MICHIGAN DEPARTMENT OF ENVIRONMENT, GREAT LAKES, AND ENERGY

INTEROFFICE COMMUNICATION

June 21, 2022

TO: Dipropylene Glycol (CAS No. 25265-71-8)

FROM: Mike Depa, Toxics Unit

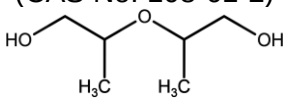
SUBJECT: Recension of Screening Level

The initial threshold screening level (ITSL) for dipropylene glycol (DPG) is rescinded. Previous ITSLs used to evaluate air emissions of DPG included 242 µg/m³ (annual averaging time) and the particulate matter (PM) National Ambient Air Quality Standards (12 µg/m³ annual, and 35 µg/m³ 24-hour). The usage of DPG in perfumes and artificial fog for entertainment events (Wikipedia, 2022) support the conclusion that DPG has low acute irritation via the inhalation exposure pathway. DPG, " …is practically non-toxic by the oral, inhalation and dermal routes." (OECD SIDS, 2001). It is anticipated that DPG will be added to Rule 120(f) as part of a list of substances that, "shall not be considered to be toxic air contaminants". Evaluation of DPG ambient air impacts resulting from air emissions from industrial sources subject to Rule 225[1] will be made on a case by case basis.

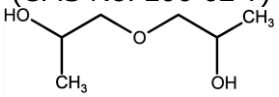
The following references or databases were searched to identify data to determine the screening level: U.S. Environmental Protection Agency (EPA) Integrated Risk Information System (IRIS), ECHA (European Chemical Agency) Registration, Evaluation, Authorization and Restriction of Chemicals (REACH), Registry for Toxic Effects of Chemical Substances (RTECS), American Conference of Governmental and Industrial Hygienists (ACGIH) Threshold Limit Values (TLVs), EPA Acute Exposure Guideline Levels (AEGLs), National Institute for Occupational Safety and Health (NIOSH) Pocket Guide to Hazardous Chemicals, Agency for Toxic Substances and Disease Registry (ATSDR) Minimal Risk Levels (MRLs), U.S. EPA Provisional Peer Reviewed Toxicity Values (PPRTVs) for Superfund, International Agency for Research on Cancer (IARC) Monographs, California Office of Environmental Health Hazard Assessment (OEHHA), Chemical Abstract Service (CAS) - SciFinder (1967 – June 2022), National Library of Medicine (NLM) Toxline, and National Toxicology Program (NTP) Status Report.

Dipropylene Glycol - Mixture
(CAS No. 25265-71-8)

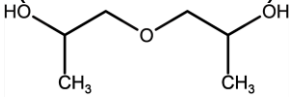
2,2'-Oxydipropanol
(CAS No. 108-61-2)



2-(2-Hydroxypropoxy)propan-1-ol
(CAS No. 106-62-7)



1,1'-Oxydi-2-propanol
(CAS No. 110-98-5)



[1] Part 55. Air Pollution Control, of the Natural Resources and Environmental Protection Act, 1994 PA 451, as amended.

DPG has low volatility (Vapor Pressure: 0.0319 mmHg @25°C, Henry's Law Constant: 5.63E-09 atm-m^3/mole @25°C).

Animal Toxicity
Six rats exposed to DPG vapors generated at 120°C and exposed for 5 hours did not die (OECD SIDS, 2001). Five of 6 rats exposed to vapors generated at 170°C died; there were no pathologic abnormalities. Reviewer's conclusion: Heating Dipropylene Glycol to 170°C resulted in toxic degradation products that did not occur from heating to 120°C and were not present in aerosols generated at room temperature or at 120°C. There was no lethality to rats or guinea pigs from aerosol of dipropylene glycol generated at room temperature. Vapor concentrations of DPG were estimated to be 6000-8000 mg/m^3 (OECD SIDS, 2001).

Excerpts from Organisation for Economic Co-operation and Development (OECD) Screening Information Dataset (SIDS)(2001):

> Dipropylene glycol (DPG) is not acutely toxic by oral (LD50[2] >13 g/kg bw/day from 7 rat studies and 17.6 g/kg bw/day from a guinea pig study), dermal (LD50 > 5g/kg bw/day in 2 rabbit studies) or inhalation (no deaths observed in rats and guinea pigs at 6 to 8 g/m3) routes of exposure. DPG is slightly irritating to the skin and eyes of rabbits. Based on human data, DPG is not a skin sensitizer. Repeated oral exposures of rats to DPG did not result in adverse effects at levels up to 5% (estimated NOAEL[3] is about 6.2 g/kg bw/day) in drinking water. At about 12.5 g/kg bw/day (10%), kidney lesions appeared in about 30% of the rats. Results from an OECD 422 combined repeat dose/reproductive/developmental toxici ty test on the structural analogue, tripropylene glycol (TPG), demonstrated a NOAEL of 200 mg/kg bw and a LOAEL of 1000 mg/kg bw for repeated dose toxicity, with increased relative weight for liver and kidney. Metabolic fate data on TPG demonstrates that TPG is readily converted to DPG, PG[4], and CO2 in rats. Thus, data from TPG are relevant to DPG. DPG did not cause fetal toxicity or teratogenicity in rats (NOAEL = 5 g/kg bw/day) or rabbits (NOAEL = 1.2 g/kg bw/day). No reproductive studies have been conducted on DPG. However, the structural analogues, propylene glycol and TPG, have been tested for reproductive effects and shown to have NOAELs of 10.1 g/kg bw in mice and 1 g/kg bw in rats, respectively. Thus, the lack of reproductive effects from TPG and the high NOAEL for PG reproductive toxicity indicate that no reproductive effects are expected in animals exposed to DPG, in the absence of maternal toxicity. DPG is not a genetic toxicant based on in vitro (bacterial and mammalian cells in culture) and in vivo (micronucleus) studies.
>
> Dipropylene glycol is slightly irritating to the skin and eyes. ... minimal skin effects were seen in a human volunteer study where 0.2 mL of 25% dipropylene glycol in water was applied semi-occlusively to 33 subjects for 24 hours. Nine subjects had mild erythema at either 30 minutes or 24 hours; two had mild erythema at both 30 minutes and 24 hours. Twenty-two subjects had no reaction after 30 minutes or 24 hours.
>
> The application of 7.2% DPG solution to rabbits' eyes for 24 hours resulted in mild irritation.

Chronic Oral Dosing Study
The National Toxicology Program (NTP,2004) published the results of a bioassay describing effects of DPG in drinking water. The doses (shown in Table 1) varied by sex and species.

[2] Lethal Dose 50%
[3] No Observed Adverse Effect Level
[4] Propylene Glycol

Table 1. Dose of DPG in Male and Female F344/N Rats and B6C3F1 Mice

Species/Sex	Low Dose mg/kg (ppm)	Mid Dose mg/kg (ppm)	High Dose mg/kg (ppm)
Rat/Male	115 (2500)	470 (10,000)	3040 (40,000)
Rat/Female	140 (2500)	530 (10,000)	2330 (40,000)
Mice/Male	735 (10,000)	1220 (20,000)	2390 (40,000)
Mice/Female	575 (10,000)	1040 (20,000)	1950 (40,000)

The groups of animals receiving 40,000 ppm dipropylene glycol weighed less than the control animals. All the male rats receiving 40,000 ppm dipropylene glycol died before the end of the study, mainly because of kidney disease. All the other animal groups survived as well as the controls. No increases in tumor rates were seen in any of the groups of rats or mice.

NTP (2004) concluded:

> Exposure to dipropylene glycol in drinking water resulted in increased incidences and severities of nephropathy in male rats, increased incidences of focal histiocytic and focal granulomatous inflammation of the liver in male rats, increased incidences of suppurative inflammation of the salivary gland in male rats, increased incidences of bile duct hyperplasia in male and female rats, increased incidences of olfactory epithelial atrophy and thrombosis of the nose in male rats, and increased incidences of olfactory epithelial degeneration of the nose in male and female rats.

Discussion

The human health toxicological hazards of dipropylene glycol indicate low acute toxicity by oral, dermal and inhalation routes of exposure. Transient signs of altered nervous system function (commonly observed with short-chain glycol exposure) are observed with oral exposure to high levels (NTP, 2004). Studies on the metabolism of structurally similar propylene glycols indicate that in the body dipropylene glycol will readily break down to propylene glycol and then to carbon dioxide (OECD SIDS 2001). Dipropylene glycol is expected to be readily absorbed by oral exposure but a study using human skin found negligible absorption for dermal exposure. This substance is slightly irritating to the skin and eye and there is no evidence of allergic skin reactions. Effects noted in repeated-exposure studies in rodents using the oral route of exposure reveal target organ effects specific to rodents and are not relevant to human health or occurred at very high dose levels of low relevance to human exposures. Tests conducted in bacteria, mammalian cells and in animals demonstrate dipropylene glycol is not mutagenic/genotoxic (OECD SIDS 2001). Long term drinking water toxicity studies conducted in two rodent species demonstrate that this substance is not a carcinogen. A reproductive toxicity study conducted with the structurally similar propylene glycol indicates dipropylene glycol does not affect fertility (OECD SIDS 2001). A repeated exposure study in animals found effects on sperm and estrous cycles at excessively high dose levels that caused significant stress related toxicity and hence these findings are not considered relevant to human health (OECD SIDS 2001).

Conclusion

DPG is used as a carrier for purfumes and fragrances and shows little evidence of inhalation toxicity. The potential health concern from ambient air impacts due to industrial emissions is low; therefore, the emissions of DPG will be evaluated on a case by case basis.

References

NTP. 2004. Technical Report on the Toxicology and Carcinogenesis Studies of Dipropylene Glycol (Cas No. 25265-71-8) In F344/N Rats And B6c3f1 Mice. (Drinking Water Studies). NTP TR 511. NIH Publication No. 04-4445. U.S. Department of Health And Human Services. Public Health Service. National Institutes of Health. Accessed January 9, 2019: https://ntp.niehs.nih.gov/ntp/htdocs/lt_rpts/tr511.pdf

Organisation for Economic Co-operation and Development (OECD) (2001). Screening Information Dataset (SIDS) Initial Assessment Report for Dipropylene Glycol, 25265-71-8. Accessed June 16, 2022: https://hpvchemicals.oecd.org/ui/AllChemicals.aspx

Wikipedia, 2022. Dipropylene Glycol. Accessed June 16, 2022. https://en.wikipedia.org/wiki/Dipropylene_glycol