MICHIGAN DEPARTMENT OF ENVIRONMENTAL QUALITY

INTEROFFICE COMMUNICATION

SEPTEMBER, 7 1999

TO: File for Hexylene Glycol (CAS# 107-41-5)

FROM: Michael Depa, Toxics Unit

SUBJECT: Screening Level Determination

The initial threshold screening level (ITSL) for hexylene glycol (2-methyl-2,4-pentanediol) is 1,210 µg/m³ based on a 1-hour averaging time.

The following references or databases were searched to identify data to determine the ITSL: EPA's Integrated Risk Information System (IRIS), Registry of Toxic Effects of Chemical Substances (RTECS), American Conference of Governmental and Industrial Hygienists (ACGIH) Threshold Limit Values (TLVs), 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 – July 3, 1999), National Library of Medicine (NLM), Health Effects Assessment Summary Tables (HEAST), and National Toxicology Program (NTP) Status Report. Occupational exposure limits (OELs) from both NIOSH and ACGIH have been set at 25 ppm (121 mg/m³). The vapor pressure of hexylene glycol is 0.05 mmHg and the molecular is 118.17 g.

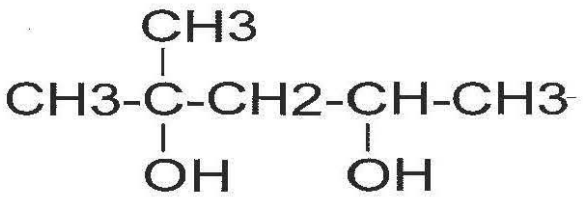

Figure 1. Molecular Structure of Hexylene Glycol (2-methyl-2,4-pentanediol)

Toxicological Studies

Human volunteers were exposed to saturated room concentrations of 50 ppm (Silverman et al., 1946). An average number of 12 subjects of both sexes were used for each solvent exposure. The exposure time was 15 minutes. The authors reported that the concentration of vapor which irritated the majority of subjects for nose and throat was >50 ppm and that the concentration of hexylene glycol that irritated the eyes was 50 ppm. The authors concluded that 50 ppm was the highest concentration which a majority of subjects estimated satisfactory for 8-hour exposure.

Acute LD50s were reported at 4.7 g/kg in rats, 3.2 g/kg in rabbits, 2.8 g/kg in guinea pigs and 3.9 g/kg in mice (Anonymous, 1985). An additional rat LD50 was reported as 4 g/kg.

Groups of 6 mice were given 5, 10 or 20 mg of hexylene glycol for 50 to 60 days (Larsen, 1958). Similar groups of mice were given the same dosages for 77 to 81 days. The dosages were given in milk which the mice drank. The average weight was approximated to be 31 g for the 5 mg dose group, 28 g for the 10 mg group, and 34 g for the 20 mg dose group. The doses in terms of mg per kg per day were determined to be 161, 357 and 588 mg/kg/day for the 5, 10 and 20 mg dose groups (respectively). The author stated that the weight loss was the same in all three groups. The author also stated that the organs from the mice treated with the highest dose for the longest time were examined histologically and that the changes found were not pronounced and that they corresponded with those described later in rats (see study below). Shortcomings of this study included: no control animals and few reported toxicological endpoints.

Groups of 10 male rats were given 0, 100 or 200 mg hexylene glycol in milk (Larsen, 1958). The rats offered pure milk willingly drank the ration, the rats from the second group less willingly and the rats from the third group still less willingly. It was estimated that the rats from the 2nd and 3rd dose group received 98 mg and 150 mg hexylene glycol daily. The average body weight of 257.2 g was then used to calculate that the doses used in this experiment were 381 and 584 mg/kg/day (respectively). The authors stated that all the livers were normal and 7 of 10 kidneys were normal in the high dosed group. The author stated that the testes of the dose groups was also normal. The author stated that no pathological signs of toxicity were observed during the experiment, including behavioral. Shortcomings of this study included inaccurate and unconventional calculation of dose and few toxicological endpoints were reported.

In a fertility experiment, 7 male rats were exposed to an average dose of 173 mg hexylene glycol (673 mg/kg) for one-hundred-thirty days (Larsen, 1958). The author stated that there was no statistically significant difference between the fertility rates of the control and the experimental groups and that histopathological examination of the testes revealed no abnormality. Similar to the other studies performed by this Larsen (1958), few toxicological details were presented; therefore, these studies will not be used to develop an ITSL.

Screening Level Calculation

The ACGIH developed the ceiling-TLV for hexylene glycol based on irritation. The ACGIH (1992) stated,

> Hexylene glycol exposure at 50 ppm [242 mg/m^3] in air for 15 minutes produced a slight odor with a few volunteer subjects noticing eye irritation. At 100 ppm for 5 minutes, the odor was plainly detectable, and slight nasal and respiratory discomfort was noted by some of the subjects. At 1000 ppm for 5 minutes, various degrees of eye irritation and throat and respiratory discomfort were noted. Since the concentration of hexylene glycol in saturated air at room temperature is 66 ppm, the reported values of 100 and 1000 ppm were probably measured in air supersaturated with a mist.

The ACGIH also stated,

> In the absence of adequate data upon which to establish an unequivocal, no effect exposure value, it is recommended that concentrations of hexylene glycol be maintained below that which causes discomfort. Accordingly, a TLV of 25 ppm as a ceiling is recommended in order to prevent eye irritation from exposure to hexylene glycol.

The ITSL was based on the c-TLV of 121 mg/m³. The ITSL was calculated pursuant to Rule 232(1)(c) as follows:

ITSL = OEL ÷ 100

ITSL = 121 mg/m³ ÷ 100

ITSL = 1.21 mg/m³

ITSL = 1,210 µg/m³ (based on a 1-hour averaging time)

A 1-hour averaging time was applied to the ITSL for hexylene glycol according to Rule 232(2)(a).

References:

ACGIH. 1992. Threshold limit values (TLVs) and biological exposure indices (BEI) documentation. American Conference of Governmental Industrial Hygienists. Cincinnati, OH, 45240-1634.

Anonymous. 1985. Final report on the safety assessment of butylene glycol, hexylene glycol, ethoxydiglycol and dipropylene glycol. Journal of the American College of Toxicology. Volume 4 Number 5, pages 223-248.

Larsen V. 1958. The toxicity of 2-methyl-pentan-2,4-diol (hexylene glycol) by chronic oral administration to rats and mice. Acta Pharmacol. et toxicol. 14: 341-349.

Silverman L, Schulte H, First M. 1946. Further studies on sensory response to certain industrial solvent vapors. Journal of industrial hygiene and toxicology. volume 28, number 4, pages 262-266.

MD:ST