EXECUTIVE SUMMARY

Propylene Glycol Monomethyl Ether (PGME) (CAS # 107-98-2) & Propylene Glycol Monomethyl Ether Acetate (PGMEA) (CAS# 108-65-6)– Oral Risk Assessment			
PARAMETER	**LEVEL**	**UNITS**	**DERIVED**
NOAEC (no-observed-adverse-effect concentration)	300	ppm	From a two-year inhalation study in Fischer 344 rats using PGME
$NOAEC_{ADJ}$ (Adjusted for continuous exposure)	36	ppm	Adjusted exposure from six hours/day, five days/ week to 24 hours, seven days/ week exposure
$NOAEL_{HED}$ (NOAEL oral human equivalent dose)	10	mg/kg-day	Conversions derived from a PBPK model developed by Corley et al. & Kirman et al. (2005)
Oral RfD (oral reference dose)	0.3	mg/kg-day	From a two-year inhalation study in Fischer 344 rats and B6C3F1 mice with a 30x uncertainty factor
TAC (total allowable concentration)	2	mg/L	For a 70 kg adult drinking 2 L/day using a 20% relative source contribution for drinking water
SPAC (single product allowable concentration)	0.2	mg/L	From the TAC, using the default 10 sources of PGME and PGMEA in drinking water
STEL (short term exposure level)	3	mg/L	From a OECD 416 inhalation study of PGME in the rat, for a 10 kg child drinking 1 L/day

EXPOSURE SUMMARY	PGME and PGMEA are high production volume solvents that are widely used in industrial and commercial applications. They have been observed as contaminants from NSF certified products in drinking water. Exposure may occur through the oral, dermal, or inhalation routes of exposure.
KEY STUDY	A two-year chronic/carcinogenicity assay in Fischer 344 rats by inhalation (Spencer et al., 2002)
CRITICAL EFFECT	Eosinophilic foci observed in the liver of rats at 1000 and 3000 ppm
UNCERTAINTY FACTORS	Factors applied in calculating the oral RfD include: • **3x** for interspecies extrapolation • **10x** for intraspecies extrapolation • **1x** for subchronic to chronic extrapolation • **1x** for LOAEL to NOAEL • **1x** for database deficiencies The total uncertainty factor is **30x**.
TOXICITY SUMMARY	PGME and PGMEA are of low acute toxicity by the oral, dermal, and inhalation routes of exposure. In rodents, portal of entry irritation at 300 ppm for PGMEA has been observed in inhalation studies that is not evident after oral exposure. Human studies revealed subjective eye irritation at ≥ 150 ppm of PGME vapor. Upon ingestion or inhalation, PGMEA is rapidly hydrolyzed to PGME followed by rapid absorption with similar distribution, metabolism, and excretion patterns that follow non-linear kinetics (due to saturation of PGME metabolism to propylene glycol and induction of microsomal enzymes) in animals and humans. Acute, short-term, subchronic, and chronic studies were consistent with occurrence of transient narcosis followed by resolution after 1-2 weeks with increased liver and kidney weights at high levels of exposure (> 1500 ppm). In a 2-year chronic inhalation study in rats and mice, histopathological changes of the kidney occurred at the lowest concentration in male rats (300 ppm), along with increased $\alpha_{2\mu}$-globulin deposition that is not considered relevant to humans. Eosinophilic foci in the liver occurred in male rats at concentrations ≥ 1000 ppm, and CNS effects were noted at a concentration of 3000 ppm. In multi-generational reproductive and developmental studies in rats and mice, reproductive effects were noted in the parental and F_1 generations at a vapor concentration of 1000 ppm (parental by inhalation) and at a drinking water concentration of 3328 mg/kg (F_1, oral exposure). Developmental effects were not reported in these studies, with the exception of a single inhalation study that reported increased incidence of delayed sternebral ossification at a vapor concentration of 3000 ppm. The weight of evidence suggests low concern for genotoxic potential, and carcinogenicity studies in rats and mice conducted via inhalation revealed increased incidence of foci in the liver without a statistically significant increase in the incidence of tumor formation at concentrations near or above the maximum tolerated concentration. Based on the available evidence, PGME and PGMEA may be classified as "*Not Likely to be Carcinogenic to Humans*" according to U.S. EPA (2005) guidelines.
CONCLUSIONS	This risk assessment utilized the available published PBPK model and a robust toxicological dataset for PGME and PGMEA. As such, these drinking water action levels are conservative and protective of public health.