

Tripropylene Glycol Methyl Ether
(CAS 25498-49-1)

(Synonyms : 2-(2-Methoxymethylethoxy)methylethoxy)propanol; Acrosolv TPM; Dowanol TPM)



Tripropylene Glycol Methyl Ether Acute REL

No studies of short term exposures were located that were suitable for the derivation of an acute REL.

Tripropylene Glycol Methyl Ether 8-hour REL

<i>Reference Exposure Level</i>	0.10 mg/m³ (0.012 ppm)
<i>Critical effects</i>	Eosinophilia
<i>Hazard Index target</i>	Liver

1 Physical and Chemical Properties of TPM

<i>Description</i>	Viscous, colorless liquid
<i>Molecular formula</i>	C ₁₀ H ₂₂ O ₄
<i>Molecular weight</i>	206.3 g/mol
<i>Specific gravity</i>	0.968 @ 25°C/25°C
<i>Boiling point</i>	243 °C
<i>Melting point</i>	-77.8 °C
<i>Vapor pressure</i>	0.021 mm Hg @ 25°C
<i>Log Kow</i>	0.309
<i>Solubility</i>	miscible @ 25°C
<i>Atmospheric half-life</i>	2 hrs
<i>Conversion factor</i>	1 ppm = 8.43 mg/m ³

2 Production, Use, and Exposure

Tripropylene glycol methyl ether is produced commercially as a mixture of up to eight isomers. It is used in the manufacture of polyester plastics. Because of its high polymer solvency and low evaporation rate, it is used in inks for ball point and felt tip pens, and in ink pads to prevent

drying. Because of its high boiling and flash points, it is used in oven cleaners and in high solids, solvent-based coatings. It is also used in rust, paint and varnish removers, and in penetrating oils. Acute inhalation and dermal exposure to TPM may occur during its application in coatings and in cleaning products. More prolonged, low level inhalation exposure may occur in confined spaces as the solvent evaporates.

The EPIWIN/APO model (U.S. EPA) estimates that the atmospheric photodegradation half-life of TPM is 2 hours, based on 12 hours of sunlight/day and an average hydroxyl radical concentration of 1.5×10^6 OH/cm³.

3 Pharmacokinetics and Metabolism

Although the primary alcohol function on glycol ethers is easily oxidized by liver alcohol dehydrogenase (ADH), propylene glycol ethers have a secondary alcohol function and are relatively poorer substrates for ADH. The ether bond in TPM may undergo microsomal o-dealkylation by mixed function oxidases to the alkyl alcohol and tripropylene glycol which is a substrate for ADH conversion to lactic acid and further to pyruvic acid (Klaassen, 1996). Via intermediate metabolism, TPM is ultimately converted to CO₂. Experiments in rats suggest TPM is absorbed, distributed and eliminated within 48 hr (Calhoun et al., 1986 in UNEP (2003).

4 Acute Toxicity of Tripropylene glycol methyl ether (TPM)

TPM is moderately irritating to the eyes with systemic effects on the liver, kidneys and central nervous system following inhalation. Dermal exposure has been associated with local irritation, weight loss and an increase in kidney weights. By analogy to other propylene glycol ethers, it is assumed to be less toxic than the equivalent ethylene glycol ethers.

Acute mammalian toxicity data were summarized in the Screening Information Data Set for TPM (Table adapted from UNEP, 2003) as follows:

Acute rat oral LD ₅₀	Acute rat inhalation LC ₅₀ (1 hr)	Acute rat dermal LD ₅₀ (24 hr)
3,500 mg/kg (95% CL: 3100-3900 mg/kg) Jones & Collier, 1986 in UNEP, 2003.	> 200,000 mg/m ³ (23,700 ppm), 1 hr exposure No deaths. Moreno, 1975 in UNEP, 2003.	15,400 mg/kg (2/4 deaths) No deaths at next lower dose 7,720 mg/kg. Kuryla, 1991 in UNEP, 2003.

To assess the toxicity of TPM by inhalation, mice and rats (5/species/sex/dose) were exposed for to TPM aerosol 6 hr/day, 5 d/wk at 0, 150, 360, 1010 mg/m³ for 9 days. Hematology and clinical chemistry data were collected prior to sacrifice. Gross necropsy and histological evaluation of 50 tissues followed sacrifice. Rats showed increased liver weights without histopathology at the mid and high doses. Mice also showed increased liver weights with eosinophilia at the highest dose giving a NOAEL of 360 mg/m³ and a LOAEL of 1010 mg/m³ (Miller 1985 in UNEP, 2003). In this study, no chemical-related reproductive damage was seen in the prostate,

epididymides, seminal vesicles and testes. This study was used in the derivation of the interim RELs described below. The LOAEL of 1010 mg/m³ is based on eosinophilia in the livers of male mice. For comparison, the LC50 for a 1-hour exposure was > 200,000 mg/m³ in rats.

5 Derivation of Interim RELs for Tripropylene glycol methyl ether (TPM).

5.1 Derivation of Acute REL for TPM

No studies of short-term exposure to TPM were located. While an LC₅₀ was reported, this value represents the upper limit for acute exposures that are compatible with survival without regard to protecting health. As such they are not the preferred basis for the derivation of an acute REL, which requires consideration of effects much less severe than lethality.

In the course of an 8-hour exposure, intermittent spikes in exposure levels are included in the time-weighted average addressed with the 8-hr REL. The values associated with 8-hr RELs are typically lower than allowed for acute 1-hr exposures, due to the longer exposure duration and possibility of recurring exposures. Therefore application of the 8-hr REL to exposure scenarios involving short-term peaks in concentration should be health protective in most cases.

5.2 Derivation of 8-Hour REL for TPM.

<i>Study</i>	Miller 1985 (see UNEP (2003))
<i>Study population</i>	Adult B6C3F1 mice
<i>Exposure method</i>	Aerosol inhalation of 0, 150, and 360, 1010 mg/m ³
<i>Exposure continuity</i>	6 hr/day, 5 d/wk
<i>Exposure duration</i>	9 days
<i>Critical effects</i>	Liver eosinophilia
<i>LOAEL</i>	1010 mg/m ³
<i>NOAEL</i>	360 mg/m ³
<i>Time-adjusted exposure</i>	C * T = K
<i>Extrapolated concentration</i>	193 mg/m ³ (360*6/8*5/7)
<i>Human concentration adjustment</i>	193 mg/m ³ (RGDR=1; systemic)
<i>LOAEL uncertainty factor</i>	1
<i>Subchronic uncertainty factor</i>	10
<i>Interspecies uncertainty factor</i>	
<i>Toxicokinetic (UF_{A-k})</i>	2
<i>Toxicodynamic (UF_{A-d})</i>	√10
<i>Intraspecies uncertainty factor</i>	
<i>Toxicokinetic (UF_{H-k})</i>	10
<i>Toxicodynamic (UF_{H-d})</i>	√10
<i>Cumulative uncertainty factor</i>	2000
<i>8-hour Reference Exposure Level</i>	0.10 mg/m³ (0.012 ppm)

The 8-hour REL was derived using the NOAEL of 360 mg/m³ for liver eosinophilia in mice. Time adjustment from this subchronic study was with the Haber's relationship, Cⁿ*T = K (n=1, default) and a subchronic UF of 10 was used. Following U.S. EPA guidelines for human concentration adjustment in the absence of chemical- or species-specific data, the regional gas dose ratio (RGDR) is taken to be 1. Based on the expected similarities to other propylene glycol ethers, the interspecies toxicokinetic UF is 2 (with use of RGDR), and the toxicodynamic UF is assigned √10 to cover variability. The intraspecies toxicokinetic UF is assigned 10 to protect sensitive subpopulation including children, while the intraspecies toxicodynamic variability is addressed with an UF of √10. The combination of the intraspecies toxicokinetic UF of 10 and the subchronic UF of 10 are expected to cover any residual deficiencies in the database. This results in a cumulative uncertainty factor of 2000 and an 8-hr REL of 0.10 mg/m³.

6 Other toxicity

Dermal toxicity of TPM has been noted in experimental animals. Rabbits topically treated with 65 applications of 0, 1, 3, 5, or 10 ml/kg/day over a 90 day period (5 d/wk, 24 hr/d) showed local skin reactions, weight loss at doses ≥ 3 ml/kg/day, and increased kidney weights. Narcosis and death in 7 of 8 animals occurred at the highest dose (10 ml/kg/d) ((Rowe et al., 1954; UNEP, 2003).

6.1 Human exposure

According to a TSCA Section 8(e) report, in 1983 a woman was hospitalized with complaints of disorientation incoordination and other unspecified nervous system effects. She had been working for 6-8 hr the day before with a floor care product containing 2.432% TPM. With the exception of water and ammonia, all other ingredients had little or no volatility. An association was made between TPM and the symptoms by the reporting officer (cited in UNEP, 2003).

7 References

Klaassen C, ed. (1996). Casarett and Doull's Toxicology; The basic science of poisons. 5th ed.. McGraw-Hill New York. p. 1111

Rowe VK, Mc Collister DD, Spencer HC, Oyen F, Hollingsworth RL and Drill VA (1954). Toxicology of mono-, di-, and tri-propylene glycol methyl ethers. A M A Arch Ind Hyg Occup Med 9(6): 509-25.

UNEP. (2003). Screening information data set for propylene glycol ethers. Organisation for Economic Co-operation and Development. Arona, Italy