Michigan Department of Natural Resources and the Environment

Interoffice Communication

TO: File for Ethylene carbonate (CAS #96-49-1)

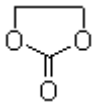
FROM: Doreen Lehner, Toxics Unit, Air Quality Division

SUBJECT: Correction of Screening Level for Ethylene carbonate (CAS #96-49-1)

DATE: March 10, 2011

The ITSL for ethylene carbonate is 30 µg/m^3 based on an annual averaging time based on an oral rat LD_{50} of 10 g/kg. There is no change from the previous ITSL of 30 µg/m^3 even though there is a correction of a mathematical algorithm (I_A) in the ITSL calculation. The correction was due to an error where a value in m^3/kg was used instead of the correct value in m^3/day.

Ethylene carbonate (MW 88.06) is an ester of ethylene glycol and carbonic acid. At room temperature (25°C) it is a transparent crystalline solid. In liquid form it is a polar solvent and is used as a high permittivity component of electrolytes in lithium batteries, as a plasticizer, and as a precursor to vinylene carbonate, which is used in polymers and in organic sythesis (http://en.wikipedia.org/wiki/Ethylene_carbonate).



A literature review was conducted to determine an initial threshold screening level (ITSL) for ethylene carbonate. 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) 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, Hazardous Substances Data Bank (HSDB), US EPA TSCATS database, and Patty's Industrial Hygiene and Toxicology.

RfC or RfD values were unavailable. However, there is an acute oral toxicity study which determined an LD_{50} for ethylene carbonate of 10g/kg in rats (Smyth et al, 1954). There is a study from Weisburger et al., 1981 who tested ethylene carbonate by oral administration in male and female Charles River CD rats. Rats were divided into 2 dose groups of 26 male and 26 female rats, with a control group of 18 rats. The doses were given at 25,000 ppm (low dose group) and 50,000 ppm (high dose group) for 78 weeks after which the animals were observed for 26 weeks before termination of the study. After 42 weeks, the males in the high dose group were taken off the dosage regimen for

two weeks, then put on a lower dose of 40,000 ppm for the remainder of the study due to excessive mortality at the higher dose level. This study was not used, as the dosage changes would not be amenable to risk assessment. Also, the "tissue counts" or number of animals for which particular sites were examined histopathologically were not recorded specifically and for certain organs an appreciable number of animals may not have had particular sites examined, therefore marginal results for such sites may be considered tentative. The basic data recorded involved animal survival at 52 weeks and at 78 weeks, which would be similar to acquiring an LD_{50} for this compound since male survival at the high dose was only 50% at 52 weeks, while females maintained a 100% survival rate at 52 weeks. This study did report that there were strongly bifringent crystals, probably oxalic acid were found in the convoluted tubules of the kidney, the collecting tubules, and sometimes in the renal pelvis and urinary bladder. The difference in toxicity and survival between males and females may relate to differences in metabolism as a function of sex, similar to that of the parent compound ethylene glycol.

A metabolic study performed by Hanley et al., 1989, confirms that ethylene carbonate (EC) has a toxicity profile which resembles that of ethylene glycol (EG). To determine whether the toxicity of EC could be explained on the basis of its metabolism to EG, male Fischer 344 rats were given 200 mg/kg of uniformly labeled [^{14}C]EC in water by gavage and the disposition of the radiolabel was then followed for 72 hr. EC was rapidly metabolized, with approximately 57 and 27% of the administered dose eliminated in the expired air as $^{14}CO_2$ and in the urine, respectively; the remainder was found in the carcass. Separation of the urinary metabolites using liquid chromatography revealed a single radioactive peak. This metabolite was unequivocally identified as ethylene glycol via gas chromatography-mass spectrometry with the aid of ^{13}C enrichment of the EC dose. Measurement of whole blood levels of EC and EG in rats given 200 mg/kg of EC by gavage revealed blood levels of EG approximately 100-fold higher than the levels of EC in these same animals, with a half-life of EG in blood of 2 hr, indicating rapid conversion of EC to EG. In view of the rapid and extensive biotransformation of EC to EG and the similarity of the existing (though limited) toxicity data base of EC compared to EG, utilization of the extensive EG systemic toxicity data base for assessing the safety of EC appears justified. The ITSL for ethylene glycol is 1,000 µg/m^3 1 hour averaging in the EPBCCD database.

There is an acute rat oral LD_{50} for ethylene carbonate at 10 gm/kg from Smyth et al, 1954. This is a lower LD_{50} than the chronic oral LD_{50} given by Weisburger et al., 1981 and therefore more protective. Based on Rule 232 (1) (h) the ITSL is determined as follows:

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

Where:
W_A = Body weight of experimental animal in kilograms (kg).
I_A = Daily inhalation rate of experimental animal in cubic meters/day.

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 m3/day
W = Body weight (kg)

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

The LD_{50} of 10 gm/kg is converted to 10,000 mg/kg to have the proper units for this equation. The resultant equation with all values added becomes:

$$ITSL = \frac{1}{500} \times \frac{1}{40} \times \frac{1}{100} \times \frac{10{,}000\,{}^{mg}\!/_{kg} \times 0.395 kg}{0.167 \times 0.373\,{}^{m^3}\!/_{day}} = \frac{3{,}950 mg}{124582 m^3} = 0.031706\,{}^{mg}\!/_{m^3} = 31.70\,{}^{\mu g}\!/_{m^3}$$

$$ITSL = 30\,{}^{\mu g}\!/_{m^3}$$

Based on Rule 232 (2) (c) the averaging time for this value is annual.

Based on the above data, the ethylene carbonate ITSL is 30 µg/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.

Hanley, T.R.; Schumann, A.M.; Langvardt, P.W.; Rusek, T.F.; and Watanabe, P.G. 1989. Metabolism and Disposition of Ethylene Carbonate in Male Fischer 344 Rats. Toxicol Appl Pharmacol. 100(1):24-31.

Smyth, H.F. Jr.; Carpenter, C.P.; Weil, C.S.; and Pozzani, U.C. 1954. Range-finding Toxicity Data: List V. AMA Arch Ind Hyg Occup Med. Jul;10(1): 61-68.

Weisburger, E.K.; Ulland, B.M.; Nam, J.m.; Gart, J.J.; and Weisburger, J.H. 1981. Carcinogenicity Tests of Certain Environmental and Industrial Chemicals. J Natl Cancer Inst. 67(1):75-88.

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