MICHIGAN DEPARTMENT OF NATURAL RESOURCES

INTEROFFICE COMMUNICATION

May 19, 1993

TO: File for Diethyl Sulfate (CAS# 64-67-5)

FROM: Mary Lee Hultin

SUBJECT: Screening level for Diethyl Sulfate

IARC classifies the evidence for carcinogenicity of diethyl sulfate as sufficient for animals and limited for humans. The primary focus of this determination for animals is work done by Druckrey, et al. Forestomach tumors were seen in rats exposed orally and local tumors were seen in rats exposed subcutaneously. In addition, offspring of pregnant rats dosed intravenously developed malignant tumors of the nervous system. However, none of the work by Druckrey is available for scrutiny as it is published only in German (CAS Online, 2/93). Furthermore, deficiencies such as lack of concurrent controls, and less than lifetime dosing periods prohibit an accurate risk assessment. Epidemiologic data is suggestive of an association with respiratory cancers, however the studies failed to clearly identify whether diethyl sulfate was the etiologic agent (J. Occ. Med., 1979, v. 21(5)).

A substantial body of literature indicates that diethyl sulfate is a mutagen. Positive results have been seen in: mouse dominant lethal tests, specific locus tests; sex linked recessive lethal tests in Drosophila sperm; chromatid breaks and somatic coat color mutation testing; host-mediated assay; and chromosomal aberrations in barley. This data adds to the concern for the carcinogenic potential of diethyl sulfate, but does not provide data for risk assessment.

No chronic or subchronic inhalation or ingestion studies were found in the literature. Two acute studies were found:

1. Smyth, et al. published a rat oral LD50 for diethyl sulfate of 0.88 gm/kg in 1949.

2. Vernot, et al., 1977, published oral LD50 studies for rats and mice as follows:

> -Male rat oral LD50 = 1410 mg/kg
> -Mice oral LD50 = 650 mg/kg

Data from the Vernot study are more appropriate for risk assessment since they are more recent and provide animal-specific data for incorporation in

the calculation. The data for mice will be used for screening level derivation since the mice appear to be more sensitive due to the lower LD50 value.

$$ITSL = \frac{1}{500} x \frac{1}{40} x \frac{1}{100} x \frac{LD50 \ x \ W_a}{0.167 \ x \ I_a}$$

$$ITSL = \frac{1}{500} x \frac{1}{40} x \frac{1}{100} x \frac{650mg/kg \ x \ 0.022kg}{0.167 \ x \ (1.99x(0.022^{1.0496})} = 1.18x10^{-3}mg/kg$$

or ITSL = 1 ug/m^3 based on annual averaging

References:

1. Druckrey, H., 1973. "Chemical Structure and Action in Transplacental Carcinogenesis and Teratogenesis", Transplacental Carcinogenesis, IARC Scientific Publication no. 4. Proceedings of a meeting held in Germany, 6-7 October 1971.
2. International Agency for Research on Cancer, 1987, IARC Monographs on the Evaluation of Carcinogenic Risks to Humans, Supplement 7.
3. Lynch, J., et al., 1979, J. Occ. Med., v. 21(5), p. 333-341.
4. Smyth, H.F., 1949, J.Ind.Hyg. & Toxicol., p. 60-62.
5. Syracuse Research Corp., 1985, Monograph on Human Exposure to Chemicals in the Workplace: Diethyl Sulfate.
6. Vernot, E.H., 1977, Toxicology and Applied Pharmacology, v. 42, p.417-423.