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DIPROPYLENE GLYCOL METHYL ETHER

CAS N°: 34590-94-8

*(Isomers: 13429-07-7, 20324-32-7; 13588-28-8;
and 55956-21-3)*

SIDS Initial Assessment Report**for
12th SIAM**

(Paris, France, 27-29 June 2001)

Chemical Name : DIPROPYLENE GLYCOL METHYL ETHER (DPGME)

CAS No: 34590-94-8

Isomers: 13429-07-7, 20324-32-7; 13588-28-8; and 55956-21-3

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SIDS INITIAL ASSESSMENT PROFILE

CAS No.	34590-94-8 (isomers: 13429-07-7, 20324-32-7; 13588-28-8; and 55956-21-3)
Chemical Name	Dipropylene Glycol Methyl Ether
Structural Formula	$\text{CH}_3\text{-(OC}_3\text{H}_6)_2\text{-OH}$

RECOMMENDATIONS

The chemical is currently of low priority for further work, based on the low hazard profile.

SUMMARY CONCLUSIONS OF THE SIAR

Human Health

Commercial Dipropylene Glycol Methyl Ether (DPGME) is a mixture of four isomers. DPGME exhibits low acute toxicity by the oral, dermal, and inhalation routes. The oral LD₅₀ ranges 5180-5400 mg/kg b.w. in rats to 7500 mg/kg b.w. in dogs. Dermal LD₅₀ values were reported to range from 9500 to >19000 mg/kg b.w. in rabbits. Acute inhalation exposures to 500 ppm (3000 mg/m³, highest attainable concentration) DPGME produced no lethality and mild, but reversible narcosis in rats. In animal and human studies, DPGME is neither a skin sensitizer nor a skin irritant, and was only slightly irritating to the eye. In repeated dose inhalation studies, NOAELs of >50 ppm to 200 ppm (> 303 mg/m³ to 1212 mg/m³) have been observed using rats, mice, rabbits, guinea pigs, and monkeys. Effects observed at higher dose levels (1818 mg/m³ to 2424 mg/m³; 300 – 400 ppm) showed signs of central nervous system depression and adaptive liver changes. In rats exposed to up to 1000 mg/kg-day DPGME via gavage for 4 weeks, tentative salivation (immediately after dosing) and adaptive liver changes were observed in animals exposed to the highest dose. No effects were observed in rats exposed to 200 mg/kg-day. Studies in rats and rabbits showed that DPGME is not teratogenic (two inhalation studies with NOAELs of 1818 mg/m³; 300 ppm). It should be noted that the beta isomer of PGME is known developmental toxicant. This isomer is unlikely to be a metabolite of DPGME. The available data indicate that DPGME is not genotoxic. Information collected for a structurally similar chemical (PGME) suggests that DPGME is not a reproductive toxicant, and is not carcinogenic. Additionally, no effects were seen on the testes and ovaries in a 90-day repeat dose inhalation toxicity study on DPGME.

Environment

DPGME is not persistent in the environment and is not expected to bioaccumulate in food webs. DPGME has a water solubility value of 1000 mg/L, a vapor pressure of 0.37 hPa and a log K_{ow} of 0.0061. The half-life of DPGME in air was measured at 5.3 hours and is estimated to be 3.4 hours due to direct reactions with photochemically generated hydroxyl radicals. DPGME is readily biodegraded under aerobic conditions, but only slightly degraded under anaerobic conditions. Although environmental monitoring data are not available for DPGME, fugacity-based modelling indicates that DPGME is likely to partition to water compartments in the environment (surface water, groundwater). Acute toxicity testing in fish, invertebrates, and algae indicate a low order of toxicity with effect concentrations exceeding 1000 mg/L. Applying an uncertainty factor of 100 to the 48-hour LC₅₀ value of 1919 mg/L for Daphnia, a PNEC of 19 mg/L was derived.

Exposure

Production in the U.S. was estimated at 35 million pounds (16 thousand tonnes) for 2000. DPGME is used in the manufacture of a wide variety of industrial and commercial products, including paints, varnishes, inks, and cleaners. In the US in 1999, DPGME was used as follows: 58% paints/coatings/inks, 28% cleaners, 10% DPGME acetate production, and 3% miscellaneous production.

NATURE OF FURTHER WORK RECOMMENDED

No further work is recommended.

FULL SIDS SUMMARY

CAS NO: 34590-94-8		SPECIES	PROTOCOL	RESULTS
PHYSICAL-CHEMICAL				
2.1	Melting Point	--	--	-83 °C
2.2	Boiling Point	--	--	190°C
2.3	Density	--	--	0.948 g/cm ³
2.4	Vapour Pressure	--	--	0.37 hPa at 20°C
2.5	Partition Coefficient (Log K _{ow})	--	--	0.0061
2.6	Water Solubility	--	--	Miscible
A.	pH	--	--	No data
B.	pKa	--	--	No data
2.12	Oxidation: Reduction Potential	--	--	No data
ENVIRONMENTAL FATE AND PATHWAY				
3.1.1	Photodegradation	--	Measured	5.3 hours
3.1.2	Stability in Water	--	Measured	Little to no degradation over short periods of time.
3.2	Monitoring Data	--	Measured	Limited occupational air sample data, product formulations generally contain 2-25%.
3.3	Transport and Distribution	--	Fugacity estimates	Primarily distributes to water compartments.
3.5	Biodegradation	--	Measured	Readily degraded under aerobic conditions; limited degradation under anaerobic conditions.
ECOTOXICOLOGY				
4.1	Acute/Prolonged Toxicity to Fish	Pimephales promelas	96-hour lethality	LC50 >10,000 mg/L
4.2	Acute Toxicity to Aquatic Invertebrates (<i>Daphnia</i>)	Daphnia magna	48-hour lethality	LC50 = 1919 mg/L
4.3	Toxicity to Aquatic Plants e.g. Algae	Selenastrum capricornum	3-4-day growth	EC10 = 133 mg/L EC50 > 969 mg/L
4.5.2	Chronic Toxicity to Aquatic Invertebrates (<i>Daphnia</i>)	Daphnia magna	22-day reproduction	NOAEL = 0.5 mg/L LOAEL > 0.5 mg/L
4.6.1	Toxicity to Soil Dwelling Organisms	--	--	No data

CAS NO: 34590-94-8		SPECIES	PROTOCOL	RESULTS
4.6.2	Toxicity to Terrestrial Plants	Glycine max	Growth	EC50 > 500,000 mg/L NOEC = 250,000 mg/L
4.6.3	Toxicity to Other Non- Mammalian Terrestrial Species (Including Birds)	--	--	No data
TOXICOLOGY				
5.1.1	Acute Oral Toxicity	Rat	Acute lethality	LD50 = 5180 – 5400 mg/kg
5.1.2	Acute Inhalation Toxicity	Rat	Acute toxicity	LOAEL = 500 ppm
5.1.3	Acute Dermal Toxicity	Rabbits	Acute lethality	LD50 = 9500 mg/kg
5.4	Repeated Dose Toxicity	Rat	4-week oral toxicity	LOAEL = 1000 mg/kg NOAEL = 200 mg/kg
		Rat	13-week inhalation	NOAEL = 200 ppm (1212 mg/m ³)
		Rat	28-week inhalation	LOAEL= 200 – 300 ppm (1212 mg/m ³ – 1818 mg/m ³) 40-60% saturated DPGME atmosphere
5.5	Genetic Toxicity In Vitro			
A.	Bacterial Test (Gene mutation)	Salmonella typhimurium	Mutagenicity	With activation: - Without activation: -
B.	Non-Bacterial In Vitro Test	Chinese hamster ovary cells	Chromosomal aberrations	With activation: - Without activation: -
5.6	Genetic Toxicity In Vivo	--	--	No data; Data for similar chemical (PGME) are negative
5.7	Carcinogenicity	--	--	No data; Data for similar chemical (PGME) are negative
5.8	Toxicity to Reproduction	--	--	Limited data; Data for similar chemical (PGME) are negative
5.9	Developmental Toxicity/ Teratogenicity	Rat	Inhalation	NOAEL = 300 ppm
		Rabbit	Inhalation	LOAEL > 300 ppm NOAEL = 300 ppm LOAEL > 300 ppm
5.11	Experience with Human Exposure	Human	Respiratory irritation	LOAEL = 35 – 75 ppm

SIDS Initial Assessment Report

1.0 IDENTITY

Dipropylene Glycol Methyl Ether (34590-94-8), or DPGME, is a liquid that possesses the following physical-chemical properties and characteristics:

Property	Value
Chemical Formula	CH ₃ -(OC ₃ H ₆) ₂ -OH
Molecular Weight	148.2 g/mol
Purity	>98%
Impurities	Water <0.1%
Melting Point	-83°C (freezing point)
Boiling Point	190°C
Density	0.948 g/cm ³
Vapor Pressure	0.37 hPa at 20°C
Partition Coefficient (Log K _{ow})	0.0061
Water Solubility g/m ³	1 x 10 ⁶
Odor Threshold	210 mg/cu m odor low; 6000 mg/cu m odor high
Synonyms	Dipropylene glycol methyl ether; Dipropylene glycol monomethyl ether; Methoxypropoxypropanol; DGME; DPGME; MDP; Arcosolv DPM; DOWANOL DPM; Solvenon DPM; Dimethyl Proxitol

DPGME is a mixture of four isomers. According to the manufacturers specification, (BUA Reports 173 and 174: Methoxypropanol (propylene glycol methyl ether), Dipropylene glycol ethyl ether. GDCh-Advisory Committee on Existing Chemicals of Environmental Relevance), the respective fractions of the structural isomers are 40-50% 1-(2-methoxypropoxy)propanol-2 (CASRN: 13429-07-7), 40-45% 1-(2-methoxy-1-methylethoxy)propanol-2 (CASRN: 20324-32-7), 2-5% 2-(2-methoxypropoxy)propanol-1 (CASRN: 13588-28-8), and 3-5% 2-(2-methoxy-1-methylethoxy)propanol-1 (CASRN: 55956-21-3). Commercial DPGME is produced only as a four-isomer mixture and hence all testing was conducted on the commercial mixture. The four individual isomers are not separated nor produced as individual chemicals.

2.0 GENERAL INFORMATION ON EXPOSURE

Estimated National Production or Import Volume

Approximately thirty eight million pounds (17 thousand tons) of DPGME were produced in the U.S. in 1999 (Appendix A). Approximately 12,000 tons of DPGME were consumed in the U.S. in 1995 (Staples and Davis, 2001). Production in the U.S. was estimated at 35 million pounds for (16 thousand tons) 2000 (Chemical Economics Handbook on Glycol Ethers (1996), SRI International). DPGME occurred in 123 products present on the Swedish market in July 1989. The estimated annual use was approximately 240-2500 tons/year (The Products Register, Swedish Chemicals Inspectorate). Manufacturers of DPGME in the Federal Republic of Germany (FRG) produced approximately 19,500 tons in 1994. No DPGME was imported into the FRG, and approximately 3,000 tons were exported. Import of DPGME with other glycols cannot be excluded, since DPGME is presumably contained in numerous finished products imported into the FRG. Consumption of DPGME in Germany for 1994 can be estimated to be at least 16,000 tons/year (GDCh-Advisory Committee on Existing Chemicals of Environmental Relevance (BUA), October 1995).

Uses and Functions

DPGME is a powerful solvent for a vast range of organic compounds. It is used as a solvent in the manufacture of water-based coatings and DPGME is also used as a coalescing agent for water based paints and inks. DPGME is an ingredient in a wide variety of industrial products including cleaning agents, cosmetic agents, detergent/wetting agents, sanitary/disinfectant cleaners, solvent for paints/varnished/inks, and stripper/degreasers. DPGME is also used in a wide variety of household and commercial cleaning products including glass, surface, paintbrush, carpet, and all-purpose cleaners, floor polish, industrial degreasers, aluminium brighteners, and rust removers. It is also used in chemicals for the oil production and drilling industry. In the U.S. in 1999, DPGME was used as follows: 58% paints/coatings/inks, 28% cleaners, 10% DPGME acetate production, and 3 % miscellaneous production (Appendix A).

Form of Marketed Product

DPGME is used in a variety of domestic, commercial, and industrial cleaners. The majority of these products may contain less than 1%-5% DPGME, however, some products contain as much as 10-25% DPGME (GDCh-Advisory Committee, 1995). A more detailed list of products and their DPGME content is provided in the SIDS Dossier for DPGME.

Sources of Potential Release to the Environment

For one facility in the Federal Republic of Germany, 3.8 tons/year were directed with plant wastewater to a biological wastewater treatment plant. At another FRG production facility 0.5 tons/year were emitted into the wastewater that fed into a biological wastewater treatment plant. In addition, unquantifiable emissions into municipal wastewater will also occur through the use of consumer and commercial products such as cleaning agents, degreasers, stripping agents, and ceiling and wall paint. Residues in packaging are expected to occur in solid municipal wastes (GDCh Advisory Committee, 1995).

2.1 Environmental Exposure and Fate

DPGME is completely miscible with water, has a vapor pressure of 0.37 hPa 20°C, and a Henry's Law constant of 1.2×10^{-4} Pa/m³ mol⁻¹ (at 25°C, calculated) (EBRC, 1995c). According to Thomas (1990), DPGME is considered to be non-volatile from water. Although there are no data available on experimentally determined values, calculated n-octanol/water partition coefficient values for DPGME range from -0.064 to -1.47 (DOW, 1992; EBRC, 1995a; Pomona, 1989). Based on the n-octanol/water partition coefficient, a bioconcentration factor (BCF) of less than or equal to 1 is estimated (Bysshe, 1990).

Based on the fact that DPGME is completely miscible with water, it is assumed that there will be no tendency for accumulation to soil and sediment in a soil-water matrix. Accordingly, a transport with leachate into groundwater can be expected from the resulting high mobility (HSDB, 1993). According to a study on

the photodegradation of DPGME by DOW (1975), a half-life of 5.3 hours in air was produced at 37.8°C, 75% relative humidity on a sunny day. Studies on the degradation of DPGME in soils are unavailable. Half-lives ranging from 5.2 to 7.6 hours in air were estimated for propylene glycol ethers (including DPGME) (Staples and Davis, 2001).

DPGME was degraded under aerobic conditions to 93% after 13 days using industrial sludge and the “Zahn-Wellens Test” (BASF, 1981). According to DOW (1998), DPGME was readily degraded under aerobic conditions to 79% after 28 days using domestic sludge and OECD 301F Manometric Respirometry Test. However, under anaerobic conditions using municipal activated sludge, DPGME degraded to 10% after 81 days (DOW 1998) with a lag period of approximately 30 days before any degradation was noted. A fugacity-based, multimedia model (Mackay Level 3) was run for DPGME (Staples and Davis, 2001). Based on an estimate of 12,000 tons of DPGME consumed in the U.S. during 1995, source terms for release to air, water, and soil were calculated to be 122, 13.7, and 1.4 kg/hour, respectively. Model predictions for the concentrations of DPGME in various compartments were as follows:

- Air: 9.24 ng/m³
- Water: 0.053 ug/L
- Soil: 0.28 ug/kg
- Sediment: 0.030 ug/kg

2.2 Human Exposure

DPGME is widely used in industrial, commercial, automotive, and household cleaners. As such, inhalation and dermal exposures are likely for worker and consumer populations. In addition, indirect exposures via the environment (*i.e.*, ingestion of surface water) are also possible. Each of these exposure scenarios is discussed below.

Occupational Exposure

The primary occupational exposure to DPGME is through inhalation of vapors or via dermal contact. In one instance, DPGME in water-based ceiling and wall paint (1% w/w) was used in a closed room. Fifteen workplace measurements were taken during painting, which measured occupational exposures of 30-40 mg/m³ (5-7 ppm) DPGME (GDCh-Advisory Committee on Existing Chemicals of Environmental Relevance (BUA), 1995).

Occupational exposure limits (OEL) for DPGME are listed below for several countries.

Exposure Limit (Country)	(mg/m ³)	(ppm)
PEL (USA)	600	100
STEL (USA)	900	150
OEL (FIN)	300	50
MAC (NL)	300	50
VME (FRA)	600	100

An evaluation of a worker's potential daily dermal dose of DPGME is presented in Appendix B. Theoretical dermal doses for a worker ranged from 0.48 to 23 mg/kg-day.

Consumer Exposure

Consumer products containing DPGME include (Appendix A; GDCh-Advisory Committee on Existing Chemicals of Environmental Relevance (BUA), 1995):

- Ceiling/wall paints;
- Glass cleaner;
- Surface cleaner;
- All purpose cleaner;
- Floor polish;
- Carpet cleaner;
- Paintbrush cleaner;
- Industrial degreaser;
- Aluminum brightener;
- Rust remover;
- Inks and dyes;
- Surface coatings; and
- Cosmetic agents.

Products containing DPGME generally contain levels between 1 and 10%, although some products may have levels that are as high as 50% (BUA, 1995). Consumer exposure to DPGME occurs through application of products including cleaning products, paints, and cosmetic agents as well as their residues in packaging (*e.g.* in packaging). A temporary accumulation of DPGME can occur in closed rooms through the use of DPGME in water-based ceiling and wall paint. In one study, 15 workplace measurements conducted during painting, DPGME concentrations of 30-40 mg/m³ (5-7ppm) were measured in the air (Hansen *et al.*, 1987).

Indirect Exposure via the Environment

Although environmental monitoring data for DPGME are not available, theoretical water, air and soil concentrations of 0.053 ug/L, 9.24 ng/m³ (0.0000016 ppm), and 0.28 ug/kg were calculated for DPGME using a Level 3 fugacity-based fate and transport modeling (Staples and Davis, 2001). Under the conservative assumptions listed in Appendix B, doses of DPGME from air, water, and soil were calculated to be 0.0000025, 0.0000015, 0.0000000038 mg/kg-day, respectively. Because DPGME does not bioconcentrate, potential exposure via consumption of fish is anticipated to be negligible.

3.0 HUMAN HEALTH HAZARDS

3.1 Effects on Human Health

Toxicokinetics and Metabolism

In a study by Miller et al. (1985), male Fischer 344 rats were given a single oral dose of carbon-14 labelled DPGME. Approximately 60% of the administered ^{14}C activity was excreted in the urine, while 27% was eliminated as $^{14}\text{CO}_2$ within 48 hours after dosing. DPGME, PGME, as well as sulfate and glucuronide conjugates of DPGME were identified in urine of animals given (^{14}C) DPGME. Major metabolic pathways for DPGME include conjugation with glucuronic acid and sulfate and hydrolysis of the methoxy group to form dipropylene glycol. Hydrolysis of the dipropylene glycol backbone of DPGME to form PGME (propylene glycol methyl ether) and propylene glycol is considered a minor metabolic pathway as indicated by the fact that conjugates of DPGME, dipropylene glycol and the parent compound accounted for more than half of the total radiolabel in the urine (Miller et al, 1985). Hence like PGME and other propylene based glycol ethers, microsomal O-demethylation is a significant route of biotransformation of DPGME. The glucuronide and sulfate conjugates of DPGME are essentially non-toxic and rapidly eliminated from the body. DPGME is less volatile and has been shown in comparable studies to be similar to, or less toxic than dipropylene glycol, PGME and propylene glycol, each of which are themselves of low toxicity.

Although tests on commercial PGME have indicated a low potential for toxicity the pure beta isomer of PGME (present at levels $\leq 0.5\%$ in commercial PGME) has produced developmental effects in animals (BASF, 1988; Hellwig et al., 1994). Unlike the alpha PGME isomer, the beta PGME isomer is an excellent substrate for alcohol/aldehyde dehydrogenases and is oxidized primarily to 2-methoxypropionic acid (2-MPA) (Miller et al., 1986). It is this alkoxyacid metabolite that is the likely mediator of developmental toxicity (Carney et al., 2000). DPGME differs from PGME in that it does not contain beta isomer and hence the formation of the primary alcohol, beta PGME, from DPGME is dependent upon the potential to hydrolyze the central ether linkage in certain isomers of DPGME. Only two of the 4 DPGME isomers have the potential to be hydrolyzed to beta PGME. If one assumes that 100% cleavage of the ether bridge occurs, only 0.6 mmol of 2-MPA can be theoretically produced for every mmol of DPGME. Although DPGME has not been studied directly for the ability to produce beta PGME, a pharmacokinetic study with a structurally similar dipropylene glycol ether, dipropylene glycol dimethyl ether (DPGDME) showed a very low potential for cleavage of the glycol ether backbone with only 4.3% of the theoretical maximum of 2-MPA recovered at low doses and 13% of the theoretical maximum at higher doses (Mendrala et al., 1993). In an in vitro liver slice metabolism assay used to investigate the formation of 2-MPA from six propylene glycol ethers including beta PGME and DPGDME, none of the di- or triether substrates evaluated were metabolized to 2-MPA as effectively as beta-PGME. The in vitro formation of 2-MPA from beta PGME ranged from 3-170-fold higher than from any of the diethers tested (Pottenger et al., 1995). The in vivo metabolism study with DPGME taken together with the in vivo and in vitro studies with structurally analogous diglycol ethers indicate that hydrolysis of the central ether linkage to form the primary alcohol beta PGME and subsequent hydrolysis to the alkoxyacid metabolite is a minor metabolic pathway for DPGME. This minor pathway is likely to result in levels of MPA that are well below the levels that produce toxicologically significant effects even at high doses of DPGME.

The database on the metabolites of DPGME also includes studies that have not been conducted with DPGME such as reproductive and chronic toxicity/oncogenicity studies. Based upon the the low probability to form beta PGME, similarities in metabolism and modes of action of DPGME and its metabolites, it is highly probable that DPGME will be similar to or less toxic than its metabolites in reproductive, chronic toxicity and carcinogenicity studies.

Acute Toxicity

Information available suggests that the acute toxicity of DPGME is low. However, generally CNS depression was found at high levels. The oral LD_{50} value for DPGME in experiments in rats ranges from 5,180 to 5,400 mg/kg (Rowe *et al.*, 1954; Smyth *et al.*, 1962). The oral LD_{50} value for dogs in an experiment

by Shideman, F.E. and Procita, L. (1951) was 7,500 mg/kg. Similarly, LC_{50} values for dermal exposure were 9,500 to >19,000 mg/kg for rabbits (Smyth *et al.*, 1962; Browning, 1965; Clayton and Clayton, 1982). Acute inhalation toxicity data includes a study by Rowe *et al.*, (1954) in which male rats were exposed to 500 ppm DPGME (saturated vapour atmosphere) for 7 hours. Mild narcosis was observed, with rapid recovery. Finally, an LD_{50} of 1230 mg/kg (1.3 ml/kg) was recorded for anaesthetised dogs exposed to DPGME via intravenous administration (Browning, 1965).

Repeated Dose Toxicity

Subchronic animal studies have been conducted for DPGME via inhalation, ingestion, and dermal contact, as summarized below:

- *Inhalation* – Laboratory animals exposed to DPGME via inhalation have reportedly developed mild symptoms of toxicity, including central nervous systems effects (sedation), adaptive hepatic changes, and decreases in body weight gain at concentrations of 140–400 ppm. NOELs ranged from >50 to 400 ppm in experiments in rats lasting 2 to 28 weeks (Landry *et al.*, 1981; Landry and Yano, 1984; Rowe *et al.*, 1954). For mice, a NOEL of >50 ppm and a LOEL of 140 ppm in an experiment lasting 2 weeks were reported (Landry *et al.*, 1981). In experiments in rabbits lasting 13 and 31 weeks, NOELs of > 200 ppm and 300–400 ppm were observed, respectively (Landry *et al.*, 1983; Rowe *et al.*, 1954). In other inhalation studies lasting 6 months, NOELs of 300 ppm and > 300 ppm were observed for monkeys and guinea pigs, respectively (Rowe *et al.*, 1954).
- *Ingestion* – In rats exposed to either 0, 40, 200, or 1000 mg/kg-day DPGME via gavage for 4 weeks, tentative salivation (immediately after dosing) and liver effects (increased relative liver weight, centrilobular hypertrophy) was observed in animals exposed to the highest dose (Dow Chemical Japan, 2000). No effects were observed in rats exposed to 200 mg/kg-day. Additionally, laboratory animals exposed to PGME (a compound similar to DPGME) via ingestion have reportedly developed central nervous system effects (mild to severe depression), enlarged livers, and weight loss. Minor kidney damage was reported following large oral doses. However, the renal effects in rats appear to be due to an a 2-microglobulin-mediated mechanism of action and therefore, are not relevant to humans. NOELs of < 459.5 and 919 mg/kg were observed in subchronic experiments lasting 13 and 5 weeks, respectively, in which PGME was administered orally to rats (Rowe *et al.*, 1954; Stenger *et al.*, 1972).
- *Dermal Contact* – Laboratory animals dermally exposed to DPGME have reportedly developed dermal effects (skin irritation, scaling, minimal inflammation, and skin thickening). Large dermal doses (10 mg/ml) can produce kidney effects (hydropic degeneration), narcosis and death. In a subchronic study in which DPGME was dermally applied to rabbits, a NOEL of 2,850 mg/kg and a LOEL of 4,750 mg/kg (90 days) were observed (Rowe *et al.*, 1954). A NOEL of 1,000mg/kg was reported for rats exposed to DPGME for 4 weeks (Fairhurst *et al.*, 1989).

Reproductive Toxicity

No effects were seen on the testes and ovaries in a 28-day repeat dose oral toxicity study on DPGME (Dow Chemical Japan, Unpublished Report #FBM 99-2691, 2000)

Additionally, in a 2-generation inhalation reproduction study sponsored by the CMA Propylene Glycol Ethers Panel with the structurally similar chemical propylene glycol monomethyl ether (PGME) no adverse fertility or reproductive effects were observed (at 1,000 ppm PGME). Levels of alpha isomer (1-methoxy-2-propanol) ranged from 97.99–98.07%, while the beta isomer (2-methoxy-1-propanol) ranged from 1.86–1.90%. Major metabolic pathways for DPGME include conjugation with glucuronic acid and sulfate; hydrolysis of the methoxy group to form dipropylene glycol; and hydrolysis of the dipropylene glycol backbone of DPGME to form PGME and propylene glycol (Miller *et al.*, 1985). The glucuronide and sulfate conjugates of DPGME are essentially non-toxic and rapidly eliminated from the body. DPGME is less volatile and has been shown in comparable studies to be similar to, or less toxic than dipropylene glycol, PGME and

propylene glycol, each of which are themselves of low toxicity. Based upon the similarities in metabolism and modes of action of DPGME and its metabolites, it is highly probable that DPGME will be similar to or less toxic than its metabolites in reproductive toxicity studies.

Developmental Toxicity/Teratogenicity

Studies in laboratory animals indicate that DPGME is neither teratogenic nor fetotoxic when administered via inhalation or ingestion.

- *Inhalation* - In a study of rats exposed to DPGME via inhalation, NOELs of 300 ppm (maternal) and 300 ppm (teratogenic) were observed (Breslin *et al.*, 1990a,b). NOELs of 300 ppm were reported for both maternal and teratogenic effects in rabbits (Breslin *et al.*, 1990 b,c). 300 ppm is the highest concentration attainable at room temperature and normal pressure.
- *Ingestion* - No developmental toxicity data is available for DPGME, however, no maternal toxicity, fetotoxicity, or teratogenicity were observed in rats, mice, and rabbits administered PGME (a compound similar to DPGME) via oral gavage. NOELs of 0.8 mL/kg, 2 mL/kg, and 1 mL/kg were observed for rats, mice, and rabbits, respectively (Stenger *et al.*, 1972). Similarly, these doses did not produce maternal or fetotoxicity in mice when administered by injection.

Although tests on commercial DPGME and PGME have been negative in developmental studies the pure beta isomer of PGME (present at levels $\leq 0.5\%$ in commercial PGME) has produced developmental effects in animals (BASF, 1988; Hellwig *et al.*, 1994). Unlike the alpha PGME isomer, the beta PGME isomer is an excellent substrate for alcohol/aldehyde dehydrogenases and is oxidized primarily to 2-methoxypropionic acid (2-MPA) (Miller *et al.*, 1986). It is this alkoxyacid metabolite that is the likely mediator of developmental toxicity (Carney *et al.*, 2000). DPGME differs from PGME in that it does not contain beta isomer thus the formation of the primary alcohol, beta PGME, from DPGME is dependent upon the potential to hydrolyze the central ether linkage in certain isomers of DPGME. Only two of the 4 DPGME isomers have the potential be hydrolyzed to beta PGME. In vivo and in vitro studies provide support that significant cleavage of the dipropylene glycol backbone does not occur (Mendrala *et al.*, 1993; Pottenger *et al.*, 1995) precluding the formation of levels of beta PGME capable of producing toxicologically significant effects even at very high doses of DPGME. The low potential to generate the beta PGME isomer taken together with negative results in developmental toxicity studies in multiple species indicate it is unlikely that DPGME would be teratogenic or fetotoxic by oral ingestion or inhalation.

Genetic Toxicity

DPGME was not mutagenic in *in vitro* tests on mammalian cells.

- *In Vitro* - No evidence of genotoxicity was reported in *Salmonella typhimurium* or *Escherichia coli*, with or without metabolic activation, using concentrations ranging from 313 to 5000 ug/plate (Dow Chemical Japan, 2000). Similarly, no evidence of chromosomal aberrations was noted in Chinese hamster lung cells exposed to 0.371-1.482 mg/L for 6 or 25 hours (Dow Chemical Japan, 2000). DPGME was not toxic to CHO cells up to 5 mg/l, but reduced survival to approximately 50% at 10 mg/l. Since metaphase analysis showed no differences between DPGME-treated and untreated cells, with or without metabolic activation, DPGME is considered not to be a chromosome mutagen for CHO cells (Kirkland, 1983). In a rat hepatocyte unscheduled DNA synthesis (UDS) assay, DPGME failed to elicit significant UDS at any concentration tested (0-0.0000316 M without metabolic activation). This result suggests an apparent lack of genotoxic activity under the test conditions (Mandrala, 1983). In a study by Kirkland and Varley (1983), DPGME was tested in a bacterial reverse mutation assay (Ames Test) on *Salmonella typhimurium* with and without metabolic activation. DPGME tested negative for genotoxic effects.

- *In Vivo* – No *in vivo* data are available for DPGME. However, concentrations up to 6,000 mg/kg PGME (a structurally similar chemical) administered to mice did not increase the frequency of micronuclei in polychromatic erythrocytes harvested from bone marrow (Elias *et al.*, 1996).

Carcinogenicity

While DPGME has not been evaluated in a chronic toxicity/oncogenicity bioassay to date, its low toxicologic potential in subacute and subchronic studies, lack of genotoxic activity, and biotransformation via the same general routes and types of metabolites as the noncarcinogen PGME, indicate that DPGME is unlikely to be carcinogenic in man or animals.

In 2-year inhalation carcinogenicity studies sponsored by the CMA PGE Panel (Cieszlak *et al.*, 1998) with the structurally similar chemical propylene glycol monomethyl ether (PGME) no evidence of carcinogenicity has been found in either rats or mice. The highest dose tested in both sexes of both species was 300 ppm. Major metabolic pathways for DPGME include conjugation with glucuronic acid and sulfate; hydrolysis of the methoxy group to form dipropylene glycol; and hydrolysis of the dipropylene glycol backbone of DPGME to form PGME and propylene glycol (Miller *et al.* 1985). The glucuronide and sulfate conjugates of DPGME are essentially non-toxic and rapidly eliminated from the body. DPGME is less volatile and has been shown in comparable studies to be similar to, or less toxic than dipropylene glycol, PGME and propylene glycol, each of which are of low toxicity, themselves. Therefore, no major differences in the systemic toxicological properties of DPGME and PGME would be anticipated, including carcinogenic potential. Consistent with this view is the fact that DPGME has been shown not to be genotoxic in several *in vitro* assay systems; DPGME was negative in an Ames bacterial gene mutation assay, did not induce unscheduled DNA synthesis (DNA damaged-induced repair) in rat hepatocytes, and was not clastogenic in CHO cells (ECETOC, 1995).

Irritation/Corrosiveness

In animal studies (rabbits), DPGME was classified as non-irritating to the skin (Ballantyne, 1983; Rowe *et al.*, 1954; Smyth *et al.*, 1962; Union Carbide, 1971). DPGME was also found to be non-irritating to the skin in human studies (Rowe *et al.*, 1954). Studies on the effects of DPGME on the eyes of rabbits resulted in non-irritating and slightly irritating results (Ballantyne, 1984a; Prehled Prumyslove Toxikol Org Latky, 1986; Union Carbide, 1971; Rowe *et al.*, 1954). Finally, DPGME (20% solution) was found to be non-irritating in human eyes in a study by Ballantyne (1984b).

Skin Sensitization

DPGME produce no evidence of primary irritation or skin sensitization in humans (Rowe *et al.*, 1954; Dow Chemical Company, 1951). The material was applied to the backs of 200 humans and allowed to remain in contact with the skin for 5 days. Three weeks later, DPGME was reapplied to the same area and allowed to remain in contact with the skin for 48 hours. In another similar study, DPGME was applied to the backs of 50 humans for 48 hours every other day until 10 applications were made. After 3 weeks, DPGME was reapplied for a period of 24-48 hours.

Human Cases

According to Cullen *et al.* (1983), three out of 7 lithographers using DPGME, ethylene glycol monoethyl ether, and a range of aliphatic, aromatic, and halogenated hydrocarbons for offset and ultraviolet-cured multicoloured printing, showed normal peripheral blood parameters; however, bone marrow specimens showed stromal injury. However, according to the authors, it is unlikely that DPGME caused the observed effects. DPGME was present along with substituted benzenes, chlorinated solvents, n-propanol, and EGEE in workplace solutions. Suspicion of DPGME as a causal agent came from personal, area air samples and wipe samples. The most intense exposure to DPGME was from an ultraviolet curing wash and air sampling revealed 0.6 to 6.43 ppm air concentrations. The authors of this article provide limited and inconclusive data that DPGME may be the cause of bone marrow injury in a small group of exposed lithographers. Because of the

small group studied, it is difficult to causally link occupational exposure with the marrow lesions. This is further confounded by a lack of published data regarding the prevalence of such marrow injury parameters in workers or the general population. Besides the hypothesis that DPGME may play a role in the observed injury, the authors also suggest that it is plausible that marrow changes represent the result of ubiquitous insults from infectious agents, drugs, alcohol, or other environmental agents or unknown factors. The most convincing evidence that DPGME is not responsible for such effects comes from a lack of recorded marrow effects in other subchronically and chronically tested PGE's (PGME, PGtBE). This is in contrast to EGME. DPGME itself when applied dermally up to 10 g/kg for 90 days produced no hematological effects even though mortality was high at the 10 g/kg level.

Probable minimum concentration of DPGME that may cause minor nasal irritation, or some tolerable eye, throat, and respiratory irritation is about 35 ppm and 75 ppm, respectively (Clayton and Clayton, 1994). Levels of 300 to 400 DPGME were very disagreeable to man. Levels of 100 ppm, which might be voluntarily tolerated without complaint, were considered safe with respect to organic injury (ACGIH 1991). Finally, no injury or adverse effects to humans have been reported from the handling and use of DPGME according to Clayton and Clayton (1994).

4.0 HAZARDS TO THE ENVIRONMENT

4.1 Aquatic Effects

In general, information on the aquatic toxicity of DPGME is limited to acute studies. Results for fish, aquatic invertebrates, and bacteria, as well as their corresponding Predicted No Effect Concentrations (PNECs), are summarized below.

- *Fish* - Two studies were identified which evaluated the toxicity of DPGME to fish. In a study by Bartlett *et al.* (1979), fathead minnow (*Pimephales promelas*) were exposed to DPGME in a static system for 96 hours. An LC₅₀ exceeding 10,000 mg/L was reported. The second study (ECOL database, Dow Chemical, 1986) reported an LC₅₀ exceeding 150 mg/L for *Notropis atherinoides* (emerald shiner) exposed to DPGME in a static system for 72 hours.
- *Invertebrates* - Available data for the acute toxicity of DPGME in aquatic invertebrates are given in the SIDS summary table. Two studies were identified that evaluated the toxicity of DPGME to aquatic invertebrates (*Daphnia magna*). In a study by Bartlett *et al.* (1979), *Daphnia magna* were exposed to DPGME in a static system for 48 hours. An LC₅₀ of 1919 mg/L was reported. In the second study by Dow Chemical (1995), *Daphnia magna* were exposed to 0.05 and 0.5 mg/L DPGME for 22 days in a flow through system. The mean reproduction per parent in the two exposure groups was greater than in the control groups. Parental mortality remained below the validity criteria of 20% in all groups; no treatment-related higher rates of mortality were recorded in the DPM test solutions. There were no adverse effects on either survival or reproductive performance at a concentration of 0.5 mg/L during the exposure period. Applying an uncertainty factor of 100 to the 48-hour LC₅₀ value, a PNEC of 19 mg/L was derived.
- *Plant and Algae* – In *Selenastrum capricornutum* exposed for 34 days, an EC₁₀ value of 133 mg/L was reported for growth inhibition (Kirk *et al.* 2000). EC₅₀ values were determined to exceed the highest concentration tests (969 mg/L). Chronic values (1166 mg/L) were estimated from ECOSAR.
- *Bacteria* – One study was identified that evaluated the effects of DPGME on bacteria. Dow Europe SA (1990) reported an EC₁₀ of 4168 mg/L for *Pseudomonas putida* bacteria. According to German classification for water pollutants, the value for bacteriotoxicity (inhibition of cell growth) is 2.4 for this aquatic test. This value was adopted as the PNEC for bacteria.

4.2 Terrestrial Effects

Other than terrestrial plants, no ecotoxicological data for DPGME were identified for terrestrial wildlife (*i.e.*, birds and mammals) or other terrestrial organisms (*i.e.*, invertebrates, bacteria, etc.). However, given the low toxicity of DPGME in laboratory animals (see Section 3.0), and the low potential for exposure in terrestrial compartments, significant toxicity in terrestrial organisms is unlikely.

- *Terrestrial Plants* – One study was identified that investigated the toxic effects of DPGME on terrestrial plants. Hart (1991) reported an EC₅₀ of greater than 500 g/l and a NOEC of 250 g/l for *Brassica napus* (rape), *Vitis vinifera* (white grape), *Glycine max* (soybean), *Lycopersicon esculentum* (tomato), and *Gossypium hirsutum* (cotton). In addition, Hart (1991) reported an EC₅₀ of greater than 500 g/l and a NOEC of 500 g/l for *Triticum aestivum* (wheat) and *Zea mays* (corn). The first endpoint investigated was growth. Hart (1991) also studied the effects

of DPGME applied to *Tritium aestivum* by overhead foliar spray (applied once). Results indicated a NOEC of greater than or equal to 1000 g/l (growth endpoint).

4.3 Other Environmental Effects

The bioaccumulation potential of DPGME is low, a BCF of <1 can be estimated on the basis of the values for the n-octanol/water partition coefficient by using a regression calculation (Byse, 1990). A $\log K_{ow}$ value of 0.0061 was reported for DPGME (Dow Chemical Japan, 2000). This value for the n-octanol/water partitioning coefficient suggests that DPGME is not expected to accumulate in biological tissue or bioaccumulate in food webs.

5.0 CONCLUSIONS AND RECOMMENDATIONS

DPGME is currently of low priority for further work.

Commercial Dipropylene Glycol Methyl Ether (DPGME) is a mixture of four isomers. DPGME exhibits low acute toxicity by the oral, dermal, and inhalation routes. The oral LD50 ranges 5180-5400 mg/kg in rats to 7500 mg/kg in dogs. Dermal LD50 values were reported to range from 9500 to >19000 mg/kg in rabbits. Acute inhalation exposures to 500 ppm DPGME produced mild, but reversible narcosis in rats. DPGME is not a skin sensitizer or skin irritant, and was only slightly irritating to the eye. In repeated dose studies, NOAELs of >50 ppm to 3000 ppm have been observed in inhalation studies using rats, mice, rabbits, guinea pigs, and monkeys. Observations included central nervous system (CNS) effects, adaptive hepatic changes, and decreases in body weight gain. In rats exposed to either 0, 40, 200, or 1000 mg/kg-day DPGME via gavage for 4 weeks, tentative salivation (immediately after dosing) and liver effects (increased relative liver weight, centrilobular hypertrophy) was observed in animals exposed to the highest dose. No effects were observed in rats exposed to 200 mg/kg-day. Studies in rats and rabbits showed that DPGME is not teratogenic (two inhalation studies with NOAELs of 300 ppm). The weight of the evidence indicates that DPGME is not genotoxic. Information collected for a structurally similar chemical (PGME) suggests that DPGME is not a reproductive toxicant, and is not carcinogenic. Additionally, no effects were seen on the testes and ovaries in a 28-day repeat dose oral toxicity study on DPGME. In humans, concentrations of 35-75 ppm may be expected to produce irritation to the eyes, nose, throat, and respiratory tract. Therefore, human exposures to concentrations of DPGME greater than 75 ppm are expected to be self-limiting.

DPGME is not persistent in the environment and is not expected to bioaccumulate in food webs. The half-life of DPGME in air was measured at 5.3 hours and is estimated to be 3.4 hours due to direct reactions with photochemically generated hydroxyl radicals. DPGME is readily biodegraded under aerobic conditions, but only slightly degraded under anaerobic conditions. Although environmental monitoring data are not available for DPGME, fugacity-based modeling indicates that PGME is likely to partition to water compartments in the environment (surface water, groundwater). Acute toxicity testing in fish, invertebrates and algae indicate a very low order of toxicity with effect concentrations exceeding 1000 mg/L. A PNEC of 19 mg/L was derived by applying an uncertainty factor of 100 to the 48-hour LC50 value of 1919 mg/L for daphnids.

Approximately 38 million pounds (17 thousand tons) of DPGME were produced in the U.S. in 1999 (Appendix A). Approximately 12,000 tons of DPGME were consumed in the U.S. in 1995 (Staples and Davis, 2001). Production in the U.S. was estimated at 35 million pounds (16 thousand tons) for 2000 (Chemical Economics Handbook on Glycol Ethers (1996), SRI International). DPGME occurred in 123 products present on the Swedish market in July 1989. DPGME is used in the manufacture of a wide variety of industrial and commercial products, including paints, varnishes, inks, and cleaners. In the US in 1999, DPGME was used as follows: 58% paints/coatings/inks, 28% cleaners, 10% DPGME acetate production and 3% miscellaneous production. Exposures to DPGME are likely to occur for workers and consumers. Inhalation exposures to relatively high concentrations of DPGME are believed to be self-limiting due to the irritant effects of the chemical. Use of protective gloves to minimize absorption is recommended when prolonged dermal exposures to DPGME are anticipated.

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Appendix A. Production and Use Information DPGME

	*1999 Production Volume	Types of Commercial End Products	US Percent Production	Industrial/ Commercial Percentage Use if Known	In Product Types Approx Weight Fraction
Dipropylene glycol methyl ether	United States	Paints, coatings and inks	58%		2-20%
34590-94-8 (mixture)	38 million pounds				
Isomer CAS #s					
20324-32-7 (40-45%)	(17 thousand tons)	Cleaners	28%		2-25%
13429-07-7 (40-50%)					
13588-28-8 (2-5%)		DPGMEA	10%		
55956-21-3 (3-5%)					
		**Misc.	3%		

*Chemical Economics Handbook, SRI International 2000. Data not reported for DPGME for other countries.

**Floor polishes, cosmetics, solvents

DPGME is a mixture of four isomers. According to the manufacturers specification, (BUA Reports 173 and 174: Methoxypropanol (propylene glycol methyl ether), Dipropylene glycol ethyl ether. GDCh-Advisory Committee on Existing Chemicals of Environmental Relevance), the respective fractions of the structural isomers are 40-50% 1-(2-methoxypropoxy)propanol-2 (CASRN: 13429-07-7), 40-45% 1-(2-methoxy-1-methylethoxy)propanol-1 (CASRN: 20324-32-7), 2-5% 2-(2-methoxypropoxy)propanol-1 (CASRN: 13588-28-8), and 3-5% 2-(2-methoxy-1-methylethoxy)propanol-1 (CASRN: 55956-21-3). Commercial DPGME is produced only as a four-isomer mixture and hence all testing was conducted on the commercial mixture. The four individual isomers are not separated nor produced as individual chemicals. 1-(2-methoxy-1-methylethoxy) propanol-1 (CASRN: 20324-32-7), was listed erroneously as an HPV chemical due to incorrect reporting of the CAS # on the 1990 IUR.

Appendix B. Quantitative Evaluation of Potential Exposures to DPGME

B.1 Predicted Environmental Concentration (PEC)

A fugacity-based, multimedia model (Level 3) was run for DPGME (Staples and Davis, 2001). Based on an estimate of 12,000 tonnes of DPGME were consumed in the U.S. during 1995, source terms for release to air, water, and soil were calculated to be 122, 13.7, and 1.4 kg/hour, respectively. Model predictions for the concentrations of DPGME in four environmental compartments were as follows:

- Air: 9.24 ng/m³
- Water: 0.053 ug/L
- Soil: 0.28 ug/kg
- Sediment: 0.030 ug/kg

B.2 Quantitative Assessment of Human Exposures

Assessment of Occupational Exposures

Exposure to DPGME in the occupational setting can occur through inhalation or dermal exposure.

- *Inhalation Exposure* - Estimated human exposures (EHE) ranging 30 to 40 mg/m³ are considered to conservatively representative of potential occupational exposures.
- *Dermal Exposure* - EHEs ranging from 0.48 mg/kg-d to 22.7 mg/kg-d were calculated using the following equation based on U.S. Environmental Protection Agency (USEPA) guidance (1989):

$$\text{Dermal Dose} = \frac{\% \text{PGME} * ET * EF * ED * SA * AR}{AT * BW}$$

Where,

Dermal Dose	=	average daily dermal dose (mg/kg-day);
% PGME	=	percent DPGME in product contacted by worker (10% and 50% assumed);
ET	=	exposure time (1 and 2 hours/day assumed);
EF	=	exposure frequency (125 and 250 days/year assumed);
ED	=	exposure duration (25 years as an upperbound for occupational tenure (EFH, 1996));
SA	=	surface area of exposed skin (840 cm ² for hands only; 1980 cm ² for hands and forearms (EFH, 1996));
AR	=	absorption rate (1.17 mg/cm ² /hr for PGME (data for DPGME not available) (Dugard <i>et al.</i> 1984));
AT	=	averaging time (9125 days based on ED assumption);
BW	=	body weight (70 kg (USEPA, 1989)).

Assessment of Consumer Exposures

Consumers may be exposed to DPGME through inhalation and dermal contact.

- *Inhalation Exposure* – EHEs ranging from 30 mg/m³ to 40 mg/m³ are considered to be conservatively representative of potential consumer exposures.

- *Dermal Exposure* - EHEs ranging from 0.005 mg/kg-d to 0.45 mg/kg-d were calculated using the following equation based on USEPA (1989) guidance:

$$\text{Dermal Dose} = \frac{\% \text{PGME} * \text{ET} * \text{EF} * \text{ED} * \text{SA} * \text{AR}}{\text{AT} * \text{BW}}$$

Where,

Dermal Dose	=	average daily dermal dose (mg/kg-day);	
%DPGME	=	percent DPGME in product contacted by consumer (1 and 10% assumed);	
ET	=	exposure time (0.5 and 1 hours/day assumed);	
EF	=	exposure frequency (25 and 50 days/years assumed);	
ED	=	exposure duration (30 years);	
SA	=	surface area of exposed skin (840 cm ² for hands only (EFH, 1996); 1980 cm ² for hands and forearms (EFH, 1996));	
AR	=	absorption rate (1.17 mg/cm ² /hr for PGME (DPGMEe data not available) (Dugard <i>et al.</i> 1984));	
AT	=	averaging time (10,950 days based on ED assumed); BW	= body weight (70 kg).

Assessment of Indirect Exposures via the Environment

Although monitoring data are not available, concentrations of DPGME in water have been estimated using fugacity-based modeling. Theoretical oral doses were calculated using the equation given below:

$$\text{Oral Dose} = \frac{C * \text{IR} * \text{EF} * \text{ED}}{\text{AT} * \text{BW}}$$

Where,

C	=	concentration of DPGME in media (air: 0.00000924 mg/m ³ ; water: 0.000053 mg/L; soil: 0.00028 mg/kg);
IR	=	intake rate for media (air: 20 m ³ /day; water: 2 L/day; soil: 0.0001 kg/day);
EF	=	exposure frequency (350 days/year);
ED	=	exposure duration (30 years);
AT	=	averaging time (10950 days); and
BW	=	body weight (70 kg).

Based on these assumptions, doses of 0.0000025, 0.0000015, 0.00000000038 mg/kg-day were calculated for human exposures to DPGME in air, water, and soil, respectively.

SIDS DOSSIER
DIPROPYLENE GLYCOL METHYL ETHER
CAS No. 34590-94-8
(Isomers: 13429-07-7, 20324-32-7; 13588-28-8; and
55956-21-3)

Sponsor Country: U.S.A.

DATE: March 2001
Updated November 2001

CONTENTS

SIDS PROFILE

SIDS SUMMARY

1. GENERAL INFORMATION

1.01 SUBSTANCE INFORMATION

- A. CAS-NUMBER
- B. NAME (IUPAC-NAME)
- C. NAME (OECD NAME)
- D. CAS DESCRIPTOR
- E. EINECS-NUMBER
- F. MOLECULAR FORMULA
- G. STRUCTURAL FORMULA
- H. SUBSTANCE GROUP
- I. SUBSTANCE REMARK
- J. MOLECULAR WEIGHT

1.02 OECD INFORMATION

- A. SPONSOR COUNTRY
- B. LEAD ORGANISATION
- C. NAME OF RESPONDER (COMPANY)

1.1 GENERAL SUBSTANCE INFORMATION

- A. TYPE OF SUBSTANCE
- B. PHYSICAL STATE
- C. PURITY

1.2 SYNONYMS

1.3 IMPURITIES

1.4 ADDITIVES

1.5 QUANTITY

1.6 LABELLING AND CLASSIFICATION (USE AND/OR TRANSPORTATION)

1.7 USE PATTERN

- A. GENERAL USE PATTERN
- B. USES IN CONSUMER PRODUCTS

1.8 OCCUPATIONAL EXPOSURE LIMIT VALUE

1.9 SOURCES OF EXPOSURE

1.10 ADDITIONAL REMARKS

- A. OPTIONS OF DISPOSAL
- B. OTHER REMARKS.

2. PHYSICAL-CHEMICAL DATA

2.1 MELTING POINT

2.2 BOILING POINT

2.3 DENSITY (RELATIVE DENSITY)

2.4 VAPOUR PRESSURE

2.5 PARTITION COEFFICIENT n-OCTANOL/WATER

2.6 WATER SOLUBILITY

- A. SOLUBILITY
- B. pH VALUE, pKa VALUE

2.7 FLASH POINT (LIQUIDS)

2.8 AUTO FLAMMABILITY (SOLID/GASES)

2.9 FLAMMABILITY

- 2.10 EXPLOSIVE PROPERTIES
 - 2.11 OXIDIZING PROPERTIES
 - 2.12 OXIDATION:REDUCTION POTENTIAL
 - 2.13 ADDITIONAL REMARKS
 - A. PARTITION CO-EFFICIENT BETWEEN SOIL/SEDIMENT AND WATER (Kd)
 - B. OTHER REMARKS
 - 3. ENVIRONMENTAL FATE AND PATHWAYS
 - 3.1 STABILITY
 - 3.1.1 PHOTODEGRADATION
 - 3.1.2 STABILITY IN WATER
 - 3.1.3 STABILITY IN SOIL
 - 3.2 MONITORING DATA (ENVIRONMENT)
 - 3.3 TRANSPORT AND DISTRIBUTION BETWEEN ENVIRONMENTAL COMPARTMENTS INCLUDING ESTIMATED ENVIRONMENTAL CONCENTRATIONS AND DISTRIBUTION PATHWAYS
 - 3.3.1 TRANSPORT
 - 3.3.2 THEORETICAL DISTRIBUTION (FUGACITY CALCULATION)
 - 3.4 MODE OF DEGRADATION IN ACTUAL USE
 - 3.5 BIODEGRADATION
 - 3.6 BOD-5, COD OR RATIO BOD-5/COD
 - 3.7 BIOACCUMULATION
 - 3.8 ADDITIONAL REMARKS
 - A. SEWAGE TREATMENT
 - B. OTHER
 - 4. ECOTOXICITY
 - 4.1 ACUTE/PROLONGED TOXICITY TO FISH
 - 4.2 ACUTE TOXICITY TO AQUATIC INVERTEBRATES
 - A. DAPHNIA
 - B. OTHER AQUATIC ORGANISMS
 - 4.3 TOXICITY TO AQUATIC PLANTS e.g., ALGAE
 - 4.4 TOXICITY TO BACTERIA
 - 4.5 CHRONIC TOXICITY TO AQUATIC ORGANISMS
 - 4.5.1 CHRONIC TOXICITY TO FISH
 - 4.5.2 CHRONIC TOXICITY TO AQUATIC INVERTEBRATES (e.g., DAPHNIA REPRODUCTION)
 - 4.6 TOXICITY TO TERRESTRIAL ORGANISMS
 - 4.6.1 TOXICITY TO SOIL DWELLING ORGANISMS
 - 4.6.2 TOXICITY TO TERRESTRIAL PLANTS
 - 4.6.3 TOXICITY TO OTHER NON-MAMMALIAN TERRESTRIAL SPECIES (INCLUDING BIRDS)
 - 4.7 BIOLOGICAL EFFECTS MONITORING (INCLUDING BIOMAGNIFICATION)
 - 4.8 BIOTRANSFORMATION AND KINETICS
 - 4.9 ADDITIONAL REMARKS
 - 5. TOXICITY
 - 5.1 ACUTE TOXICITY
 - 5.1.1 ACUTE ORAL TOXICITY
 - 5.1.2 ACUTE INHALATION TOXICITY
 - 5.1.3 ACUTE DERMAL TOXICITY
 - 5.1.4 ACUTE TOXICITY BY OTHER ROUTES OF ADMINISTRATION
 - 5.2 CORROSIVENESS/IRRITATION
-

- 5.2.1 SKIN IRRITATION/CORROSION
- 5.2.2 EYE IRRITATION/CORROSION
- 5.3 SKIN SENSITISATION
- 5.4 REPEATED DOSE TOXICITY
- 5.5 GENETIC TOXICITY IN VITRO
 - A. BACTERIAL TEST
 - B. NON-BACTERIAL IN VITRO TEST
- 5.6 GENETIC TOXICITY IN VIVO
- 5.7 CARCINOGENICITY
- 5.8 TOXICITY TO REPRODUCTION
- 5.9 DEVELOPMENTAL TOXICITY / TERATOGENICITY
- 5.10 OTHER RELEVANT INFORMATION
 - A. SPECIFIC TOXICITIES (NEUROTOXICITY, IMMUNOTOXICITY etc.)
 - B. TOXICODYNAMICS, TOXICOKINETICS
- 5.11 EXPERIENCE WITH HUMAN EXPOSURE
- 6. REFERENCES

Note: Data elements in the SIDS
Data elements specially required for inorganic chemicals

SIDS PROFILE

DATE: March 2001

1.01 A.	CAS No.	34590-94-8 (isomers: 13429-07-7, 20324-32-7; 13588-28-8; and 55956-21-3)
1.01 C.	CHEMICAL NAME (OECD Name)	2-Methoxymethylethoxy-propanol
1.01 D.	CAS DESCRIPTOR	Not applicable in this case.
1.01 G.	STRUCTURAL FORMULA	CH ₃ -(OC ₃ H ₆) ₂ -OH
	OTHER CHEMICAL IDENTITY INFORMATION	Mixture of 4 isomers.
1.5	QUANTITY	In FRG approx 19,500 tonnes in 1994. In US 38 million pounds (17 thousand tons) in 1999.
1.7	USE PATTERN	(a) Wide dispersive use in domestic, commercial and industrial cleaners. (b) Wide dispersive use in formulation of inks, paints, coatings, and cleaners.
1.9	SOURCES AND LEVELS OF EXPOSURE	1. Accumulation of DPGME in air of closed rooms during use of water-based paints was measured at 30-40 mg/m ³ or approximately 10% of the 8 hr TWA of 308 mg/m ³ . 2. Exposures to DPGME as a solvent component in screen printing inks have been documented to be as high as 22 mg/m ³ in the absence of local exhaust ventilation.
ISSUES FOR DISCUSSION (IDENTIFY, IF ANY)		

SIDS SUMMARY Date: January 1999

CAS No: 34590-94-8		Info Available Y/N	OECD Study Y/N	GLP Y/N	Other Study Y/N	Estimation Method Y/N	Acceptable Y/N	Testing Required Y/N
Study								
PHYSICAL CHEMICAL DATA								
2.1	Melting Point	Y	N	?	Y	N	Y	
2.2	Boiling Point	Y	N	?	Y	N	Y	
2.3	Density	Y	N	?	Y	N	Y	
2.4	Vapor Pressure	Y	N	?	Y	N	Y	
2.5	Partition Coefficient	Y	Y	Y	N	N	Y	
2.6.	Water Solubility	Y	N	?	Y	N	Y	
	pH and PkA values	N						
2.12	Oxidation Reduction Potential	N						
OTHER P/C STUDIES RECEIVED		N						
ENVIRONMENTAL FATE and PATHWAYS								
3.1.1	Photodegradation	Y	N	?	Y	Y	Y	
3.1.2	Stability in water	Y						
3.2	Monitoring data	Y						
3.3	Transport and Distribution	Y						
3.5	Biodegradation	Y	Y	Y	Y	N	Y	
OTHER ENVI FATE STUDIES RECEIVED		N						
ECOTOXICITY								
4.1	Acute Toxicity to Fish	Y	N	?	Y	N	Y	
4.2	Acute Toxicity to Daphnia	Y	N	?	Y	N	Y	
4.3	Toxicity to Algae	Y	Y	Y				
4.5.2	Chronic Toxicity to Daphnia	Y	Y	Y				
4.6.1	Toxicity to Soil Dwelling Organisms	N						
4.6.2	Toxicity to Terrestrial Plants	Y	Y	Y	Y	N	Y	
4.6.3	Toxicity to Birds	N						

SIDS SUMMARY (Continued)

CAS No: 34590-94-8		Info Available Y/N	OECD Study Y/N	GLP Y/N	Other Study Y/N	Estimation Method Y/N	Acceptable Y/N	Testing Required Y/N
Study								
TOXICITY								
5.1.1	Acute Oral	Y	N	N	Y	N	Y	
5.1.2	Acute Inhalation	Y	N	N	Y	N	Y	
5.1.3	Acute Dermal	Y	N	N	Y	N	Y	
5.4	Repeated Dose	Y	N	Y	Y	N	Y	
5.5	Genetic Toxicity <i>in vitro</i>							
	-Gene Mutation	Y	Y	Y	Y	N	Y	
	-Chromosome Aberration	Y	Y	Y	Y	N	Y	
5.6	Genetic Toxicity <i>in vivo</i>	N						
5.8	Reproduction Toxicity	N						
5.9	Development/Teratogenicity	Y	N	Y	Y	N	Y	
5.11	Human Experience	Y	N	N	Y	N	Y	
OTHER TOXICITY STUDIES RECEIVED		Y						

1. GENERAL INFORMATION**1.01 SUBSTANCE INFORMATION**

- A. CAS-Number** 34590-94-8 (for commercial grade)
(Isomers: 13429-07-7, 20324-32-7; 13588-28-8; and 55956-21-3)
- B. Name (IUPAC name)** (2-methoxymethylethoxy) propanol
- C. Name (OECD name)** 2-methoxymethylethoxy propanol
- D. CAS Descriptor** Not applicable in this case
- E. EINECS-Number** 252-104-2
- F. Molecular Formula** C7 H16 O3
- G. Structural Formula** CH₃-(OC₃H₆)₂-OH
- H. Substance Group** Not applicable
- I. Substance Remark**
- J. Molecular Weight** 148.2 g/mol

1.02 OECD INFORMATION

- A. Sponsor Country:** US
- B. Lead Organisation:**
 Name of Lead Organisation: American Chemistry Council
 Contact person: Dr. Susan Anderson Lewis
 Address: 1300 Wilson Blvd.
 Arlington, VA 22209
 U.S.A.
 Tel: (703) 741-5635
 Fax: (703) 741-6091
 susan_lewis@americanchemistry.com

1.1 GENERAL SUBSTANCE INFORMATION

- A. Type of Substance**
 element []; inorganic []; natural substance []; organic [X]; organometallic [];
 petroleum product []
- B. Physical State** (at 20°C and 1.013 hPa)
 gaseous []; liquid [X]; solid []
- C. Purity** >98%, with a maximum of 0.1% water
 1-(2-methoxy-1-methylethoxy) propanol-2 (CAS No. 20324-32-7): 40-45%
 1-(2-methoxypropoxy) propanol-2 (CAS No. 13429-07-7): 40-50%
 2-(2-methoxypropoxy) propanol-1 (CAS No. 13588-28-8): 2-5%
 2-(2-methoxy-1-methylethoxy) propanol-1 (CAS No. 55956-21-3): 3-5%

Reference: BUA. 1995. BUA Reports 173 and 174: Methoxypropanol (propylene glycol methyl ether), Dipropylene glycol ethyl ether. GDCh-Advisory Committee on Existing Chemicals of Environmental Relevance (BUA).

Remarks: DPGME is a mixture of four isomers. According to the manufacturers specification, (BUA Reports 173 and 174: Methoxypropanol (propylene glycol methyl ether), Dipropylene glycol ethyl ether. GDCh-Advisory Committee on Existing Chemicals of Environmental Relevance), the respective fractions of the structural isomers are 40-50% 1-(2-methoxypropoxy)propanol-2 (CASRN: 13429-07-7), 40-45% 1-(2-methoxy-1-methylethoxy)propanol-1 (CASRN: 20324-32-7), 2-5% 2-(2-methoxypropoxy)propanol-1 (CASRN: 13588-28-8), and 3-5% 2-(2-methoxy-1-methylethoxy)propanol-1 (CASRN: 55956-21-3). Commercial DPGME is produced only as a four-isomer mixture and hence all testing was conducted on the commercial mixture. The four individual isomers are not separated nor produced as individual chemicals. 1-(2-methoxy-1-methylethoxy) propanol-1 (CASRN: 20324-32-7), was listed erroneously as an HPV chemical due to incorrect reporting of the CAS # on the 1990 IUR.

1.2 SYNONYMS

Dipropylene glycol methyl ether
Dipropylene glycol monomethyl ether
Methoxypropoxypropanol
DGME
DPGME
MDP
Arcosolv DPM
DOWANOL DPM
Solvenon DPM
Dimethyl Proxitol

1.3 IMPURITIES

Remarks: < 2% with 0.1% water

1.4 ADDITIVES

Remarks: None

1.5 QUANTITY

Remarks: Thirty-eight million pounds (17 thousand tons) was produced in the US in 1999.

Reference: Appendix A.

Remarks: Thirty-one million pounds was produced in the US in 1995.

Reference: Chemical Economics Handbook, SRI International, 1996

Remarks: DPGME occurred in 123 products present on the Swedish market in July 1989. The estimated annual use was 240 - 2500 tons/year.

- Reference: The Products Register, Swedish Chemicals Inspectorate.
- Remarks: Manufacturers of DPGME in the Federal Republic of Germany produced approximately 19,500 tons in 1994. No DPGME was imported into the FRG; approximately 3,000 tons were exported. Import of DPGME with other glycols cannot be excluded, since DPGME is presumably contained in numerous finished products imported into the FRG. Consumption of DPGME in Germany for 1994 can be estimated to be at least 16,000 tons/year.
- Reference: GDCh-Advisory Committee on Existing Chemicals of Environmental Relevance (BUA), October 1995.

1.6 LABELLING AND CLASSIFICATION

Labelling

Remarks: Does not meet any of the classification criteria of the EC.

Classification

Remarks: Does not meet any of the classification criteria of the EC.

1.7 USE PATTERN

A. General

DPGME is a colorless, relatively slow evaporating, hygroscopic liquid with a mild odour. It is a powerful solvent for a vast range of organic compounds. DPGME is used as a solvent in the manufacture of water-based coatings. DPGME is also used as a coalescing agent for water based paints and inks. DPGME is also used in a wide variety of household, commercial and industrial cleaning products. It is also used in chemicals for the oil production and drilling industry. Of the 38 million pounds produced in 1999, 58% was used for paints/coatings/inks, 28% for cleaners, 10% for DPGME acetate production, and 3% miscellaneous (Appendix A).

Type of Use: **Category:** Non dispersive

Industrial Chemical Industry: used as a formulation aid and a starting material for production of esters.

Type of Use: **Category:** Wide dispersive

Industrial Ingredient in a variety of products:
Industrial/commercial cleaning agents
Cosmetic agent
Detergent/wetting agents
Sanitary/disinfectant cleaners
Solvent for paints/varnishes/inks
Stripper/degreaser

Remarks: The application concentration for DPGME in most products ranges from 1% to 10%; may reach concentrations of 50%, especially in typical solvent-containing cleaners used for surface cleaning or the graphics industry.

Reference: GDCh-Advisory Committee on Existing Chemicals of Environmental Relevance (BAU), October 1995.

B. Uses in Consumer Products

DPGME is used in a variety of domestic, commercial and industrial cleaners. Examples of cleaning formulations that utilise DPGME (along with approximate percentages) are below:

<u>Function</u>	<u>Amount present</u>	<u>Physical state</u>
Glass cleaner	less than 5%	liquid
Surface cleaner	less than 1%	liquid
All purpose cleaner	less than 3%	liquid
Floor polish	less than 5%	liquid
Carpet cleaner	less than 5%	foam
Paintbrush cleaner	less than 3%	liquid
Industrial degreaser	approx 15-20%	liquid
Aluminium brightner	less than 25%	liquid
Rust remover	less than 12%	liquid

Reference: GDCh-Advisory Committee, October 1995.

1.8 OCCUPATIONAL EXPOSURE LIMIT VALUEExposure limit value

Type:	European ILV
Value:	50 ppm (approx. 300 mg/m ³)
Type:	ARAB (B, LUX)
Value:	100 ppm (approx. 600 mg/m ³)
Type:	AGSM (Denmark)
Value:	50 ppm (approx. 300 mg/m ³)
Type:	OEL (Finland)
Value:	50 ppm (approx. 300 mg/m ³)
Type:	VME (France)
Value:	100 ppm (approx. 600 mg/m ³)
Type:	MAK (G, CH, Austria)
Value:	50 ppm (approx. 300 mg/m ³)
Type:	MAC
Value:	50 ppm (approx. 300 mg/m ³)
Type:	PEL (USA)
Value:	100 ppm (approx. 600 mg/m ³)
Type:	TLV (USA, I, P, Sp.)
Value:	100 ppm (approx. 600 mg/m ³)

Short term exposure limit value (STEL)

Value:	150 ppm (approx. 900 mg/m ³)
Length of exposure period:	15 minutes
Frequency:	no more than 4 times per day
Remarks:	Skin notation
Reference:	ACGIH, Threshold Limit Value 1998

Value: 150 ppm (approx. 900 mg/m³)
 Reference: Finland

Value: 100 ppm (approx. 600 mg/m³)
 Reference: Germany and Austria

1.9 SOURCES OF EXPOSURE

(a)

Source: Media of release: waste water from a production site
 Quantities per media: at one facility in the Federal Republic of Germany, 3.8 tons/year were directed with plant wastewater to a biological wastewater treatment plant. At another FRG production facility, 0.5 tons/year were emitted into the wastewater that fed into a biological wastewater treatment plant.

Remarks: Unquantifiable emissions into municipal wastewater will also occur through the use of consumer and commercial products such as cleaning agents, degreasers, and stripping agents. Residues in packaging are expected to occur in solid municipal wastes.

Reference: GDCh-Advisory Committee on Existing Chemicals of Environmental Relevance (BUA), October 1995.

(b)

Source: Media of release: Air from closed rooms without local exhaust ventilation.

Remarks: DPGME in water-based ceiling and wall paint (1% w/w) was used in closed rooms. In one study, 15 workplace measurements were taken during painting; occupational exposures to DPGME concentrations of 30-40 mg/m³ were recorded.

References: GDCh-Advisory Committee on Existing Chemicals of Environmental Relevance (BUA), October 1995.

1.10 ADDITIONAL REMARKS

A. Options for disposal

Remarks: No studies located

B. Other remarks

Remarks: No studies located

2 PHYSICAL-CHEMICAL DATA

2.1 MELTING POINT/FREEZING POINT

(a)
 Value: = -83 °C (freezing point)
 Decomposition: Yes ☐ No ☒ Ambiguous ☐
 Sublimation: Yes ☐ No ☒ Ambiguous ☐
 Method: Other
 GLP: Yes ☐ No ☐ ? ☒
 Reference: Dow Europe, S.A. 1994.

2.2 BOILING POINT

(a)
 Value: = 190°C
 Pressure: at 1013.25 hPa
 Decomposition: Yes ☐ No ☒ Ambiguous ☐
 Method: Other
 GLP: Yes ☐ No ☐ ? ☒
 Reference: Dow Europe, S.A., 1994.

(b)
 Value: = 189.6°C
 Pressure: at 101.3 kPa
 Decomposition: Yes ☐ No ☒ Ambiguous ☐
 Method: Other
 GLP: Yes ☐ No ☐ ? ☒
 Reference: DHHS (NIOSH) Publication 91-103, 1991.

(c)
 Value: = 184 - 197 °C
 Pressure: 1013 hPa
 Decomposition: Yes ☐ No ☒ Ambiguous ☐
 Method: Other
 GLP: Yes ☐ No ☐ ? ☒
 Reference: ECETOC Technical Report No. 64, 1995.

2.3 DENSITY (Relative density)

(a)
 Type: Bulk density ☐; Density ☐; Relative Density ☒
 Value: 0.948
 Temperature: 25°C
 Method: Other
 GLP: Yes ☐ No ☐ ? ☒
 Remarks: Liquid density was measured (25 °C/4 °C)
 Reference: NIOSH Publication 91-103, 1991

(b)
 Type: Bulk density ☐; Density ☐; Relative Density ☒

Value: 0.95
 Temperature: 20°C
 Method: Other
 GLP: Yes ☐ No ☐ ? ☒
 Remarks: Specific gravity in relation to water (water = 1.0)
 Reference: Dow Europe, S.A. 1994.

2.4 VAPOUR PRESSURE

(a)
 Value: = 0.37 hPa
 Temperature: 20 °C
 Method: calculated ☒; measured ☐
 GLP: Yes ☐ No ☐ ? ☒
 Reference: Dow Europe, SA., 1994.

(b)
 Value: = 0.6 hPa
 Temperature: 20 °C
 Method: calculated ☒; measured ☐
 GLP: Yes ☐ No ☒ ? ☐
 Reference: Henschler, D. (ed)., 1992.

2.5 PARTITION COEFFICIENT log10Pow

Log Pow: = 0.0061
 Temperature: 25°C
 Method: calculated ☐; measured ☒
 GLP: Yes ☒ No ☐ ? ☐
 Reference: Dow Chemical Japan, Unpublished Report # 0006P (2000)

Log Pow: = - 0.064
 Temperature: 20°C
 Method: calculated ☒; measured ☐
 GLP: Yes ☐ No ☒ ? ☐
 Reference: Dow Europe, SA., 1994.

2.6 WATER SOLUBILITY

A. Solubility

Value: 100%
 Temperature: Ambient
 Description: Miscible☒; Of very high solubility ☐;
 Of high solubility ☐; Soluble ☐; Slightly soluble ☐;
 Of low solubility ☐; Of very low solubility ☐; Not soluble ☐
 Method: Other
 GLP: Yes ☐ No ☐ ? ☒
 Reference: Dow Europe, SA., 1994.

B. pH Value, pKa Value

pH Value: No data available
 pKa value: No data available

2.7 FLASH POINT

Value: 75 °C
 Type of test: Closed cup [X]; Open cup []; Other []
 Method: ASTM D-3828-87
 GLP: Yes [] No [] ? [X]
 Remarks: SETA closed cup test and equipment as described by ASTM D-3828-87.
 Reference: Dow Europe, SA., 1994.

2.8 AUTO FLAMMABILITY

Value: 270 °C
 Pressure:
 Method: Other
 GLP: Yes [] No [] ? [X]
 Reference: Dow Europe, SA., 1994.

2.9 FLAMMABILITY

Results: Extremely flammable []; Extremely flammable - liquified gas [];
 Highly Flammable []; Flammable []; Non flammable [X];
 Spontaneously flammable in air []; Contact with water liberates highly
 flammable gases []; Other []
 Method: Other
 GLP: Yes [] No [] ? [X]
 Remarks: Lower and upper flammability limit (% vol./vol.) is 1.1 (at 100 °C) and 14.0
 (at 150 °C), respectively.
 Reference: Dow Europe, SA., 1994.

2.10 EXPLOSIVE PROPERTIES

Results: Explosive under influence of a flame [];
 More sensitive to friction than m-dinitrobenzene [];
 More sensitive to shock than m-dinitrobenzene []; Not explosive [X];
 Other []
 Method: Other
 GLP: Yes [] No [] ? [X]
 Reference: Dow Europe, SA., 1994.

2.11 OXIDIZING PROPERTIES

Results: Maximum burning rate equal or higher than reference mixture [];
 Vigorous reaction in preliminary test [];
 No oxidising properties [X]; Other []
 Method: Other

GLP: Yes ☐ No ☐ ? ☒ [X]
Remarks: Contact with oxidising materials should be avoided.
Reference: Dow Europe, SA., 1994.

2.12 OXIDATION: REDUCTION POTENTIAL

Results: No data available

2.13 ADDITIONAL DATA

A. Partition co-efficient between soil/sediment and water (K_d)

Results: No data available

B. Other data

Results: Calculated
Remarks: Calculation coefficient for DPGME is:
1 ppm (ml/m³) = 6.15 mg/m³ at 20 °C
1 mg/m³ = 0.163 ppm (ml/m³) at 20 °C
Reference: Dow Europe, SA, 1994

3. ENVIRONMENTAL FATE AND PATHWAYS

3.1 STABILITY

3.1.1 PHOTODEGRADATION

Type: Air ☐; Water ☐; Soil ☐; Other ☐
 Light source: Sun light ☐, Xenon lamp ☐; Other ☐
 Direct photolysis:
 Half-life: ca 3.4 hour
 Degradation:
 Quantum yield:
 Method: calculated ☒; measured ☐
 GLP: Yes ☐ No ☐ ? ☒
 Test substance: No data
 Reference: GEMS, FAB Database, 1986.

3.1.2 STABILITY IN WATER

(a)
 Method: calculated ☐; measured ☒
 GLP: Yes ☒ No ☐ ? ☐
 Test substance: No data
 Remarks: While determining Log Pow, little to no degradation of DPGME was observed after 24 hours at 25 °C. Recovery of DPGME ranged from 96-101%.
 Reference: Dow Chemical Japan, Unpublished Report # S-0001 (2000)

(b)
 Remarks: In water, DPGME would not be expected to sorb to sediments or to bioconcentrate. The main degradation mechanism in water is, in all likelihood, biodegradation, while photolysis and hydrolysis are probably insignificant. Evaporative transfer from water to the atmosphere is expected to be minimal.
 Reference: Hawley, G.G., 1977.

3.1.3 STABILITY IN SOIL

Remarks: No data available

3.2 MONITORING DATA (ENVIRONMENT)

(a)
 Type of Measurement: Background ☐; At contaminated site ☐; Other ☒
 Media: Other
 Results: Detected
 Remarks: DPGME was found in the effluents from three different wastewater treatment plants. Due to its diverse uses, DPGME is probably a constituent of the effluents from many other treatment facilities. DPGME was also detected in water from a landfill recovery well. Because of its high solubility and low vapour pressure, DPGME would be expected to partition to the aquatic phase of the environment.
 Reference: G.G. Hawley, 1977.

3.3 TRANSPORT AND DISTRIBUTION BETWEEN ENVIRONMENTAL COMPARTMENTS INCLUDING ESTIMATED ENVIRONMENTAL CONCENTRATIONS AND DISTRIBUTION PATHWAYS

3.3.1 TRANSPORT

(a)

Type: Adsorption []; Desorption []; Volatility []; Other [X]
 Media: Other
 Method: Other; estimations based on physical-chemical properties
 Remarks: Based on physical-chemical data there is little disappearance from water to air, high solubility in water, will not absorb to soils or sediments, would be expected to leach through soil.
 Reference: G.G. Hawley, 1977.

(b)

Type: Adsorption []; Desorption []; Volatility []; Other [X]
 Media: Other
 Method: Other
 Remarks: Because of water solubility, no tendency for accumulation to soil and sediment in a soil-water matrix is assumed. Therefore, transport with leachate into groundwater can be expected from the resultant high mobility.
 Reference: HSDB, 1993.

3.3.2 THEORETICAL DISTRIBUTION (FUGACITY CALCULATION)

Type: Fugacity predictions
 Media: Water, air, soil, sediment
 Method: Level 3
 Remarks: An estimate of 12,000 tonnes of DPGME were consumed in the U.S. during 1995. Source terms for release to air, water, and soil were calculated to be 122, 13.7, and 1.4 kg/hour, respectively.
 Results: Estimated Distribution and Media Concentration: Air: 9.24 ng/m³; Water: 0.053 ug/L; Soil: 0.28 ug/kg; Sediment: 0.030 ug/kg. Results for soil and sediment are expressed in dry weight
 Reference: Staples CA, Davis JW. 2001. An environmental risk assessment of propylene glycol ethers (in prep).

3.4 IDENTIFICATION OF MAIN MODE OF DEGRADABILITY IN ACTUAL USE

Remarks: Main mode of degradation in actual use: biodegradation in water, photodegradation in air.
 Reference: G.G. Hawley, 1977.

3.5 BIODEGRADATION

(a)

Type: aerobic [X]; anaerobic []
 Inoculum: adapted []; non-adapted [X]; activated sludge, industrial [X]
 Concentration of the chemical: 400 mg/l related to COD []; DOC [X]; Test substance []
 Medium: water [X]; water-sediment []; soil []; sewage treatment []
 Degradation: 93% after 13 days
 Results: Readily biodeg. []; Inherently biodeg. [X]; under test condition no biodegradation observed [], Other []

Method: Modified Zahn-Wellens test
 GLP: Yes [X] No [] ? []
 Test substance: As prescribed by 1.1 - 1.4
 Remarks: DPGME is considered ultimately biodegradable. Test substance used was Solvenon DPM from BASF containing dipropylene glycol methyl ether. The activated sludge originated from the BASF wastewater treatment plant.
 Reference: BASF, 1981.

(b)

Type: aerobic [X]; anaerobic []
 Inoculum: adapted []; non-adapted [X]; activated sludge, domestic [X]
 Concentration of the chemical: 25.7 mg/l related to COD []; DOC [X]; Test substance [];
 Medium: water [X]; water-sediment []; soil []; sewage treatment []
 Degradation: 79% after 28 days
 Results: Readily biodeg. [X]; Inherently biodeg. []; under test condition no biodegradation observed [], Other []
 Kinetic: 10 % at 10.7 days
 60% at 16.1 days
 Method: OECD 301 F Manometric Respirometry Test
GLP: **Yes [X] No [] ? []**
 Test substance: As prescribed by 1.1 – 1.4
 Remarks: The mean percent biodegradation occurring after 28 days from aqueous medium dosed with sodium benzoate was >99% (60% after first 2.1 days) of the initial sodium benzoate applied.
 Reference: Dow Chemical U.S., Unpublished Report #98111 (1998)

(c)

Type: aerobic [X]; anaerobic []
 Inoculum: adapted [X]; non-adapted []; activated sludge, domestic []
 Concentration of the chemical: 10 mg/l related to COD []; DOC []; Test substance [X];
 Medium: water [X]; water-sediment []; soil []; sewage treatment []
 Degradation: 34% after 28 days
 Results: Readily biodeg. []; Inherently biodeg. [X]; under test condition no biodegradation observed [], Other []
 Method: Other
 GLP: Yes [] No [] ? [X]
 Test substance: As prescribed by 1.1 - 1.4
 Remarks: At a concentration of 20 mg/l degradation was <10% after 28 days.
 Reference: Dow Europe, S.A., 1990.

(d)

Type: aerobic [X]; anaerobic []
 Inoculum: adapted []; non-adapted []; activated sludge, industrial [X]
 Concentration of the chemical: 17.61 mg/l related to COD []; DOC [X]; Test substance [];
 Medium: water [X]; water-sediment []; soil []; sewage treatment []
 Degradation: 72.9% after 28 days
 Results: Readily biodeg. []; Inherently biodeg. []; under test condition no biodegradation observed [], Other [X]
 Kinetic: 4.5% at 7 days
 30.2% at 14 days
 62.7% at 21 days
 Method: Other
 GLP: Yes [] No [] ? [X]
 Test substance: No data

Remarks:	The mean percent biodegradation occurring after 28 days from aqueous medium dosed with sodium benzoate was 97.3% (90.8% after first 7 days) of the initial sodium benzoate applied (17.7 and 17.52 C/l) according to DOC analysis.
Reference:	McLaughlin, 1993.
(e)	
Type:	aerobic <input type="checkbox"/> ; anaerobic <input checked="" type="checkbox"/>
Inoculum:	adapted <input type="checkbox"/> ; non-adapted <input type="checkbox"/> ; activated sludge, municipal <input checked="" type="checkbox"/>
Concentration of the chemical:	50 mg/l related to COD <input type="checkbox"/> ; DOC <input type="checkbox"/> ; Test substance <input checked="" type="checkbox"/>
Medium:	water <input type="checkbox"/> ; water-sediment <input type="checkbox"/> ; soil <input type="checkbox"/> ; sewage treatment <input checked="" type="checkbox"/>
Degradation:	10% after 81 days
Results:	Readily biodeg. <input type="checkbox"/> ; Inherently biodeg. <input type="checkbox"/> ; under test condition no biodegradation observed <input type="checkbox"/> ; Other <input checked="" type="checkbox"/>
Kinetic:	0% at 28 days 10% at 42 days 10% at 81 days
Method:	ASTM E 1196-92
GLP:	Yes <input checked="" type="checkbox"/> No <input type="checkbox"/> ? <input type="checkbox"/>
Test substance:	As prescribed by 1.1 – 1.4
Remarks:	A lag period of approximately 30 days was noted before any degradation was observed. No signs of toxicity to inoculum (as determined from gas production from standard substrates) from DPGME was observed.
Reference:	Dow Chemical U.S., Unpublished Report #971174 (1998)

3.6 BOD₅, COD OR RATIO BOD₅/COD

BOD₅

Method:	Other (1990)
Value:	=0 mg O ₂ /L
GLP:	Yes <input type="checkbox"/> No <input type="checkbox"/> ? <input checked="" type="checkbox"/>

COD

Method:	Other
Value:	= 2.02 mg O ₂ /g
GLP:	Yes <input type="checkbox"/> No <input type="checkbox"/> ? <input checked="" type="checkbox"/>

Ratio BOD₅/COD:

Remarks:	According to Dow publication, the BOD ₂₀ is 0.65 parts/part, the ThOD is 2.06 and the index of biodegradability (BOD ₂₀ /ThOD) is 31.6%.
Reference:	ECOL Database, Dow Chemical Company, 1990.

3.7 BIOACCUMULATION

Method:	Calculation
Remarks:	A BCF of ≤ 1 can be estimated on the basis of the values calculated for the n-octanol/water partition coefficient by using a regression calculation.
Reference:	Bysse, 1990 as cited in GDCh-Advisory Committee on Existing Chemicals of Environmental Relevance (BUA), October 1995.

3.8 ADDITIONAL REMARKS

No additional remarks

4. ECOTOXICOLOGICAL DATA**4.1 ACUTE/PROLONGED TOXICITY TO FISH**

(a)

Type of test: static [X]; semi-static []; flow-through []; other [] open-system [X]; closed-system []
 Species: *Notropis atherinoides*
 Exposure period: 72 hr
 Results: LC₅₀ > 150 mg/l
 Analytical monitoring: Yes [] No [] ? [X]
 Method: Other
 GLP: Yes [] No [] ? [X]
 Test substance: No data
 Remarks: The maximum safe concentration for emerald shiners was 150 mg/l.
 Reference: ECOL Database, Dow Chemical Company, 1986.

(b)

Type of test: static [X]; semi-static []; flow-through []; other [] open-system [X]; closed-system []
 Species: *Pimephales promelas*
 Exposure period: 96 hr
 Results: LC₅₀ > 10,000 mg/l
 Analytical monitoring: Yes [] No [] ? [X]
 Method: Other
 GLP: Yes [] No [] ? [X]
 Test substance: As prescribed by 1.1 - 1.4
 Reference: Bartlett, E.A., 1979.

4.2 ACUTE TOXICITY TO AQUATIC INVERTEBRATES**A. Daphnia**

Type of test: static [X]; semi-static []; flow-through []; other []; open-system []; closed-system []
 Species: *Daphnia magna*
 Exposure period: 48 hr
 Results: LC₅₀ = 1919 mg/l
 Analytical monitoring: Yes [] No [] ? [X]
 Method: Other (1979)
 GLP: Yes [] No [] ? [X]
 Test substance: As prescribed by 1.1-1.4
 Reference: Bartlett, E.A., 1979.

B. Other aquatic organisms

Type of test: static []; semi-static []; flow-through [X]; other []; open-system []; closed-system [] **Note:** With daily renewal
 Species: *Crangon crangon*
 Exposure period: 96 hr
 Results: LC₅₀ > 1000 mg/
 Analytical monitoring: Yes [] No [] ? [X]
 Method: Other
 GLP: Yes [X] No [] ? []
 Test substance: As prescribed by 1.1-1.4

Reference: Thompson, R.S., 1987.

4.3 TOXICITY TO AQUATIC PLANTS e.g. Algae

Type: Aquatic ☒; Field ☐; Soil ☐; Other ☐
 Species: *Selenastrum capricornutum* Printz
 Exposure Period: 96 hr
 Results: For 3-day exposures, an EC10 value of 133 mg/L was reported for growth inhibition. 3- and 4-day EC50 values exceeded the highest concentration tested (>969 mg/L). NOEC = 969 mg/L; LOEC > 969 mg/L
 Analytical monitoring: Yes ☒ No ☐ ? ☐
 Method: OECD No. 221 "Algal, Growth Inhibition Test"
 GLP: Yes ☒ No ☐ ? ☐
 Test substance: DPGME
 Remarks: Average initial cell density was 12466 cells/mL; Temperature = 24.3 C; light intensity = 4644 kux; pH = 6.9-7.6 without algae or 8.0-9.3 with algae. DPGME is classified as "practically non-toxic" to *S. capricornutum*.
 Reference: Kirk et al. (2000): Unpublished Study by Dow Chemical Company # 001212

4.4 TOXICITY TO BACTERIA

Type: Aquatic ☒; Field ☐; Soil ☐; Other ☐
 Species: *Pseudomonas putida*
 Exposure Period: 18 hr
 Results: EC₁₀ = 4168 mg/l
 Analytical monitoring: Yes ☐ No ☐ ? ☒
 Method: Other
 GLP: Yes ☐ No ☐ ? ☒
 Test substance: As prescribed by 1.1-1.4
 Remarks: Value for bacteriotoxicity (inhibition of cell growth) = 2.4 according to German classification for water pollutants.
 Reference: Dow Europe, S.A., 1990b.

4.5 CHRONIC TOXICITY TO AQUATIC ORGANISMS

4.5.1 CHRONIC TOXICITY TO FISH

Remarks: No data available

4.5.2 CHRONIC TOXICITY TO AQUATIC INVERTEBRATES

A. Daphnia

Type of test: static ☐; semi-static ☐; flow-through ☒; other ☐; open-system ☐; closed-system ☐
 Species: *Daphnia magna*
 Exposure period: 22-day
 Dose: 0.05 and 0.5 mg/ml
 Results: The normal 21-day exposure period was extended one day in order to meet the validity criterion of 60 young per parent. The mean reproduction per parent in the two exposure groups was actually greater than in the control groups (62.3, and 94.5 offspring/parent at

0.05 and 0.5 mg/L, respectively, vs. 59.3 offspring/parent in the controls). Parental mortality remained below the validity criteria of 20% in all groups, and no treatment-related higher rates of mortality were recorded in the DPM test solutions. There were no adverse effects on either survival or reproductive performance at a concentration of 0.5 mg/L during 22 days of exposure.

Analytical monitoring: Yes ☐ No ☐ ? ☒
 Method: OECD Guideline No. 22
 GLP: Yes ☒ No ☐ ? ☐
 Test substance: As prescribed by 1.1-1.4
 Reference: Dow Report DET -2255, 1995 (unpublished)

4.6 TOXICITY TO TERRESTRIAL ORGANISMS

Remarks: No data available

4.6.1 TOXICITY TO SOIL DWELLING ORGANISMS

Remarks: No data available

4.6.2 TOXICITY TO TERRESTRIAL PLANTS

(a)

Species: *Brassica napus* (rape), *Vitis vinifera* (wine grape), *Glycine max* (soybean), *Lycopersicon esculentum* (tomato), *Gossypium hirsutum* (cotton)
 End-point: Emergence ☐; Growth ☒; Other ☐
 Exposure period: Applied once as an overhead foliar spray.
 Results: EC₅₀ = >500 g/l
 NOEC = 250 g/l
 Method: Other
 GLP: Yes ☐ No ☐ ? ☒
 Test substance: As prescribed by 1.1-1.4
 Remarks: First endpoint was growth (i.e. fresh weight after 21 days; second endpoint was crop injury to foliage. Crop injury to foliage was found after DPGME at a dose of >=500 g/l.
 Reference: Hart, D., 1991.

(b)

Species: *Triticum aestivum* (wheat), *Zea mays* (corn)
 End-point: Emergence ☐; Growth ☒; Other ☐
 Exposure period: Applied once as an overhead foliar spray.
 Results: EC₅₀ >500 g/l
 NOEC = 500 g/l
 Method: Other
 GLP: Yes ☐ No ☐ ? ☒
 Test substance: As prescribed by 1.1-1.4
 Remarks: Crop injury to foliage was found after DPGME at a dose of >500 g/l.
 Reference: Hart, D., 1991.

(c)

Species: *Triticum aestivum* (Monocotyledon)
 End-point: Emergence ☐; Growth ☒; Other ☐
 Exposure period: DPGME was applied once as an overhead foliar spray.
 Results: EC₅₀ =
 NOEC = >= 1000 g/l

Method: LOEC =
Other
GLP: Yes ☐ No ☐ ? ☒
Test substance: As prescribed by 1.1-1.4
Remarks: A first endpoint was growth (i.e. fresh weight after 21 days); a second endpoint was crop injury to foliage. DPGME was also not phytotoxic to monocotyledon at any of the diluted concentrations.
See also: BUA Report 174 (October 1995) on dipropylene glycol methyl ether.
Reference: Hart, D., 1991.

4.6.3 TOXICITY TO OTHER NON MAMMALIAN TERRESTRIAL SPECIES (INCLUDING AVIAN)

Results: No data available.

4.7 BIOLOGICAL EFFECTS MONITORING (INCLUDING BIOMAGNIFICATION)

Results: No data available.

4.8 BIOTRANSFORMATION AND KINETICS

Results: No data available

4.9 ADDITIONAL REMARKS

Remarks: No additional remarks

5. TOXICITY**5.1 ACUTE TOXICITY****5.1.1 ACUTE ORAL TOXICITY****(a) Preferred Result**

Type: LD₀ []; LD₁₀₀ []; LD₅₀ [X]; LDL₀ []; Other []
 Species/strain: Rat
 Value: = 5230 mg/kg (males)
 = 5180 mg/kg (females)
 Method: Other
 GLP: Yes [] No [X] ? []
 Test substance: As prescribed by 1.1 - 1.4
 Remarks: LD50 for female rats was comparable to value obtained for males.
 Depression of CNS was observed.
 See also: Clayton GD and Clayton, FE (eds.), Patty's Industrial Hygiene and
 Toxicology, 3rd Ed., Vol. 2C, p. 3989 and 4th Ed., Vol. 2D, p. 2882.
 Reference: Rowe *et al.*, 1954.

(b)

Type: LD₀ []; LD₁₀₀ []; LD₅₀ [X]; LDL₀ []; Other []
 Species/strain: Rat
 Value: =5400 mg/kg
 Method: Other
 GLP: Yes [] No [X] ? []
 Test substance: No data
 Remarks: Total number of animals tested was 5 male rats.
 See also: Clayton GD and Clayton, FE (eds.), Patty's Industrial Hygiene and
 Toxicology, 3rd Ed., Vol. 2C, p. 3989 and 4th Ed., Vol. 2D, p. 2882.
 Reference: Smyth *et al.*, 1962.

(c)

Type: LD₀ []; LD₁₀₀ []; LD₅₀ [X]; LDL₀ []; Other []
 Species/strain: Dog
 Value: =7500 mg/kg
 Method: Other
 GLP: Yes [] No [X] ? []
 Test substance: No data
 Remarks: Mortality within 48 hr. Signs of toxicity included respiratory paralysis.
 See also: Clayton GD and Clayton, FE (eds.), Patty's Industrial Hygiene and
 Toxicology, 3rd Ed., Vol. 2C, p. 3989 and 4th Ed., Vol. 2D, p. 2882.
 Reference: Shideman, F.E. and Procita, L., 1951.

5.1.2 ACUTE INHALATION TOXICITY**(a)**

Type: LC₀ []; LC₁₀₀ []; LC₅₀ []; LCL₀ []; Other [X]
 Species/strain: Rat
 Exposure time: 7 hours
 Value: >500 ppm
 Method: Other
 GLP: Yes [] No [X] ? []
 Test substance: No data

Remarks: Male rats were exposed for 7 hr to a saturated vapour (fog) atmosphere. Animals were wet with the test material at the end of the exposure interval. Mild narcosis was observed, with rapid recovery. See also: Clayton GD and Clayton, FE (eds.), Patty's Industrial Hygiene and Toxicology, 3rd Ed., Vol. 2C, p. 3991 and 4th Ed., Vol. 2D, p. 2882.

Reference: Rowe *et al.*, 1954.

5.1.3 ACUTE DERMAL TOXICITY

(a) Preferred Result

Type: LD₀ []; LD₁₀₀ []; LD₅₀ [X]; LD_{L0} []; Other []

Species/strain: Rabbit (New Zealand white)

Value: 13,000 - 14,000 mg/kg

Method: Other

GLP: Yes [] No [X] ? []

Test substance: No data

Remarks: See also: Clayton GD and Clayton, FE (eds.), Patty's Industrial Hygiene and Toxicology, 3rd Ed., Vol. 2C, p. 3990 and 4th Ed., Vol. 2D, p. 2882. See also: Henscheler, D., 1992.

Reference: Browning, E., 1965.

(b)

Type: LD₀ []; LD₁₀₀ []; LD₅₀ [X]; LD_{L0} []; Other []

Species/strain: Rabbit

Value: > 19,000 mg/kg

Method: Other

GLP: Yes [] No [X] ? []

Test substance: No data

Remarks: A single application of 20 ml/kg was held in continuous contact with a large area of the rabbits' skin for 24 hours. There were no deaths, however, transient narcosis was reported.

Reference: Unpublished data as reported in Clayton G.D. and Clayton, F.E. (eds.), Patty's Industrial Hygiene and Toxicology, 3rd Ed. 1982

(c)

Type: LD₀ []; LD₁₀₀ []; LD₅₀ [X]; LD_{L0} []; Other []

Species/strain: Rabbit

Value: 9500 mg/kg

Method: Other

GLP: Yes [] No [X] ? []

Test substance: No data

Remarks: A total of 4 female rabbits were tested.

Reference: Smyth *et al.*, 1962.

(d)

Type: LD₀ []; LD₁₀₀ []; LD₅₀ [X]; LD_{L0} []; Other []

Species/strain: Rabbit

Value: 10,100 mg/kg

Method: Other

GLP: Yes [] No [X] ? []

Test substance: No data

Reference: Unpublished data as reported in Clayton G.D. and Clayton, F.E. (eds.), Patty's Industrial Hygiene and Toxicology, 1982.

5.1.4 ACUTE TOXICITY, OTHER ROUTES OF ADMINISTRATION

Type: LC₀ []; LC₁₀₀ []; LC₅₀ []; LCL₀ []; Other []
 LD₀ []; LD₁₀₀ []; LD₅₀ [X]; LDL₀ []; Other []

Species/strain: Dog

Route of Administration: i.m. []; i.p. []; i.v. [X]; infusion []; s.c. []; other []

Exposure time: N.A.

Value: 330 - 470 mg/kg

Method: Other

GLP: Yes [] No [X] ? []

Test substance: No data

Remarks: Test was performed on anaesthetised dogs. The LD₅₀ for artificially respired dogs was 1230 mg/kg (1.3 ml/kg).
 See also: Clayton GD and Clayton, FE (eds.), Patty's Industrial Hygiene and Toxicology, 3rd Ed., Vol. 2C, p. 3990 and 4th Ed., Vol. 2D, p. 2882

Reference: Browning, E., 1965.

5.2 CORROSIVENESS/IRRITATION**5.2.1 SKIN IRRITATION/CORROSION**

(a)

Species/strain: Rabbit (New Zealand White)

Results: Highly corrosive []; Corrosive []; Highly irritating []; Irritating [];
 Moderate irritating []; Slightly irritating []; Not irritating [X]

Classification: Highly corrosive (causes severe burns) []; Corrosive (caused burns) [];
 Irritating []; Not irritating [X]

Method: Other

GLP: Yes [] No [] ? [X]

Test substance: No data

Reference: Ballantyne, B., 1983

(b)

Species/strain: Rabbit

Results: Highly corrosive []; Corrosive []; Highly irritating []; Irritating [];
 Moderate irritating []; Slightly irritating [X]; Not irritating []

Classification: Highly corrosive (causes severe burns) [];
 Corrosive (caused burns) []; Irritating []; Not irritating [X]

Method: Other

GLP: Yes [] No [X] ? []

Test substance: As prescribed by 1.1-1.4

Remarks: Continuous skin contact over 90 days caused only very minor irritation in the form of slight scaliness; narcotic deaths were observed among rabbits receiving 10,000 mg/kg/day.
 See also: Clayton GD and Clayton, FE (eds.), Patty's Industrial Hygiene and Toxicology, 3rd Ed., Vol. 2C, p. 3990 and 4th Ed., Vol. 2D, p. 2884.

Reference: Rowe *et al*, 1954.

(c)

Species/strain: Rabbit

Results: Highly corrosive []; Corrosive []; Highly irritating []; Irritating [];
 Moderate irritating []; Slightly irritating []; Not irritating [X]

Classification: Highly corrosive (causes severe burns) [];
 Corrosive (caused burns) []; Irritating []; Not irritating [X]

Method:	Other
GLP:	Yes <input type="checkbox"/> No <input type="checkbox"/> ? <input checked="" type="checkbox"/>
Test substance:	No data
Reference:	Smyth <i>et al.</i> , 1962.
(d)	
Species/strain:	Rabbit
Results:	Highly corrosive <input type="checkbox"/> ; Corrosive <input type="checkbox"/> ; Highly irritating <input type="checkbox"/> ; Irritating <input type="checkbox"/> ; Moderate irritating <input type="checkbox"/> ; Slightly irritating <input type="checkbox"/> ; Not irritating <input checked="" type="checkbox"/>
Classification:	Highly corrosive (causes severe burns) <input type="checkbox"/> ; Corrosive (caused burns) <input type="checkbox"/> ; Irritating <input type="checkbox"/> ; Not irritating <input checked="" type="checkbox"/>
Method:	Other
GLP:	Yes <input type="checkbox"/> No <input type="checkbox"/> ? <input checked="" type="checkbox"/>
Test substance:	No data
Remarks:	500 mg was applied without occlusion.
Reference:	Union Carbide Data Sheet, 1971.
(e)	
Species/strain:	Human
Results:	Highly corrosive <input type="checkbox"/> ; Corrosive <input type="checkbox"/> ; Highly irritating <input type="checkbox"/> ; Irritating <input type="checkbox"/> ; Moderate irritating <input type="checkbox"/> ; Slightly irritating <input type="checkbox"/> ; Not irritating <input checked="" type="checkbox"/>
Classification:	Highly corrosive (causes severe burns) <input type="checkbox"/> ; Corrosive (caused burns) <input type="checkbox"/> ; Irritating <input type="checkbox"/> ; Not irritating <input checked="" type="checkbox"/>
Method:	Other
GLP:	Yes <input type="checkbox"/> No <input checked="" type="checkbox"/> ? <input type="checkbox"/>
Test substance:	No data
Remarks:	Undiluted DPGME was applied to the backs of 200 human subjects and remained in direct contact with the skin for a period of 5 days.
Reference:	Dow Chemical Company, 1951. Rowe <i>et al.</i> , 1954.

5.2.2 EYE IRRITATION/CORROSION

(a)	
Species/strain:	Rabbit
Results:	Highly corrosive <input type="checkbox"/> ; Corrosive <input type="checkbox"/> ; Highly irritating <input type="checkbox"/> ; Irritating <input type="checkbox"/> ; Moderate irritating <input type="checkbox"/> ; Slightly irritating <input checked="" type="checkbox"/> ; Not irritating <input type="checkbox"/>
Classification:	Irritating <input type="checkbox"/> ; Not irritating <input checked="" type="checkbox"/> ; Risk of serious damage to eyes <input type="checkbox"/>
Method:	Other
GLP:	Yes <input type="checkbox"/> No <input type="checkbox"/> ? <input checked="" type="checkbox"/>
Test substance:	No data
Remarks:	A volume of 0.1 ml was applied undiluted. Signs of irritation to the conjunctiva and margins of the eyelid were observed. Effects had resolved by 7 days. There were only minor changes in corneal thickness and intra-ocular pressure, indicating minimal effects on the corneal epithelium.
Reference:	Ballantyne, 1984.
(b)	
Species/strain:	Rabbit
Results:	Highly corrosive <input type="checkbox"/> ; Corrosive <input type="checkbox"/> ; Highly irritating <input type="checkbox"/> ; Irritating <input type="checkbox"/> ; Moderate irritating <input type="checkbox"/> ; Slightly irritating <input type="checkbox"/> ; Not irritating <input checked="" type="checkbox"/>
Classification:	Irritating <input type="checkbox"/> ; Not irritating <input checked="" type="checkbox"/> ; Risk of serious damage to eyes <input type="checkbox"/>
Method:	Other
GLP:	Yes <input type="checkbox"/> No <input type="checkbox"/> ? <input checked="" type="checkbox"/>
Test substance:	No data

Remarks:	The dose administered was 500 mg/24 hr.
Reference:	Prehled Prumyslove Toxikol Org Latky, 1986.
(c)	
Species/strain:	Rabbit
Results:	Highly corrosive []; Corrosive []; Highly irritating []; Irritating []; Moderate irritating []; Slightly irritating []; Not irritating [X]
Classification:	Irritating []; Not irritating [X]; Risk of serious damage to eyes []
Method:	Other
GLP:	Yes [] No [X] ? []
Test substance:	No data
Remarks:	The dose administered was 500 mg.
Reference:	Union Carbide Data Sheet, 1971.
(d)	
Species/strain:	Rabbit
Results:	Highly corrosive []; Corrosive []; Highly irritating []; Irritating []; Moderate irritating [X]; Slightly irritating []; Not irritating [X]
Classification:	Irritating []; Not irritating [X]; Risk of serious damage to eyes []
Method:	Other
GLP:	Yes [] No [X] ? []
Test substance:	As prescribed in 1.1-1.4
Remarks:	One drop of undiluted DPGME was placed in the eyes of rabbits on each of 5 consecutive days. This caused only transitory mild conjunctival irritation, but no corneal damage. The dose administered was 238 mg.
Reference:	Rowe <i>et al.</i> , 1954.
(e)	
Species/strain:	Human
Results:	Highly corrosive []; Corrosive []; Highly irritating []; Irritating []; Moderate irritating [X]; Slightly irritating []; Not irritating [X]
Classification:	Irritating []; Not irritating [X]; Risk of serious damage to eyes []
Method:	Other
GLP:	Yes [] No [] ? [X]
Test substance:	No data
Remarks:	Application of a 0.04 ml of a 20% aqueous solution to human eyes produced mild transient sensory irritation, hyperemia of conjunctival vessels and a small increase in intraocular pressure. All effects disappeared within 2 hr.
Reference:	Ballantyne, 1984b.

5.3 SKIN SENSITISATION

(a)	
Type:	Other
Species/strain:	Human
Results:	Sensitising []; Not sensitising [X]; ambiguous []
Classification:	Sensitising []; Not sensitising [X]
Method:	Other
GLP:	Yes [] No [X] ? []
Test substance:	As prescribed by 1.1 - 1.4
Remarks:	Undiluted DPGME was applied to the backs of 200 unselected human subjects, 100 males and 100 females, and allowed to remain in direct contact with the skin for 5 days. Three weeks later, DPGME was again applied to the backs of the same subjects and allowed to remain in contact with the skin for a period of 48 hours.

DPGME was tested by a repeated insult method on 50 unselected human subjects, 25 males and 25 females. The material was applied to the back of each subject for 4 to 8 hours every other day until 10 applications had been made. After a lapse of 3 weeks, the material was reapplied for a period of 24 to 48 hours.

Reference: Rowe *et al.*, 1954.
Dow Chemical Company, 1951.

5.4 REPEATED DOSE TOXICITY

a)

Species/strain: Rat/Sprague-Dawley
Sex: Female ☐; Male ☐; Male/Female ☒; No data ☐
Route of Administration: Oral gavage
Exposure period: 4 weeks
Frequency of treatment: Daily
Post exposure observation period: 2 weeks
Dose: 0, 40, 200, 1000 mg/kg-day
Control group: Yes ☒; No ☐; No data ☐
Concurrent no treatment ☐; Concurrent vehicle ☒; Historical ☐
Results: Changes in liver histology were observed
Method: Kanpogyo 700, Yakuhatsu 1039, Kikyoku 1014
GLP: Yes ☒ No ☐ ? ☐
Test substance: DPGME
Remarks: No effects were noted on body weight or survival. No hematological effects were reported. Tentative salivation noted immediately after exposure beginning on day 11. Evidence of hepatotoxicity also noted at the highest dose. Liver weight (absolute and relative) remained significantly elevated in male rats following a two-week recovery period. No other treatment related effects were observed. 1000 mg/kg is identified as a LOAEL for tentative salivation, significantly increased relative liver weight, and centrilobular hypertrophy. 200 mg/kg is identified as a NOAEL.
Reference: Dow Chemical Japan, Unpublished Report #FBM 99-2691 (2000)

b)

Species/strain: Rat/Fischer 344
Sex: Female ☐; Male ☐; Male/Female ☒; No data ☐
Route of Administration: Inhalation
Exposure period: 13 weeks
Frequency of treatment: 6 hours/day; 5 days/week
Post exposure observation period: No data
Dose: 0, 15, 50, 200 ppm
Control group: Yes ☒; No ☐; No data ☐
Concurrent no treatment ☐; Concurrent vehicle ☒; Historical ☐
NOEL: 200 ppm
Results: There were no effects attributed to exposure to DPGME at any exposure concentrations in male or female rats.
Remarks: Concentrations of 15, 50 and 200 ppm DPGME correspond to 91, 303, and 1212 mg/m³ DPM respectively. 200 ppm was approximately 40% of a saturated DPGME atmosphere.
Method: OECD Guideline 413: Subchronic Inhalation Toxicity: 90-day Study
GLP: Yes ☐ No ☐ ? ☒
Test substance: As prescribed by 1.1 - 1.4
Reference: Landry, T.D. and Yano, B.L., 1984.

- (c)
- Species/strain: Rat
- Sex: Female []; Male []; Male/Female [X]; No data []
- Route of Administration: Inhalation
- Exposure period: 28 weeks
- Frequency of treatment: 7 hours/day; 5 days/week
- Post exposure observation period: No data
- Dose: 300-400 ppm
- Control group: Yes []; No []; No data [X];
Concurrent no treatment []; Concurrent vehicle []; Historical []
- Results: Increased liver weight was observed.
- Method: Other
- GLP: Yes [] No [X] ? []
- Test substance: As prescribed by 1.1 - 1.4
- Remarks: Total tested animals were 13 male and 17 female rats. Transient narcosis was reportedly observed during the first few weeks of the study.
See also: Clayton GD and Clayton, FE (eds.), *Patty's Industrial Hygiene and Toxicology*, 3rd Ed., Vol. 2C, p. 3991 and 4th Ed., Vol. 2D, p. 2884
- Reference: Rowe *et al.*, 1954.
- (d)
- Species/strain: Rat /Wistar
- Sex: Female []; Male [X] ; Male/Female []; No data []
- Route of Administration: Dermal
- Exposure period: 4 weeks
- Frequency of treatment: 4 hours/day; 5 days/week
- Post exposure observation period: No data
- Dose: 100, 1000 mg/kg/d
- Control group: Yes [X]; No []; No data [];
Concurrent no treatment []; Concurrent vehicle [X]; Historical []
- NOEL: > 1000 mg/kg/day
- Results: No significant changes in clinical chemistry, hematology, or gross pathology were found.
- Method: Other
- GLP: Yes [] No [] ? [X]
- Test substance: No data
- Remarks: DPGME was applied to male rats under occluded and non-occluded conditions.
- Reference: Fairhurst *et al.*, 1989.
- (e)
- Species/strain: Mouse/B6C3F1
- Sex: Female []; Male []; Male/Female [X]; No data []
- Route of Administration: Inhalation
- Exposure period: 2 weeks (9 exposures)
- Frequency of treatment: 6 hours/day; 5 days/week
- Post exposure observation period: No data
- Dose: 50, 140, 330 ppm
- Control group: Yes [X]; No []; No data [];
Concurrent no treatment [X]; Concurrent vehicle []; Historical []
- NOEL: >50 ppm
- LOEL: 140 ppm
- Results: There were no treatment-related effects with respect to post-exposure clinical observations, body weights and urinalysis. Relative liver weights increased in female mice.
- Method: Other

GLP: Yes ☐ No ☒ ? ☐
 Substance: as prescribed by 1.1-1.4
 Remarks: Based on histopathology, these effects on liver weight were suggested not to represent adverse effects of DPGME.
 See also: Clayton GD and Clayton, FE (eds.), Patty's Industrial Hygiene and Toxicology, 3rd Ed., Vol. 2C, p. 3991 and 4th Ed., Vol. 2D, p. 2884
 Reference: Landry *et al.*, 1981.

(f)

Species/strain: Rabbit/New Zealand White
 Sex: Female ☐; Male ☐; Male/Female ☒; No data ☐
 Route of Administration: Inhalation
 Exposure period: 13 weeks
 Frequency of treatment: 6 hours/day; 5 days/week
 Post exposure observation period: No data
 Dose: 0, 15, 50, 200 ppm
 Control group: Yes ☒; No ☐; No data ☐;
 Concurrent no treatment ☐; Concurrent vehicle ☒; Historical ☐
 NOEL: >200 ppm
 Results: There were no effects attributed to exposure to DPGME at any exposure concentration in male or female rabbits.
 Remarks: Concentrations of 15, 50 and 200 ppm DPGME correspond to 91, 303, and 1212 mg/m³ DPGME respectively. 200 ppm was approximately 40% of a saturated DPGME atmosphere.
 Method: OECD Guideline 413: Subchronic Inhalation Toxicity: 90-day Study
 See also: Clayton GD and Clayton, FE (eds.), Patty's Industrial Hygiene and Toxicology, 3rd Ed., Vol. 2C, p. 3991 and 4th Ed., Vol. 2D, p. 2884
 GLP: Yes ☐ No ☒ ? ☐
 Test substance: As prescribed by 1.1 - 1.4
 Reference: Landry, T.D. and Yano, B.L., 1984.

(g)

Species/strain: Rat/Fischer 344
 Sex: Female ☐; Male ☐ Male/Female ☒; No data ☐
 Route of Administration: Inhalation
 Exposure period: 2 weeks (9 exposures)
 Frequency of treatment: 6 hours/day; 5 days/week
 Post exposure observation period: No data
 Dose: 50, 140, 330 ppm
 Control group: Yes ☒; No ☐; No data ☐;
 Concurrent no treatment ☐; Concurrent vehicle ☒; Historical ☐
 NOEL: >50 ppm
 LOEL: 140 ppm
 Results: There were no treatment-related effects with respect to post-exposure clinical observations, body weights and urinalysis.
 Relative liver weights increased in male rats at all DPGME dosages and absolute liver weight increased in male rats exposed to 330 ppm.
 Method: Other
 GLP: Yes ☐ No ☒ ? ☐
 Substance: As prescribed by 1.1 - 1.4
 Remarks: Based on histopathology, these effects on liver weight were suggested not to represent adverse effects of DPGME.
 See also: Clayton GD and Clayton, FE (eds.), Patty's Industrial Hygiene and Toxicology, 3rd Ed., Vol. 2C, p. 3991 and 4th Ed., Vol. 2D, p. 2884
 Reference: Landry *et al.*, 1981.

(h)

Species/strain: Rabbit

Sex: Female []; Male []; Male/Female [X]; No data []

Route of Administration: Inhalation

Exposure period: 31 weeks

Frequency of treatment: 7 hours/day; 5 days/week

Post exposure observation period: No data

Dose: 300-400 ppm

Control group: Yes []; No []; No data [X];
Concurrent no treatment []; Concurrent vehicle []; Historical []

Results: Changes in liver histology were observed.

Method: Other

GLP: Yes [] No [X] ? []

Test substance: As prescribed by 1.1 - 1.4

Remarks: Total tested animals were 2 male and 2 female rabbits.
See also: Clayton GD and Clayton, FE (eds.), *Patty's Industrial Hygiene and Toxicology*, 3rd Ed., Vole 2C, p. 3991 and 4th Ed., Vol. 2D, p. 2884

Reference: Rowe *et al.*, 1954.

(i)

Species/strain: Rabbit

Sex: Female []; Male [X]; Male/Female []; No data []

Route of Administration: Dermal

Exposure period: 90 days

Frequency of treatment: 5 days/week

Post exposure observation period: No data

Dose: 1, 3, 5, 10 ml/kg

Control group: Yes [X]; No []; No data [];
Concurrent no treatment []; Concurrent vehicle []; Historical []

NOEL: 2850 mg/kg

LOEL: 4750 mg/kg

Results: Prolonged and repeated dermal application resulted in minor skin irritation.
Narcosis and deaths were reported at doses of 5 and 10 ml/kg. An increase in hydropic degeneration of the kidney was reported in animals in the 10 ml/kg group.

Method: Other

GLP: Yes [] No [] ? [X]

Test substance: As prescribed in 1.1 - 1.4

Remarks: See also: Clayton GD and Clayton, FE (eds.), *Patty's Industrial Hygiene and Toxicology*, 3rd Ed., Vol. 2C, p. 3991 and 4th Ed., Vol. 2D, p. 2884

Reference: Rowe *et al.*, 1954.

(j)

Species/strain: Guinea pig

Sex: Female []; Male []; Male/Female [X]; No data []

Route of Administration: Inhalation

Exposure period: 26 weeks

Frequency of treatment: 7 hours/day; 5 days/week

Post exposure observation period: No data

Dose: 300 - 400 ppm

Control group: Yes []; No []; No data [X];
Concurrent no treatment []; Concurrent vehicle []; Historical []

Results: Changes in liver histology in females were observed.

Method: Other

GLP: Yes [] No [X] ? []

Test substance: As prescribed in 1.1 - 1.4
 Remarks: Total tested animals were 7 male and 5 female guinea pigs.
 See also: Clayton GD and Clayton, FE (eds.), Patty's Industrial Hygiene and Toxicology, 3rd Ed., Vol. 2C, p. 3991 and 4th Ed., Vol. 2D, p. 2884
 Reference: Rowe *et al.*, 1954.

(k)
 Species/strain: Monkey
 Sex: Female ☐; Male ☐; Male/Female ☒; No data ☐
 Route of Administration: Inhalation
 Exposure period: 31 weeks
 Frequency of treatment: 7 hours/day; 5 days/week
 Post exposure observation period: No data
 Dose: 300 - 400 ppm
 Control group: Yes ☐; No ☐; No data ☒
 Concurrent no treatment ☐; Concurrent vehicle ☐; Historical ☐
 Results: Changes in liver histology were observed
 Method: Other
 GLP: Yes ☐ No ☒ ? ☐
 Test substance: As prescribed in 1.1 - 1.4
 Remarks: Total tested animals were 1 male and 1 female monkey.
 See also: Clayton GD and Clayton, FE (eds.), Patty's Industrial Hygiene and Toxicology, 3rd Ed., Vol. 2C, p. 3991 and 4th Ed., Vol. 2D, p. 2884.
 See also: NIOSH, 1991.
 Reference: Rowe *et al.*, 1954.

(l)
 Species/strain: Rat/
 Sex: Female ☐; Male ☐; Male/Female ☐; No data ☒
 Route of Administration: oral gavage
 Exposure period: 35 days
 Frequency of treatment: daily, 5 doses/week
 Post exposure observation period: no data
 Dose: 91.9, 275.7, 919, 2757 mg/kg
 Control group: Yes ☒; No ☐; No data ☐
 Concurrent no treatment ☐; Concurrent vehicle ☒; Historical ☐
 NOEL: 919 mg/kg bw
 LOEL: 2757 mg/kg bw
 Results: No mortalities were found. At 2757 mg/kg, some animals initially lost body weight, but they recovered quickly. The final body weight was not significantly different from that of controls.
 2757 mg/kg produced only minor effects on liver and kidney.
 Method: Other
 GLP: Yes ☐ No ☒ ? ☐
 Test substance: PGME (a metabolically related compound)
 Remark: Method similar to OECD guideline 407
 See also: Patty's Industrial Hygiene and Toxicology (1994)
 4th edition, Vol IID, p. 2865-2872.
 Reference: Rowe VK et al. (1954) Arch Ind Hyg Occup Med, 9, 509-525

(m)
 Species/strain: Dog
 Sex: Female ☐; Male ☒; Male/Female ☐; No data ☐
 Route of Administration: oral feed
 Exposure period: 14 weeks
 Frequency of treatment: 5 days per week

Post exposure observation period: no data
 Dose: 459.5, 919, 1836, 3672 mg/kg (0.5, 1.0, 2.0, 3.0 ml/kg/day)
 Control group: Yes ☐ ; No ☐ ; No data ☒ ;
 Concurrent no treatment ☐ ; Concurrent vehicle ☐ ; Historical ☐
 NOEL: < 459.5 mg/kg bw
 LOEL: 459.5 mg/kg bw
 Results: Mild to severe central nervous system depression in a dose-related manner was observed. Male dogs developed numerous spermiphages in the epididymis. There were minor kidney changes at higher doses.
 Method: Other
 GLP: Yes ☐ No ☐ ? ☒
 Test substance: PGME (a metabolically related compound)
 Remark: Method similar to OECD guideline 409
 See also: Patty's Industrial Hygiene and Toxicology (1994) 4th edition, Vol IID, p. 2865-2872.
 Reference: Stenger, EG et al., (1972) *Arzneim. Forsch.*, 22, 569-574

5.5 GENETIC TOXICITY IN VITRO

A. BACTERIAL TEST

(a)
 Type: Bacterial reverse mutation assay (Ames Test)
 System of testing: Species/strain: *Salmonella. typhimurium* TA98, TA1537, TA100;
Escherichia coli WP2uvrA
 Concentration: 313, 625, 1250, 2500, 5000 ug/plate
 Metabolic activation: With ☐ ; Without ☐ ; With and Without ☒ ; No data ☐
 Results: Genotoxic effects: + ? -
 With metabolic activation: ☐ ☐ ☒
 Without metabolic activation: ☐ ☐ ☒
 Method: Other
 GLP: Yes ☒ No ☐ ? ☐
 Test substance: DPGME
 Reference: Dow Chemical Japan, Unpublished Report #FBM 00-8026 (2000)

(b)
 Type: Bacterial reverse mutation assay (Ames Test)
 System of testing: Species/strain: *Salmonella. typhimurium* TA 98, TA 100, TA 1535,
 TA 1537, TA 1538
 Concentration: 0, 2, 10, 50, 250, 1250, 6250 ug/plate
 Metabolic activation: With ☐ ; Without ☐ ; With and Without ☒ ; No data ☐
 Results: Genotoxic effects: + ? -
 With metabolic activation: ☐ ☐ ☒
 Without metabolic activation: ☐ ☐ ☒
 Method: Other
 GLP: Yes ☒ No ☐ ? ☐
 Test substance: As prescribed by 1.1 - 1.4
 Reference: Kirkland, D.Y. and Varley, R., 1983.

B. NON-BACTERIAL IN VITRO TEST

(a)
 Type: Chromosomal aberrations
 System of testing: Chinese hamster lung cells

Concentration: Incubated with 0.371, 0.741, 1.482 mg/L
 Metabolic activation: With ☐; Without ☐; With and Without ☒; No data ☐
 Results: Genotoxic effects: + ? -
 With metabolic activation: ☐ ☐ ☒
 Without metabolic activation: ☐ ☐ ☒
 Method: Kanpogyo 700; Yakuhatsu 1039; Kikyoku 1014
 GLP: Yes ☒ No ☐ ? ☐
 Test substance: DPGME
 Remarks: DPGME shows no evidence of potential to cause cytotoxicity or structural/numerical abnormalities in chromosomes of CHL/IU cells.
 Reference: Dow Chemical Japan, Unpublished Report #FBM 00-8027 (2000)

(b)

Type: Cytogenetics Assay
 System of testing: Metaphase analysis of Chinese Hamster Ovary (CHO) cells
 Concentration: Incubated with 0, 1.25, 2.5, 5.0, 10 mg/l.
 Metabolic activation: With ☐; Without ☐; With and Without ☒; No data ☐
 Results: Cytotoxicity conc:
 With metabolic activation: 10 mg/l
 Without metabolic activation: 10 mg/l
 Genotoxic effects: + ? -
 With metabolic activation: ☐ ☐ ☒
 Without metabolic activation: ☐ ☐ ☒
 Method: Other
 GLP: Yes ☒ No ☐ ? ☐
 Test substance: As prescribed by 1.1 - 1.4
 Remarks: DPGME was not toxic to CHO cells up to 5 mg/l, but reduced survival to approximately 50% at 10 mg/l. Since metaphase analysis showed no differences between DPGME-treated and untreated cells, with or without metabolic activation, DPGME is considered not to be a chromosome mutagen for CHO cells.
 Reference: Kirkland, 1983.

(c)

Type: Unscheduled DNA Synthesis
 System of testing: Rat hepatocyte unscheduled DNA synthesis assay (DNA repair test)
 Concentration: Incubated with 0, 0.01, 0.00316, 0.001, 0.000316, 0.0001, 0.0000316 M
 Metabolic activation: With ☐; Without ☒; With and Without ☐; No data ☐
 Results: Genotoxic effects: + ? -
 With metabolic activation: ☐ ☐ ☐
 Without metabolic activation: ☐ ☐ ☒
 Method: OECD Guideline 482: Genetic Toxicology: DNA Damage and Repair/ Unscheduled DNA Synthesis in Mamalian Cells in vitro.
 GLP: Yes ☒ No ☐ ? ☐
 Test substance: As prescribed by 1.1 - 1.4
 Remarks: DPGME failed to elicit significant UDS at any concentration tested. This result suggests an apparent lack of genotoxic activity under the test conditions.
 Reference: Mendrala, A.L., 1983.

5.6 GENETIC TOXICITY IN VIVO

Results: No data available

Comments:

Concentrations up to 6,000 mg/kg PGME (a structurally similar chemical) administered to mice did not increase the frequency of micronuclei in polychromatic erythrocytes harvested from bone marrow (Elias et al., 1996)

5.7 CARCINOGENICITY

Results: No data available

Comments:

While DPGME has not been evaluated in a chronic toxicity/oncogenicity bioassay to date, its low toxicologic potential in subacute and subchronic studies, lack of genotoxic activity, and biotransformation via the same general routes and types of metabolites as the noncarcinogen PGME, indicate that DPGME is unlikely to be carcinogenic in man or animals.

In 2-year inhalation carcinogenicity studies sponsored by the CMA PGE Panel with the structurally similar chemical propylene glycol monomethyl ether (PGME) no evidence of carcinogenicity has been found in either rats or mice. The No Observed Adverse Effect Levels (NOEL's) in both sexes of both species were 300 ppm. Major metabolic pathways for DPGME include conjugation with glucuronic acid and sulfate; hydrolysis of the methoxy group to form dipropylene glycol; and hydrolysis of the dipropylene glycol backbone of DPGME to form PGME and propylene glycol (Miller *et al* 1985). The glucuronide and sulfate conjugates of DPGME are essentially non-toxic and rapidly eliminated from the body. DPGME is less volatile and has been shown in comparable studies to be similar to, or less toxic than dipropylene glycol, PGME and propylene glycol, each of which are of low toxicity, themselves. Therefore, no major differences in the systemic toxicological properties of DPGME and PGME would be anticipated, including carcinogenic potential. Consistent with this view is the fact that DPGME has been shown not to be genotoxic in several *in vitro* assay systems; DPGME was negative in an Ames bacterial gene mutation assay, did not induce unscheduled DNA synthesis (DNA damaged-induced repair) in rat hepatocytes, and was not clastogenic in CHO cells (ECETOC, 1995).

5.8 TOXICITY TO REPRODUCTION

Results: No data available

Comments:

In a 2-generation inhalation reproduction study sponsored by the CMA Propylene Glycol Ethers Panel with the structurally similar chemical propylene glycol monomethyl ether (PGME) no adverse fertility or reproductive effects were observed at 1,000 ppm PGME. Major metabolic pathways for DPGME include conjugation with glucuronic acid and sulfate; hydrolysis of the methoxy group to form dipropylene glycol; and hydrolysis of the dipropylene glycol backbone of DPGME to form PGME and propylene glycol (Miller *et al*, 1985). The glucuronide and sulfate conjugates of DPGME are essentially non-toxic and rapidly eliminated from the body. DPGME is less volatile and has been shown in comparable studies to be similar to, or less toxic than dipropylene glycol, PGME and propylene glycol, each of which are of low toxicity, themselves. Based upon the similarities in metabolism and modes of action of DPGME and its metabolites, it is highly probable that DPGME will be similar to or less toxic than its metabolites in reproductive toxicity studies.

Additionally, no effects were seen on the testes and ovaries in a 28-day repeat dose oral toxicity study (Dow Chemical Japan, Unpublished Report #FBM 99-2691, 2000)

5.9 DEVELOPMENTAL TOXICITY/TERATOGENICITY

(a)

Species/strain: Rat/Fischer 344
 Sex: Female [X]; Male []; Male/Female []; No data []
 Route of Administration: Inhalation
 Exposure period: days 6 -15 of gestation
 Frequency of treatment: 6 hours/day
 Doses: 0, 50, 150, 300 ppm
 Control group: Yes [X]; No []; No data [];
 Concurrent no treatment []; Concurrent vehicle [X]; Historical []
 NOEL Maternal Toxicity: \geq 300 ppm
 NOEL Teratogenicity: \geq 300 ppm
 Results: 300 ppm/day was the highest concentration attainable. DPGME at this concentration was not toxic, embryo/fetotoxic, or teratogenic.
 Method: Other
 GLP: Yes [X] No [] ? []
 Test substance: As prescribed by 1.1 - 1.4
 Remarks: These results indicate that DPGME is not embryo-fetotoxic or teratogenic in rats when administered by an appropriate route of potential human exposure (inhalation) at the highest concentration (300 ppm) that is practicably attainable at room temperature and normal pressure.
 Reference: Breslin *et al*, 1990a and 1990b.

(b)

Species/strain: Rabbit/New Zealand White
 Sex: Female [X]; Male []; Male/Female []; No data []
 Route of Administration: Inhalation
 Exposure period: days 7 - 19 of gestation
 Frequency of treatment: 6 hours/day
 Doses: 0, 50, 150, 300 ppm
 Control group: Yes [X]; No []; No data [];
 Concurrent no treatment []; Concurrent vehicle [X]; Historical []
 NOEL Maternal Toxicity: \geq 300 ppm
 NOEL Teratogenicity: \geq 300 ppm
 Results: No significant treatment-related effects were observed in any maternal or fetal parameters at any exposure level.
 Method: Other
 GLP: Yes [X] No [] ? []
 Test substance: As prescribed by 1.1 - 1.4
 Remarks: These results indicate that DPGME is not embryo-fetotoxic or teratogenic in rabbits when administered by an appropriate route of potential human exposure (inhalation) at the highest concentration (300 ppm) that is practicably attainable at room temperature and normal pressure.
 Reference: Breslin *et al*, 1990b. and 1990c.

5.10 OTHER RELEVANT INFORMATION

A. Specific toxicities

Results: No studies located

B. Toxicodynamics, toxicokinetics

Type: Metabolism
 Remarks: Male Fischer 344 rats were given a single oral dose of carbon-14 labelled DPGME. Approximately 60% of the administered ¹⁴C activity was excreted in the urine, while 27% was eliminated as ¹⁴CO₂ within 48 hours after dosing. DPMGE, PGME (propylene glycol methyl ether), as well as sulfate and glucuronide conjugates of DPGME were identified in urine of animals given (¹⁴C)DPGME.
 References: Miller *et al*, 1985.

Comments:

The toxicity of DPGME has been evaluated in a series of acute, subacute, subchronic and developmental toxicity studies. In addition, the metabolic profile of DPGME supports the use of extensive metabolite databases to evaluate the potential toxicity of DPGME. Major metabolic pathways for DPGME include conjugation with glucuronic acid and sulfate; hydrolysis of the methoxy group to form dipropylene glycol; and hydrolysis of the dipropylene glycol backbone of DPGME to form PGME and propylene glycol (Miller *et al*, 1985). The glucuronide and sulfate conjugates of DPGME are essentially non-toxic and rapidly eliminated from the body. DPM is less volatile and has been shown in comparable studies to be similar to, or less toxic than dipropylene glycol, PGME and propylene glycol, each of which are of low toxicity, themselves. The database on the metabolites of DPGME also includes studies that have not been conducted with DPGME such as reproductive and chronic toxicity/oncogenicity studies. Based upon the similarities in metabolism and modes of action of DPGME and its metabolites, it is highly probable that DPGME will be similar to or less toxic than its metabolites in reproductive, chronic toxicity and carcinogenicity studies.

5.11 EXPERIENCE WITH HUMAN EXPOSURE

(a)
 Remarks: No injury or adverse effects to humans have been reported from the handling and use of DPGME.
 Reference: Clayton GD and Clayton, FE (eds.), Patty's Industrial Hygiene and Toxicology, 4th Ed., 1994.

(b)
 Remarks: Three out of 7 lithographers using DPGME, ethylene glycol monoethyl ether, and a range of aliphatic, aromatic and halogenated hydrocarbons for offset and ultraviolet-cured multicoloured printing, showed normal peripheral blood parameters; however, bone marrow specimens showed stromal injury. It is unlikely that DPGME caused the observed effects. DPGME was present along with substituted benzenes, chlorinated solvents, n-propanol, and EGEE in workplace solutions. Suspicion of DPGME as a causal agent came from personal, area air samples and wipe samples. The most intense exposure to DPGME was from an ultraviolet curing wash and air sampling revealed 0.6 to 6.43 ppm air concentrations.

The authors of this article provide limited and inconclusive data that DPGME may be the cause of bone marrow injury in a small group of exposed lithographers. Because of the small group studied, it is difficult to causally link occupational exposure with the marrow lesions. This is further confounded by a lack of published data regarding the prevalence of such marrow injury parameters in

workers or the general population. Besides the hypothesis that DPGME may play a role in the observed injury, the authors also suggest that it is plausible that marrow changes represent the result of ubiquitous insults from infectious agents, drugs, alcohol, or other environmental agents or unknown factors.

The most convincing evidence that DPGME is not responsible for such effects comes from a lack of recorded marrow effects in other subchronically and chronically tested PGE's (PGME, PGtBE). This is in contrast to EGME. DPGME itself when applied dermally up to 10 g/kg for 90 days produced no hematologicaleffects even though mortality was high at the 10 g/kg level.

Reference:

Cullen *et al.*, 1983.

(c)

Remarks:

Probable minimum concentration of DPGME that may cause minor nasal irritation, or some tolerable eye, throat, and respiratory irritation is about 35 ppm and 75 ppm (450 mg/m³), respectively.

Reference:

Clayton GD and Clayton, FE (eds.), Patty's Industrial Hygiene and Toxicology, 4th Ed., 1994.

(d)

Remarks:

Levels of 300 to 400 DPGME were very disagreeable to man. Levels of 100 ppm, which might be voluntarily tolerated without complaint, were considered safe with respect to organic injury.

Reference:

ACGIH, 1991.

(e)

Remarks:

DPGME caused neither irritation nor sensitisation when tested on human subjects. It is low in toxicity by inhalation. Hazards to health associated with handling and ordinary use of this material seem to be minimal.

Reference:

Clayton, G.D. and Clayton, F.E. (eds), Patty's Industrial Hygiene and Toxicology, 4th Ed., 1994.

(f)

Remarks:

Application of 0.4 ml of a 20% solution of DPGME to one eye of each of ten human male volunteers caused a minor stinging sensation for 30-45 seconds, and was accompanied by slight excess lacrimation and blepharospasm for about 1 minute. A mild injection of the conjunctival vessels and a minor increase in intraocular tension were observed during the first hour.

Reference:

Ballantyne, 1984b.

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SIDS ROBUST SUMMARIES
DIPROPYLENE GLYCOL METHYL ETHER
(DPGME)
CAS No. 34590-94-8
(Isomers: 13429-07-7, 20324-32-7; 13588-28-8; and
55956-21-3)

Data Quality
March 2001

Updated December, 2001

Klimisch Scores
1= reliable without restrictions
2=reliable with restrictions
3=not reliable
4=not assignable

PHYSICAL/CHEMICAL ELEMENTS**MELTING POINT****TEST SUBSTANCE**

- Dipropylene glycol methyl ether (DPGME)

METHOD

- Method ?
- GLP:?
- Year (study performed): 1994
- Remarks:

RESULTS

- Melting point: -83 °C
- Decomposition: No
- Sublimation: No
- Remarks:

CONCLUSIONS

- The melting point for DPGME is -83 °C

DATA QUALITY = 2

REFERENCES

- Dow Europe S.A., (1994). Safety Data Sheet

OTHER

BOILING POINT**TEST SUBSTANCE**

- Dipropylene glycol methyl ether (DPGME)

METHOD

- Method: ?
- GLP: ?
- Year (study performed): 1994
- Remarks:

RESULTS

- Boiling point: 190 °C
- Pressure:
- Pressure unit:
- Decomposition (yes/no/ambiguous)
- Remarks:

CONCLUSIONS

- The boiling point for DPGME is 190 °C

DATA QUALITY = 2**REFERENCES**

- Dow Europe S.A., (1994). Safety Data Sheet

OTHER

- Values ranging from 184-197 °C have been reported for DPGME (ECETOC Technical Report # 64, 1995).

VAPOUR PRESSURE**TEST SUBSTANCE**

- Dipropylene glycol methyl ether (DPGME)

METHOD

- Method: Calculated
- GLP: ?
- Year (study performed): 1994
- Remarks:

RESULTS

- Vapor Pressure: 0.37 hPa
- Temperature: 20 °C
- Decomposition:
- Remarks:

CONCLUSIONS

- The vapor pressure for DPGME is 0.37 hPa.

DATA QUALITY = 2**REFERENCES**

- Dow Europe S.A., (1994). Safety Data Sheet

OTHER

PARTITION COEFFICIENT**TEST SUBSTANCE**

- Dipropylene glycol methyl ether (DPGME)
- Remarks: 99% pure (w/w)

METHOD

- Method: OECD 107
- GLP: Yes
- Year (study performed): 2000
- Remarks: 5 minute shaking time at 20 rpm in stainless steel centrifuge tubes

RESULTS

- Log Pow: 0.0061
- Temperature: 25 °C
- Remarks: Chemical analyses conducted by gas chromatography. Recoveries ranging from 99-101% were reported.

CONCLUSIONS

- The Log Pow value for DPGME is 0.0061 (range: -0.014 to 0.0086).

DATA QUALITY = 1**REFERENCES**

- Dow Chemical Japan, Unpublished Report # 0006P (2000)

OTHER

WATER SOLUBILITY**TEST SUBSTANCE**

- Identity: Dipropylene glycol methyl ether (DPGME)

METHOD

- Method: ?
- GLP: ?
- Year (study performed): 1994
- Remarks:

RESULTS

- Value: 100%
- Description of solubility: miscible
- pH value and concentration at temperature °C:
- pKa value at 25 °C:
- Remarks:

CONCLUSIONS

- DPGME is miscible in water in all proportions.

DATA QUALITY = 1

REFERENCES

- Dow Europe S.A. 1994. Safety Data Sheet

OTHER

ENVIRONMENTAL FATE ELEMENTS AND PATHWAYS**PHOTODEGRADATION****TEST SUBSTANCE**

- Dipropylene glycol methyl ether (DPGME)

METHOD

- Method: ?
- GLP: No
- Year (study performed): 1975

RESULTS

- Direct photolysis:
- Half-life $t_{1/2}$: 5.3 hours
- Remarks: 37.8°C at 75% humidity on a sunny day

CONCLUSIONS

- A half-life of 5.3 hours was measured for DPGME due to direct photolysis

DATA QUALITY = 2**REFERENCES**

- Photodecomposition of Dowanol glycol ethers. Unpublished report of DOW Chemical Company, 33p, 1975

OTHER

- A half-life of 3.4 hours was estimated for DPGME due to direct photolysis (GEMs FAB Database, 1986)
- Measured half-life values for structurally similar chemicals (propylene glycol ethers) were reported to range from 3.1 to 16.1 hours (Staples and Davis, 2001).

STABILITY IN WATER**TEST SUBSTANCE**

- Dipropylene glycol methyl ether (DPGME)
- Remarks: 99% pure (w/w)

METHOD

- Method: ?
- Type (test type): Log Pow determination
- GLP: yes
- Year (study performed): 2000
- Remarks: measurements made during Log Pow determination
- Duration: 24 hours
- Positive Controls: none
- Negative Controls: none
- Analytical procedures: gas chromatography

RESULTS

- Measured value: Recovery of DPGME ranged from 96-101%
- Degradation: little to no degradation apparent 25 °C after 24 hours
- Breakdown products: none
- Remarks:

CONCLUSIONS

- DPGME is relatively stable for relatively short periods of time.

DATA QUALITY = 1**REFERENCES**

- Dow Chemical Japan, Unpublished Report # S-0001 (2000)

OTHER

TRANSPORT BETWEEN ENVIRONMENTAL COMPARTMENTS (FUGACITY)**TEST SUBSTANCE**

- Dipropylene glycol methyl ether (DPGME)

METHOD

- Test (test type): Fugacity predictions
- Method: Level 3
- Year (study performed): 2001
- Remarks: An estimate of 12,000 tons of DPGME were consumed in the U.S. during 1995. Source terms for release to air, water, and soil were calculated to be 122, 13.7, and 1.4 kg/hour, respectively.

RESULTS

- Media: Air, soil, water and sediment concentrations were estimated.
- Estimated Distribution and Media Concentration:
 - o Air: 9.24 ng/m³
 - o Water: 0.053 ug/L
 - o Soil: 0.28 ug/kg
 - o Sediment: 0.030 ug/kg
- Remarks: Results for soil and sediment are expressed in dry weight

CONCLUSIONS

- The estimated concentrations for DPGME in environmental media are well below the levels required to produce adverse environmental effects.

DATA QUALITY = 1**REFERENCES (Free Text)**

- Staples CA, Davis JW. 2001. An environmental risk assessment of propylene glycol ethers (in prep).

OTHER

BIODEGRADATION**TEST SUBSTANCE**

- Dipropylene glycol methyl ether (DPGME)

METHOD

- Method/guideline: OECD 301 F Manometric Respirometry Test
- Test Type: aerobic
- GLP: Yes
- Year (study performed): 1998
- Contact time (units): 28 days
- Inoculum: Domestic sludge
- Concentration of test chemical: 27.7mg/l related to COD
- Temperature of incubation: ambient

RESULTS

- Degradation was 79% after 28 days. (Kinetic: 10% at 10.7 days and 60% at 16.1 days).
-

CONCLUSIONS

DPGME is considered readily biodegradable. The mean percent biodegradation occurring after 28 days from aqueous medium dosed with sodium benzoate was >99% (60% after first 2.1 days) of the initial sodium benzoate applied.

DATA QUALITY = 1

REFERENCES

Dow Chemical U.S., Unpublished Report #98111 (1998)

OTHER

- Under aerobic conditions this chemical is rapidly and extensively biodegraded, for which half-life estimates ranging from 7 to 28 days for DPGME in soil or water have been estimated (Staples and Davis, 2001 in prep.).

BIODEGRADATION**TEST SUBSTANCE**

- Dipropylene glycol methyl ether (DPGME)

METHOD

- Method/guideline: Modified Zahn-Wellens Test
- Test Type: aerobic
- GLP: Yes
- Year (study performed): 1981
- Contact time (units): 13 days
- Inoculum: BASF wastewater sludge
- Concentration of test chemical: 400mg/l DOC (734 mg/l test substance)
- Temperature of incubation: ambient

RESULTS

- Degradation was 93% after 13 days.

CONCLUSIONS

- Dipropylene glycol methyl ether is considered ultimately biodegradable. No significant adsorption on activated sludge and no abiotic elimination were observed.

DATA QUALITY = 2

REFERENCES

- BASF product literature for dipropylene glycol methyl ether in the Zahn-Weller test. (1981)

BIODEGRADATION**TEST SUBSTANCE**

- Dipropylene glycol methyl ether (DPGME)

METHOD

- Method/guideline: ASTM E 1196-92
- Test Type: anaerobic
- GLP: Yes
- Year (study performed): 1998
- Contact time (units): 81 days
- Inoculum: municipal digester sludge:
- Inoculum (concentration and source): 10% (Midland municipal waste water treatment plant)
- Concentration of test chemical, vehicle used, pre-acclimation conditions: 50 mg/L, mineral medium, glovebox atmosphere = 70% N₂, 28% CO₂ and 2% H₂
- Temperature of incubation: 34.8 °C
- Sampling frequency: day 10, 17, 28, 42, 56, 70, 81
- Appropriate controls and blank system used? Yes
- Analytical method used to measure biodegradation: Gas production
- Method of calculating measured concentrations: arithmetic mean

RESULTS

- Degradation % after time: 10% degradation after 81 days
- For each time period %: 0% up to day 28; 10% from day 42 on
- Breakdown products: None specified.
- Remarks field for Results: A lag period of approximately 30 days was noted before any degradation was observed. No signs of toxicity to inoculum (as determined from gas production from standard substrates) from DPGME was observed.

CONCLUSIONS

- DPGME is only slightly biodegradable under anaerobic conditions

DATA QUALITY = 1**REFERENCES**

- Dow Chemical U.S., Unpublished Report #971174 (1998)

OTHER

ECOTOXICITY ELEMENTS**ACUTE TOXICITY TO FISH****TEST SUBSTANCE**

- Dipropylene glycol methyl ether (DPGME)

METHOD

- Method/guideline: ?
- Type (test type):
- GLP: ?
- Year (study performed): 1979
- Species/Strain/Supplier: Pimephales promelus
- Analytical monitoring:
- Exposure period (unit): 96 hours
- Statistical methods: descriptive
- Details of test: static
- Remarks:

RESULTS

- Nominal concentrations:
- Element value: LC50 value exceeds 10,000 mg/L
- Statistical results:

CONCLUSIONS

- DPGME is essentially non-toxic to Pimephalus promelus following acute exposures.

DATA QUALITY = 2**REFERENCES**

- Bartlett EA. 1979. Unpublished Dow Chemical Report: Toxicity of Dowanol DPM to freshwater organisms

OTHER

ACUTE TOXICITY TO AQUATIC INVERTEBRATES (E.G., DAPHNIA)**TEST SUBSTANCE**

- Dipropylene glycol methyl ether (DPGME)

METHOD

- Method/guideline: ?
- Test type:
- GLP: ?
- Year (study performed): 1979
- Species/Strain: *Daphnia magna*
- Test details: static
- Statistical methods: descriptive
- Exposure period: 48 hours
- Remarks:

RESULTS

- Nominal concentrations:
- Unit:
- 48 hours: $LC_{50} = 1919$ mg/L
- Statistical results:
- Remarks:

CONCLUSIONS

- DPGME is slightly toxic to *Daphnia magna* following acute exposures.

DATA QUALITY = 2**REFERENCES**

- Bartlett EA. 1979. Unpublished Dow Chemical Report: Toxicity of Dowanol DPM to freshwater organisms

OTHER

- These results are supported by a 22-day reproduction study in *Daphnia* in which no adverse effects were observed at concentration of 0.5 mg/L (Dow Chemical Report #DET-2255, 1995).

TOXICITY TO AQUATIC PLANTS (E.G., ALGAE)**TEST SUBSTANCE**

- Dipropylene glycol methyl ether (DPGME)
- Remarks: 99.5% pure

METHOD

- Method/guideline: OECD 201
- Test type (static/other): static
- GLP: Yes
- Year (study performed): 2000
- Species/strain # and source: *Selenastrum capricornutum* Printz (Strain 1648)
- Element basis: Algal cell densities were determined by electron particle counting using a Coulter Multisizer.
- Exposure period, date of start and end of the test [Duration]: 3 and 4 days
- Analytical monitoring: GC/FID analysis on days 0 and 4
- Statistical methods: arithmetic mean of 3 replicates per test concentration
- Remarks: Average initial cell density was 12466 cells/mL; Temperature = 24.3 C; light intensity = 4644 kux; pH = 6.9-7.6 without algae or 8.0-9.3 with algae.

RESULTS

- Nominal concentrations: 31.3 - 1000 mg/L
- Measured concentrations: 27.9, 63.1, 123, 254, 503, 969 mg/L
- Unit:
- Element value: For 3-day exposures, an EC10 value of 133 mg/L was reported for growth inhibition. 3- and 4-day EC50 values exceeded the highest concentration tested (>969 mg/L).
- NOEC, LOEC, or NOEL, LOEL: NOEC = 969 mg/L; LOEC > 969 mg/L
- Was control response satisfactory: Yes
- Statistical results: Effects of DPGME on cell growth were not statistically significant. Remarks: An EC10 of 133 mg/l and NOEC of 969 mg/l is not an inconsistency. The conclusion of a 3-day NOEC of 969 mg/L is based on three factors the first being a lack of a dose response, the second being that there was only 11 percent inhibition of growth at 969 mg/L when compared to the control group, and the third being the standard deviation associated with the data generated on day 3 for this dose level. The last point is the one taken into consideration by the statistical package used to evaluate the data.

CONCLUSIONS

- According to a categorization system used by USEPA, DPGME is classified as "practically non-toxic" to *S. capricornutum*.

DATA QUALITY = 1**REFERENCES**

- Kirk et al. (2000): Unpublished Study by Dow Chemical Company # 001212

OTHER

HEALTH ELEMENTS**ACUTE TOXICITY****TEST SUBSTANCE**

- Dipropylene glycol methyl ether (DPGME)
- Remarks:

METHOD

- Method/guideline:
- Type (test type): lethality study
- GLP: No
- Year (study performed): 1954
- Species/Strain: young rats/white
- Sex: male/female
- No. of animals per sex per dose: 169 rats placed into 9 dose levels (breakdown not specified)
- Vehicle: none
- Route of administration: oral
- Remarks: A series of toxicity studies are reported. Few details are presented. Statistical methods described by Litchfield and Wilcoxon used to evaluate dose-response. All surviving animals were observed until full recovery from loss of weight (approximately 2 weeks).

RESULTS

- LD₅₀ Value: 5.4 mL/kg (95% confidence limit 4.9 – 6.9 mL/kg), corresponding to 5230 mg/kg (males) and 5180 mg/kg (females)
- Number of deaths at each dose level: Not specified
- Remarks: Although few details provided, this study defines an oral LD₅₀ value with a high level of confidence.

CONCLUSIONS

- The acute oral toxicity of DPGME is relatively low.

DATA QUALITY = 2**REFERENCES**

- Rowe VK, et al. (1954). Toxicology of mono-, di-, and tripropylene glycol methyl ethers. Indust Hyg Occup Med

OTHER

- Acute inhalation toxicity in rat
 - Acute Dermal toxicity in rabbits
- LOAEL = 500 ppm (Rowe et al. 1954)
LC 50 = 9500 mg/kg (Smyth et al, 1962),

REPEATED DOSE TOXICITY**TEST SUBSTANCE**

- Dipropylene glycol methyl ether (DPGME)

METHOD

- Method/guideline followed: Kanpogyo 700, Yakuhatsu 1039, Kikyoku 1014
- Test type: Oral repeated-dose toxicity study
- GLP: Yes
- Year (study performed): 2000
- Species: Rat
- Strain: Sprague-Dawley
- Route of administration: oral (gavage)
- Duration of test: 4 weeks
- Doses/concentration levels: 0, 40, 200, 1000 mg/kg
- Sex: male & female
- Exposure period: 4 weeks
- Frequency of treatment: daily
- Control group and treatment: vehicle
- Post exposure observation period: 2 weeks (controls and high dose)
- Statistical methods: descriptive
- Remarks field for Test Conditions.
- Test Subjects
- Age at study initiation: 6 weeks
- No. of animals per sex per dose: 5-10
- Study Design
- Vehicle: water
- Clinical observations performed and frequency: 3x/day
- Organs examined at necropsy: Brain, pituitary, thyroid, heart, thymus, esophagus, stomach, duodenum, ileum, colon, kidneys, adrenals, urinary bladder, testes, epididymes, prostate, ovaries, uterus, femoral bone, spinal cord, sciatic, lymph nodes

RESULTS

- NOAEL (NOEL): 200 mg/kg
- LOAEL (LOEL): 1000 mg/kg
- Toxic response/effects by dose level:
1000 mg/kg: tentative salivation, significantly increased relative liver weight, centrilobular hypertrophy
- Remarks No effects were noted on body weight or survival. No hematological effects were reported. Tentative salivation noted immediately after exposure beginning on day 11. Evidence of hepatotoxicity also noted at the highest dose. Liver weight (absolute and relative) remained significantly elevated in male rats following a two week recovery period. No other treatment related effects were observed.

CONCLUSIONS

- It is concluded that 200 mg/kg-day represents a NOAEL in rats under the conditions of this oral study.

DATA QUALITY = 1

REFERENCES

- Dow Chemical Japan, Unpublished Report #FBM 99-2691 (2000)

OTHER

REPEATED DOSE TOXICITY**TEST SUBSTANCE**

- Dipropylene glycol methyl ether (DPGME)

METHOD

- Method/guideline: OECD Guideline 413
- Test type: Sub-chronic inhalation study
- GLP): No
- Year (study performed): 1984
- Species: Rat
- Strain: Fischer 344
- Route of administration: Inhalation (whole-body)
- Duration of test: 13 weeks
- Doses/concentration levels: 0, 15, 50, 200 ppm
- Sex: male & female
- Exposure period: 13 weeks
- Frequency of treatment: 6 hours/day; 5 days/week
- Control group and treatment: vehicle

RESULTS

- NOAEL (NOEL): 200 ppm
Toxic response: There were no effects attributable to exposure to DPGME at any exposure concentrations in male or female rats.
- Remarks field for Results: Concentrations of 15, 50 and 2000 ppm DPGME correspond to 91, 303, and 1212 mg/m³ DPGME respectively. 200 ppm was approximately 40% of a saturated DPGME atmosphere.

CONCLUSIONS

- It is concluded that 200 ppm represents a NOAEL in rats under the conditions of this study.

DATA QUALITY = 2**REFERENCES**

Landry, T.D. and Yano, B.L. 1984. Dipropylene glycol monomethyl ether: A 13 week inhalation toxicity study in rats and rabbits. *Fundam. Appl. Toxicol.* 4, 612-617.

REPEATED DOSE TOXICITY**TEST SUBSTANCE**

- Dipropylene glycol methyl ether (DPGME)

METHOD

- Method/guideline followed: ?
- Type: 28 week inhalation study
- GLP: No
- Year (study performed): 1954
- Species/Strain: Rat
- Route of administration: inhalation ((whole-body)
- Duration of test: 28 weeks
- Doses/concentration levels: 300-400 ppm
- Sex: 13 male & 17 female
- Exposure period: 28 weeks
- Frequency of treatment: 7 hours/day; 5 days/week
- Control group and treatment: ?

RESULTS

- Transient narcosis was reportedly observed during the first few weeks of the study. No effects other than increased liver weight was observed.

CONCLUSIONS

- The LOAEL for this study was 200 – 300 ppm (1212 – 1818 mg/m³: 40 – 60% saturated DPGME vapor).

DATA QUALITY = 2**REFERENCES**

- Rowe, V.K., McCollister, D.D., Spencer, H.C. et al. (1954). AMA Arch Ind Hug Occup Med 9: 509-525.

GENETIC TOXICITY ELEMENTS**GENETIC TOXICITY IN VITRO (GENE MUTATIONS)****TEST SUBSTANCE**

- Dipropylene glycol methyl ether (DPGME)

METHOD

- Method/guideline: Kanpogyo 700; Yakuhatsu 1039; Kikyoku 1014; Kanpoan 298; Eisie 127; Kikyoku 2
- Type: reverse mutation assay
- System of testing: Bacterial
- GLP: Yes
- Year (study performed): 2000
- Cell line: Salmonella typhimurium TA98, TA1537, TA100; Escherichia coli WP2uvrA
- Metabolic activation: Liver S-9, uninduced
- Concentrations tested: 313, 625, 1250, 2500, 5000 ug/plate
- Statistical Methods: descriptive
- Number of replicates: 3
- Positive and negative control groups and treatment: 2-aminofluorene, 9-aminoacridine, sodium azide
- Criteria for evaluating results (e.g. cell evaluated per dose group): doubling of mean revertants in negative control

RESULTS

- Genotoxic effects
- With metabolic activation: negative
- Without metabolic activation: negative

CONCLUSIONS

- DPGME shows no evidence of mutagenic activity under the conditions of this assay.

DATA QUALITY =1**REFERENCES**

- Dow Chemical Japan, Unpublished Report #FBM 00-8026 (2000)

OTHER

GENETIC TOXICITY IN VITRO (CHROMOSOMAL ABERRATIONS)**TEST SUBSTANCE**

- Dipropylene glycol methyl ether (DPGME)

METHOD

- Method/guideline: Kanpogyo 700; Yakuhatsu 1039; Kikyoku 1014
- Type (test type): chromosomal aberrations
- GLP: Yes
- Year (study performed): 2000
- Cells: Chinese Hamster Lung
- Concentration levels: 0.371, 0.741, 1.482 mg/L
- Exposure period: 6 hours, 25 hours
- Statistical methods: descriptive
- Remarks: In vitro evaluation of cytotoxicity and chromosomal aberrations under pulse (6 hours) and continuous (25 hours) treatments. A broader range of concentrations was evaluated for cytotoxicity (0.0029 – 1.482 mg/L)
- Control groups: dimethylnitrosamine, methylmethanesulfonate
- Criteria for evaluating results: aberration incidence = <5% (negative), 5-10% (semi-positive), >10% (positive)

RESULTS

- Cytotoxicity:
 - With metabolic activation: negative
 - Without metabolic activation: negative
- Chromosomal Aberrations
 - Pulse treatment
 - With metabolic activation: negative
 - Without metabolic activation: negative
 - Continuous treatment
 - With metabolic activation: negative
 - Without metabolic activation: negative

CONCLUSIONS

- DPGME shows no evidence of potential to cause structural or numerical abnormalities in chromosomes of CHL/IU cells.

DATA QUALITY = 1**REFERENCES**

- Dow Chemical Japan, Unpublished Report #FBM 00-8027 (2000)

OTHER (genetic toxicity in vivo)

- Concentrations up to 6,000 mg/kg PGME (a structurally similar chemical) administered to mice did not increase the frequency of micronuclei in polychromatic erythrocytes harvested from bone marrow (Elias et al., 1996).

CARCINOGENICITY**TEST SUBSTANCE**

Propylene Glycol Methyl Ether (PGME)

Levels of alpha isomer (1-methoxy-2-propanol) ranged from 97.99-98.07%, while the beta isomer (2-methoxy-1-propanol) ranged from 1.86-1.90%.

METHOD.

Method: OECD 453
 GLP: Yes [X] No [] ? []
Test substance: **PGME**
 Species/strain: Rat/Fischer 344
 Sex: Female []; Male []; Male/Female [X]; No data []
 Route of Administration: inhalation (whole body)
 Exposure period: 2 years
 Frequency of treatment: 6 hr/day, 5 days/week
 Postexposure observation period: none
 Doses: 0, 300, 1000, 3000 ppm
 Control group: Yes [X]; No []; No data []; Concurrent no treatment []; Concurrent vehicle [X]; Historical []
 NOEL: 300 ppm
 LOEL: 1000 ppm

RESULTS :

PGME-induced sedation at 3000 ppm resolved in all animals during the second week of exposure in conjunction with the appearance of adaptive changes in the liver (MFO induction and hepatocellular proliferation-from previous work). MFO activities (PROD) subsequently dropped to near-control values by week 52, coinciding with a return of sedation at 3000 ppm PGME. In male rats, the loss of metabolic adaptation was followed by a dose-related increase in eosinophilic foci of altered hepatocytes after two years of exposure to 1000 or 3000 ppm PGME. Kidney toxicity was observed in male rats only, which was confirmed immunohistochemically as an alpha 2μ-globin nephropathy. No statistically-identified increases in tumors were observed in any tissue, however, a numerical increase in kidney tumors (3/50) were observed in male rats from the intermediate exposure level with 1/50 observed at 3000 ppm PGME.

CONCLUSIONS

It is concluded that 300 ppm represents a NOEL in rats under the conditions of this study.

REMARKS

The lack of statistical significance or a dose-response relationship in renal tumors, in conjunction with the induction of the male rat-specific alpha 2μ-globulin nephropathy, render these minimal renal observations irrelevant for human risk assessment purposes.

DATA QUALITY = 1**REFERENCES**

Cieszlak, F.S., *et al.* 1998a. Propylene Glycol Monomethyl Ether: A 2-year Vapor Inhalation Chronic Toxicity/Oncogenicity Study and Evaluation of Hepatic and Renal Cellular Proliferation, P450 Enzyme Induction and Protein Droplet Nephropathy in Fischer 344 Rats. Unpublished report (in preparation) of the Dow Chemical Company (sponsored by the Chemical Manufacturers Association P-Series Glycol Ethers Panel, Arlington, VA).

CARCINOGENICITY**TEST SUBSTANCE**

Propylene Glycol Methyl Ether (PGME)

Levels of alpha isomer (1-methoxy-2-propanol) ranged from 97.99-98.07%, while the beta isomer (2-methoxy-1-propanol) ranged from 1.86-1.90%.

METHOD

Method: OECD 453
GLP: Yes ☒ No ☐ ? ☐
Test substance: PGME
Species/strain: Mouse/B6C3F1
Sex: Female ☐; Male ☐; Male/Female ☒; No data ☐
Route of Administration: inhalation(whole body)
Exposure period: 2 years
Frequency of treatment: 6 hr/day, 5 days/week
Postexposure observation period: none
Doses: 0, 300, 1000, 3000 ppm
Control group: Yes ☒; No ☐; No data ☐;
Concurrent no treatment ☐; Concurrent vehicle ☒; Historical ☐
NOEL: 300 ppm
LOEL: 1000 ppm

RESULTS

A transient sedation of mice inhaling 3000 ppm PGME during the first week of exposures was observed; however, this resolved during the second week concomitant with adaptive changes in the livers of these animals (previous study results). Mice exposed to 3000 ppm had increased mortality (males), decreased in-life body weights and body weight gains relative to controls, over much of the exposure period, as well as minimal increases in absolute and relative liver weights and hepatic MFO activity. No treatment-related histopathological changes accompanied these liver effects, nor were histopathological changes observed in any other tissues. These data, along with the occurrence of chronic, albeit small increases in hepatocellular proliferation in mice inhaling 3000 ppm suggested minimal regenerative response in the liver, likely related to shortened life span metabolically stressed hepatocytes. Decreases in body weights were also observed, although less frequently, in both sexes exposed to 1000 ppm. No treatment-related increases in tumors were observed in any tissue of male or female mice.

CONCLUSIONS

It is concluded that 300 ppm represents a NOEL in mice under the conditions of this study.

DATA QUALITY = 1**REFERENCES**

Cieszlak, F.S., *et al.* 1998b. Propylene Glycol Monomethyl Ether: A 2-year Vapor Inhalation Chronic Toxicity/Oncogenicity Study and Evaluation of Hepatic Cellular Proliferation in B6C3F1 Mice. Unpublished report (in preparation) of the Dow Chemical Company (sponsored by the Chemical Manufacturers Association P-Series Glycol Ethers Panel, Arlington, VA).

OTHER

While DPGME has not been evaluated in a chronic toxicity/oncogenicity bioassay to date, its low toxicologic potential in subacute and subchronic studies, lack of genotoxic activity, and biotransformation via the same general routes and types of metabolites as the noncarcinogen PGME, indicate that DPGME is unlikely to be carcinogenic in man or animals.

In 2-year inhalation carcinogenicity studies sponsored by the CMA PGE Panel with the structurally similar chemical propylene glycol monomethyl ether (PGME) no evidence of carcinogenicity has been found in either rats or mice. The No Observed Adverse Effect Levels (NOEL's) in both sexes of both species were 300 ppm. Major metabolic pathways for DPGME include conjugation with glucuronic acid and sulfate; hydrolysis of the methoxy group to form dipropylene glycol; and hydrolysis of the dipropylene glycol backbone of DPGME to form PGME and propylene glycol (Miller *et al* 1985). The glucuronide and sulfate conjugates of DPGME are essentially non-toxic and rapidly eliminated from the body. DPGME is less volatile and has been shown in comparable studies to be similar to, or less toxic than dipropylene glycol, PGME and propylene glycol, each of which are of low toxicity, themselves. Therefore, no major differences in the systemic toxicological properties of DPGME and PGME would be anticipated, including carcinogenic potential. Consistent with this view is the fact that DPGME has been shown not to be genotoxic in several *in vitro* assay systems; DPGME was negative in an Ames bacterial gene mutation assay, did not induce unscheduled DNA synthesis (DNA damaged-induced repair) in rat hepatocytes, and was not clastogenic in CHO cells (ECETOC, 1995).

TOXICITY TO REPRODUCTION**TEST SUBSTANCE**

Propylene Glycol Methyl Ether (PGME)

Levels of alpha isomer (1-methoxy-2-propanol) ranged from 97.99- 98.07%, while the beta isomer (2-methoxy-1-propanol) ranged from 1.86-1.90%.

METHOD

Method: OECD 416
 GLP: Yes ☒ No ☐ ? ☐
 Test substance: PGME
 Type: Fertility ☐ ; One generation study ☐ ; Two generation study ☒ ;
 Other ☐
 Species/strain: Rat/Sprague-Dawley
 Sex: Female ☐ ; Male ☐ ; Male/Female ☒ ; No data ☐
 Route of Administration: inhalation
 Exposure period: 6 hours/day
 Frequency of treatment: 5 days/week prior to mating and 7 days/week during mating,
 gestation and lactation
 Postexposure observation period: NA
 Premating exposure period: male: NA, female: NA
 Doses: 0, 300, 1000 and 3000 ppm
 Control group: Yes ☒ ; No ☐ ; No data ☐ ;
 Concurrent no treatment ☐ ; Concurrent vehicle ☒ ; Historical ☐
 NOEL Parental: 300 ppm
 NOEL F1 Offspring: 1000 ppm
 NOEL F2 Offspring: 1000 ppm

RESULTS :

At 3000 ppm, toxicity in the P1 and P2 adults was marked, as evidenced by sedation during and after exposure for several weeks, and mean body weights which were as much as 21% lower than controls. This marked parental toxicity was accompanied by lengthened estrous cycles, decreased fertility, decreased ovary weights, reduced pup survival and litter size, slight delays in puberty onset, and histologic changes in the liver and thymus of the F1 and F2 offspring. At 3000 ppm, there was an increase in histologic ovarian atrophy in P1 and P2 females, and at 1000 ppm, there was a decrease in pre-mating body weight in the P1 and P2 females. No treatment-related differences in sperm counts or motility were observed among the P1 or P2 males.

REMARKS:

The nature of the reproductive/neonatal effects and their close individual correlation with decreased paternal body weights suggest that these effects were secondary to general toxicity and/or nutritional stress. No such effects were observed at 1000 ppm, a concentration which caused less marked, but significant body weights effects without sedation.

QUALITY = 1**REFERENCES**

E.W. Carney, J.W. Crissman, A.B. Liberacki, C.M. Clements, and W.J. Breslin, "Two-Generation Inhalation Reproduction Study with Propylene Glycol Monomethyl Ether in Sprague-Dawley Rats," Toxicol.Sci. 50, 249-258 (1999)

OTHER

- In a 2-generation inhalation reproduction study sponsored by the CMA Propylene Glycol Ethers Panel with the structurally similar chemical propylene glycol monomethyl ether (PGME) no adverse fertility or reproductive effects were observed at 1,000 ppm PGME. Major metabolic pathways for DPGME include conjugation with glucuronic acid and sulfate; hydrolysis of the methoxy group to form dipropylene glycol; and hydrolysis of the dipropylene glycol backbone of DPGME to form PGME and propylene glycol (Miller et al, 1985). The glucuronide and sulfate conjugates of DPGME are essentially non-toxic and rapidly eliminated from the body. DPGME is less volatile and has been shown in comparable studies to be similar to, or less toxic than dipropylene glycol, PGME and propylene glycol, each of which are themselves of low toxicity. Based upon the similarities in metabolism and modes of action of DPGME and its metabolites, it is highly probable that DPGME will be similar to or less toxic than its metabolites in reproductive toxicity studies.

Additionally, no effects were seen on the testes and ovaries in a 28-day repeat dose oral toxicity study (Dow Chemical Japan, Unpublished Report #FBM 99-2691, 2000)

DEVELOPMENTAL TOXICITY/TERATOGENICITY**TEST SUBSTANCE**

- Dipropylene glycol methyl ether (DPGME)

METHOD

- Method/guideline: Other
- GLP: Yes
- Year (study performed): 1990
- Species: Rat
- Strain: F344
- Route of administration: inhalation
- Doses/concentration levels: 0, 50, 150, 300 ppm
- Sex: Female
- Exposure period: Gestation days 6-15
- Frequency of treatment: Daily
- Control group and treatment: Vehicle
- Duration of test: 6 hours/day
- Statistical methods: Descriptive

RESULTS

- Maternal toxicity: NOAEL = 300 ppm; LOAEL \geq 300 ppm
- Developmental toxicity: NOAEL = 300 ppm; LOAEL \geq 300 ppm
- Remarks: 300 ppm/day was the highest concentration attainable

CONCLUSIONS

- DPGME is not maternally toxic, fetotoxic, or teratogenic in rats exposed to concentrations as high as 300 ppm during gestation.

DATA QUALITY = 1**REFERENCES**

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OTHER

- The results of this study are supported by observations made in similarly treated rabbits.

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