

MICHIGAN DEPARTMENT OF ENVIRONMENTAL QUALITY

INTEROFFICE COMMUNICATION

TO: File for Propylene glycol monomethyl ether (CAS # 107-98-2)

FROM: Keisha Williams, Air Quality Division

DATE: October 10, 2017

SUBJECT: Screening Level Update

The initial threshold screening level (ITSL) for exposure to propylene glycol monomethyl ether (PGME) is 3,700 $\mu\text{g}/\text{m}^3$ (1-hour averaging time) based on the Michigan Department of Environmental Quality (MDEQ), Air Quality Division (AQD) Rule 336.1232(1)(c)¹. The ITSL of 2,000 $\mu\text{g}/\text{m}^3$ (annual averaging time) established on January 25, 2017 is rescinded based on this updated review.

The following references and databases were searched to identify data for screening level derivation: United States Environmental Protection Agency's (USEPA) Integrated Risk Information System (IRIS), the Registry of Toxic Effects of Chemical Substances, the American Conference of Governmental Industrial Hygienists (ACGIH) Threshold Limit Values (TLV), National Institute of Occupational Safety and Health (NIOSH) Pocket Guide to Hazardous Chemicals, MDEQ Library, International Agency for Research on Cancer Monographs, National Library of Medicine, Health Effects Assessment Summary Tables (HEAST), National Toxicology Program (NTP) Status Report, USEPA Toxic Substances Control Act Test Submissions database, USEPA Superfund Provisional Peer Reviewed Toxicity Values, USEPA Acute Exposure Guideline Levels for Airborne Chemicals, USEPA High Production Volume Database, United States Department of Labor Occupational Safety and Health Administration Permissible Exposure Limits, Spacecraft Maximum Allowable Concentrations, Agency for Toxic Substances and Disease Registry's (ATSDR) Toxicological Profiles, California Office of Environmental Health Hazard Assessment's Reference Exposure Levels, Texas Commission on Environmental Quality Effects Screening Levels, Maximum Workplace Concentrations (Maximale Arbeitsplatzkonzentrationen) for Germany, USEPA School Air Toxics Benchmarks, USEPA National Air Toxics Assessment Benchmarks, World Health Organization Air Quality Guidelines, and European Chemicals Agency Registered Substances Dossiers.

Background Information

PGME (Figure 1) is used as a solvent, and in surface coatings and cleaning products (ACGIH, 2013; Kirman et al., 2005). This chemical has been described as "the most widely used propylene glycol ether solvent" (Kirman et al, 2005). Chemical properties are listed in Table 1.

¹ 336.1232. Air Pollution Control Rules in Michigan Administrative Code promulgated pursuant to Article II Pollution Control, Part 55 (Sections 324.5501-324.5542), Air Pollution Control, of the Natural Resources and Environmental Protection Act, 1994. PA 451, as amended (NRUSEPA).

Figure 1. Chemical structure for PGME

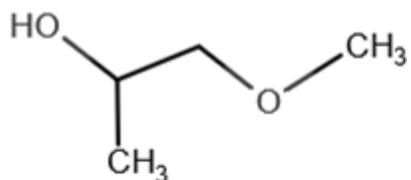


Table 1. Chemical and physical properties of PGME

Molecular weight: 90.122 grams/mole
Melting point: -139°F
Boiling point: 248°F at 760 mm Hg
Vapor pressure: 11.8 mm Hg at 77°F
Physical state: liquid
Color: colorless
Odor: mild, ethereal

Reference: National Center for Biotechnology Information, <https://pubchem.ncbi.nlm.nih.gov/compound/7900>

PGME has been shown to be a portal of entry irritant, as well as a hepatotoxicant, nephrotoxicant, central nervous system, reproductive and general toxicant (Spencer, 2002; Carney, 1999; ACGIH, 2013). There have been significant research studies on the pharmacokinetic and toxicokinetic properties of inhaled PGME, including controlled human studies, a two-generation reproductive/developmental study in rodents, a lifetime exposure study in two different species, and a sub-chronic study in two different species. Table 2 provides a list of health benchmark values that are designed to protect against adverse effects with inhalation exposure.

Table 2. Health benchmark values for inhaled PGME

Agency	Benchmark Value
American Conference of Governmental Industrial Hygienists (ACGIH)	Threshold limit value (TLV): 50 ppm (184 mg/m ³) 8-hour time-weighted average 100 ppm (369 mg/m ³) short-term exposure limit (STEL) (ACGIH, 2013)
Office for Environmental Health Hazard Assessment (OEHHA)	Reference Exposure Level (REL): 7,000 µg/m ³ for chronic inhalation (OEHHA, 2008)
United States Environmental Protection Agency (USEPA)	Reference Concentration (RfC): 2 mg/m ³ for chronic exposure (USEPA, 1991)
National Institute for Occupational Safety and Health (NIOSH)	REL: 360 mg/m ³ , 8-hour averaging time 540 mg/m ³ , STEL (NIOSH, 2016)
Texas Commission on Environmental Quality (TCEQ)	Effects Screening Level (ESL): 3,700 µg/m ³ for short-term exposure 370 µg/m ³ for long-term exposure (TCEQ, 2017) ²

² ESL Detail Report states that this ESL was derived from the NIOSH REL.

The mechanisms of action for adverse effects such as central nervous system depression (or sedation) are not known (Kirman et al., 2005). However, it has been observed that increased metabolism of the primary isomer of commercial PGME, 1-methoxy-2-propanol, leads to decreased sedation (Corley et al., 2005). Thus, unmetabolized, free PGME is considered relatively toxic as compared to its metabolites.

Controlled, human studies have been reported (ACGIH, 2013; Emmen et al, 2003; Hopf et al., 2012; Tomicic et al, 2011), where eye and upper respiratory tract irritation are the critical effects. Irritation symptoms have been reported at 50 ppm after a 2-hour exposure (Tomicic et al., 2011).

A lifetime inhalation exposure study was conducted in Fischer 344 rats and B6C3F1 mice at concentrations of 0, 300, 1,000 and 3,000 ppm PGME (Spencer, 2002). No significant increase in benign or malignant cancers was found. As a result, PGME is not classifiable as a carcinogen. Non-carcinogenic effects were only observed at the highest exposure concentration in this study. This same concentration range was also used in a two-generation inhalation study in Sprague-Dawley rats and a sub-chronic inhalation study on which the USEPA RfC is derived (Carney et al., 1999; USEPA, 1991). The lowest no-observable effect level (NOEL) was 300 ppm (Carney et al, 1999; Spencer et al, 2002). It should be noted that this NOEL is higher than the effects level observed in short-term human exposure studies (Emmen et al., 2003; Hopf et al., 2012; and Tomicic et al., 2011). Furthermore, the human equivalent concentrations, and respective health benchmarks, derived from the NOEL of 300 ppm, are also higher than the effects level observed in the short-term human exposure studies (USEPA, 1991; OEHHA, 2008; Kirman et al, 2005; Corley et al., 2005). Thus, portal of entry effects observed in the human studies are the most sensitive effect with PGME inhalation exposure and will be the basis for the ITSL derivation.

Within the TLV documentation, the authors note, “A TLV-TWA of 50 ppm (184 mg/m³) and a TLV-STEL of 100 ppm (369 mg/m³) are recommended for occupational exposure to 1-methoxy-2-propanol (PGME) (α-isomer PGME or technical grade PGME containing <0.5% β-isomer). This is based on a human volunteer study where, at 100 ppm the odor was initially reported to be intolerably strong by 4 of 6 subjects but after 25 minutes the subjects habituated. However, eye irritation was reported by two subjects after two hours of exposure... This TLV should protect against the liver, kidney and lung effects seen in chronic and subchronic animal inhalation studies at 1000 and 1500 ppm” (ACGIH, 2013). The TLV used a controlled, human study as the key study; it is appropriate to use for health protective effects seen with chronic exposure. An ITSL can be derived based on the ACGIH TLV-STEL of 100 ppm (369 mg/m³) health benchmark using Equation 1 below:

Equation 1. Based on AQD 232 (1)(c)

$$ITSL = \frac{OEL}{100}$$

$$ITSL = \frac{369 \text{ mg/m}^3}{100} = 3.69 \frac{\text{mg}}{\text{m}^3} \times \frac{10^3 \mu\text{g}}{\text{mg}} = 3690 \frac{\mu\text{g}}{\text{m}^3} \approx 3700 \frac{\mu\text{g}}{\text{m}^3}, 1 \text{ hour averaging time}$$

It should be noted that a 2011 publication from Tomicic et al. described irritation symptoms in exposed volunteers after exposures of 50 ppm in a 6-hour exposure. While the TLV-STEL is twice this exposure concentration, the AQD Rules provide adequate protection by using an uncertainty factor of 100.

Therefore, the acute ITSL is 3,700 µg/m³, 1-hour averaging time.

References

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KW:lh

MICHIGAN DEPARTMENT OF ENVIRONMENTAL QUALITY

INTEROFFICE COMMUNICATION

TO: File for Propylene glycol monomethyl ether (CAS# 107-98-2)

FROM: Doreen Lehner, Toxics Unit, Air Quality Division

DATE: January 25, 2017

SUBJECT: Propylene glycol monomethyl ether (CAS# 107-98-2) ITSL change in the averaging time from 24 hours to annual

The initial threshold screening level (ITSL) for propylene glycol monomethyl ether is 2000 $\mu\text{g}/\text{m}^3$ based on an annual averaging time. The ITSL was originally established on 7/8/1992 and was set at 2000 $\mu\text{g}/\text{m}^3$ based a 24-hour averaging time. The ITSL is based on an EPA (1991) reference concentration (RfC) of 2000 $\mu\text{g}/\text{m}^3$ which was derived from a 13-week inhalation study by Landry et al., (1983). Fischer 344 rats (10/sex/dose) and New Zealand White rabbits (7/sex/dose) were exposed to 0, 300, 1000, or 3000 ppm (0, 1106, 3686, or 11060 mg/m^3) for 6 hours/day, 5 days/week, for 13 weeks. The critical effect was mild reversible sedation. EPA calculated the no observed adverse effect level (NOAEL) human equivalent concentration (HEC) at 658 mg/m^3 . The current file review concludes that the averaging time may appropriately be set at annual, as the key study is a subchronic inhalation study. Therefore, the averaging time is being changed from 24 hours to annual.

References:

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

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Michigan Department of Natural Resources

Interoffice Communication

July 8, 1992

To : Propylene glycol monomethyl ether File (CAS #107-98-2)

From : Gary Butterfield

Subject : ITSL for Propylene glycol monomethyl ether

A CAS-on-line search (Jan 1991 to Apr 1992) found no 'hits' for new toxicity studies published since EPA's RfC was verified, in April 1991. It can be concluded that the RfC is still based on the best and most recent data. Therefore, it is appropriate for the ITSL to be equivalent to the RfC of 2 mg/m³, with a 24 hour averaging time.