MICHIGAN DEPARTMENT OF NATURAL RESOURCES

INTEROFFICE COMMUNICATION

OCTOBER 18, 1994

TO: File for Anhydro-dimethylamino Hexose Reductone (CAS# 63937-30-4)

FROM: Michael Depa, Toxics Unit

SUBJECT: Screening Level Determination

The initial threshold screening level (ITSL) for anhydro-dimethylamino hexose reductone is 0.6 $\mu g/m^3$ based on an annual averaging time.

The following references or databases were searched to identify data to determine the ITSL: IRIS, RTECS, ACGIH Threshold Limit Values, NIOSH Pocket Guide to Hazardous Chemicals, Environmental Protection Bureau Library, IARC Monographs, CAS Online (1967-August 20, 1994), National Library of Medicine, Health Effects Assessment Summary Tables, and NTP Status Report. Review of these sources found that EPA has not established an RfC or RfD for anhydro-dimethylamino hexose reductone. Occupational exposure limits were not available. A report was available where the researchers performed a 100 day feed study and an LD50 study (Ambrose, 1961). The feed study reported that all dose levels produced growth rate retardation. However, few details of how this study was performed were reported. Consequently, the quality of the feed study could not be assessed and it could not be used to determine the ITSL. Only the LD50 study provided enough toxicity information and enough details of the test conditions to determine a screening level. This study is described below.

Groups of eight to ten mice (strain unspecified) weighing 15 to 20 g each were administered oral doses ranging from 0 to 1500 mg/kg[1] of anhydro-dimethylamino hexose reductone (suspended in 20% gum acacia) (Ambrose, 1961). No deaths and no

[1]Although reported as mg, it was assumed that the researchers meant to report the dose levels as mg/kg. See the discussion concerning the quality of the study.

symptoms occurred in 4 controls given gum acacia, nor in 8 mice receiving 200 mg/kg. Five of 10 mice given 300 mg/kg and 4 of 8 given 400 mg/kg died in 1 to 2 hours. Dosage levels of 500 and 800 mg/kg produced 75% mortality, and mortality was 100% in the higher dose groups. Convulsions occurred before death, and the heart stopped in systole. No symptoms were noted in any of the survivors. The LD50 was reported as 300 mg/kg.

The quality of the Ambrose study was scrutinized, and several problems were identified. The dose unit was described with the unit of milligram (mg) but the LD50 was reported in mg/kg. If it is assumed that the dose was measured in mg then the LD50 corresponding to the lowest dose with 50% mortality would be 300 mg divided by 0.0175 kg (average weight of a mouse) or 17,000 mg/kg. This corresponds to an LD50 of 17 g/kg. Since it was reported that the LD50 was 300 mg/kg instead of 17 g/kg, it was concluded that the researchers dosed the mice with units of mg/kg and had simply made a typographical error in reporting these dosing units. This study also failed to report the strain and sex of the mice, the observation period, and the method used to determine the LD50.

Despite the problems with this study there was useful toxicity data. As reported by Ambrose the LD50 was 300 mg/kg, however, given the dose and mortality data reported in the study an LD50 of 350 mg/kg was calculated according to the Litchfield and Wilcoxon method (1949)(see attached graph). It was decided to use the more conservative reported LD50 of 300 mg/kg rather than the calculated LD50 of 350 mg/kg given the uncertainties of this study. Thus, the LD50 of 300 mg/kg was used to determine the ITSL pursuant of Rule 232 (1)(h) as follows:

$$ITSL = \frac{1}{500} \times \frac{1}{40} \times \frac{1}{100} \times \frac{LD50\ (mg/kg) \times W_a}{0.167 \times I_a}$$

$$ITSL = \frac{1}{500 \times 40 \times 100} \times \frac{300\ mg/kg \times 0.018\ kg}{0.167 \times 0.029\ m^3}$$

$$ITSL = 5.58 \times 10^{-4}\ mg/m^3$$

$$ITSL = 0.6\ mg/m^3$$

Where: W_a is the default weight of the mouse (EPA, 1988) and
I_a is the default inhalation rate of the mouse (EPA, 1988).

The ITSL for anhydro-dimethylamino hexose reductone is 0.6 $\mu g/m^3$ based on an annual averaging time.

Ambrose, A., Robbins, D., and DeEds, F. 1961. Acute and subacute toxicity of amino-hexose-reductones. Proceedings of the Society for Experimental Biology and Medicine. 106: 656-659.

EPA. 1988. Recommendations for and documentation of biological values for use in risk assessment. PB 88-179874.

Litchfield, J., and Wilcoxon, F. 1949. A simplified method of evaluating dose-effect experiments. Journal of Pharmacology and Experimental Therapy. 96:99-115.