

MICHIGAN DEPARTMENT OF ENVIRONMENTAL QUALITY

INTEROFFICE COMMUNICATION

TO: File for Diethyl Carbonate (CAS # 105-58-8)

FROM: Robert Sills, AQD Toxics Unit Supervisor

SUBJECT: Diethyl Carbonate ITSL change in the averaging time from 24 hrs to annual

DATE: December 28, 2016

The current ITSL for Diethyl Carbonate is 5000 ug/m³, with annual averaging time (AT).

Previously, the ITSL was established on September 8, 2010 at 5000 ug/m³ with 24 hr averaging time (attached). The averaging time (AT) assigned to the ITSL at that time was 24 hours, as per the default methodology at that time (Rule 232(2)(b)). The ITSL was based on a chronic (83 week) oral (drinking water) mouse bioassay. The ITSL derivation utilized a total uncertainty factor (UF) = 100 consisting of a UF = 10 for each interspecies extrapolation and intraspecies variability. The current file review concludes that the AT for the ITSL may appropriately be set at annual, based on the nature and duration of the key study and the ITSL value derivation, as allowed under Rule 229(2)(b).

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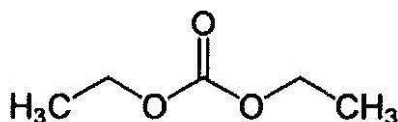
FROM: Doreen Lehner, Toxics Unit, Air Quality Division

SUBJECT: Screening Level for Diethyl carbonate (CAS # 105-58-8)

DATE: September 8, 2010

A NOEL based initial threshold screening level (ITSL) for diethyl carbonate (CAS # 105-58-8) is 5,000 ug/m³ for 24-hour averaging time. This interim ITSL is based on a NOEL of 140 mg/kg/day from an 83-week mouse oral study by Brown et al (1978).

Diethyl carbonate (CAS # 105-58-8) MW 118.13, is a clear liquid room temperature (25°C) with a low flash point which is used as an evaporating agent for nitrocellulose, cellulose esters, synthetic and natural resins, an intermediate in Phenobarbital synthesis, a neutral lacquer solvent, and is a component of electrolytes in lithium batteries.



A literature review was conducted to determine an initial threshold screening level (ITSL) for diethyl carbonate. The following references and databases were searched to derive the above screening level: EPBCCD, United States Environmental Protection Agency (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) 2008 guide, National Toxicology Program (NTP) Study Database, International Agency for Research on Cancer (IARC), Acute Database, Chemical Abstract Service (CAS) Online, National Library of Medicine (NLM)-online, EPA Aggregated Computational Toxicology Resource (ACToR) Database, US EPA TSCATS database, and Hazardous Substances Data Bank (HSDB).

There is not much toxicity data available for diethyl carbonate. There is an oral mouse LD_{Lo} of 500 mg/kg (Biochemical Pharmacology, 1959) and an oral rat LD_{Lo} of 15 g/kg (Lewis R.J., 1996). As these LD_{Lo}s are cited from secondary sources, without further information from the primary source, these values cannot be used to derive an ITSL. The study used to determine the interim ITSL is from Brown et al, 1978 *Long-term Toxicity of Diethyl Carbonate in Mice*. Groups of 48 male and 50 female mice were

given drinking water containing 0,50, 250, or 1,000 ppm diethyl carbonate for 83 weeks. There was no effect on mortality, rate of body weight gain or the incidence of histopathological findings, including tumors. There were isolated differences between treated and control mice in the findings of the haematological examinations and in the liver weights of female mice but these were not considered to be related to treatment. It is concluded that no carcinogenic effect could be detected and that the no-untoward-effect level of 1,000 ppm (approx. 140 mg/kg/day).

The 83 week study NOEL of ~ 140 mg/kg/day was used to calculate the ITSL for diethyl carbonate. The EPA uses the following equation to determine an RfD from a NOAEL:

$$RfD = \frac{NOAEL}{UF \times MF} = \frac{NOAEL}{UF_H \times UF_A \times MF} = \frac{140 \text{ mg/kg/day}}{10 \times 10 \times 1} = 1.4 \text{ mg/kg/day}$$

Where:

UF = The uncertainty factor used to account for differences between the available data and the possible effects in the human population, usually expressed as factors of 10.

UF_H = Uncertainty factor used to account for the variation in sensitivity among individuals of the human population.

UF_A = Uncertainty factor used to account for the extrapolation from animal data to humans.

MF = The modifying factor which is an additional scientific uncertainty of the study not accounted for in the uncertainty factor. Usually expressed as a value greater than 0 and less than or equal to 10.

Rule 232 (1) (b) uses an oral RfD to determine an ITSL using the following equation:

$$ITSL = \text{Oral } \dots RfD \times \frac{70 \text{ kg}}{20 \text{ m}^3} = 1.4 \text{ mg/kg/day} \times 3.5 \frac{\text{kg}}{\text{m}^3} = 4.9 \frac{\text{mg}}{\text{m}^3} = 4,900 \frac{\mu\text{g}}{\text{m}^3}$$

The ITSL is reported in $\mu\text{g}/\text{m}^3$, so rounding 4,900 $\mu\text{g}/\text{m}^3$ to 1 significant figure making the final ITSL 5,000 $\mu\text{g}/\text{m}^3$. Rule 232 (2) (b) the averaging time is 24 hours.

Based on the above data, the ITSL for diethyl carbonate (CAS # 105-58-8) is 5,000 $\mu\text{g}/\text{m}^3$ for 24-hour averaging time.

References:

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

BCPCA6 Biochemical Pharmacology, (Pergamon Press Inc., Maxwell House, Fairview Park, Elmsford, NY 10523) V.1-1958 (2), pp 168, 1959.

Brown D., Gaunt I.F., Hardy J., Kiss I.S., and Butterworth K.R. 1978. Long-term Toxicity of Diethyl Carbonate in Mice. Toxicology 10, pp 291-295.

Lewis, R.J. Sax's Dangerous Properties of Industrial Materials. 9th ed. Volumes 1-3.
New York, NY: Van Nostrand Reinhold, 1996., p. 2205.

Reference Dose (RfD): Description and Use in Health Risk Assessments. Last updated
March 16, 2010. <http://www.epa.gov/ncea/iris/rfd.htm>