on amyl alcohol: IRIS, HEAST, Environmental Protection Bureau Library, and CAS Online.

Very little toxicological data were available for amyl alcohol. Relevant studies included an acute oral and inhalation study (Scala and Burtis, 1973), a 13 week oral toxicity study in rats (Butterworth et al, 1978), and a developmental toxicity study in rats exposed via inhalation (Nelson et al, 1989). Scala and Burtis (1973) reported an LD50 of 2.69 g/kg in male Sprague-Dawley rats. They also exposed groups of 10 Swiss mice, Wistar rats, and English short haired guinea pigs to a calculated concentration of 14,000 mg/m3 amyl alcohol (as an aerosol) for a single 6 hour period. Mortality observed included the following: 7/10 for mice, 2/10 for rats, and 0/10 for guinea pigs. Effects observed in all animals included irritation of the mucous membranes of the eyes, nose, throat, and respiratory passages, CNS effects, and an increase size of the deep proximal convoluted tubules associated with an increase size of the epithelial cells lining the tubules. Pulmonary edema was also noted in mice. The amyl alcohol used by Scala and Burtis in their studies was a commercial grade consisting typically of 74 wt% 1-pentanol, 25 wt% 2-methyl-1-butanol, and 1 wt% 3-methyl-1-butanol.

In the developmental toxicity study by Nelson et al (1989), 15 Sprague-Dawley rats were exposed for 7 hr/day on gestation days 1 - 19 to a concentration of 14,000 mg/m3. This is the highest concentration the authors said could be generated as a vapor. The test material utilized was reagent grade 1-pentanol with a purity of $\geq$ 99%. The only effects observed were a significant decrease in maternal food consumption and a non-significant decrease in weight gain. No teratogenic or developmental effects were observed in this study.

The results of the study by Nelson et al (1989) conflict with those by Scala and Burtis (1973) in that animals from both studies were exposed

to the same concentration of amyl alcohol (14,000 mg/m3), yet little or no effects were observed by Nelson et al, whereas Scala and Burtis saw a number of adverse effects including mortality. The reason for this difference isn't entirely clear and may be due to the difference in composition of the test material, or the fact that one exposure occurred as an aerosol and one as a vapor.

In the study by Butterworth, a 13 week oral rat NOAEL of 1000 mg/kg/day was identified. In this study, rats were exposed by gavage to 50, 150, or 1000 mg/kg/day amyl alcohol (purity, min. 97%).

The study by Nelson et al was used to determine the ITSL for amyl alcohol using the algorithm in Rule 232(1)(d) with an additional 10-fold uncertainty factor for using a LOAEL as follows:

$$\text{ITSL} = \frac{14{,}000\ \text{mg/m}^3}{35 \times 100 \times 10} \times \frac{7\ \text{hr}}{24\ \text{hr}} = 0.117\ \text{mg/m}^3 = 120\ \mu\text{g/m}^3$$

Although the algorithm in Rule 232(1)(d) is for calculating an ITSL from a 7-day NOAEL, the uncertainty factors utilized in the equation were considered appropriate, taking into account the uncertainty associated with the effects at 14,000 mg/m3 from the Scala and Burtis study, as well as the fact that Nelson et al were only looking at the single endpoint of developmental toxicity. More weight was given to the Nelson et al study as the test material was reagent grade of $\geq$ 99% purity. Although the 13 week oral study (Butterworth et al) was considered a better quality study, the uncertainty of extrapolating from this route of exposure, given the existing inhalation studies, over rode the use of this study for determining the ITSL. The results of the Butterworth study do not conflict with the inhalation studies, and resulting ITSL, if it is assumed that absorption by the oral and inhalation routes are equal, and no other factors are relevant for dose conversion. Based on these assumptions, an equivalent daily inhalation exposure for 1000 mg/kg/day (the highest dose tested) would be approximately 1000 mg/m3 (assuming a mean rat body weight of 342 grams, and a daily inhalation rate of 0.332 m3/day).

REFERENCES

Butterworth K.R. et al. 1978. Short term toxicity of n-amyl alcohol in rats. Food and Cosmetic Toxicology 16:203-207.

Nelson B.K. et al. 1989. Developmental toxicology evaluation of 1-pentanol, 1-hexanol, and 2-ethyl-1-hexanol administered by inhalation to rats. Journal of the American College of Toxicology 8:405-410.

Scala R.A. and E.G. Burtis. 1973. Acute toxicity of a homologous series of branched-chain primary alcohols. American Industrial Hygiene Association Journal 34:493-499.

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