MICHIGAN DEPARTMENT OF ENVIRONMENTAL QUALITY

INTEROFFICE COMMUNICATION

DRAFT

March 19, 2001

TO: File for 2-Ethylhexanal (CAS No. 123-05-7)

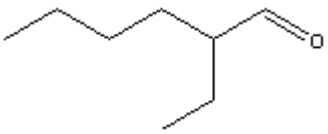
FROM: Michael Depa, Toxics Unit, Air Quality Division

SUBJECT: Development of the Screening Level

The initial threshold screening level (ITSL) for 2-ethylhexanal is 10 µg/m³ (annual averaging time).

The following references or databases were searched to identify data to determine the screening level: Environmental Protection Agency's (EPA's) Integrated Risk Information System (IRIS), the Registry of Toxic Effects of Chemical Substances (RTECS), the American Conference of Governmental Industrial Hygienists (ACGIH) Threshold Limit Values (TLV), National Institute of Occupational Safety and Health (NIOSH) Pocket Guide to Hazardous Chemicals, Environmental Protection Bureau Library, International Agency for Research on Cancer (IARC) Monographs, Chemical Abstract Service (CAS) Online (1967- September 2000), National Library of Medicine (NLM), Health Effects Assessment Summary Tables (HEAST), and National Toxicology Program (NTP) Status Report. The EPA has not established a reference concentration (RfC) or reference dose (RfD) for 2-ethylhexanal. The molecular weight is 128.2 g, and the molecular formula is C8H16O. The molecular structure is pictured in Figure 1. The boiling point is 163ºC. 2-Ethylhexanal is a yellow liquid at standard temperature and pressure. The vapor pressure is 1.8 mmHg at 20ºC.

Figure 1. Molecular Structure of 2-Ethylhexanal



Toxicity Studies

In an LD50 study, groups of 5 male and female CD rats received doses of 1250, 2500 and 5000 mg/kg 2-ethylhexanal as a single dose and observed for 14-days (Eastman Kodak, 1991). All rats in the 5000 mg/kg dose group died on day 1. One male in the 2500 mg/kg dose group died on day 1 with the remaining rats surviving the duration of the 14-day observation period. No rats died in the 1250 mg/kg dose group. The authors stated that the surviving animals gained weight normally. The authors also noticed that some of the animals displayed weakness after dosing. The oral LD50 for males was 3078 mg/kg (95% Confidence Interval = 2333 - 4061 mg/kg). The oral LD50 for females was 3536 mg/kg (95% Confidence Interval = 2679 - 4665 mg/kg).

In an acute inhalation study (Eastman Kodak, 1991) a group of three rats were exposed to 130 mg/L (130,000 mg/m³). The authors stated that the animals exhibited symptoms of vasodilation,

convulsions, and after death it was found that the lungs were bright red and the blood failed to clot. In a follow-up study, three rats were exposed to 30.1 mg/L (30,000 mg/m³) for 42 minutes. It was reported that there were no deaths after a 14 day observation period. Three hours after the 42 minute exposure it was found that the rats had clotting times of 3.5, 5.5 and 9 minutes respectively. Control rats had a clotting time of 3.5 minutes. The authors stated that the effect on blood is uncertain from this data. The animals gained weight normally in this 14-day observation period following exposure.

In a brief report by Eastman Kodak (1991) rats survived without symptoms, concentrations of 145 ppm for 6 hours. No other information was provided, including the duration of observation period.

In a dietary study, a group of 5 male F344 rats were administered 2-ethylhexanal (i.e., 2-ethylhexyl aldehyde) in the feed at a concentration of 2% (Moody and Reddy, 1982). Based on the feed consumption of male F344 rats of 0.078 kg/kg body weight (EPA, 1988) the dosage was calculated as 1560 mg/kg/day. The serum cholesterol and serum triglyceride were significantly lower than control rats. No other toxicological endpoints were reported.

In an acute oral study, the LD50 was reported as 3,730 mg/kg (95% confidence interval = 2.43 - 5.74) (Smyth, et al., 1951). A four hour inhalation study at 4000 ppm (20,973 mg/m³) resulted in 1 of six rats dying within 14 days. No other details were reported. Because of this, an ITSL could not be developed from the inhalation toxicity data.

Derivation of Screening Level

The inhalation toxicity studies were of poor quality. In the Eastman Kodak (1991) study, three rats were exposed for 42 minutes resulting in no mortality within 14 days. Few animals and inadequate reporting of results detract from the usefulness of this study. Furthermore, the study duration of 42 minutes is somewhat less than 1-hr (60 minutes) typically used for Rule 232(1)(g) to develop an ITSL. Forty-two minutes is 70% of 60 minutes. However, if this study was adequate an ITSL of 15 µg/m³ could be developed if one assumes that the 30,000 µg/m³ is the 1-hr LC50. Since there were too many problems with this study and the Smyth (1951) study, the oral toxicity data was evaluated in order to develop an ITSL.

Unfortunately the two week dietary study did not look at body weights, organ weights or any endpoints other than serum cholesterol and triglycerides. Therefore, the Eastman Kodak (1991) LD50 study was determined to provide the best data for ITSL derivation.

The ITSL pursuant to Rule 232(1)(h).

$ITSL = 1/(500 \times 40 \times 100) \times LD50/(0.167) \times W_a/I_a$

$ITSL = (5 \times 10^{-7}) \times (3078 mg/kg)/(0.167) \times (0.470 kg)/(0.431 m^3)$

$ITSL = 1.01 \times 10^{-2} mg/m^3$

$ITSL = 10 \mu g/m^3$ (annual averaging time)

The ITSL for 2-ethylhexanal is 10 µg/m³ based on annual averaging time.

References

Eastman Kodak. 1991. Letter from Eastman Kodak Company to USEPA submitting enclosed toxicity and health hazard summary, material safety data sheet and toxicity reports on 2-ethylhexanal with attachments. USEPA microfiche # (TSCA 8D): 86-920000057.

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

Moody DE, Reddy JK. 1982. Serum triglyceride and cholesterol contents in male rats receiving diets containing plasticizers and analogues of the ester 2-ethylhexanol. Toxicology Letters 10: 379-383.

Smyth HF, Carpenter CP, Weil CS. 1951. Range-finding toxicity data: List IV. Archives of Industrial Hygiene and Occupational Medicine. 4: 119-22.