MICHIGAN DEPARTMENT OF ENVIRONMENTAL QUALITY

INTEROFFICE COMMUNICATION

August 12, 1997

TO: File for Triethanolamine (CAS #102-71-6)

FROM: Marco Bianchi, Toxics Unit, Air Quality Division

SUBJECT: Initial Threshold Screening Level

The *final* Initial Threshold Screening Level (ITSL) for triethanolamine is 50 ug/m^3 based on an 8 hr. averaging time. This compound was initially evaluated by AQD staff in 1993, using interim ITSL procedures to derive a screening level of 50 ug/m^3 for an 8 hr averaging time. In an effort to finalize all interim chemical screening levels, this chemical was re-reviewed to set a final ITSL/(IRSL). The following references or databases were searched to identify data to determine the ITSL/IRSL: IRIS, HEAST, NTP Management Status Report, RTECS, EPB-CCD, EPB library, CAS-online, NLM-online, IARC, NIOSH Pocket Guide, and ACGIH Guide.

Triethanolamine may be absorbed through the skin and in the gastrointestinal tract. In mice that received a single 1,000 mg/kg dermal application, approximately 60% of the radioactivity was recovered from the urine and 20% was recovered from the feces 48 hours after dosing; less than 10% was detected in the skin at the site of application. More than 95% of the radioactivity recovered in the urine was identified as the parent compound, indicating that triethanolamine does not undergo extensive biotransformation in mice. Rats dosed with this compound also showed similar metabolism. A single oral dose (2 to 3 mg/kg) of [^{14}C]-triethanolamine was rapidly absorbed and excreted mainly in the urine as unchanged parent compound. Twenty-four hours after dosing, 53% of the radioactivity was recovered in the urine and 20% was recovered in the feces. For humans, no information on the pharmacokinetics and metabolism of triethanolamine was reported in the literature.

Acute oral studies have shown that triethanolamine is relatively non-toxic. In RTECS, LD_{50} values for rats were listed at 8680 and 9110 mg/kg, and for mice and guinea pigs, 1450 mg/kg and 8000 mg/kg, respectively. Erythema and slight edema were observed on rabbit skin, after application of 560 mg triethanolamine. However, solutions containing 6% and 15% of this compound showed no sensitizing properties when applied to the skin of guinea pigs. Another study (Kindsvatter, 1940) showed that when guinea pigs were administered 8 g/kg/day, 5 days/week of either commercial or high purity grade triethanolamine to the shaved and subsequently bandaged skin, the guinea pigs died between the second and seventeenth application. Necrosis of the epithelium was observed. Kidneys and liver showed cloudy swelling and congestion; fatty changes were seen in the central ascini of the liver and lung and adrenal congestion were observed.

Subchronic oral studies resulted in outcomes similar to the acute oral exposures mentioned above. In one representative study (Kindsvatter, 1940), groups of 24 guinea pigs and 24 albino rats were administered 200, 400, 800, or 1600 mg/kg body weight of commercial or high purity grades of triethanolamine by gavage, 5 days/week (guinea pigs) or in the diet (rats). One-third of the animals were sacrificed after 12 weeks (60 doses), the second one-third after 24 weeks (120 doses), and the remaining one-third after 24 weeks, but followed by a 3-month no dosing period. Adverse effects followed a dose-

response trend with increasing severity as the dose and exposure times increased. At the high-end dose range, kidney damage consisted of cloudy swelling of the convoluted tubules and Henli loop. Liver damage consisted of slight cloudy swelling in the peripheries of the acini along with some fatty changes in the inner halves of the acini - most prominent around the larger central veins. Sciatic nerves showed scattered degeneration in the myelin sheath of the individual fibers. Kidney regeneration was not as complete as liver regeneration at the end of the recovery period. In contrast, at the 200 mg/kg dosage, kidneys showed some light, cloudy swelling; and peripheral nerves, light scattered degeneration of the fibers. No NOEL was determined from this study. In another study by Smyth (1951), groups of ten rats that were administered triethanolamine in the diet at dosages of 0.005 to 2.61 g/kg for 30 days. Detailed responses were not listed, but generally included reduced growth, altered organ weights, microscopic lesions, and death. A NOEL of 0.08 g/kg was reported.

Mosberg (1985), exposed both Fischer 344 rats and B6C3F1 mice in separate 14-day inhalation studies to 0, 125, 250, 500, 1000, and 2000 mg/m^3 triethanolamine (TEA) for 6 hrs/day, 5 days/wk. Exposure groups consisted of 5 animals/sex/dose. At necropsy, intact body weight and the weights of the heart, brain, lungs, thymus, liver, right kidney, and right testicle were recorded. Forty target tissues were selected from rats in the control group and the highest dose group for microscopic examination. Target tissues were selected based upon the histopathologic examination of the animals from the highest dose and control groups, and were examined in rats from the lower dose groups to a no-effect level. Hematology was performed on all rats. Assays for hemoglobin, hematocrit, RBC and WBC count, platelet and reticulocyte count were performed.

Results were similar for test animals in each of the inhalation studies. No mortality occurred in the rat study, and only one control animal died in the mouse study. No abnormal clinical signs were observed in any of the treatment groups during testing. There were no significant changes observed in the group mean body weights of either sex for rats, but both male and female mice-treated animals exhibited a decrease in body weight as compared to controls. Likewise, both studies showed changes in body to organ weight ratios for all dose groups. Microscopically, the sole lesion considered to be treatment related was a minimal to slight inflammation of the laryngeal submucosa for animals in both studies. Minor lesions were seen in most dose groups, but didn't appear to be dose related. This inflammation was characterized by an infiltration of a few lymphocytes, plasma cells and neutrophils in the loose submucosal connective tissue and around the mucosal glands. According to the pathologist report, the significance of this lesion is undetermined and equivocal as it often appeared in one section of larynges that had multiple sections provided.

Hoshino et al., 1978 found that ICR-JCL mice fed a diet containing 0.3% or 0.03% triethanolamine developed malignant tumors. Females showed a high incidence of tumors in lymphoid tissues, while this type was absent in males. By contrast, in a 104-week carcinogenic bioassay (Maekawa, 1986), triethanolamine was administered in drinking water at levels of 0%, 1% or 2% to groups of 50 male and 50 female rats. A positive trend was noted in the occurrence of hepatic tumors in males and of uterine endometrial sarcomas and renal-cell adenomas in females. However, the authors concluded that triethanolamine under the condition of the study was not carcinogenic. Additionally, short-term genotoxic toxicity testing did not induce mutations in bacteria, gene conversions in yeast, or chromosome damage in a cultured rat-liver cell line. These studies tend to lend support of the weak carcinogenic potential of triethanolamine.

ACGIH documentation has reported that allergic contact dermatitis, erythematous vesicular lesions, eczema, contact dermatitis, and irritation in workers has been caused by triethanolamine exposure in industrial occupations. A cohort study in which cancer morbidity and mortality were investigated in workers exposed to cutting fluids with nitrates and amines (including TEA) had negative results. The effects on workers industrially exposed to metalworking coolants containing sodium nitrate and

triethanolamine solutions were investigated in a Russian study. Observed vascular effects were attributed to sodium nitrite; no effects were attributed to triethanolamine.

The ACGIH recommends a Threshold Limit Value TLV of 5 mg/m^3 for triethanolamine to minimize the potential for skin and eye irritation, and acute and chronic effects. This value was originally used to set an interim ITSL of 50 ug/m^3. Because none of the reviewed literature supported the derivation of an RfC(D), the interim value will be used again and become the final ITSL. According to Air Toxics Rule 232 1(c); if an Occupational Exposure Level (OEL) e.g., Threshold Limit Value (TLV), exists for a toxic air contaminant, the initial threshold screening level equals the OEL.

The ITSL was determined as follows:

ACGIH TLV = 5 mg/m^3

5 mg/m^3 ÷ 100 = 0.05 mg/m^3

$$0.05\ mg/m^3 \times \frac{1000\ ug/m^3}{1\ mg/m^3} = 50\ ug/m^3$$

The ITSL for triethanolamine = 50 $\mu g/m^3$ based on 8 hr. averaging.

References:

1. Documentation of Threshold Limit Values and Biological Exposure Indices. 1991. Triethanolamine. American Conference of Governmental Industrial Hygienists (ACGIH), 6th Edition.

2. Hoshino H. et al., 1978. Carcinogenicity of Triethanolamine in Mice and Its Mutagenicity after Reaction with Sodium Nitrate in Bacteria. Cancer Research 38, 3918-3921.

3. Kindsvatter V. 1940. Acute and Chronic Toxicity of Triethanolamine. Journal of Industrial Hygiene and Toxicology 22;6 pp. 206-212.

4. Maekawa, A. et al., 1986. Lack of Carcinogenicity of Triethanolamine in 344 Rats. Toxicology and Environmental Health 19:345-357.

5. Mosberg A. et al., 1985. Final Report on The Repeated Dose Inhalation Study of Triethanolamine (CAS No. 102-71-6) in Fischer 344 Rats to National Toxicology Program. Battelle - Columbus, OH. K-725-(100).

6. Mosberg A. et al., 1985. Final Report on The Repeated Dose Inhalation Study of Triethanolamine (CAS No. 102-71-6) in B6C3F1 Mice to National Toxicology Program. Battelle - Columbus, OH. K-725-(100).

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