MICHIGAN DEPARTMENT OF ENVIRONMENTAL QUALITY

INTEROFFICE COMMUNICATION

July 26, 1999

TO: File for diethylene glycol mono-2-ethylhexyl ether [DGEHE] (1559-36-0)

FROM: Dan O'Brien, Toxics Unit

SUBJECT: Initial Threshold Screening Level

**The initial threshold screening level (ITSL) for DGEHE is 22 µg/m$^3$ based on an annual averaging time.**

The following references or databases were searched to identify data to determine the ITSL: AQD chemical files; EPA's Integrated Risk Information System (IRIS) and Health Effects Assessment Summary Tables (HEAST); American Conference of Governmental Industrial Hygienists (ACGIH) Threshold Limit Value (TLV) Booklet; National Institute for Occupational Safety and Health (NIOSH) Pocket Guide to Chemical Hazards and Registry of Toxic Effects of Chemical Substances (RTECS); National Toxicology Program (NTP) World Wide Website (WWW), MDEQ Library; International Agency for Research on Cancer (IARC) WWW; Chemical Abstract Service (CAS) On-line and National Library of Medicine (NLM) Toxline (1967–April 19, 1999), Chemical Evaluation Search And Retrieval System (CESARS), Handbook of Environmental Data on Organic Chemicals, Patty's Industrial Hygiene and Toxicology, Merck Index and the Condensed Chemical Dictionary.

No specific information on the uses of DGEHE was noted in our searches, but it seems likely that, similar to other glycol ethers, it is employed primarily as a solvent. Ethylene-based glycol ethers are used primarily by the coatings industry, where their relatively slow rate of evaporation is particularly useful. Other uses include inks, cleaners, chemical intermediates, process solvents, brake fluids and deicers (Gingell *et al.*, 1994).

Little toxicological information is available for DGEHE. No data derived from long-term studies by any route of exposure were located in our searches. With respect to acute exposure, a CAS on-line search for the chemical cited a range-finding toxicity study (Smyth *et al.*, 1969), which suggests that that study should hold toxicity information on DGEHE. Unfortunately, the study does not reference chemicals by CAS #, and attempts to identify data specific to DGEHE by chemical name were ambiguous. Having scrutinized the chemical names listed in the study, no exact match to the chemical names listed in the CAS identity search for DGEHE was found, but the most similar chemical name appeared to be "2-hexyloxy-2-ethoxyethyl ether". A Lethal Dose $(LD)_{50}$ for that compound determined in rats and its 95% confidence limits was found to be 3.73 (2.68, 5.21) ml/kg. Given a specific gravity of 0.9429 g/ml (Stott, 1999), this

dose would translate into an $LD_{50}$ of 3.52 g/kg. Attempts to definitively identify the chemical studied by Smyth and coworkers as DGEHE using various cross-references were unsuccessful. Thus, these data were not considered reliable for use as the basis of a screening level for DGEHE.

The only other toxicological data found were from an unpublished study from Union Carbide Corporation (1992). The cover letter to the study specifically references DGEHE by CAS # 1559-36-0, meaning the study results, if of acceptable quality, could form the basis of a screening level. Sections of the copy available for our review (specifically labeled "Best copy available" by the EPA Library) were nearly illegible, both in fiche and paper copy, making examination of study details difficult. However, it could be discerned that groups of 5 strain and sex-unspecified rats were dosed with "as received" DGEHE at dose levels ranging from 2 to 16 ml/kg (1.89 to 15.09 g/kg). Experimental conditions were referred to as "standard", with reference made to an attachment of standard procedures which was not part of the fiche available for our review. The oral $LD_{50}$ and its confidence limits are listed as 7.46 (4.63, 12.0) ml/kg. Given a specific gravity of 0.9429 g/ml (Stott, 1999), this dose would translate into an $LD_{50}$ of 7.03 (4.37, 11.3) g/kg. Gross pathology results listed for victims included pale, distended, gas-filled stomachs and blood and gas filled intestines, while for survivors, "nothing remarkable" is noted. Sluggishness, unsteady gait and prostration were the reported clinical signs in intoxicated individuals. The same document also notes a dermal $LD_{50}$ of 2.52 (1.54, 4.11) ml/kg in rabbits, and that DGEHE elicits trace skin irritation and severe eye irritation in rabbits. A six hour inhalation exposure to substantially saturated DGEHE vapor atmospheres produced no deaths in six rats.

*Derivation of the ITSL*: The only toxicological data available to use in screening level derivation that are verifiably specific to DGEHE are those from the Union Carbide (1992) acute studies. While fewer study details were provided than one would desire, the relatively low toxicity evidenced by the magnitude of the $LD_{50}$ (> 7 g/kg body weight) suggests that setting the screening level at the default trace concentration of 0.1 $\mu g/m^3$ (based on insufficient data for screening level development) is likely to be an inappropriate and excessively conservative alternative. Consequently, the Union Carbide $LD_{50}$ is considered to be of sufficient quality for screening level development, and is used as the basis for the ITSL for DGEHE. Per R232(1)(h) of part 55, Act 451, as amended:

$$ITSL = \frac{1}{500} \times \frac{1}{40} \times \frac{1}{100} \frac{LD_{50}\,(mg/kg) \times W_A}{0.167 \times I_A}$$

where:

$W_A$ = Default body weight of a strain- and sex-unspecified rat (from MDEQ, 1996 and EPA, 1988) and

$I_A$ = Default daily inhalation rate of a strain- and sex-unspecified rat (from MDEQ, 1996 and EPA, 1988)

So,

$$\textbf{ITSL} = (0.002)\times(0.025)\times(0.01)\times\frac{(7030\,\text{mg/kg})\times(0.395\,\text{kg})}{(0.167)\times(0.945\,\text{m}^3/\text{kg})\times(0.395\,\text{kg})}$$

$$= (0.0000005)\times\frac{7030\,\text{mg/kg}}{0.158\,\text{m}^3/\text{day}}$$

$$= (0.0000005)\times(44{,}493\,\text{mg/m}^3)$$

$$= (0.0222\,\text{mg/m}^3)\times\frac{1000\,\mu\text{g}}{1\,\text{mg}}$$

$$= \mathbf{22.2\,\mu g/m^3 \approx 22\,\mu g/m^3}$$

Per 232(2)(c), an **annual averaging** time would apply.

*References*

Chemical Hygiene Fellowship (1992). Initial Submission: 2-ethylhexyl Carbitol: Range Finding Toxicity Studies (Final Report) with Cover Letter Dated 011492. Submitted by the Chemical Hygiene Fellowship, Carnegie-Mellon University, Pittsburgh, PA, for the Union Carbide Corp., Danbury, CT. Submitted to U.S. Environmental Protection Agency, Office of Toxic Substances, Washington, DC. EPA Document #88-920000668, 12 pp.

EPA (1988). Recommendations For and Documentation of Biological Values For Use in Risk Assessment. Cincinnati, OH: Environmental Criteria and Assessment Office, Office of Health and Environmental Assessment, Office of Research and Development, U.S. Environmental Protection Agency. Document # PB88-179874, EPA Report # EPA/600/6-87/008, 200+ pp. (2/1988).

Gingell R, Boatman RJ, Bus JS, Cawley TJ, Knaak JB, Krasavage WJ, Skoulis NP, Stack CR and Tyler TR (1994). A. Ethers of the ethylene glycols. *In*: Patty's Industrial Hygiene and Toxicology, 4th Ed. (Clayton GD and Clayton FE, Eds.), Volume II, Part D, Chapter Thirty One: Glycol Ethers and Other Selected Glycol Derivatives. John Wiley and Sons, Inc., New York, p. 2762.

MDEQ (1996). Default animal data for risk assessment (as based on U.S. EPA, 1988, Recommendations for and documentation of biological values for use in risk assessment, EPA Document # PB 88-179874).

Smyth HF, Carpenter CP, Weil CS, Pozzani UC, Striegel JA Nycum JS (1969). Range-finding toxicity data: List VII. *Am Indus Hyg Assoc J* **30**(5):470-476.

Stott W (1999). William Stott, Research and Development, Dow Chemical Company. Personal communication with M. Bianchi, MDEQ-AQD, 5/13/99.

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