

## Michigan Department of Environmental Quality

### Interoffice Communication

TO: File for 2,6-Dimethyl-4-heptanol (CAS # 108-82-7)

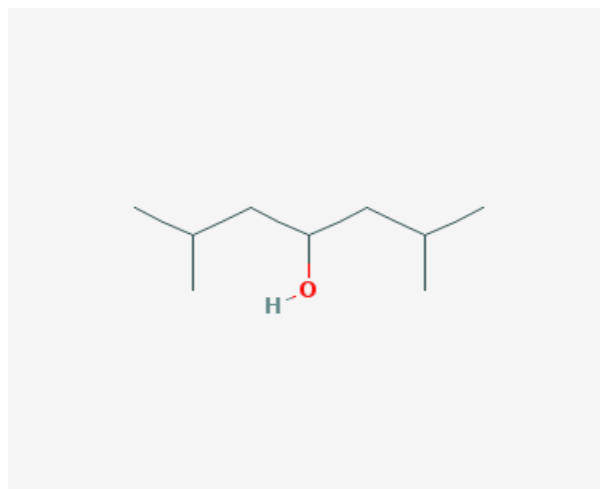
FROM: Doreen Lehner, Toxics Unit, Air Quality Division

SUBJECT: Screening Level for 2,6-Dimethyl-4-heptanol (CAS # 108-82-7)

DATE: March 6, 2012

The initial threshold screening level (ITSL) for 2,6-dimethyl-4-heptanol (CAS # 108-82-7) is 30 µg/m<sup>3</sup> annual averaging time.

2,6-Dimethyl-4-heptanol (CAS # 108-82-7) also known as diisobutyl carbinol, secondary nonyl alcohol, and sec-nonyl alcohol is a transparent, colorless liquid with a sweet odor. It is commonly used in mining, fabric softeners, textile and paper manufacturing, as a lubricant additive intermediate, defoamer in adhesives, coupling solvent for synthetic resins, dispersing agent in coatings, chemical manufacturing processing solvent, chemical intermediate in the production of perfumes and flavors, and as a process solvent in the production of hydrogen peroxide.



A literature review was conducted to determine an initial threshold screening level (ITSL) for 2,6-dimethyl-4-heptanol. The following references and databases were searched to derive the above screening level: EPBCCD, United States Environmental Protection Agency (US EPA) Integrated Risk Information System (IRIS), National Institute for Occupational Safety and Health (NIOSH), American Conference of Governmental Industrial Hygienists (ACGIH) Threshold Limit Values and Biological Exposure Indices (TLV/BEI) 2010 guide, National

Toxicology Program (NTP) Study Database, International Agency for Research on Cancer (IARC), Acute Database, CAS Online (searched 3/4/12), National Library of Medicine (NLM)-online, EPA Aggregated Computational Toxicology Resource (ACToR) Database, US EPA TSCATS database, Hazardous Substances Data Bank (HSDB), and US EPA High Production Volume Information System (HPVIS).

A study on human subjects was performed by Silverman et al., (1946) which found that 2,6-dimethyl-4-heptanol produced eye irritation in the majority of subjects at less than 5 ppm (30 mg/m<sup>3</sup>).

A combined repeated dose study with the reproductive/developmental toxicity study was performed on 12 Crl:CDE(SD) rats sex/group using OECD guideline # 422. Doses were 0, 50, 150, and 500 mg/kg/day of 2,6-dimethyl-4-heptanol in 0.5% methocel A4M (used as the vehicle) administered by gavage once daily for 34 days for males and 60 days for females. "Treatment-related statistically significant increases in mean absolute liver weights were noted in males of the middle (17% increase) and high dose (28% increase) groups, as well as the high dose females (10% increase). These changes correlated with increases in relative liver weights that were also statistically significant as compared to controls. The higher liver weights corresponded with very slight liver hypertrophy of centrilobular hepatocytes in males at 150 or 500 mg/kg/day and females 500 mg/kg/day. A no-observed effect level (NOEL) for general toxicity was 50 mg/kg/day. The NOEL for reproductive and neurological effects was 500 mg/kg/day, the highest dose tested" (HPVIS, 2012).

Using this study it is possible to derive an ITSL using Rule 232(1)(e):

$$ITSL = \frac{NOAEL(\text{mg}/\text{kg}/\text{day})}{20 \times 100} \times \frac{W_A}{I_A} \times \frac{b}{a}$$

Where:

$W_A$  = Body weight of experimental animal in kilograms (kg).

$I_A$  = 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.

The original value in the denominator of 35 was changed to 20 in recognition that the study used is much longer than 7 days (34 days for males and 60 days for females) and therefore there is less uncertainty connected with the results.

The NOEL is 50 mg/kg/day for the rat repeated dose oral toxicity study. The  $W_A$  is the default value for a non-gender rat is 0.395 kg. The  $I_A$  is determined by the following equation taken from EPA 1988 determined below:

$$I_A = 0.80 \times W^{0.8206}$$

Where:

I = Inhalation rates in cubic meters/day.

W = Body weight (kg).

$$I_A = 0.80 \times 0.395^{0.8206} = 0.373 \text{ m}^3/\text{day}$$

The value b/a is not known and therefore a default value of 1 is used. Using the above equation:

$$ITSL = \frac{50 \text{ mg/kg/day}}{20 \times 100} \times \frac{0.395 \text{ kg}}{0.373 \text{ m}^3/\text{day}} \times 1 = 0.02647 \text{ mg/m}^3 = 26.47 \text{ } \mu\text{g/m}^3$$

The ITSL rounded to one significant figure is 30  $\mu\text{g/m}^3$ . Based on rule 232(2)(c) the averaging time is annual.

Based on the above data, the ITSL for 2,6-dimethyl-4-heptanol is 30  $\mu\text{g/m}^3$  based on an annual averaging time.

#### References:

Act 451 of 1994, Natural Resources and Environmental Protection Act and Air Pollution Control Rules, Michigan Department of Environmental Quality.

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

HPVIS. 2012. 4-Heptanol, 2,6-dimethyl- (Diisobutyl Carbinol; CAS RN 108-82-7) High Production Volume (HPV) Chemical Challenge Test Plan and Data Review Prepared for: The Dow Chemical Company Prepared by: Toxicology/Regulatory Services, Inc. October 4, 2006. Document ID#'s 201-16401A and 201-16401B available at:

<http://www.epa.gov/chemrtk/pubs/summaries/4hept26d/c15004tc.htm> .

OECD 422. 1996. OECD Guideline for Testing of Chemicals. Combined Repeated Dose Toxicity Study with the Reproduction/Developmental Toxicity Screening Test. Available at:

[http://iccvam.niehs.nih.gov/SuppDocs/FedDocs/OECD/OECD\\_GL422.pdf](http://iccvam.niehs.nih.gov/SuppDocs/FedDocs/OECD/OECD_GL422.pdf) .

Silverman, L.; Schulte, H.F.; and First, M.W. 1946. Further Studies on Sensory Response to Certain Industrial Solvent Vapors. J. Ind. Hyg. Toxicol. 28(6):262-266.

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