MICHIGAN DEPARTMENT OF ENVIRONMENTAL QUALITY

INTEROFFICE COMMUNICATION

July 7, 1997

TO: File for Diisopropanolamine (Cas # 110-97-4)

FROM: Marco Bianchi, Toxics Unit, Air Quality Division

SUBJECT: Re-evaluation of Initial Threshold Screening Level Due to New Data

The new Initial Threshold Screening Level (ITSL) for diisopropanolamine is 4 ug/m^3 based on an annual averaging time. This compound was initially evaluated by Air Quality Division (AQD) staff in 1994, but no data could be found to set an ITSL other than trace (0.04 ug/m^3, annual averaging time). Since that time, Dow Chemical Company has recently submitted a two-week oral rat study for AQD's evaluation and re-determination of the ITSL.

Dow Chemical submitted an internal study entitled, *Diisopropanolamine: Results of a Two-Week Study in the Drinking Water of CDF Fischer 344 Rats*. In this study, Groups of 5 male and 5 female CDF Fischer 344 rats received diisopropanolamine in their drinking water for 2 weeks in concentrations calculated to administered doses of 0, 100, 300, 600, 1200 or 3000 mg/kg body weight/day.

According to the report, the targeted dose of 3000 mg/kg/day was poorly tolerated; two of the five males did not survive to the scheduled terminal necrospy. Both sexes of rats at this dose showed markedly reduced water and food intake and loss of body weight. Gross necropsy observations of marked reductions in body size, body fat, and size of organs, along with various alterations in clinical biochemical parameters and organ weights, were all reflections of an emaciated state as a result of decreased water and food intake. Histopathologic examinations of kidneys and urinary bladder from rats at the highest dose revealed evidence of acute inflammation and degeneration; these alterations in the kidneys and urinary bladder, slight in severity, were considered to be due to the chemical or its metabolite(s). The authors concluded that the degree of change in the kidney and urinary bladder was probably potentiated by the decreased water intake with a resultant concentration of toxicant in these tissues. Male and female rats receiving the targeted dose of 1200 mg/kg/day showed slight decreases in water and food intake; minimally decreased body weight gain was observed in males, but not females. Relative kidney weights were slightly increased in both sexes at 1200 mg/kg/day. Additionally, statistically significant increases in relative kidney weights of females at doses of 100, 300, or 600 mg/kg/day were minimal in magnitude, and appeared to the authors to be the consequence of the lower mean fasted body weights of those treated groups compared the control mean. A microscopically observed alteration in the kidney of one male rat at 1200 mg/kg/day, similar to that observed at 3000 mg/kg/day, was the only histopathologic evidence of a treatment-related effect at this dose.

The study concluded by stating that administration of diisopropanolamine in the drinking water to CDF Fischer 344 rats for 2 weeks did not produce any significant toxicological effects at doses of 600 mg/kg/day or below. The statistically significant increases in relative kidney weights of females at doses of 100, 300, or 600 mg/kg/day was thought to be the consequence of the lower mean fasted body weights of the treated groups compared to the control mean. AQD, however, disagrees with this interpretation. The significant change in mean fasted body weights was not evident in the summary tables provided. Simply dismissing the statistically significant change in kidney weights due to changes in body weight alone seems inappropriate, especially when the kidney is the target organ of toxicity. The terminal kidney weights provided in the study suggest a statistically significant dose-related trend in the 100 to 1200 mg/kg/day dose groups. The kidney appears to be the organ most sensitive to the effects of ingestion of high levels of diisopropanolamine. Treatment-related changes which were microscopically detected in the kidneys and urinary bladder suggest that the material being excreted was irritating to the transitional epithelium - especially in the highest dose group. The reduced water intake at this level probably resulted in a marked concentration of the urine and the excretion product of diisopropanolamine such that irritation to the epithelium resulted. Therefore, assessing this data holistically would indicate that 100 mg/kg/day (121 mg/kg/day actual average dose adjusted for group mean body weight and water comsumption data) was a lowest-observable-adverse-effect-level (LOAEL), since there was a statistically significant increase in kidney weight at this lowest exposure level.

The ITSL was determined as follows:

WA	=	body weight of experimental animal in kilograms (kg)
IA	=	daily inhalation rate of experimental animal in cubic meters/day
b	=	absorption efficiency by the oral route of exposure
a	=	absorption efficiency by the inhalation route of exposure
35	=	adjustable safety factor dependent upon the length of the study
LOAEL	=	10-fold uncertainty factor in denominator

$$ITSL = \frac{LOAEL\ (mg/kg/day)}{35 \times 100 \times 10} \times \frac{W_A}{I_A} \times \frac{b}{a}$$

$$ITSL = \frac{121\ mg/kg/day}{30 \times 100 \times 10} \times \frac{1}{0.990} \times \frac{1}{1}$$

$$ITSL = 0.004\ mg/m^3 \times 1000\ ug/mg = 4\ ug/m^3$$

The ITSL for diisopropanolamine = 4 $\mu g/m^3$ based on annual averaging.

MB:slb