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Response to Public Comments for Propylene glycol monomethyl ether (CAS # 107-98-2)

Summary:

Based on public comments, the Air Quality Division (AQD) has reviewed the Initial Threshold Screening Level (ITSL) for propylene glycol monomethyl ether (PGME). Because of that review, the AQD agrees with the commenter that the ITSL of 2000 µg/m^3 (annual averaging time) is outdated and no longer appropriate. Therefore, the ITSL of 2000 µg/m^3 (annual averaging time) is rescinded and replaced with an ITSL of 3700 µg/m^3 (1-hour averaging time).

Background:

Revisions to the Air Pollution Control Rules[1] were promulgated December 22, 2016. Subsequently, the Michigan Department of Environmental Quality (MDEQ), Air Quality Division (AQD) published toxic air contaminant screening levels and their basis as required by Rule 230(1). Pursuant to Rule 230(2), the AQD solicited and received public comments on these screening levels for 60 days: February 14 through April 14, 2017. The AQD must respond to these comments within 180 days; the latest date for response is October 11, 2017.

Comments and Responses:

[1] 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 (NREPA).

Comment:
The commenter pointed out that since the 1992 derivation of the propylene glycol monomethyl ether (PGME) ITSL, there have been several research studies and publications on PGME.

Response:
The AQD reviewed both our standard list of references and the references provided by the commenter, and we agree that there have been important research reports and publications on PGME since the adoption of the 1991 PGME Reference Concentration (RfC).

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. Tomicic et al. (2011) reported respiratory irritation in workers after a 2 hour exposure of 50 ppm PGME.

A lifetime inhalation exposure study was conducted in Fischer 344 rats and B6C3F1 mice at concentrations of 0, 300, 1000 and 3000 ppm PGME (Spencer, 2002). No significant increase in benign or malignant cancers was found. As a result, PGME is not classifiable as a carcinogen. Furthermore, non-carcinogenic effects were only observed at the highest exposure concentration in this study. This same concentration range was also used in the two-generation inhalation study in Sprague-Dawley rats and the sub-chronic inhalation study on which the U.S. EPA RfC is derived (Carney et al., 1999; US EPA, 1991). 300 ppm was the lowest no-observable effect level (NOEL) (Carney et al, 1999; Landry et al., 1983; Spencer et al, 2002). It should be noted that the NOEL identified from the animal studies is at a higher level than the effects level observed in the acute human studies. Furthermore, the human equivalent concentrations, and respective health benchmarks, derived from this NOEL are also higher than the effects level observed in the acute human studies (US EPA, 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/m^3) and a TLV-STEL of 100 ppm (369 mg/m^3) 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 the health protective effects seen with chronic exposure. An ITSL can be derived based on the ACGIH TLV-STEL of 100 ppm (369 mg/m^3) health benchmark in Equation 1 below:

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

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

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

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. Personal communication with the authors revealed that these effects were minimal and found to not be important enough to include in a subsequent study on a sensitive population. Furthermore, 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 3700 µg/m^3, 1-hour averaging time.

Summary and Conclusions:

The AQD agrees with the commenter that there is more relevant research available, and the ITSL of 2000 µg/m^3 (annual averaging time) is rescinded and the ITSL of 3700 µg/m^3 (1-hour averaging time) is adopted.

The primary AQD reviewer for these comments was Keisha Williams, AQD Toxics Unit Toxicologist. The secondary (peer) reviewer was Doreen Lehner, AQD Toxics Unit Toxicologist.

References:

ACGIH. 2013. 1-Methoxy-2-propanol. CAS number: 107-98-2. Documentation of the Threshold Limit Values and Biological Exposure Indices. American Conference of Governmental Industrial Hygienists, Cincinnati, OH.

Carney, E. W., Crissman, J. W., Liberacki, A. B., Clements, C. M., Breslin, W. J. 1999. Assessment of adult and neonatal reproductive parameters in Sprague-Dawley rats exposed to propylene glycol monomethyl ether vapors for two generations. *Toxicological sciences: an official journal of the Society of Toxicology*, 50(2), 249-258.

Corley, R. A., Gies, R. A., Wu, H., Weitz, K. K. 2005. Development of a physiologically based pharmacokinetic model for propylene glycol monomethyl ether and its acetate in rats and humans. *Toxicology letters*, 156(1), 193-213.

Emmen, H. H., Muijser, H., Arts, J. H. E., Prinsen, M. K. 2003. Human volunteer study with PGME: eye irritation during vapour exposure. *Toxicology letters*, 140, 249-259.

Hopf, N. B., Vernez, D., Berthet, A., Charriere, N., Arnoux, C., Tomicic, C. 2012. Effect of age on toxicokinetics among human volunteers exposed to propylene glycol methyl ether (PGME). *Toxicology letters,* 211(1), 77-84.

Kirman, C. R., Sweeney, L. M., Corley, R., Gargas, M. L. 2005. Using Physiologically-Based Pharmacokinetic Modeling to Address Nonlinear Kinetics and Changes in Rodent Physiology and Metabolism Due to Aging and Adaptation in Deriving Reference Values for Propylene Glycol Methyl Ether and Propylene Glycol Methyl Ether Acetate. *Risk analysis*, 25(2), 271-284.

Landry, T. D., Gushow, T. S., Yano, B. L. (1983). Propylene glycol monomethyl ether: a 13-week inhalation toxicity study in rats and rabbits. *Fundamental and Applied Toxicology*, 3(6), 627-630.

National Center for Biotechnology Information. PubChem Compound Database; CID=7900, https://pubchem.ncbi.nlm.nih.gov/compound/7900 (Accessed September 28, 2017).

NIOSH. 2016. Propylene glycol monomethyl ether. https://www.cdc.gov/niosh/npg/npgd0536.html (Accessed September 28, 2017). The page was last reviewed and updated on April 11, 2016.

OEHHA. 2008. Chronic Toxicology Summary: Propylene glycol monomethyl ether. Pp. 466-470 in Appendix D.3 Chronic RELs and toxicity summaries using the previous version of the Hot Spots Risk Assessment Guidelines (OEHHA 1999), Technical Support Document for the Derivation of Noncancer Reference Exposure Levels. Air Toxicology and Epidemiology Branch, Office of Environmental Health Hazard Assessment, California Environmental Protection Agency, Oakland, CA: [online]. Available: https://oehha.ca.gov/media/downloads/crnr/appendixd3final.pdf (accessed September 28, 2017).

Spencer, P. J., Crissman, J. W., Stott, W. T., Corley, R. A., Cieszlak, F. S., Schumann, A. M., Hardisty, J. F. 2002. Propylene glycol monomethyl ether (PGME): inhalation toxicity and carcinogenicity in Fischer 344 rats and B6C3F1 mice. *Toxicologic pathology*, 30(5), 570-579.

TCEQ. 2017. Effects Screening Levels (ESL) Lists Used in the Review of Air Permitting Data: Query the TCEQ Toxicity Factor Database. (Accessed September 28, 2017). http://www.tceq.texas.gov/toxicology/esl/list_main.html/#esl_1

Tomicic, C., Berode, M., Oppliger, A., Castella, V., Leyvraz, F., Praz-Christinaz, S. M., Danuser, B. 2011. Sex differences in urinary levels of several biological indicators of exposure: A human volunteer study. *Toxicology letters*, 202(3), 218-225.

U.S. EPA. 1991. IRIS database. Propylene glycol monomethyl ether (CASRN 107-98-2). https://cfpub.epa.gov/ncea/iris2/chemicalLanding.cfm?substance_nmbr=404 (Accessed on September 28, 2017).