FOREWORD INTRODUCTION

DIPROPYLENE GLYCOL

(MIXED ISOMERS AND DOMINANT ISOMER)

CAS N°:25265-71-8 & 110-98-5)

SIDS Initial Assessment Report
for
11th SIAM

(USA, January 23-26, 2001)

Chemical Name: Dipropylene glycol, mixed isomers and dominant isomer

CAS No: 25265-71-8 and 110-98-5

Sponsor Country: U.S.A

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HISTORY: At SIAM 11 the recommendation of Low Priority for Further Work was agreed. Revisions to the SIAR and preparation of Robust Summaries were requested and agreed.

COMMENTS:

Deadline for circulation:

Date of Circulation:

SIDS INITIAL ASSESSMENT PROFILE

CAS No.	25265-71-8 and 110-98-5
Chemical Name	Dipropylene glycol, mixed isomers and dominant isomer
Structural Formula	CH_3-CHOH-CH_2O-CH_2-CHOH-CH_3

RECOMMENDATIONS

The chemical is currently of low priority for further work.

SUMMARY CONCLUSIONS OF THE SIAR

Human Health

Dipropylene glycol (DPG) is not acutely toxic by oral (LD_{50} $\geq$13 g/kg bw/day from 7 rat studies and 17.6 g/kg bw/day from a guinea pig study), dermal (LD_{50} > 5g/kg bw/day in 2 rabbit studies) or inhalation (no deaths observed in rats and guinea pigs at 6 to 8 g/m^3) routes of exposure. DPG is slightly irritating to the skin and eyes of rabbits. Based on human data, DPG is not a skin sensitizer. Repeated exposures of rats to DPG did not result in adverse effects at levels up to 5% (estimated NOAEL is about 6.2 g/kg bw/day) in drinking water. At about 12.5 g/kg bw/day (10%), kidney lesions appeared in about 30% of the rats. Results from an OECD 422 combined repeat dose/reproductive/developmental toxicity test on the structural analogue, tripropylene glycol (TPG), demonstrated a NOAEL of 200 mg/kg bw and a LOAEL of 1000 mg/kg bw for repeated dose toxicity, with increased relative weight for liver and kidney. Metabolic fate data on TPG demonstrates that TPG is readily converted to DPG, PG, and CO_2 in rats. Thus, data from TPG are relevant to DPG. DPG did not cause fetal toxicity or teratogenicity in rats (NOAEL = 5 g/kg bw/day) or rabbits (NOAEL = 1.2 g/kg bw/day). No reproductive studies have been conducted on DPG. However, the structural analogues, propylene glycol and TPG, have been tested for reproductive effects and shown to have NOAELs of 10.1 g/kg bw in mice and 1 g/kg bw in rats, respectively. Thus, the lack of reproductive effects from TPG and the high NOAEL for PG reproductive toxicity indicate that no reproductive effects are expected in animals exposed to DPG, in the absence of maternal toxicity. DPG is not a genetic toxicant based on *in vitro* (bacterial and mammalian cells in culture) and *in vivo* (micronucleus) studies.

Environment

Dipropylene glycol (DPG) is not volatile, but is miscible with water. Air monitoring data are not available, but concentrations of dipropylene glycol in the atmosphere are expected to be extremely low because of its low vapor pressure and high water solubility. Low levels of DPG (0.4 ng/l) in drinking water were reported in one study. It is biodegraded in water and expected to be biodegraded in soil, as indicated by >70% degradation after 28d in a Zahn-Wellens test. It is not expected to bioaccumulate, with measured BCFs between 0.3 and 4.6 in fish. Measured aquatic toxicity data on fish and amphibians report toxicity at >5,000 and 3,181 mg/L, respectively. Based on QSAR data for Daphnia and algal toxicity, and the measured data for fish and amphibians, DPG is not expected to be toxic to aquatic organisms except at very high concentrations. Using an assessment factor of 100 and the fish 96-hour LC_{50}, the PNEC is >50 mg/l; if the amphibian data are used, the PNEC is 32 mg/l.

Exposure

Dipropylene glycol is produced as a byproduct of the manufacture of propylene glycol. The US production capacity of DPG was 131 million pounds (59.5 kilotonnes) in 1998; the demand was 108 million pounds (49 kilotonnes). DPG is used (percent of demand) as follows: plasticizers, 38 percent; unsaturated polyester resins, 23 percent; cosmetics and fragrances, 10 percent; polyurethane polyols, 8 percent; alkyd resins, 7 percent; miscellaneous, including solvents and functional fluids (specialty de-icers, inks, lubricants), 14 percent.

NATURE OF FURTHER WORK RECOMMENDED

No further work is recommended.

FULL SIDS SUMMARY

CAS NO: 25265-71-8, 110-98-5		SPECIES	PROTOCOL	RESULTS
PHYSICAL-CHEMICAL				
2.1	Melting Point	--	NG	<-39°C
2.2	Boiling Point	--	NG	228-236°C
2.3	Density	--	NG	1.022 g/cm3 at 25°C
2.4	Vapour Pressure	--	NG	0.0128 hPa at 20°C
2.5	Partition Coefficient (Log K_{ow})	--	NG	-1.486
2.6 A.	Water Solubility	--	NG	Miscible at at 25°C
B.	PH	--	--	
	Pka	--	--	
2.12	Oxidation: Reduction Potential	--	--	
ENVIRONMENTAL FATE AND PATHWAY				
3.1.1	Photodegradation	--	--	---
3.1.2	Stability in Water	--	NG	No hydrolyzable groups
3.2	Monitoring Data	--	--	
3.3	Transport and Distribution	--	Fugacity model Level III	0.11% to air; 46.1% to water; 53.7% to soil; 0.08% to sediments.
3.5	Biodegradation		a. Other TG: EEC-87/302	a. >70% after 28 days (pre-adapted)
			b. OECD TG 301C	b. No degradation.
3.6	BOD5, COD		Other TG:	BOD5 = 92 mgO2/L
			APHA 219	COD = 1840 mg/g
3.7	Bioaccumulation	Cyprinus carpio	OECD TG 305C	BCF of 0.3-1.4 (42 days at 3 mg/L)
				BCF of <2.2-4.6 (42 days at 3 mg/L)
ECOTOXICOLOGY				
4.1	Acute/Prolonged Toxicity to Fish	Carassius auratus	24-hr lethality Other TG: APHA 1971	LC50 = >5000 mg/L (static)
4.2	Acute Toxicity to Aquatic Invertebrates *(Daphnia)*	--	--	No data
4.3	Toxicity to Aquatic Plants e.g. Algae	--	--	No data

CAS NO: 25265-71-8, 110-98-5		SPECIES	PROTOCOL	RESULTS
4.4	Toxicity to Microorganisms	Pseudomonas putida	Other TG: LTwS-Nr 10	EC10 = 1000 mg/L (static, 18 hr)
4.5.1	Chronic Toxicity to Fish	--	--	No Data
4.5.2	Chronic Toxicity to Aquatic Invertebrates (*Daphnia*)	--	--	No Data
4.6.1	Toxicity to Soil Dwelling Organisms	--	--	No Data
4.6.2	Toxicity to Terrestrial Plants	--	--	No Data
4.6.3	Toxicity to Other Non-Mammalian Terrestrial Species (Including Birds)			No Data
4.9	Additional Remarks	Xenopus laevis	NG	LC50 = 3,181 mg/L (48 hr, static)
TOXICOLOGY				
5.1.1	Acute Oral Toxicity	a. Rat	Acute lethality NG	a. LD50 = 16,000 mg/kg (est. from 15.8 mL/kg)
		b. Mouse		b. LD50 = >2,000 mg/kg
5.1.2	Acute Inhalation Toxicity	Rat, guinea pig	Acute lethality NG	Not lethal: 6000-8000 mg/m3 (aerosol, nominal concentration)
5.1.3	Acute Dermal Toxicity	Rabbit	Acute lethality NG	LD50 > 5000 mg/kg
5.2.1	Skin Irritation	a. Rabbit	a. Draize test NG	a. Slightly irritating (500 mg, 24 hr, occluded)
		b. Human	b. NG	b. None to mild irritation (2 mL of 25% solution; 24 hr; semi-occluded)
5.2.2	Eye Irritation	Rabbit	Draize test NG	Slightly irritating (0.1 mL of 100% solution; 4 hr)
5.3	Skin Sensitization	Human	NG	1 of 503 was sensitized to synthesis grade
5.4	Repeated Dose Toxicity	Rat	9-77 days, in drinking water. NG	NOAEL 5% LOAEL = 10%
		Dog	4 or 6 gavage doses NG	NOAEL 20 mL/kg
		Rat	15 wk, oral NG	NOAEL = 12% in diet
5.5	Genetic Toxicity In Vitro			

CAS NO: 25265-71-8, 110-98-5		**SPECIES**	**PROTOCOL**	**RESULTS**
A.	Bacterial Test (Gene mutation)	Salmonella typhimurium	Mutagenicity; Ames test NG	Negative (with and without activation) (TA 98, 100, 1535, 1537)
B.	Non-Bacterial In Vitro Test	Mouse	Lymphoma assay; NG	Negative (with and without activation)
5.6	Genetic Toxicity In Vivo	Mice	Micronucleus assay OECD TG 474 EPA 870.5395	Negative (2000 mg/kg, gavage)
5.7	Carcinogenicity	--	--	No Data
5.8	Toxicity to Reproduction	--	--	No Data
5.9	Developmental Toxicity/ Teratogenicity	Rat	Gavage Other TG: NTP	NOAEL = 800 mg/kg maternal toxicity NOAEL = 5000 mg/kg teratogenicity
		Rabbit	Gavage Other TG: NTP	NOAEL = 1200 mg/kg maternal toxicity NOAEL = 1200 mg/kg teratogenicity
5.10	Other Relevant Information	Rat	104 wk, oral NG	Propylene glycol tested: No treatment related increase in tumors at dietary levels up to 50000 ppm propylene glycol (approx. 1700-2100 mg/kg/day)
		Mouse	Drinking water; continuous from 7 days prior to mating NG	Propylene glycol tested: NOAEL = 5% (parents) NOAEL = 5% (F1 offspring) NOAEL = 5% (F2) offspring 5% propylene glycol = 10,000 mg/kg
		Rat	Gavage; premating through Day 3 of lactation OECD TG 422	Tripropylene glycol tested: NOAEL = 200 mg/kg (parents) NOAEL = 1000 mg/kg (reproductive) NOAEL = 1000 mg/kg (developmental)
5.11	Experience with Human Exposure		ss	No Data

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1. Identity

Commercial dipropylene glycol (CAS # 25265-71-8; (CH_3-CHOH-CH_2O-CH_2-CHOH-CH_3) is composed of 3 isomers (2,2'-dihydroxydiisopropylether (CAS-No.: 108-61-2); 2,2'-dihydroxydipropylether (CAS-No.: 110-98-5); 2-hydroxypropyl-2'-hydroxyisopropyl-ether (CAS-No.: 106-62-7) and is typically 98% pure. It is a liquid that possesses the following physico-chemical properties and characteristics:

Property	Value
Chemical Formula	$(CH_3CHOCH_2)_2O$
Molecular Weight	134.2
Purity	>= 98% w/w
Impurities	
Solubility	Miscible with water
Melting Point	< -39 °C
Boiling Point	222.2 – 236 °C
Density	1022-1025 mg/ml at 20 °C
Vapor Pressure	0.01 hPa at 20°C 0.05 hPa at 21°C
Log Kow	-1.486
Synonyms	DPG; Di-1,2-propyleneglycol; oxybispropanol; Practical

2. General Information on Exposure

2.1 Production

Dipropylene glycol is produced as a byproduct of the manufacture of propylene glycol. The United States (US) production capacity of dipropylene glycol (i.e., byproduct production capacities of propylene glycol plants) was 131 million pounds (60 thousand tonnes) in 1998. The US Domestic demand in 1998 was 108 million pounds (49 thousand tonnes). In 1998, dipropylene glycol was produced in the US by The Dow Chemical Company, Eastman Chemical Company, Huntsman Corporation, Lyondell Chemical Company, and Olin Corporation. (ChemExpo Chemical Profile, 1998). Worldwide capacity is estimated at 235 million pounds (107 thousand tonnes).

2.2 Use

Dipropylene glycol is used primarily as an industrial intermediate, but is also used as a substance in consumer products, and as an ingredient in pesticidal formulations. Uses of dipropylene glycol as a substance capitalize on its superior performance as a plasticizer as well as properties (e.g., high solvency, high viscosity) that permit dipropylene glycol to act as a functional ingredient of fluids. The uses of dipropylene glycol are listed in the following table.

USES OF DIPROPYLENE GLYCOL

USES	APPLICATION	**FUNCTION**	**% PRODUCTION**
Intermediate	Specialty plasticizer	Plasticizer	38 %
Intermediate	Non-reinforced polyesters	Resin monomer	23 %
Substance	Cosmetics and Fragrances	Humectant, Emollient	10 %
Intermediate	Polyurethane polyols	Plasticizer	10 %
Intermediate	Alkyd resins	Resin monomer	7 %
Substance, Intermediate	Miscellaneous (e.g., dyes & inks, paints & coatings; functional uses in hydraulic brake fluids; cutting oils)	Solvent, functional fluid, coolant	14%

(Source: ChemExpo Chemical Profile (1998)).

The uses listed in the table above have been grouped and assigned a publicly available percentage of production. The Environmental Defense (ED) Scorecard website (Source: www.scorecard.org). for dipropylene glycol lists 6 consumer product types and 18 pesticidal products containing dipropylene glycol. Data available from the US EPA indicates that in 2001 there are two pesticidal products containing dipropylene glycol as an ingredient registered in the US, whereas 20 such products have been registered over time (Source: California Department of Pesticide Registration website, http://www.cdpr.ca.gov/cgi-bin/epa/chemdet.pl?pccode=068604).

2.3 Exposure

As most dipropylene glycol in the US is used in industrial applications, occupational exposures via the dermal or inhalation route present a potential for exposure. In the commercial service and consumer settings use as a functional fluid (e.g. in hydraulic brake fluids, cutting oils) or as an ingredient in pesticides present a potential for inhalation exposure in addition to dermal exposure.

In the consumer setting, dermal exposure, and to a lesser degree inhalation exposure are to be expected where dipropylene glycol is formulated into cosmetic or fragrance products.

DIPROPYLENE GLYCOL EXPOSURE POTENTIAL

POPULATION	ROUTE(S) OF EXPOSURE	SOURCE(S)
Occupational Exposure	Dermal Inhalation	Manufacturing Industrial use as Intermediate Commercial Service
Consumer	Dermal Inhalation	Cosmetics, fragrances, germicidal products

The use concentration of dipropylene glycol in branded pesticidal products is also available. This is summarized in the following table.

PESTICIDAL FORMULATIONS CONTAINING DIPROPYLENE GLYCOL

RANGE OF CONCENTRATION (%)			
	<1	**1-5**	**>5**
No. of Brand Name Products	1	16	1

(Source: EDF Website: www.scorecard.org)

Only two of the 18 branded products shown in the above table currently (May, 2001) maintain active registrations in the US, and both contain dipropylene glycol in the 1 to 5 percent range.

Exposure of dipropylene glycol from environmental sources is expected to be low. Very low levels of dipropylene glycol have been reported in drinking water (0.2 and 0.4 ng/l) and 5 paper mill waste water treatment plants effluents (11 µg/l). Because of its low volatility detection of dipropylene glycol in air samples is not expected.

3. Environment

3.1 Environmental Exposure

Based on the available data, dipropylene glycol is expected to present a low hazard to the environment. If released into the environment, it will preferentially partition into water. Because of its low soil sorption coefficient (K_{oc}), dipropylene glycol is expected to mobilize if spilled on soil and will not adsorb to particles. Volatility is not expected to be a significant fate process for this material due to its low vapor pressure and high water solubility. Photodegradation of the material in air or water is also not expected to be a significant fate process. Once in the environment, dipropylene glycol is capable of being degraded under aerobic conditions by bacteria present in soil and water. As is typical for ethers and glycols, dipropylene glycol is hydrolytically stable. Results of the octanol/water partition coefficient (expressed as log K_{ow}) and from bioaccumulation studies with carp (MITI, 1992) indicate that dipropylene glycol is not expected to significantly accumulate in aquatic organisms (BCF 0.3 to 4.6).

3.2 Environmental Partitioning

Based on the EPIWIN Level III Fugacity Model (Mackay, 1991), dipropylene glycol is expected to partition primarily to water and soil.

Compartment	Percent
Air	0.107
Water	46.1
Soil	53.7
Sediment	0.0768

The results predicted by the model are consistent with study data generated on dipropylene glycol. Based on the low soil sorption coefficient (K_{oc} 3 to 56.2), dipropylene glycol would be expected to mobilize following exposure to soil and would not bind to sediment or soil particles. Mathematical modeling of photodegradation gives an estimated atmospheric half-life of 13 hours, supporting the model results suggesting that the air compartment is not a significant fate process following release of dipropylene glycol. Hydrolysis of dipropylene glycol in water and soil is also not expected to be an important fate process.

Results from biodegradation studies show that dipropylene glycol is biodegraded in water and expected to be biodegraded in soil. Degradation (>70% in 28 days) was observed when the Zahn-Wellens test was used (BASF, 1989), but not when the same compound was evaluated in the MITI test (MITI, 1992). Differences in the technique used to add dipropylene glycol to the test flasks was an important variable in determining the potential degradation of the test substance under the conditions used in these tests. Additional biodegradation tests with *Corynebacterium* sp. under vigorous shaking conditions and with soil bacteria confirmed that dipropylene glycol is biodegradable when contact between the test substance and bacteria is enhanced (Kawai *et al.*, 1977, 1985). Evaluation of the BOD5/COD plants (Bridie *et al.*, 1979b) and the acute toxicity of dipropylene glycol to *Pseudomonas putida* (Claussen, 1993) demonstrate that dipropylene glycol is not expected to be toxic or to cause a significant oxidative load to wastewater treatment

3.3 Effects on the Environment

Based on a combination of test data, quantitative structure activity relationship analysis (QSAR), and data on analogs (propylene glycol, tripropylene glycol), dipropylene glycol presents a low hazard concern for the environment. Representative results for dipropylene glycol include:

Organism	Duration (hrs.)	LC_{50}/EC_{50} (mg/l)	Source
Fish			
Carassium auratus	24	>5,000	Bridie *et al.*, 1979a
Amphibians			
Rana brevipoda porosa	48	5,300	Nishiuchi, 1984
Xenopus laevis	48	3,181	DeZwart and Slooff, 1987
Bacteria			
Pseudomonas putida	18	1,000 (EC_{10})	Claussen, 1993

Toxicity predictions using QSAR support the general conclusions of low toxicity. QSAR predictions for dipropylene glycol based on SARs (chemical class = alcohol ether) for neutral organic chemicals include:

Fish 96-hour LC_{50}	>10,000 mg/l
Daphnid 48-hour LC_{50}	>10,000 mg/l
Green algal 96-hour LC_{50}	>10,000 mg/l
Fish chronic value (ChV)	>1,000 mg/l
Daphnid ChV	470 mg/l
Algal ChV	340 mg/l

Toxicity values for the analogs propylene glycol and tripropylene glycol also support the expected lack of aquatic toxicity, with fish LC_{50} values of >46,000 mg/l and >1,000 mg/l, invertebrate EC_{50} values of 10,000 mg/l and > 1,000 mg/l and aquatic plant EC_{50} values of 19,000 mg/l and >1,000 mg/l for propylene glycol and tripropylene glycol, respectively. Although chronic study data for dipropylene glycol are not available, QSAR predictions suggest that this test substance will not cause chronic toxicity to aquatic organisms. Published studies are not available on the effects of dipropylene glycol on terrestrial organisms or plants, however, little effect is expected, since dipropylene glycol degrades in soil, has very low bioaccumulation potential, and is of low toxicity to aquatic organisms.

Based on the QSAR data for Daphnia and algal toxicity, and the measured data for fish and amphibians, dipropylene glycol is not expected to be toxic to aquatic organisms except at very high concentrations. Using an assessment factor of 100 and the goldfish (*Carassius auratus*) data (LC_{50} >5,000 mg/l), a predicted no effect concentration (PNEC) of >50 mg/l is obtained. Using the clawed toad (*Xenopus laevis*) data (LC_{50} 3,181 mg/l), and an assessment factor of 100, the PNEC is 32 mg/l.

4. Human Health

4.1 Toxicity Studies

4.1.1. Acute Toxicity

Dipropylene glycol is not acutely toxic by oral, dermal, or inhalation exposure. Acute oral toxicity has been examined in the rat, mouse, and guinea pig and the reported LD_{50}s were 15.8 ml/kg (16000 mg/kg), >2000 mg/kg and 17600 mg/kg, respectively. The study that provides the best documentation of design and results was reported by Spanjers and Til, 1980. The authors dosed 5 groups of animals with graded amounts of dipropylene glycol. There was no indication of clinical signs in the report, but the necropsy examination after death or at the end of the 14-day observation period was reported to have found no gross alterations of the internal organs. The authors determined an LD_{50} for the study of 15.8 ml/kg (approximately 16000 mg/kg). In a study designed to assess micronuclei, 6 male mice received two consecutive daily doses of dipropylene glycol via oral gavage; survivors were terminated 24 hours later. There were no deaths in the study; therefore, the LD_{50} for this study was >2000 mg/kg (Dow, 1999).

Dipropylene glycol vapor and aerosol has been examined for acute inhalation toxicity. An aerosol atmosphere of 6000 to 8000 mg/m3 dipropylene glycol was not lethal to rats or guinea pigs (Oettel and Hofmann, 1961), but vaporized degradation products produced by heating dipropylene glycol to 170 °C was lethal to 5 of 6 rats exposed for 8 hours. No mortality occurred from vapors generated at 120°C. Pathologic abnormalities were not observed in any of the animals (Oettel and Hofmann, 1961).

Dipropylene glycol did not produce deaths when administered to the skin of animals. Rabbits that were reportedly administered 5000 and 20000 mg/kg dipropylene glycol to their skin did not die from the treatment (BIBRA, 1991; Opdyke, 1978; Deichman and Gerarde, 1969). Details of these studies are not available.

Based on the above acute data, dipropylene glycol is practically non-toxic by the oral, inhalation and dermal routes.

4.1.2. Irritation and Sensitization

Dipropylene glycol is slightly irritating to the skin and eyes. Dipropylene glycol was described as slightly irritating to rabbit skin in a report that did not provide details on test conditions or results (BIBRA, 1991). Similar minimal skin effects were seen in a human volunteer study where 0.2 ml of 25% dipropylene glycol in water was applied semi-occlusively to 33 subjects for 24 hours. Nine subjects had mild erythema at either 30 minutes or 24 hours; two had mild erythema at both 30 minutes and 24 hours. Twenty-two subjects had no reaction after 30 minutes or 24 hours (Acklin and Plaza, 1995).

Dipropylene glycol was reported to be mildly irritating when it was placed full strength in rabbit eyes, but only transient eye irritation was reported from a formulation containing 7.2% dipropylene glycol (BIBRA, 1991). The details of the study were not provided.

Dipropylene glycol appears to have low potential to produce allergic skin reactions. There are no experimental animal studies reported, but there is a human clinical study. A

dermatology clinic tested 503 (212 men, 291 women) consecutive patients with eczema for sensitivity to dipropylene glycol, using 1 to 10% dipropylene glycol applied for 2 days. This was not a standard sensitization test because there was no specific induction phase and the subjects at the onset of the study were not clinically normal. One individual was found to be sensitized; 22 had questionable erythema; and 480 were unreactive (Johansen *et al.*, 1995).

4.1.3. Repeated Dose Toxicity

The available information indicates that dipropylene glycol has a low order of repeated exposure toxicity. Dipropylene glycol repeatedly administered at very high doses produced lethality, kidney damage, and apparent neurobehavioral changes in laboratory animals. Dipropylene glycol was administered at 10% in the drinking water of twenty five rats for 9 to 68 days. Seven animals died between days 10 and 30; five had kidney lesions described as hydropic degeneration of renal epithelium. Four of the 18 animals that survived to termination also had kidney lesions. The severity of kidney lesions was not reported. No effects were seen in seven rats given dipropylene glycol in the drinking water at 1 to 5% for 33 to 77 days (Kesten *et al.*, 1939). Interpretation of this study is difficult due to the very high doses administered (10%). Under current guidelines, materials are not normally administered at greater than 5% in diet or drinking water because of concerns about interference with normal nutrition. Thus in this study, it can not be discerned whether these effects were directly related to dipropylene glycol or to nutritional imbalance; however, the NOAEL was established to be >5% in the drinking water.

In another study, investigators administered dipropylene glycol at 12% of the diet to rats for 15 weeks. The purpose of the study was to compare effects of dipropylene glycol with propylene glycol on running behavior. Administration of dipropylene glycol at 12% in the diet resulted in decreased running activity (van Winkle and Kennedy, 1940). The magnitude and temporal nature (relative to daily dosing and over the course of the study) to the changes in running behavior were not reported. The lack of details on study design, assessment method, and results limit the interpretation of this study.

There is a study of dogs that received multiple doses of dipropylene glycol over the apparent course of a couple of days. Dipropylene glycol was administered to dogs by gavage as follows: one dog received 6 doses of 1.5 cc/kg/dose (9 cc/kg); two dogs received 6 doses of 2.0 cc/kg/dose (12 cc/kg), and one dog received 4 doses of 5 cc/kg/dose (20 cc/kg). Based on the density of dipropylene glycol, these administered dosages are approximately equivalent to total doses of 9400, 12500, and 20800 mg/kg. Frequency of administration was not stated, but it was probably 3 times per day. Emesis and recovery was observed in one dog of the middle dose. No deaths and no other signs of toxicity were observed in any of the dogs (Hanzlik *et al.*, 1939). The design limitations of the study hamper its applicability to the repeated exposure hazard characterization for dipropylene glycol.

In a study that was designed to assess effects of dipropylene glycol on the development of offspring to dams, investigators exposed pregnant rats to dipropylene glycol on gestation days 6 to 15. At 2000 mg/kg/day and above, some rats died and there were signs of toxicity as well as reduced body weight, food consumption and increased water consumption. The NOAEL for maternal toxicity was 800 mg/kg/day. In pregnant rabbits exposed on gestation days 6-19, no maternal toxicity was seen; hence, the NOAEL for the study was 1200 mg/kg/day (Bates *et al.*, 1992a; 1992b).

A repeat exposure/reproductive screen study was conducted on tripropylene glycol, which is rapidly converted to dipropylene glycol *in vivo*. Males and females exposed by gavage to tripropylene glycol for 14 days at 1000 mg/kg/day had increased liver weights; thus the study NOAEL was 200 mg/kg/day (Tanaka *et al.*, year not reported).

The available data from repeated dosing studies indicate toxic effects only at very high doses of dipropylene glycol. The studies are summarized below:

Species	**Treatment**	**NOAEL/LOAEL** (mg/kg bw/day)	**Comments**	**Source**
Rat	1% - 10% in drinking water for 9-77 d	5% in drinking water; data do not permit calculation in terms of mg/kg/day	Some animals from 10% exposure group died ; some had hydropic degeneration of tubule epithelium in kidneys.	Kesten *et al*., 1939
Rat	12% in feed for 15 weeks	Not established	Decreased running activity after 15 weeks.	van Winkle and Kennedy, 1940
Dog	Total dose of 9, 12 or 20 cc/kg divided among multiple doses	9400	One of two dogs dosed at 12 cc/kg (12500 mg/kg) had emesis, but recovered. No other indication of toxicity in study.	Hanzlik *et al.*, 1939
Rat	800, 2000, and 5000 mg/kg/day days 6-15 of gestation	800 mg/kg/day	Deaths, reduced food consumption and body weight at two higher doses	Bates *et al.*, 1992a
Rabbit	200, 400, 800, and 1200 mg/kg/day days 6-19 of gestation	1200	No adverse effects seen.	Bates *et al*., 1992b

4.1.4. Genotoxicity

Dipropylene glycol is not toxic to genetic material based on *in vitro* and *in vivo* study findings. The National Cancer Institute (NCI) conducted Ames assays of dipropylene glycol using S9 from livers of rats and hamsters induced by feeding of Aroclor 1254, and without metabolic activation, using strains TA98, TA100, TA 1535 and TA1537. It was a standard plate assay with concentrations of dipropylene glycol up to 10000 µg/plate. Tables of revertants at each dose level were not provided, but the results were characterized by NCI as negative (CCRIS, 2001). Similarly NCI conducted a mouse lymphoma assay of dipropylene glycol using L5178 (TK+/TK-) cells. Testing was conducted with and without metabolic activation using S9 from livers of rats fed Aroclor 1254. Concentrations of dipropylene glycol were 29-60 µl/ml without metabolic activation and 30-50 µl/ml with activation. Detailed results were not provided, but were characterized by NCI as negative (CCRIS, 2001).

Male CD-1 mice (6 per treatment group) were treated by gavage with 0, 500, 1000, or 2000 mg/kg/day dipropylene glycol for 2 consecutive days. Cyclophosphamide (120 mg/kg) was administered as a positive control. Bone marrow was isolated and stained for examination of 2000 polychromatic erythrocytes (PCE) for the presence of micronuclei. The number of cells with micronuclei ranged from 1.3 to 2.8 cells/2000 PCE in the treated and negative controls groups (Dow, 1999). None of the treated groups had significantly

more micronuclei than the controls or a change in the percentage of PCEs. In contrast, cyclophosphamide caused 40 micronuclei/2000 PCE, indicating the assay was sufficiently sensitive to detect induction of micronuclei by a known clastogen.

4.1.5. Carcinogenicity

Dipropylene glycol has not been tested specifically for carcinogenicity; however, based on the results of a cancer bioassay of propylene glycol (to which dipropylene glycol is rapidly converted), dipropylene glycol is not expected to have carcinogenic potential. Propylene glycol was administered in the diet of male and female Crl:CD rats at concentrations of 0, 6250, 12500, 25000, and 50000 ppm for 104 weeks. No increases in tumor incidence were found in the treated rats compared to the controls. Daily exposure to propylene glycol in the high-dose group was calculated at 1700 to 2100 mg/kg/day (Gaunt *et al.*, 1972).

4.1.6. Reproductive/Developmental Toxicity

No reproduction studies have been conducted for dipropylene glycol; however the structural analogues tripropylene glycol and propylene glycol have been tested for reproductive effects and no effects on fertility and reproductive performance were found at doses that did not result in maternal toxicity. The negative reproductive findings for tripropylene glycol and propylene glycol support an expected similar lack of reproductive toxicity for dipropylene glycol because the metabolism data demonstrates that tripropylene glycol is rapidly hydrolyzed to dipropylene glycol, which is further rapidly hydrolyzed to propylene glycol.

Tripropylene glycol was administered by gavage from premating through day 3 of lactation at doses of 0, 8, 40, 200, and 1000 mg/kg/day to groups of 12 male and 12 female Crj:CD rats. There was no effect on paternal body weight, food consumption, hematology, clinical chemistry, necropsy or histopathology. Males and females that received 1000 mg/kg/day had increased liver weights and males also had increased kidney weights. The NOAEL for parental effects was 200 mg/kg/day. There were no differences in estrus cycle, mating, pregnancy rate, length of gestation, gestation index, mean litter size, mean live litter size, pup survival through day 4, sex ratio, or external abnormalities. The NOAEL for reproduction and developmental effects was >1000 mg/kg/day (Tanaka *et al.*, year not reported).

In a continuous breeding study in mice, propylene glycol was administered at 0, 1, 2.5 and 5% in the drinking water of male and female CD-1 mice for 7 days premating and through 98 additional days of cohabitation. Estimated daily doses were: 1800, 4800 and 10100 mg/kg/day. The outcome of the study was that no adverse effects were found in the F0, F1 or F2 generation animals or in their ability to reproduce (Morrissey *et al.*, 1989).

Developmental toxicity has been studied for dipropylene glycol using rats and rabbits. These studies found no differences in developmental parameters between exposed and control animals when dipropylene glycol was administered to rats at up to 5000 mg/kg/day days 6-15 of gestation or to rabbits at up to 1200 mg/kg/day days 6-19 of gestation.

Dipropylene glycol was administered to groups of 26 or 27 pregnant Crl:CD rats by gavage at doses of 800, 2000 or 5000 mg/kg/day on days 6-15 of gestation. Dams were necropsied on gestation day 20. One dam at 2000 mg/kg/day and two dams at 5000 mg/kg/day died prior to termination. At 2000 and 5000 mg/kg/day ataxia, unstable gait

and piloerection were seen in the dams. At 5000 mg/kg/day, dams also had reduced body weight gain, reduced food consumption and increased water consumption. Dipropylene glycol did not affect resorptions, number of live fetuses, sex ratio, fetal weight, or skeletal or visceral abnormalities or variations (Bates *et al.*, 1992a).

Dipropylene glycol was administered to groups of 24 pregnant New Zealand White rabbits by gavage at doses of 200, 400, 800, or 1200 mg/kg/day on days 6-19 of gestation. Dams were necropsied on gestation day 30. There was no evidence of maternal toxicity, although mortality was seen in a preliminary study at 800 and 1500 mg/kg/day. Dipropylene glycol did not affect resorptions, number of live fetuses, sex ratio, fetal weight, or skeletal or visceral abnormalities or variations (Bates *et al.*, 1992b).

The following NOAELS and LOAELS were obtained :

Species	**Treatment mg/kg bw/d**	**Treatment period**	**Maternal**		**Fetal**	
			LOAEL	**NOAEL**	**LOAEL**	**NOAEL**
Rat	800, 2000, 5000	GD 6-15	2000	800	NA	>5000
Rabbit	200, 400, 800, 1200	GD 6-19	NA	>1200	NA	>1200

Thus based on reproduction studies with tripropylene glycol and propylene glycol and developmental toxicity studies in rats and rabbits with dipropylene glycol, dipropylene glycol represents a low hazard potential for developmental or reproductive effects in humans.

4.1.7. Toxicokinetics

Dipropylene glycol is readily absorbed from the gastrointestinal tract. Once absorbed it is readily converted into propylene glycol, which is further converted to lactic and pyruvic acids. These acids are normal body constituents and are further broken down to carbon dioxide and water or incorporated into glycogen. Propylene glycol that is not metabolized is excreted into the urine. These conclusions are drawn from a metabolism study of tripropylene glycol and propylene glycol (Dow, 1995). ^{14}C-Labelled tripropylene glycol was administered by gavage to male F344 rats; exhaled air, urine and feces were collected for 24 hours. After 24 hours the animals were sacrificed for collection of blood, liver, kidney, fat, brain, muscle, and the remaining carcass. 73% of administered dose was recovered as CO_2 (21%) or urinary metabolites (53%); 10% remained in the tissues. The urine contained 13 %, 8%, and 4% of administered dose as tripropylene glycol + tripropylene glycol conjugates, dipropylene glycol + dipropylene glycol conjugates, and propylene glycol + propylene glycol conjugates, respectively. When propylene glycol was similarly administered, only urine was collected. 12% of the administered dose was found in the urine. This study demonstrates that tripropylene glycol is rapidly metabolized to dipropylene glycol which is further metabolized to propylene glycol to lactic and pyruvic acids which either enter the citric acid cycle with exhaled CO_2 as a byproduct of energy production, or are incorporated into tissue components such as glycogen.

5. Conclusions and Recommendations

5.1 Conclusions

Commercial dipropylene glycol (CAS # 25265-71-8; (CH_3-CHOH-CH_2O-CH_2-CHOH-CH_3) is composed of 3 isomers and is typically 98% pure. The commercial product is typically composed of up to 48% isomer 110-98-5. Dipropylene glycol is produced as a byproduct of the manufacture of propylene glycol. The US production capacity of dipropylene glycol was 131 million pounds (60 thousand tonnes) in 1998. Dipropylene glycol is used as both a reactive intermediate and as a solvent. Reactive intermediate end uses in the US include: plasticizers, unsaturated polyester resins, polyurethane polyols, and alkyd resins. Solvent end uses in the US include: cosmetics, pesticides and functional fluids: specialty deicers, inks, lubricants.

Dipropylene glycol is a liquid at room temperature, it has a low vapor pressure, and is miscible with water. Releases to the environment are expected to partition primarily to water and soil where they will be degraded. It is not expected to bioaccumulate due to BCFs measured at 0.3 to 4.6. Testing in aquatic species showed a low hazard concern. PNECs of >50 mg/L were obtained from a fish LC_{50} of 5000 mg/l and 32 mg/l from a clawed toad (*Xenopus laevis*) LC_{50} of 3181 mg/l. The mammalian acute toxicity of dipropylene glycol is low, with values around 16000 mg/kg reported in tests in rats. Dipropylene glycol is only minimally irritating to the skin and eye. It appears to have low potential to produce allergic skin reactions, as only 1 of 503 patients with eczema reacted to dipropylene glycol. Longer-term studies of dipropylene glycol and the structural analogues, propylene glycol and tripropylene glcyol, demonstrate a low concern for chronic, reproductive, and developmental effects. Dipropylene glycol is not genotoxic and not expected to be carcinogenic.

5.2 Recommendations

The chemical is currently a low priority for further work.

6. References

Acklin, A., and Plaza, M.E. (1995). Evaluation of Primary Irritation Potential in Humans. Hill Top Research, Inc. Report No. 94-1373-70. Submitted to The Dow Chemical Company, Midland, Michigan.

BASF. (1989). Dipropylene Glycol. DIN-Sicherheitsdatenblatt com Juli 1989, BASF Aktiengesellschaft, Ludwigshafen, 2 S.

Bates, K.H. *et al*. (1992a). Final Report on the Developmental Toxicity of Dipropylene Glycol (CAS-No. 25265-71-8) in Sprague-Dawley (CD) Rats. National Toxicology Program, National Institute of Environmental Health Sciences, PO Box 12233, Research Triangle Park, NC 27709; NTIS # PB92-196179.

Bates, K.H. *et al*. (1992b). Final Report on the Developmental Toxicity of Dipropylene Glycol (CAS-No. 25265-71-8) in New Zealand White Rabbits. National Toxicology Program, National Institute of Environmental Health Sciences, PO Box 12233, Research Triangle Park, NC 27709; NTIS # PB92-238294.

BIBRA Toxicology International (1991). Dipropylene glycol - Toxicity profile. BIBRA Toxicology International - British Industrial Biological Research Association, 1-4.

Bridie, A.L. *et al*. (1979b). BOD and COD of some petrochemicals. *Water Res*. 13, 627-630.

Bridie, A.L., Wolff, C.J.M., Winter, M. (1979a). The acute toxicity of some petrochemicals to goldfish. *Water Res.* 13, 623-626.

CCRIS (Chemical Carcinogenesis Research Information System from National Cancer Institute). Dipropylene glycol; available online through ToxNet, listing on 4/25/01 at http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?CCRIS.

CDPR (California Department of Pesticide Registration). (2001). Available online at http://www.cdpr.ca.gov/cgi-bin/epa/chemdet.pl?pccode=068604.

ChemExpo Chemical Profile of Dipropylene Glycol (1998). Available online at http://www.chemexpo.com/news/PROFILE980720.cfm

Claussen, T. (1993). Dipropylene Glycol. Determination of the Acute Toxicity to *Pseudomonas putida*. Unpublished report, The Dow Chemical Company, Horgen, Switzerland.

De Zwart, D., Slooff, W. (1987). Toxicity of mixtures of heavy metals and petrochemicals to *Xenopus laevis*. *Bull. Environ. Contam. Toxicol.* 38: 345-351.

Deichmann, W.B., Gerarde, H.W. (1969). Acute toxicity of glycols. Toxicology of Drugs and Chemicals, 4. AFL., Academic Press, New York, 731.

The Dow Chemical Company. (1995). Metabolism of tripropylene glycol in rats. Unpublished report, The Dow Chemical Company, Midland, Michigan, pp. 1-36.

The Dow Chemical Company. (1999). Evaluation of dipropylene glycol in the mouse bone marrow micronucleus test. Unpublished report, The Dow Chemical Company, Midland, Michigan.

Gaunt, I.F., Carpanini, F.M.B., Grasso, P., Lansdown, A.B.G. (1972). Long-term toxicity of propylene glycol in rats. *Fd. Cosmet. Toxicol.*10, 151 – 162.

Hanzlik, P.J. *et al.* (1939). Toxicity, fats and excretion of propylene glycol and other glycols. *J. Pharmacol. Exp. Therap*. 65: 101-113.

Johansen, J.D., Jemec, G.B.E., Rastogi, S.C. (1995). Contact sensitization to dipropylene glycol in an eczema population. *Contact Dermatitis*. 33: 211-212.

Kawai, F., Hanada, K., Tani, Y., Ogata, K. (1977). Bacterial degradation of water-insoluble polymer (polypropylene glycol). *J. Ferment. Technol.* 55: 89-96.

Kawai, F., Okamoto, T., Suzuki, T. (1985). Aerobic degradation of polypropylene glycol by corynebacterium sp. *J. Ferment. Technol.* 63: 239-244.

Kesten, H.D. *et al.* (1939). Pathologic effects of certain glycols and related compounds. *Archives of Pathology* 27: 447-465.

Mackay, D. (1991). Multimedia Environmental Models, Chelsea, Lewis Publishers, 185-227.

MITI (1992). Dipropylene glycol. Chemicals inspection and testing institute Japan: Data of existing chemicals based on the CSCL Japan. Japan Chemical Industry Ecology-Toxicology and Information Center, 2-56.

Morrissey, R.E., Lamb, J.C., Morris, R.W., Chapin, R.E., Gulati, D.K., Heindel, J.J. (1989). Results and evaluations of 48 continuous breeding reproduction studies conducted in mice. *Fund. Appl. Toxicol.* 13, 747 – 777.

Nishiuchi, K. (1984). Toxicity of agrochemicals to freshwater organisms. CIII. Solvents. *Suisan Zoshoku - The Aquiculture Japan* 31: 115-119.

Oettel, H., Hofmann, H .T. (1961). Dipropylene Glycol. Report of Acute Inhalation of Dipropylene Glycol n Rats and Guinea Pigs. BASF internal report, 2 pages.

Opdyke, D.J. (1978). Dipropylene glycol. Food and Cosmetics Toxicology 16, Suppl. In: Monographs on Fragrance of Raw Materials, 729-730.

Spanjers, M.T., Til, H.P. (1980). Determination of the acute oral toxicity of dipropylene glycol in rats. Unpublished report, The Dow Chemical Company, Horgen, Switzerland.

Tanaka, N., Yamakage, K., Kusakabe, H., Hashimoto, K., Shibuya, T., Hara, T., Kato, M., Ishihara, N. (no date). Toxicity studies with tripropylene glycol. Research Report; Hatano Research Institute, Food and Drug Safety Center, Hadano, Kanagawa, Japan, pp. 253-276.

Van Winkle, W. jr., Kennedy, N.K. (1940). Voluntary activity of rats fed propylene glycol and other glycols. *J.Pharmac. exp. Ther.* 69: 140.

SIDS DOSSIER
Dipropylene glycol, mixed isomers and dominant isomer (DPG)
(CAS No. 25265-71-8 and 110-98-5)

Sponsor Country: U.S.A.

1. GENERAL INFORMATION

1.01 SUBSTANCE INFORMATION

A. CAS-Number: 25265-71-8 and 110-98-5

B. Name *(IUPAC name)* dipropylene glycol, mixed isomers and dominant isomer structural isomers (as mixture in the technical product):
(1) 2,2'-dihydroxydiisopropropylether (CAS-No.: 108-61-2);
(2) 2,2'-dihydroxydipropylether (CAS-No.: 110-98-5);
(3) 2-hydroxypropyl-2'-hydroxyisopropylether (CAS-No.: 106-62-7);

C. Name *(OECD name):* DPG

D. CAS Descriptor

E. EINECS-Number

F. Molecular Formula $C_6H_{14}O_3$

G. Structural Formula CH_3-CHOH-CH_2O-CH_2-CHOH-CH_3

H. Substance Group

I. Substance Remark

J. Molecular Weight

1.02 OECD INFORMATION

A. Sponsor Country: U.S.A.

B. Lead Organisation:

Name of Sponsor Country: United States of America
Contact point: Oscar Hernandez
EPA/Office of Toxic Substances RAD (7403M)
1200 Pennsylvania Ave, NW
Washington, D.C. 20460
Telephone: (202) 564-7649
Fax: (202)-564-7450

Name of Lead Organisation: American Chemistry Council Propylene Glycol Ethers Panel
Contact person: Anne LeHuray.
Address: American Chemistry Council
1300 Wilson Blvd.
Arlington, VA 22209
U.S.A.
Tel: 703-741-5630
Fax: 703-741-6091
Email:LeHuray_Anne@americanchemistry.com

1.1 GENERAL SUBSTANCE INFORMATION

A. Type of Substance element [ ]; inorganic [ ]; natural substance [ ]; organic [X]; organometalic [ ]; petroleum product [ ]

B. Physical State *(at 20°C and 1.013 hPa)*
gaseous [ ]; liquid [X]; solid [ ]

C. Purity *(indicate the percentage by weight/weight)*

1.2 SYNONYMS:

1,1'-Oxybis-2-propanol; 1,1'-Oxydi-2-propanol; 2,2'-Dihydroxydipropylether; Bis(2-hydroxypropyl)ether; Di-1,2-propylenglycol; dipropylene glycol; dipropyleneglycol2-(2-hydroxypropoxy)-1-propanol (CAS No. 108-61-2)
2,2'oxybis-1-propanol (CAS No. 106-62-7)

1.3 IMPURITIES

1.4 ADDITIVES

1.5 QUANTITY

Dipropylene glycol is produced as a byproduct of the manufacture of propylene glycol. The United States (US) production capacity of dipropylene glycol (i.e., byproduct production capacities of propylene glycol plants) was 131 million pounds (60 thousand tonnes) in 1998. The US Domestic demand in 1998 was 108 million pounds (49 thousand tonnes). In 1998, dipropylene glycol was produced in the US by The Dow Chemical Company, Eastman Chemical Company, Huntsman Corporation, Lyondell Chemical Company, and Olin Corporation. (ChemExpo Chemical Profile, 1998). Worldwide capacity is estimated at 235 million pounds (107 thousand tonnes).

1.6 LABELLING AND CLASSIFICATION

Labelling
Type:
Specific limits:
Symbols:
Nota:
R-phrases:
S-phrases:
Text of S-phrases:
Remarks:

Classification
Type:
Category of danger:
R-phrases:
Remarks:

1.7 USE PATTERN

A. General

Type of Use:

USES OF DIPROPYLENE GLYCOL

USES	APPLICATION	FUNCTION	% PRODUCTION
Intermediate	Specialty plasticizer	Plasticizer	38 %
Intermediate	Non-reinforced polyesters	Resin monomer	23 %
Substance	Cosmetics and Fragrances	Humectant, Emollient	10 %
Intermediate	Polyurethane polyols	Plasticizer	10 %
Intermediate	Alkyd resins	Resin monomer	7 %
Substance, Intermediate	Miscellaneous (e.g., dyes & inks, paints & coatings; functional uses in hydraulic brake fluids; cutting oils)	Solvent, functional fluid, coolant	14%

(Source: ChemExpo Chemical Profile (1998)).

B. Uses in Consumer Products

Cosmetics, fragrances, germicidal products

The use concentration of dipropylene glycol in branded pesticidal products is also available. This is summarized in the following table.

PESTICIDAL FORMULATIONS CONTAINING DIPRO PYLENE GLYCOL

RANGE OF CONCENTRATION (%)			
	<1	**1-5**	**>5**
No. of Brand Name Products	1	16	1

(Source: EDF Website: www.scorecard.org)

1.8 OCCUPATIONAL EXPOSURE LIMIT VALUE

1.9 SOURCES OF EXPOSURE

(a)
Media of release:
Source:
Remarks:
Reference:

(b)
Media of release:
Source:
Remarks:
Reference:

1.10 ADDITIONAL REMARKS

A. Options for disposal

Remarks:
Reference:

B. Other remarks

2. PHYSICAL-CHEMICAL DATA

2.1 MELTING POINT

Value = - 39 degree C – pour point
Method
GLP: No data

Reference: Brown, E.S.; Hauser, C.F.; Ream, B.C.; Berthold, R.V. (1980): Glycols. Kirk-Othmer Ency clopedia of Chemical Technology, Band 11, 3. Auf 1., John Wiley & Sons, New York, ISBN -0-471-02063-8; 933-956.
Hommel, G. (1983): Dipropyleneglycol. Handbuch der gefaehrlichen Gueter, 3 ueberarb. Auflage, Springer Verlag, Berlin, Merkblatt 478.

2.2 BOILING POINT

Value = 222.2 - 225.7 degree C
Pressure: 1013 hPa
Decomposition
GLP: No data
Reference: Sexton, A.R.; Britton, E.C. (1953): Synthesis and identification of dipropylene glycol isomers. *J. Am. Chem. Soc.* 75: 4357-4358.

Value = 232 degree C
Pressure
Decomposition
GLP: No data
Reference: Brown, E.S.; Hauser, C.F.; Ream, B.C.; Berthold, R.V. (1980): Glycols. Kirk-Othmer Encyclopedia of Chemical Technology, Band 11, 3. Auf 1., John Wiley & Sons, New York, ISBN -0-471-02063-8; 933-956.

Value = 233 degree C
Pressure
Decomposition
GLP: No data
Reference: Hawley, G.G. (1981): Dipropylene Glycol. Hawley, G.G.: The Condensed Chemical Dictionary, 10. Auflage, New York: van Nostrand Reinhold, 383.

2.3 DENSITY

Value = 1.023 g/cm3
Temperature: 20 degree C
GLP: No data
Reference: Elm, R.; Falbe, J.; Hahn, H.-D., Gelbke, H.-P. (1980): Propandiole. Ullmanns Enzyklopaedie der technischen Chemie, 4. neubearb. u. er. AFL. Band 19, Verlag Chemie, Wenham. 427-432.

Value = 1.0252 g/cm3
Temperature: 20 degree C
GLP: No data
Reference: Browning, E. (1965): Dipropylene Glycol. Toxicity and metabolism of industrial solvents, Elsevier Verlag, Amsterdam, 653-655.

2.4 VAPOUR PRESSURE

Value = <.01 hPa
Temperature: 20 degree C
GLP: No data

Reference: Browning, E. (1965): Dipropylene Glycol. Toxicity and metabolism of industrial solvents, Elsevier Verlag, Amsterdam, 653-655.

Value = <.013 hPa
Temperature: 20 degree C
GLP: No data

Reference: Brown, E.S.; Hauser, C.F.; Ream, B.C.; Berthold, R.V. (1980): Glycols. Kirk-Othmer Encyclopedia of Chemical Technology, Band 11, 3. AFL., John Wiley & Sons, New York, ISBN 0-471-02063-8; 933-956.

Value = .05 hPa
Temperature: 21 degree C
GLP: No data

Reference: DOW (1991a): Dipropylene Glycol. DIN-Sicherheitsdatenblatt vom Juni 1991, DOW Deutschland Inc., Frankfurt, 5 S.

2.5 PARTITION COEFFICIENT $\log_{10}P_{ow}$

log Pow = -1.486
Temperature degree C
GLP: No data

Reference: Battersby, R.V. (1993c): Berechnung eines Verteilungs - koeffizienten fuer Dipropylenglykol. Schriftliche Mitteilung vom 18.10.1993, IBR Forschungs GmbH, Hannover, 9S.

log Pow = -.687
Temperature degree C
GLP: No data

Reference: Pomona College, Medicinal Chemistry Project (1987): Dipropylene glycol. MedChem Software Manual, Release 3.52, Medicinal Chemistry Project, Pomona College, Claremont.

2.6 WATER SOLUBILITY

Described as miscible
GLP: No data

Reference: DOW (1991): Dipropylene Glycol. DIN-Sicherheitsdatenblatt vom Juni 1991, DOW Deutschland Inc., Frankfurt, 5 S.
Reference: Elm, R.; Falbe, J.; Hahn, H.-D.; Gelbke, H.-P. (1980): Propandiole. Ullmanns Enzyklopaedie der technischen chemie, 4. neubearb. u. er. AFL. Band 19, Verlag Chemie, Wenham, 427-432.

2.7 FLASH POINT *(liquids)*

Value = 118 degree C
Type: other
GLP: No data
Method: ASTM D56.

Reference: Brown, E.S.; Hauser, C.F.; Ream, B.C.; Berthold, R.V. (1980): Glycols. Kirk-Othmer Encyclopedia of Chemical Technology, Band 11, 3. AFL., John Wiley & sons, New York, ISBN 0-471-02063-8; 933-956.

Value = 120 degree C
Type: closed cup
GLP: No data
Method: DIN 51758

Reference: Elm, R.; Falbe, J.; Hahn, H.-D.; Gelbke, H.-P. (1980): Propandiole. Ullmanns Enzyklopaedie der technischen Chemie, 4. neubearb. u. er. AFL. Band 19, Verlag Chemie, Wenham, 427-432.

Value = 121 degree C
Type: closed cup
GLP: No data
Method: Pensky Martens

Reference: DOW (1991a): Dipropylene Glycol. DIN-Sicherheitsdatenblatt com Juni 1991, DOW Deutschland Inc., Frankfurt, 5 S.

Value = 138 degree C
Type: other
GLP: No data
Method: other

Reference: Hommel, G. (1983): Dipropylenglykol. Handbuch der gefaehrlichen Gueter, 3. Ueberarb. Auflage, Springer Verlag, Berline, Merkblatt 478.

Merck (1992): Dipropyleneglycol. Reagenzien, Diagnostica, Chemikalien 1992/93 - Merck-Katalog, 522.

2.8 AUTO FLAMMABILITY *(solid/gases)*

Value = 371 degree C
Pressure
GLP: No data

Reference: Material Safety Data Sheet, Arco Chemical Company, 1993

2.9 FLAMMABILITY

No data

2.10 EXPLOSIVE PROPERTIES

No data

2.11 OXIDIZING PROPERTIES

No data

2.12 ADDITIONAL REMARKS

Remarks: No additional remarks

2.13 ADDITIONAL DATA

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

Value:
Method:
GLP:
Remarks: No studies located
Reference:

B. Other data

Results: No studies located
Remarks:
Reference:

3. ENVIRONMENTAL FATE AND PATHWAYS

3.1 STABILITY

3.1.1 PHOTODEGRADATION

(a)
Type: Air [X]; Water [ ]; Soil [ ]; Other [ ]
Light source: Sun light [ ]; Xenon lamp [ ]; Other [X]
Light spectrum:
Relative intensity:
Concentration of Substance: molecule/cm3

Temperature:
Direct photolysis:
Half life: 13 hours
Degradation:
Quantum yield:

Method: calculated [ ]; measured [ ]
Other
GLP: Yes [ ] No [ ] ? [x]
Test substance:
Remarks:
Result: The rate constant for the reaction of DPG with photochemically induced OH radicals was calculated by a mathematical model (AOP) to a value of 29.7 x 10^{-11} cm^3/molecule x sec at a temperature of 25 degrees C. This results in an atmospheric half life of ca. 13 hours at an atmospheric concentration of 5 x 10^5 OH radicals per cm^3.

Reference: AOP (1992): Atmospheric Oxidation Program, Version 1.5. An Adaptation of the Atkinson Estimation Methodology, Syracuse Research Corporation, Syracuse.

Type: Air [ ]; Water [X]; Soil [ ]; Other [ ]
Rel. Intens. .. based on Intensity of Sunlight
Spectrum of Substance
lambda (max) nm epsilon (max)
Test condition:
Rate Constant cm^3/(molecule*sec)
GLP: no data
Rate constant:
Remark: According to the V-spectrum of DPG (i.e., no relevant UV absorption above 290 nm) only a minimal tendency for direct photolysis can be expected.
Reference: BUA report (1994): Dipropylenglykol.

3.1.2 STABILITY IN WATER

Remark: Ethers and glycols are generally regarded as resistant towards hydrolysis. Therefore, DPG is not expected to undergo hydrolysis under environmentally relevant conditions.
Reference: Lyman, W.J. (1982); Adsorption coefficient for soils and sediments. Lyman W.J.; Reehl, W.F.; Rosenblatt, D.H. (publisher): Handbook of chemical property estimation methods. Environmental behavior of Organic Compounds, New York, McGraw-Hill, 4.1 - 4.33.

3.1.3 STABILITY IN SOIL

No data available

3.2 MONITORING DATA (ENVIRONMENT)

Medium other: drinking water

Remark In a study on drinking water and waste water in Ohio (USA) during 1978-1980, DPG was found in samples of drinking water at concentrations between 0.2 and 0.4 ng/L.

Reference: Lin, D.D.D.; Melton, R.G.; Kopfler, F.C.; Lucas, S.V. (1981); Glass capillary gas chromatographic/mass spectrometric analysis of organic
Medium other: effluent from waste water treatment plant

Remark: A study on the priority pollutants found in the effluent of 5 paper mill waste water treatment plants in USA and Canada revealed a DPG concentration of 11 µg/l in the effluent of one of the plants. It was not detected in the influent stream nor in the untreated waste stream.

Reference: Turoski, V.E.; Woltman, D.L.; Vincent, B.F. (1983): Determination of organic priority pollutants in the paper industry by GC/MS. *Tappi J.* 66: 89-90.

Medium other: ground water

Remark The occurrence of DPG in ground water samples taken in the vicinity of a landfill in Norman, Oklahoma (USA) was demonstrated qualitatively in a study performed during 1972-1973.

Reference: Dunlap, W.J.; Shew, D.C. (1976); Organic pollutants contributed to ground water by a landfill. U.S. EPA, EPA - 600/9-76-004 PB - 251161, 96-110.
concentrates from drinking and advanced waste treatment water. Advances in the identification and analysis of organic pollutants in water/ Keith, L.H. (Publisher) - Vol 2 - Ann Arbor Science Publishers, Collingwood, ISBN 0-250-40398-6, 861-906.

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

3.3.1 TRANSPORT BETWEEN ENVIRONMENTAL COMPARTMENTS

Type: Adsorption [X]: Desorption [ ]; Volatility [ ]: Other [ ]
Media: Water-Soil
Method: Other
Remarks: Due to lack of valid data, a rough estimation was made on the basis of a calculated range for the log P_{ow} value of -0.69 to -1.486. These theoretical considerations lead to an expected range for the K_{oc} value of DPG = 3.0 - 56.2.

The tendency of DPG to adsorb onto soil must be regarded as very low.

Reference: BUA report (1994): Dipropylenglykol.
Litz, N. (1990): Schultz vor weiteren anthorpogenen Organika-Eintrogen. Blume, H.P. (Ed.): Handbuch des Bodenschutzes. Bodenokologie und -belastung: Vorbeugende und absehrende Schutzmassnahmen.
Ecomed Verlagsgesellschaft, Landsberg/Lech, 579-584.

Type: Adsorption [ ]: Desorption [ ]; Volatility [ ]: Other [X]
Media: Water-Air
Method: Other
Remarks: Henry Law Constant: 3.6 x 10^{-4} Pa*m^3/mole.
The volatility of DPG from water can, therefore, be considered as minimal.

Reference: Hine, J.; Mookerjee, P.K. (1975): The intrinsic hydrophilic character of organic compounds. Correlations in terms of structural contributions. *J. Org. Chem* . 40, 292-298.

Mackay, D. (1991): Multimedia Environmental Models, Chelsea, Lewis Publishers, 185-227.

Thomas, R.G. (1990): Volatilization from water. Lyman, W.J.; Reehl, W.F.; Rosenblatt, D.H. (Publisher): Handbook of chemical property estimation methods. Environmental Behavior of Organic Compounds, New York, McGraw-Hill, 15.1 - 15.34.

3.3.2 THEORETICAL DISTRIBUTION (FUGACITY CALCULATION)

No data available

3.4 IDENTIFICATION OF MAIN MODE OF DEGRADABILITY IN ACTUAL USE

No data available

3.5 BIODEGRADATION

Type: aerobic
Inoculum: activated sludge, adapted
Test condition: Directive 87/302/EEC, part C. p. 99 “Biodegradation: Zahn-Wellens test”
Concentration:
GLP: No data
Results: > 70 % degraded after 28 day
Reference: BASF (1989): Dipropylene Glycol. DIN-Sicherheitsdatenblatt com Juli 1989, BASF Aktiengesellschaft, Ludwigshafen, 2 S.

Type: aerobic
Inoculum: activated sludge
Method: not given; 30 mg/1 substance; 100 mg/l sludge
GLP: No data
Results: under test conditions no biodegradation observed
Reference: MITI (1992): Dipropylene glycol. Chemicals inspection and testing institute Japan: Data of existing chemicals based on the CSCL Japan. Japan Chemical Industry Ecology-Toxicology and Information Center, 2-56.

Type: aerobic
Inoculum: Corynebacterium sp. (Bacteria)
Concentration: 5 g/l
GLP: No data
Results: Degradation: > 90 % after 23 hour
Remark Degradation of DPG to propylene glycol and ketones depended on the shaking conditions. In stationary culture, DPG was scarcely degraded. With vigorous shaking (about 120 rpm), over 90% of DPG was consumed within 23 h, but traces

of metabolites accumulated in the reaction mixture. The metabolites were characterized by GC-MS analysis using a capillary column.

Reference: Kawai, F.; Hanada, K.; Tani, Y.; Ogata, K. (1977): Bacterial degradation of water-insoluble polymer (polypropylene glycol). *J. Ferment. Technol*. 55: 89-96.

Kawai, F. Okamoto, T.; Suzuki, T. (1985): Aerobic degradation of polypropylene glycol by *corynebacterium* sp. *J. Ferment. Technol*. 63: 239-244.

Type: aerobic
Inoculum: other: soil bacterium (aerobic. gram-negative)
Concentration: 671 ug/1
Results: Degradation: >70% after 28 day; 2% degradation after 4 hours related to oxygen uptake.
GLP: No data
Remark: The bacterium was isolated from soil enriched with triethylene glycol. Cells to be assayed for oxidative activity were cultured at 30 degree C on a shaker for 72 to 96 hr in basal medium.
Reference: Fincer, E.L.; Payne, W.J. (1962): Bacterial utilization of ether glycols. *Appl. Microbiol*. 10: 542-630.

3.6 BOD_5,COD OR RATIO BOD_5/COD

BOD5/COD

Method: APHA standard methods: No. 219
GLP: No data
Results: BOD5 = 92 mg/l
COD = 1840 mg/g
BOD5/COD = .049
Reference: Bridie, A.L. et al. (1979b): BOD and COD of some petrochemicals. *Water Res*. 13, 627-630.

3.7 BIOACCUMULATION

Species: *Cyprinus carpio* (Fish, fresh water)
Method OECD Guideline 305C "Bioaccumulation: Test for the Degree of Bioconcentration in Fish"
Exposure Period: 42 days; Temperature 25 degree C; Concentration: 3 mg/l
Elimination: No data
GLP: No data
BCF: 0.3 to 1.4
Reference: MITI (1992): Dipropylene glycol. Chemicals inspection and testing institute Japan: Data of existing chemicals based on the CSCL Japan. Japan Chemical Industry Ecology-Toxicology and Information Center, 2-56.

Species: *Cyprinus carpio* (Fish, fresh water)
Method OECD Guideline 305C "Bioaccumulation: Test for the Degree of Bioconcentration in Fish"
Exposure Period: 42 days; Temperature 25 degree C; Concentration: 3 mg/l
Elimination: No data
GLP: No data
BCF: <2.2 to 4.6
Reference: MITI (1992): Dipropylene glycol. Chemicals inspection and testing institute Japan: Data of existing chemicals based on the CSCL Japan. Japan Chemical Industry Ecology-Toxicology and Information Center, 2-56.

3.8 ADDITIONAL REMARKS

A. Sewage Treatment

Remarks: No additional remarks

B. Other

Remarks: No additional remarks

4. ECOTOXICOLOGICAL DATA

4.1 ACUTE/PROLONGED TOXICITY TO FISH

Type: static
Species: *Carassius auratus* (Fish, fresh water)
Method: Static-tank acute toxicity test. Standard methods for the examination of water and wastewater. APHA method No. 231.; Exposure Period 96 hour
Analyt. Monitoring: no data
GLP: No data
Results: LC50 = >5000 mg/l
Reference: Bridie, A.L.; Wolff, C.J.M.; Winter, M. (1979a): The acute toxicity of some petrochemicals to goldfish. *Water Res*. 13, 623-626.

4.2 ACUTE TOXICITY TO AQUATIC INVERTEBRATES

No data available

4.3 TOXICITY TO AQUATIC PLANTS e.g. Algae

No data available

4.4 TOXICITY TO BACTERIA

Species: Bacterium *Pseudomonas putida*
Method: UBA Richtlinie LTWS - Nr. 10; DIN 38412L8; Exposure Period: 18 hr
GLP: No data
Results: Bacterial growth was inhibited (13.5%) at a concentration of 100 mg/l DPG.
Reference: NATEC (1992): Pruefbericht Bestimmung der akuten Bakterientoxizitaet an Pseudomonas putida mit der Pruefsubstanz Dipropylene glycol. Pruefnummer NA 91 1212. Unveroeffentlichter Bericht vom 28.02.1992, NATEC Institut, Hamburg.

Species: Bacterium *Pseudomonas putida*
Method Conformed to German Water Hazard classification; Exposure Period 18 hour
Analyt. Monitoring: yes
GLP: Yes
Results: The mean concentration of dipropylene glycol which demonstrated a 10% growth inhibition (EC10) of *Pseudomonas putida* was 1,000 mg/L.
Reference: Claussen, T. (1992). Dipropylene Glycol: Determination of the Acute Toxicity to *Pseudomonas putida.* Research and Development Report, Health & Environmental Sciences, Dow Europe.

4.5 CHRONIC TOXICITY TO AQUATIC ORGANISMS

4.5.1. CHRONIC TOXICITY TO FISH

No data available

4.5.2. CHRONIC TOXICITY TO AQUATIC INVERTEBRATES

No data available

4.6 TOXICITY TO TERRESTRIAL ORGANISMS

4.6.1 TOXICITY TO SOIL DWELLING ORGANISMS

No data available

4.6.2 TOXICITY TO TERRESTRIAL PLANTS

No data available

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

No data available

4.7 BIOLOGICAL EFFECTS MONITORING (INCLUDING BIOMAGNIFICATION)

No data available

4.8 BIOTRANSFORMATION AND KINETICS

No data available

4.9 ADDITIONAL REMARKS

Toxicity to Aquatic Animals:

Species:	*Rana brevipoda porosa*
Method:	not specified; Exposure Period: 48 hours
GLP:	No data
Results:	LC50 = 5300 mg/l
Reference:	Nishiuchi, K. (1984): Toxicity of agrochemicals to freshwater organisms. CIII. Solvents. *Suisan Zoshoku - The Aquiculture Japan* 31: 115-119.

Species:	*Xenopus laevis*
Method:	not specified; Exposure Period 48 hour
GLP:	No data
Results:	LC50 = 3181 mg/l
Reference:	De Zwart, D.; Slooff, W. (1987): Toxicity of mixtures of heavy metals and petrochemicals to *Xenopus laevis*. *Bull. Environ. Contam. Toxicol*. 38: 345-351.

5. TOXICITY

5.1 ACUTE TOXICITY

5.1.1 ACUTE ORAL TOXICITY

Species: rat
Method: details not given
GLP: no data
Results: LD50 = 14800 mg/kg
Effects: Details not Reported.
Reference: Opdyke, D.J. (1978): Dipropylene glycol. Food and Cosmetics Toxicology 16, Suppl. In: Monographs on fragrance of raw materials, 729-730.

Patty, F. (1982): Dipropylene glycol. In: Patty's Industrial Hygiene and Toxicology / G.D. Clayton, F.E. Clayton (Hrsg.) 3. Bearb. AFL., Vol. 2C Toxicology. Wiley-Interscience Verlag, New York, 3863-3865.

Species: rat
Method: details not given
GLP: No data
Results: LD50 = 14850 mg/kg
Reference: Shaffer, C.B. et al. (1951): A toxicological study of some polypropylene (polypropylene) glycols. *Arch. Ind. Hyg. Occup. Med.* 3: 448-453.

Species: rat
Method: details not given
GLP: No data
Results: LD50 = 15000 mg/kg
Reference: CIR Cosmetic Ingredient Review (1982): Scientific Literature Review on butylene glycol, hexylene glycol, ethoxydiglycol, dipropylene glycol. Cosmetic Ingredient Review (CIR), 202/331-0651, 1-31.

Patty, F. (1982): Dipropylene glycol. In: Patty's Industrial Hygiene and Toxicology / G.D. Clayton, F.E. Clayton (Hrsg.) 3. Bearb. AFL., Vol. 2C Toxicology. Wiley-Interscience Verlag, New York, 3863-3865.

Species: rat
Method: Single oral dose; details not given
GLP: No data
Results: LD50 : 15000 mg/kg
Reference: Sax, N.J. (1979): Dipropylene glycol. Dangerous Properties of Industrial Materials, 5. Ed., published by Van Nostrand Rheinhold, New York, 627.

Species: rat
Method: details not given
GLP: No data
Results: LD50 = 13300 mg/kg
Reference: BASF (1989): Dipropylene Glycol. DIN-Sicherheitsdatenblatt vom Juli 1989, BASF Aktiengesellschaft, Ludwigshafen, 2 S.

Species: Rat
Method: oral dose; details not given
GLP: No data
Results: LD50 = 15.0 and 8.0 ml/kg-bw for males and females, respectively
Reference: Dow Chemical Europe, Horgen, Switzerland. Determination of the acute oral toxicity of dipropylene glycol in rats with cover letter dated 03/28/94 (sanitized). Doc ID# 86940000276S.

Species: Rat
Method: details not given
GLP: No data
Results: LD0 = 3000 mg/kg; LD100 = 15000 mg/kg
Reference: Spencer, H.C. (1946): A summary of the toxicological information on dipropylene glycol and a discussion of the hazards associated with its handling and use. Dow Chemical Company - Biochemical Research Laboratory.

Species: Guinea pig
Method: details not given
GLP: No data
Results: LD50 = 17600 mg/kg
Reference: BIBRA Toxicology International (1991): Dipropylene glycol - Toxicity profile. BIBRA Toxicology International - British Industrial Biological Research Association, 1-4.

5.1.2 ACUTE INHALATION TOXICITY

Species: Rat
Method: details not given
GLP: No data
Results: LC50 = 6000 mg/m^3
Reference: BASF (1989): Dipropylene Glycol. DIN-Sicherheitsdatenblatt vom Juli 1989, BASF Aktiengesellschaft, Ludwigshafen, 2 S.

5.1.3 ACUTE DERMAL TOXICITY

Species: rabbit
Method: not specified
GLP: No data
Results: LD50 = >5000 mg/kg
Reference: BIBRA Toxicology International (1991): Dipropylene glycol - Toxicity profile. BIBRA Toxicology International - British Industrial Biological Research Association, 1-4.

Opdyke, D.J. (1978): Dipropylene glycol. Food and Cosmetics Toxicology 16, Suppl. In: Monographs on fragrance of raw materials, 729-730.

Species: rabbit
Method: not specified
GLP: No data
Results: LD50 = >20000 mg/kg
Reference: Deichmann, W.B.; Gerarde, H.W. (1969): Acute toxicity of glycols. Toxicology of Drugs and Chemicals, 4. AFL., Academic Press, New York, 731.

5.1.4 ACUTE TOXICITY, OTHER ROUTES OF ADMINISTRATION

Species: rat
Route: i.p.
Method: details not given
GLP: No data
Results: LD50 = 10000 mg/kg.
Reference: CIR Cosmetic Ingredient Review (1982): Scientific Literature Review on butylene glycol, hexylene glycol, ethoxydiglycol, dipropylene glycol. Cosmetic Ingredient Review (CIR), 202/331-0651, 1-31.

Species: rat
Route: i.p

Method: details not given
GLP: No data
Results: LD50 = 10300 mg/kg.
Reference: Browning, E. (1965): Dipropylene Glycol. Toxicity and metabolism of industrial solvents, Elsevier Verlag, Amsterdam, 653-655.
Opdyke, D.J. (1978): Dipropylene glycol. Food and Cosmetics Toxicology 16, Suppl. In: Monographs on fragrance of raw materials, 729-730.

Species: rat
Route: i.p
Method: details not given
GLP: No data
Results: LD50 = 10590 mg/kg
Reference: Shaffer, C.B. et al. (1951): A toxicological study of some polypropylene (polyoxypropylene) glycols. *Arch. Ind. Hyg. Occup. Med*. 3: 448-453.

Species: mouse
Route: i.p.
Method: details not given
GLP: No data
Results: LD50 = 4600 mg/kg.
Reference: CIR Cosmetic Ingredient Review (1982): Scientific Literature Review on butylene glycol, hexylene glycol, ethoxydiglycol, dipropylene glycol. Cosmetic Ingredient Review (CIR), 202/331-0651, 1-31.

Opdyke, D.J. (1978): Dipropylene glycol. Food and Cosmetics Toxicology 16, Suppl. In: Monographs on fragrance of raw materials, 729-730.

Species: mouse
Route: i.p.
Method: details not given
GLP: No data
Results: LD50 = 4500 mg/kg
Reference: BIBRA Toxicology International (1991): Dipropylene glycol Toxicity profile. BIBRA Toxicology International - British Industrial Biological Research Association, 1-4.

Species: dog
Route: i.p.
Method: details not given
GLP: No data
Results: LD50 = 11500 mg/kg
Reference: CIR Cosmetic Ingredient Review (1982): Scientific Literature Review on butylene glycol, hexylene glycol, ethoxydiglycol, dipropylene glycol. Cosmetic Ingredient Review (CIR), 202/331-0651, 1-31.
Hanzlik, P.J. et al. (1939): Toxicity, fats and excretion of propylene glycol and other glycols. *J. Pharmacol. Exp. Therap*. 65, 101-113.

Species: rat
Route: i.v.
Method: details not given
GLP: No data
Results: LD50 = 5800 mg/kg
Reference: CIR Cosmetic Ingredient Review (1982): Scientific Literature Review on butylene glycol, hexylene glycol, ethoxydiglycol, dipropylene glycol. Cosmetic Ingredient Review (CIR), 202/331-0651, 1-31.
Shaffer, C.B. et al. (1951): A toxicological study of some polypropylene (polyoxypropylene) glycols. *Arch. Ind. Hyg. Occup. Med*. 3: 448-453.

Species: dog

Route: i.v.
Method: details not given
GLP: No data
Results: fatal dose = 11.5 cc/kg
Reference: Hanzlik, P.J. Newman, H.W., Van Winkle, W., Jr., Lehman, A.J., and Kennedy, N.K.. (1939): Toxicity, fats and excretion of propylene glycol and other glycols. *J. Pharmacol. Exp. Therap*. 67: 101-113.

5.2 CORROSIVENESS/IRRITATION

5.2.1 SKIN IRRITATION/CORROSION

Species: rabbit
Method: other
GLP: No data
Results: 10 applications of DPG over 12 days produced negligible irritation of rabbit skin.
Reference: BIBRA Toxicology International (1991): Dipropylene glycol - Toxicity profile. BIBRA Toxicology International - British Industrial Biological Research Association, 1-4.
Patty, F. (1982): Dipropylene glycol. In: Patty's Industrial Hygiene and Toxicology. G.D. Clayton, F.E. Clayton (Hrsg.) 3. Bearb. AFL., Vol. 2C Toxicology. Wiley-Interscience Verlag, New York, 3863-3865.

Species: rabbit
Method: uncovered applications, 5 days/w for 6 w.
GLP: no data
Results: neat material showed only slight irritation, while a 10% aqueous solution did not cause any local reactions in rabbits.
Reference: BIBRA Toxicology International (1991): Dipropylene glycol - Toxicity profile. BIBRA Toxicology International - British Industrial Biological Research Association, 1-4.

Species: rabbit
Method: not specified
GLP: No data
Results: slightly irritating; Application (generally covered) of DPG caused slight irritation for 24 h to intact or abraded rabbit skin.
Reference: BIBRA Toxicology International (1991): Dipropylene glycol - Toxicity profile. BIBRA Toxicology International - British Industrial Biological Research Association, 1-4.
Opdyke, D.J. (1978): Dipropylene glycol. Food and Cosmetics Toxicology 15, Suppl. In: Monographs on fragrance of raw materials, 729-730.

Species: rabbit
Method: 500 mg undiluted DPG was applied to rabbit skin for 24 hours.
GLP: No data
Results: slightly irritating
Reference: CIR Cosmetic Ingredient Review (1982): Scientific Literature Review on butylene glycol, hexylene glycol, ethoxydiglycol, dipropylene glycol. Cosmetic Ingredient Review (CIR), 202/331-0651: 1-31.
CIR, Cosmetic Ingredient Review (1985): Final report on the safety assessment of butylene glycol, hexylene glycol, ethoxydiglycol and dipropylene glycol. *J. Am. Coll. Toxicol*. 4: 223-248.

Species: rabbit
Method: not specified
GLP: No data
Results: not irritating

Reference: Patty, F. (1982): Dipropylene glycol. In: Patty's Industrial Hygiene and Toxicology. G.D. Clayton, F.E. Wiley-Interscience Verlag, New York, 3863-3865.
Spencer, H.C. (1946): A Summary of the toxicological information on dipropylene glycol and a discussion of the hazards associated with its handling and use. Dow Chemical Company - Biochemical Research Laboratory.

5.2.2 EYE IRRITATION/CORROSION

Species: rabbit
Method: not specified
GLP: No data
Results: not irritating.
Reference: Carpenter, C.P.; Smyth, H.F., Jr. (1946): Chemical burns of the rabbit cornea. *Amer. J.Opthalmol.* 29, 1363-1372.
Patty, F. (1982): Dipropylene glycol. In: Patty's Industrial Hygiene and Toxicology. G.D. Clayton, F.E. Wiley-Interscience Verlag, New York, 3863-3865.

Species: rabbit
Method: Dose: 500 mg DPG for 24 hours or a formulation containing 7.2% of DPG
GLP: No data
Results: from neat DPG - mild irritation. No more than minimal transient irritation from 7.2% DPG formulation
Reference: BIBRA Toxicology International (1991): Dipropylene glycol Toxicity profile. BIBRA Toxicology International - British Industrial Biological Research Association, 1-4.
CIR, Cosmetic Ingredient Review (1985): Final report on the safety assessment of butylene glycol, hexylene glycol, ethoxydiglycol and dipropylene glycol. *J. Am. Coll. Toxicol.* 4: 223-248.
Deichmann, W.B.; Gerarde, H.W. (1969): Acute toxicity of glycols. Toxicology of Drugs and Chemicals, 4. AFL., Academic Press, New York, 731.

5.3 SKIN SENSITISATION

No animal data available. Please see section 5.11.

5.4 REPEATED DOSE TOXICITY

Oral:

Species: male/female rats, strain not reported

Method: not reported
Exposure Period: 9-77 days
Doses: 1-10% in drinkng water
GLP: No data
Results: No adverse effects in rats exposed up to 5%. In rats exposed to 10% DPG in drinking water 9-68 days, 36% developed kidney lesions; 7 of 25 died.
Reference: Kesten, H.D. et al (1939): Pathologic effects of certain glycols and related compounds. Arch. Pathol. 27: 447-465.

Species: dog, strain and sex not reported
Method: By gavage. Dosing described as "divided doses", no specifications on how frequenctly doses were administered; in another part of the study doses of diethylene glycol were administered 3 times daily.
Exposure Period: not stated
Doses: 20 cc/kg bw in 4 applications; 9 cc/kg bw in 6 applications; 12 cc/kg bw in 6 applications

GLP: No data
Results: No effects in 3 of 4 dogs; 1 at 12 cc/kg – emesis and recovery; minimal liver damage; moderate degeneration of kidneys in 2 of 4 dogs.
Reference: Hanzlik, P.J. Newman, H.W., Van Winkle, W., Jr., Lehman, A.J., and Kennedy, N.K.. (1939): Toxicity, fats and excretion of propylene glycol and other glycols. *J. Pharmacol. Exp. Therap.* 67: 101-113.

Species: rat; strain and sex not specified
Method: not reported
Exposure Period: 15 weeks
Feed Concentrations: 0, 12%
GLP: No data
Results:
Reference: Browning, E. (1965): Dipropylene Glycol. Toxicity and metabolism of industrial solvents, Elsevier Verlag, Amsterdam, 653-655.
Opdyke, D.J. (1978): Dipropylene glycol. Food and Cosmetics Toxicology 16, Suppl. In: Monographs on fragrance of raw materials, 729-730.

Species: chicks; strain and sex not specified
Method: not reported
Exposure Period: 27 days
Feed Concentrations: 5% (approximately 6.25 g/kg bw/day)
GLP: No data
Results: No adverse effects
Reference: BIBRA Toxicology International (1991): Dipropylene glycol – Toxicity profile. BIBRA Toxicology International – British Industrial Biological Research Association, 1-4.
Patty, F. (1982): Dipropylene glycol. In: Patty's Industrial Hygiene and Toxicology / G.D. Clayton, F.E. Clayton (Hrsg.) 3. Bearb. AFL., Vol. 2C Toxicology. Wiley-Interscience Verlag, New York, 3863-3865.
Yoshida, M., Woshii, H., and Morimoto, H. (1969): Nippon Kakim Gakkaishi 6: 73.

Intravenous Studies:

Species: rabbit; strain and sex not specified
Method: not given
Duration: 1-21 days
Doses: 2-4 cc/kg
GLP: No data
Results: Dosing at 4 cc/kg/day resulted in 50% incidence of renal changes (not specifically described) and 40% mortality. No effect was seen at 2 cc/kg.
Reference: Kesten, H.D. et al (1939): Pathologic effects of certain glycols and related compounds. Arch. Pathol. 27: 447-465.

5.5 GENETIC TOXICITY IN VITRO

A. BACTERIAL IN VITRO TEST

Type: Ames test
System of Testing: Salmonella typhimurium TA 98, TA 100, TA 1535, TA 1537
Concentration: 100 – 10,000 µg/plate
GLP: No data
Result: Negative
Reference: CCRIS (1992): Data Bank Recherche vom 17.11.1992.

Type: Ames test
System of Testing: TA98, TA100, TA1535, TA1537, TA1538 with and without metabolic activation

Concentration:	0.102 - 102 µg/plate
Method:	OECD Guideline 471 "Genetic Toxicology: *Salmonella thyphimurium* Reverse Mutation Assay"
GLP:	No data
Result:	Negative
Reference:	Leuschner, J. (1992): Pruefbericht Mutagenicity study of dipropylene glycol in the AMES Salmonella/Microsome plate test (in Vitro). LPT Report No. 7112/91. Unveroeffentlicher Bericht vom 04.03.1992, Laboratory of Pharmacology and Toxicology (LPT) in Hamburg

B. NON-BACTERIAL IN VITRO TEST

Type:	Mouse lymphoma assay
Method:	OECD Guideline 473
System of Testing:	L5178Y (Tk+/TK-) with and without metabolic activation
Concentration:	30 - 60 µl/ml
GLP:	Yes
Result:	Negative.
Reference:	CCRIS (1992): Data Bank Recherche com 17.11.1992.

5.6 GENETIC TOXICITY IN VIVO

Test type: Micronucleus assay

Test Species:	CD-1 mouse, male
Test Substance:	Dipropylene glycol
Test Method:	OECD #474 (1997); EPA OPPTS 870.5395 (1998)
Route of Exposure:	oral gavage
Frequency of Exposure:	once per day
Duration of Exposure:	2 consecutive days
Post Exposure Observation Period:	none
Doses:	0, 500, 1000, 2000 mg/kg/day
GLP:	Yes
Test Results:	The study was negative.
Reference:	Dow Chemical Company. (1999): Evaluation of Dipropylene glycol in the mouse bone marrow micronucleus test. Unpublished report of The Dow Chemical Company, 24 March 1999.

5.7 CARCINOGENICITY

No data available.

5.8 TOXICITY TO REPRODUCTION

No data available

5.9 DEVELOPMENTAL TOXICITY/TERATOGENICITY

Type:	Teratology
Method:	not specified
Species:	female Sprague-Dawley rat
Route of Administration:	gavage
Doses:	0, 800, 2000, 5000 mg/kg of DPG daily days 6-15 of gestation period
GLP:	No data

Results: Maternal Effects: Maternal toxicity and lethality were observed at 2000 and 5000 mg/kg/day (mortality rate: 4% and 9%), establishing the maternal NOAEL as 800 mg/kg/day.

Embryo/Fetal Effects: There were no significant differences between the DPG exposed groups and the control. NOAEL was 5000 mg/kg/day.

Reference: Bates, K.H. et al (1992): Final Report on the Development Toxicity of Dipropylene Glycol (CAS-No. 25265-71-8) in Sprague-Dawley (CD) Rats. National Toxicology Program, National Institute of Environmental Health Sciences, PO Box 12233, Research Triangle Park, NC 27709; NTIS # PB92-196179.

Type: Teratology
Method: not specified
Species: female New Zealand White rabbit
Route of Administration: gavage
Doses: 0, 200, 400, 800, 1200 mg/kg of DPG daily days 6-19 of gestation period
GLP: No data
Results: Maternal Effects: No maternal toxicity or lethality was observed at any doses level.
Embryo/Fetal Effects: There were no significant differences between the DPG exposed groups and the control. NOAEL was 1200 mg/kg/day.
Reference: Bates, K.H. et al (1992): Final Report on the Development Toxicity of Dipropylene Glycol (CAS-No. 25265-71-8) in New Zealand White Rabbits. National Toxicology Program, National Institute of Environmental Health Sciences, PO Box 12233, Research Triangle Park, NC 27709; NTIS # PB92-238294.

5.10 OTHER RELEVANT INFORMATION

Type: metabolism
Remark: Tripropylene glycol was administered by oral gavage to male F344 rats. TPG was readily converted to DPG and then to PG, which was further metabolized via the citric acid cycle to CO_2 or excreted in the urine.
Reference: Dow Chemical Company. (1995): Metabolism of tripropylene glycol in rats. Unpublished Report from The Toxicology Research Laboratory, The Dow Chemical Company, Midland, Michigan, pp. 1-36.

Type: Biochemical or cellular interactions
Remark: In experiments with mice the exposure of DPG (contained in a commercial deodorant spray) for 2 hours caused a rise in the ozone sensibility of the liver (measured as an increase of the reduced form of ascorbic acid in the liver).
Reference: Veninga, T.; Wagenaar, J. (1977): Reinforcement of ozone action in mice by additional environmental compounds. VDI-Berichte Nr. 270, 119-122.

Type: Excretion of Bile
Remark The application of 1 ml/kg DPG (intraduodenal) to rats increased the excretion of bile.
Reference: Croce, G.; Ferrini, R. (1973): Modificazioni della coleresi nel ratto con alcuni solvent e disperdenti usati come veicoli di farmaci - Modification of choleresis in the rat. Bollettino - societa italiana biologia sperimentale 49, 653-659.

5.11 EXPERIENCE WITH HUMAN EXPOSURE

Skin Irritation:

Species: Human
Method: 0.2 ml of a 25% solution of dipropylene glycol in distilled water for 24 hours via semi-occluded patches. 33 subjects
GLP: No data
Results: 2 subjects no effects at 30 min. but mild erythema at 24 hrs.
2 subjects mild to moderate erythema at 30 min. and mild erythema at 24 hrs.
7 subjects mild to moderate erythema at 30 min. but no effects at 24 hrs.
22 subjects no reaction at 30 min or 24 hr.
Reference: Acklin, A., and Plaza, M.E. (1995). Evaluation of Primary Irritation Potential in Humans. Hill Top Research, Inc. Report No. 94-1373-70. Submitted to Dow Chemical Company.

Species: Human
Method: Covered 48-h application of a 20% or 50% solution of DPG in petrolatum.
7.2% in shaving prep
GLP: No data
Results: 50% solution caused irritation in 14 of 34 persons and was equivocally an irritant in a further 17.
20% solution caused no irritation number tested not stated.
7.2% shaving prep no irritation open application, mild irritation in 6 of 101 subjects in closed patch.
Reference: BIBRA Toxicology International (1991): Dipropylene glycol - Toxicity profile. BIBRA Toxicology International - British Industrial Biological Research Association, 1-4.

Sensitization:

Species: Human
Method: Not specified
GLP: No data
Results: Only 1 patient out of 503 eczema patients displayed a positive patch test to dipropylene glycol (96% purity) in an eczematous population.
Reference: Johansen, J.D., G.B.E. Jemec, and S.C. Rastogi. (1995). Contact sensitization to dipropylene glycol in an eczema population. *Contact Dermatitis*. 33:211-212.

Species: Human
Method: 24/48-h (presumably covered) patches, 3 days/week for 3 weeks, followed by a challenge patch after a 2-w rest period. Supplemental exposure to UV light after application of the first four patches and the challenge patch. 50 subjects
GLP: No data
Results: No indication of sensitization or photosensitization.
Reference: BIBRA Toxicology International (1991): Dipropylene glycol - Toxicity profile. BIBRA Toxicology International - British Industrial Biological Research Association, 1-4.

6. REFERENCES

Acklin, A., and Plaza, M.E. (1995). Evaluation of Primary Irritation Potential in Humans. Hill Top Research, Inc. Report No. 94-1373-70. Submitted to Dow Chemical Company.

AOP (1992): Atmospheric Oxidation Program, Version 1.5. An Adaptation of the Atkinson Estimation Methodology, Syracuse Research Corporation, Syracuse.

BASF (1989): Dipropylene Glycol. DIN-Sicherheitsdatenblatt com Juli 1989, BASF Aktiengesellschaft, Ludwigshafen, 2 S.

Bates, K.H. et al (1992): Final Report on the Development Toxicity of Dipropylene Glycol (CAS-No. 25265-71-8) in Sprague-Dawley (CD) Rats. National Toxicology Program, National Institute of Environmental Health Sciences, PO Box 12233, Research Triangle Park, NC 27709; NTIS # PB92-196179.

Bates, K.H. et al (1992): Final Report on the Development Toxicity of Dipropylene Glycol (CAS-No. 25265-71-8) in New Zealand White Rabbits. National Toxicology Program, National Institute of Environmental Health Sciences, PO Box 12233, Research Triangle Park, NC 27709; NTIS # PB92-238294.

Bridie, A.L. et al. (1979b): BOD and COD of some petrochemicals. *Water Res*. 13, 627-630.

Bridie, A.L.; Wolff, C.J.M.; Winter, M. (1979a): The acute toxicity of some petrochemicals to goldfish. *Water Res*. 13, 623-626.

Brown, E.S.; Hauser, C.F.; Ream, B.C.; Berthold, R.V. (1980): Glycols. Kirk-Othmer Encyclopedia of Chemical Technology, Band 11, 3. Auf 1., John Wiley & Sons, New York, ISBN -0-471-02063-8; 933-956.

Browning, E. (1965): Dipropylene Glycol. Toxicity and metabolism of industrial solvents, Elsevier Verlag, Amsterdam, 653-655.

BUA report (1994): Dipropylenglykol

CCRIS (1992): Data Bank Recherche vom 17.11.1992.

CIR, Cosmetic Ingredient Review (1985): Final report on the safety assessment of butylene glycol, hexylene glycol, ethoxydiglycol and dipropylene glycol. *J. Am. Coll. Toxicol.* 4: 223-248.

CIR Cosmetic Ingredient Review (1982): Scientific Literature Review on butylene glycol, hexylene glycol, ethoxydiglycol, dipropylene glycol. Cosmetic Ingredient Review (CIR), 202/331-0651, 1-31.

Claussen, T. (1992). Dipropylene Glycol: Determination of the Acute Toxicity to *Pseudomonas putida*. Research and Development Report, Health & Environmental Sciences, Dow Europe.

Croce, G.; Ferrini, R. (1973): Modificazioni della coleresi nel ratto con alcuni solvent e disperdenti usati come veicoli di farmaci - Modification of choleresis in the rat. Bollettino - societa italiana biologia sperimentale 49, 653-659.

Deichmann, W.B.; Gerarde, H.W. (1969): Acute toxicity of glycols. Toxicology of Drugs and Chemicals, 4. AFL., Academic Press, New York, 731

Deichmann, W.B.; Gerarde, H.W. (1969): Acute toxicity of glycols. Toxicology Johansen, J.D., G.B.E. Jemec, and S.C.

Rastogi. (1995). Contact sensitization to dipropylene glycol in an eczema population. *Contact Dermatitis*. 33:211-212.

De Zwart, D.; Slooff, W. (1987): Toxicity of mixtures of heavy metals and petrochemicals to *Xenopus laevis*. *Bull.Environ. Contam. Toxicol*. 38: 345-351.

DOW (1991): Dipropylene Glycol. DIN -Sicherheitsdatenblatt vom Juni 1991, DOW Deutschland Inc., Frankfurt, 5 S.

DOW (1991a): Dipropylene Glycol. DIN-Sicherheitsdatenblatt com Juni 1991, DOW Deutschland Inc., Frankfurt, 5 S.

Dow Chemical Company. (1995): Metabolism of tripropylene glycol in rats. Unpublished Report from The Toxicology
Research Laboratory, The Dow Chemical Company, Midland, Michigan, pp. 1-36.

Dow Chemical Company. (1999): Evaluation of Dipropylene glycol in the mouse bone marrow micronucleus test. Unpublished report of The Dow Chemical Company, 24 March 1999

Dow Chemical Europe, Horgen, Switzerland. Determination of the acute oral toxicity of dipropylene glycol in rats with cover letter dated 03/28/94 (sanitized). Doc ID# 86940000276S.

Dunlap, W.J.; Shew, D.C. (1976); Organic pollutants contributed to ground water by a landfill. U.S. EPA, EPA - 600/9-76-004 PB - 251161, 96-110.

Elm, R.; Falbe, J.; Hahn, H.-D.; Gelbke, H.-P. (1980): Propandiole. Ullmanns Enzyklopaedie der technischen chemie, 4. neubearb. u. er. AFL. Band 19, Verlag Chemie, Wenham, 427-432.

Fincer, E.L.; Payne, W.J. (1962): Bacterial utilization of ether glycols. *Appl. Microbiol*. 10: 542-630.
MITI (1992): Dipropylene glycol. Chemicals inspection and testing institute Japan: Data of existing chemicals based on the CSCL Japan. Japan Chemical Industry Ecology -Toxicology and Information Center, 2-56.

Hanzlik, P.J. Newman, H.W., Van Winkle, W., Jr., Lehman, A.J., and Kennedy, N.K.. (1939): Toxicity, fats and excretion of propylene glycol and other glycols. *J. Pharmacol. Exp. Therap*. 67: 101-113.

Hawley, G.G. (1981): Dipropylene Glycol. Hawley, G.G.: The Condensed Chemical Dictionary, 10. Auflage, New York: van Nostrand Reinhold, 383.

Hine, J.; Mookerjee, P.K. (1975): The intrinsic hydrophilic character of organic compounds. Correlations in terms of structural contributions. *J. Org. Chem*. 40, 292-298.

Hommel, G. (1983): Dipropyleneglycol. Handbuch der gefaehrlichen Gueter, 3 ueberarb. Auflage, Springer Verlag, Berlin, Merkblatt 478.

Kawai, F.; Hanada, K.; Tani, Y.; Ogata, K. (1977): Bacterial degradation of water- insoluble polymer (polypropylene
glycol). *J. Ferment. Technol*. 55: 89-96.

Kawai, F. Okamoto, T.; Suzuki, T. (1985): Aerobic degradation of polypropylene glycol by *corynebacterium* sp. *J.*
Ferment. Technol. 63: 239-244.

Kesten, H.D. et al (1939): Pathologic effects of certain glycols and related compounds. Arch. Pathol. 27: 447-465.

Laboratory Carpenter, C.P.; Smyth, H.F., Jr. (1946): Chemical burns of the rabbit cornea. *Amer. J. Opthalmol.* 29, 1363-1372.

Leuschner, J. (1992): Pruefbericht Mutagenicity study of dipropylene glycol in the AMES Salmonella/Microsome plate test (in Vitro). LPT Report No. 7112/91. Unveroeffentlicher Bericht vom 04.03.1992, Laboratory of Pharmacology and Toxicology (LPT) in Hamburg

Lin, D.D.D.; Melton, R.G.; Kopfler, F.C.; Lucas, S.V. (1981); Glass capillary gas chromatographic/mass spectrometric analysis of organic concentrates from drinking and advanced waste treatment water. Advances in the identification and analysis of organic pollutants in water/ Keith, L.H. (Publisher) - Vol 2 - Ann Arbor Science Publishers, Collingwood, ISBN 0-250-40398-6, 861-906.

Litz, N. (1990): Schultz vor weiteren anthorpogenen Organika-Eintrogen. Blume, H.P. (Ed.): Handbuch desBodenschutzes. Bodenokologie und -belastung: Vorbeugende und absehrende Schutzmassnahmen. Ecomed Verlagsgesellschaft, Landsberg/Lech, 579-584.

Lyman, W.J. (1982); Adsorption coefficient for soils and sediments. Lyman W.J.; Reehl, W.F.; Rosenblatt, D.H. (publisher): Handbook of chemical property estimation methods. Environmental behavior of Organic Compounds, New York, McGraw -Hill, 4.1 - 4.33.

Mackay, D. (1991): Multimedia Environmental Models, Chelsea, Lewis Publishers, 185-227.

Material Safety Data Sheet, Arco Chemical Company, 1993

Merck (1992): Dipropyleneglycol. Reagenzien, Diagnostica, Chemikalien 1992/93 - Merck-Katalog, 522.

MITI (1992): Dipropylene glycol. Chemicals inspection and testing institute Japan: Data of existing chemicals based on The CSCL Japan. Japan Chemical Industry Ecology-Toxicology and Information Center, 2-56.

NATEC (1992): Pruefbericht Bestimmung der akuten Bakterientoxizitaet an Pseudomonas putida mit der Pruefsubstanz Dipropylene glycol. Pruefnummer NA 91 1212. Unveroeffentlichter Bericht vom 28.02.1992, NATEC Institut, Hamburg.

Nishiuchi, K. (1984): Toxicity of agrochemicals to freshwater organisms. CIII. Solvents. *Suisan Zoshoku – The Aquiculture Japan* 31: 115-119.

Opdyke, D.J. (1978): Dipropylene glycol. Food and Cosmetics Toxicology 16, Suppl. In: Monographs on fragrance of Raw materials, 729-730.

Patty, F. (1982): Dipropylene glycol. In: Patty's Industrial Hygiene and Toxicology / G.D. Clayton, F.E. Clayton (Hrsg.) 3. Bearb. AFL., Vol. 2C Toxicology. Wiley-Interscience Verlag, New York, 3863-3865.

Sax, N.J. (1979): Dipropylene glycol. Dangerous Properties of Industrial Materials, 5. Ed., published by Van Nostrand Rheinhold, New York, 627.

Sexton, A.R.; Britton, E.C. (1953): Synthesis and identification of dipropylene glycol isomers. *J. Am. Chem. Soc*. 75: 4357-4358.

Shaffer, C.B. et al. (1951): A toxicological study of some polypropylene (polypropylene) glycols. *Arch. Ind. Hyg. Occup. Med.* 3: 448-453.

Spencer, H.C. (1946): A summary of the toxicological information on dipropylene glycol and a discussion of the hazards associated with its handling and use. Dow Chemical Company - Biochemical Research Laboratory.

Thomas, R.G. (1990): Volatilization from water. Lyman, W.J.; Reehl, W.F.; Rosenblatt, D.H. (Publisher): Handbook of chemical property estimation methods. Environmental Behavior of Organic Compounds, New York, McGraw-Hill, 15.1 - 15.34.

Turoski, V.E.; Woltman, D.L.; Vincent, B.F. (1983): Determination of organic priority pollutants in the paper industry by GC/MS. *Tappi J.* 66: 89-90.

Veninga, T.; Wagenaar, J. (1977): Reinforcement of ozone action in mice by additional environmental compounds. VDI-Berichte Nr. 270, 119-122.

Yoshida, M., Woshii, H., and Morimoto, H. (1969): Nippon Kakim Gakkaishi 6: 73.

I U C L I D Data Set

Existing Chemical	:	ID: 25265-71-8
CAS No.	:	25265-71-8
EINECS Name	:	oxydipropanol
EINECS No.	:	246-770-3
TSCA Name	:	Propanol, oxybis -
Molecular Formula	:	C6H14O3

Producer Related Part

Company	:	ACC Propylene Oxide/Propylene Glycol Panel
Creation date	:	23.05.2001

Substance Related Part

Company	:	ACC Propylene Oxide/Propylene Glycol Panel
Creation date	:	23.05.2001
Memo	:	
Printing date	:	30.05.2001
Revision date	:	
Date of last Update	:	30.05.2001
Number of Pages	:	3
Chapter (profile)	:	Chapter: 1, 2, 3, 4, 5, 7
Reliability (profile)	:	Reliability: without reliability, 1, 2, 3, 4
Flags (profile)	:	Flags: without flag, confidential, non confidential, WGK (DE), TA-Luft (DE), Material Safety Dataset, Risk Assessment, Directive 67/548/EEC, SIDS

1.0.1 OECD AND COMPANY INFORMATION

Type :
Name : Lyondell Chemical Company
Partner :
Date :
Street : 1221 McKinney Street Suite 1600
Town : 77010 Houston Texas
Country : United States
Phone : 713-652-7200
Telefax :
Telex :
Cedex :
Source : Lyondell Chemical Co. Houston, Texas
11.05.2001

Type :
Name : Huntsman Corporation
Partner :
Date :
Street : 500 Huntsman Way
Town : 84108 Salt Lake City, Utah
Country : United States
Phone : 1-800-421-2411
Telefax : 801-584-5781
Telex :
Cedex :
Source : Lyondell Chemical Co. Houston, Texas
30.05.2001

Type :
Name : The Dow Chemical Company
Partner :
Date :
Street : 2030 Dow Center
Town : 48674 Midland, MI
Country : United States
Phone : 517-636-1000
Telefax : 517-636-4033
Telex :
Cedex :
Source : Lyondell Chemical Co. Houston, Texas
29.05.2001

1.0.2 LOCATION OF PRODUCTION SITE

1.0.3 IDENTITY OF RECIPIENTS

1.1 GENERAL SUBSTANCE INFORMATION

Substance type : organic
Physical status : liquid

Purity : >= 98 % w/w
Source : Lyondell Chemical Co. Houston, Texas
30.04.2001

1.1.0 DETAILS ON TEM PLATE

1.1.1 SPECTRA

1.2 SYNONYMS

Di-1,2-propyleneglycol
Remark : common name:
dipropyleneglycol

structural isomers (as mixture in the technical product):
(1) 2,2-Dihydroxydiisopropylether (CAS-No.: 108-61-2);
(2) 2,2-Dihydroxydipropylether (CAS-No.: 110-98-5);
(3) 2-Hydroxypropyl-2'-hydroxyisopropylether
(CAS-No.:106-62-7);
Source : Lyondell Chemical Co. Houston, Texas
Flag : Critical study for SIDS endpoint
21.05.2001

1.3 IMPURITIES

1.4 ADDITIVES

1.5 QUANTITY

1.6.1 LABELLING

1.6.2 CLASSIFICATION

1.7 USE PATTERN

Type : type
Category : Non dispersive use
Source : Lyondell Chemical Co. Houston, Texas
09.05.2001

Type : type
Category : Use resulting in inclusion into or onto matrix
Source : Lyondell Chemical Co. Houston, Texas
09.05.2001

Type : type

Category : Wide dispersive use
Source : Lyondell Chemical Co. Houston, Texas
09.05.2001

Type : industrial
Category : Basic industry: basic chemicals
Source : Lyondell Chemical Co. Houston, Texas
09.05.2001

Type : industrial
Category : Chemical industry: used in synthesis
Source : Lyondell Chemical Co. Houston, Texas
09.05.2001

Type : industrial
Category : Electrical/electronic engineering industry
Source : Lyondell Chemical Co. Houston, Texas
09.05.2001

Type : industrial
Category : Leather processing industry
Source : Lyondell Chemical Co. Houston, Texas
09.05.2001

Type : industrial
Category : Personal and domestic use
Source : Lyondell Chemical Co. Houston, Texas
09.05.2001

Type : industrial
Category : Public domain
Source : Lyondell Chemical Co. Houston, Texas
09.05.2001

Type : industrial
Category : Textile processing industry
Source : Lyondell Chemical Co. Houston, Texas
09.05.2001

Type : use
Category : Cleaning/washing agents and disinfectants
Source : Lyondell Chemical Co. Houston, Texas
09.05.2001

Type : use
Category : Cosmetics
Source : Lyondell Chemical Co. Houston, Texas
09.05.2001

Type : use
Category : Intermediates
Source : Lyondell Chemical Co. Houston, Texas
09.05.2001

Type : use
Category : Odour agents
Source : Lyondell Chemical Co. Houston, Texas
21.05.2001

Type : use

Category : Solvents
Source : Lyondell Chemical Co. Houston, Texas
09.05.2001

Type : use
Category : Stabilizers
Source : Lyondell Chemical Co. Houston, Texas
09.05.2001

1.7.1 TECHNOLOGY PRODUCTION/USE

1.8 OCCUPATIONAL EXPOSURE LIMIT VALUES

1.9 SOURCE OF EXPOSURE

1.10.1 RECOMMENDATIONS/PRECAUTIONARY MEASURES

1.10.2 EMERGENCY MEASURES

1.11 PACKAGING

1.12 POSSIB. OF RENDERING SUBST. HARMLES S

1.13 STATEMENTS CONCERNING WASTE

1.14.1 WATER POLLUTION

1.14.2 MAJOR ACCIDENT HAZARDS

1.14.3 AIR POLLUTION

1.15 ADDITIONAL REMARKS

1.16 LAST LITERATURE SEARCH

1.17 REVIEW

1.18 LISTINGS E.G. CHEMICAL INVENTORIES

2.1 MELTING POINT

Value : < -39 ° C
Sublimation :
Method :
Year : 1980
GLP :
Test substance :
Source : Lyondell C hemical Co. Houston, Texas
Flag : Critical study for SIDS endpoint
22.05.2001 (9)

2.2 BOILING POINT

Value : = 222.2 - 233 ° C at
Source : Lyondell Chemical Co. Houston, Texas
29.05.2001 (32)

Value : = 228 - 236 ° C at
Source : Lyondell Chemical Co. Houston, Texas
Flag : Critical study for SIDS endpoint
29.05.2001 (20)

2.3 DENSITY

Type :
Value : = 1.025 g/cm3 at 20° C
Source : Lyondell Chemical Co. Houston, Texas
29.05.2001 (10)

Type :
Value : = 1.022 g/cm3 at 25° C
Source : Lyondell Chemical Co. Houston, Texas
Flag : Critical study for SIDS endpoint
29.05.2001 (25)

2.3.1 GRANULOMETRY

2.4 VAPOUR PRESSURE

Value : = .05 hPa at 21° C
Source : Lyondell Chemical Co. Houston, Texas
29.05.2001 (16)

Value : = .0128 hPa at 20° C
Source : Lyondell Chemical Co. Houston, Texas
Flag : Critical study for SIDS endpoint
29.05.2001 (34)

2.5 PARTITION COEFFICIENT

Log pow : = -1.486 at ° C

Method
Year : 1993
GLP :
Test substance :
Source : Lyondell Chemical Co. Houston, Texas
Flag : Critical study for SIDS endpoint
23.05.2001 (5)

2.6.1 WATER SOLUBILITY

Value : at ° C
Qualitative : other: Described as miscible
Pka : at 25 ° C
PH : at and ° C
Source : Lyondell Chemical Co. Houston, Texas
Flag : Critical study for SIDS endpoint
29.05.2001 (16)

2.6.2 SURFACE TENSION

2.7 FLASH POINT

Value : = 118 ° C
Type : other
Method :
Year : 1980
GLP :
Test substance :
Method : ASTM D56
Source : Lyondell Chemical Co. Houston, Texas
Flag : Critical study for SIDS endpoint
22.05.2001 (9)

2.8 AUTO FLAMMABILITY

Value : = 371 ° C at
Method :
Year : 1993
GLP :
Test substance :
Method : ATSM D56
Source : Lyondell Chemical Co. Houston, Texas
Flag : Critical study for SIDS endpoint
22.05.2001 (27)

2.9 FLAMMABILITY

2.10 EXPLOSIVE PROPERTIES

2.11 OXIDIZING PROPERTIES

2.12 ADDITIONAL REMARKS

3.1.1 PHOTODEGRADATION

3.1.2 STABILITY IN WATER

Remark : no hydrolyzable groups
Source : Lyondell Chemical Co. Houston, Texas
Flag : Critical study for SIDS endpoint
22.05.2001

3.1.3 STABILITY IN SOIL

3.2 MONITORING DATA

3.3.1 TRANSPORT BETW EEN ENVIRONMENTAL COMPARTMENTS

Type : fugacity model level III
Media :
Air (level I) :
Water (level I) :
Soil (level I) :
Biota (level II / III) :
Soil (level II / III) :
Method : other: calculated
Year :
Method : EPIWIN (Estimation Program Interface for Windows) Version 3.05
LEVEL III FUGACITY MODEL

Melting Point (deg C): -39
Boiling Point (deg C): 222.20
Vapor Pressure (mm Hg): 0.05
Log Kow (octanol-water): -1.49

Default Emissions of 1000 Kg/h for air, water and soil (provided by EPIWIN)

Result : Concentration (Percent)
Half Life (hours)
Emissions (Kg/hr)

Air
0.107
8.19
1000

Water
46.1
360
1000

Soil
53.7
360
1000

Sediment
0.0768
1.44e+003
0

Henry's Law Constant: 3.58E-009 atm-m3/mole (EPIWIN estimate)
Volatization From Water (EPIWIN estimate)

River
Lake

Water depth (meters)
1
1

Wind Velocity (m/sec)
5
0.5

Current Velocity (m/sec)
1
0.05

HALF-LIFE (hours)
1.894E+005
2.067+006

HALF-LIFE (days)
7893
8.611E+004

HALF-LIFE (years)
21.61
235.8

Source : Lyondell Chemical Co. Houston, Texas
Conclusion : According to EPIWIN, assuming equal emissions to air, water, and soil, this chemical will concentrate mostly in water (46.1 %) and soil (53.7 %).

This chemical will take about 21.61 years to volatilize from a model river, and 235.8 years to volatilize from a model lake.
Flag : Critical study for SIDS endpoint
22.05.2001 (19)

3.3.2 DISTRIBUTION

3.4 MODE OF DEGRADATION IN ACTUAL USE

3.5 BIODEGRADATION

Type : aerobic
Inoculum : activated sludge, adapted
Contact time :
Degradation : > 70 % after 28 day
Result :

Deg. Product	:	
Method	:	Directive 87/302/EEC, part C, p. 99 "Biodegradation: Zahn-Wellens test"
Year	:	1989
GLP	:	no data
Test substance	:	no data
Method	:	Flasks containing test solution shaken continuously during the study period. Carbon dioxide production measured at intervals during the test. No additional study details given. Extent of pre-adaptation of bacteria not given.
Remark	:	Original reference not available for review, so methods and results were described based on a reputable secondary source.
Result	:	Following pre-adaptation of bacteria, significant degradation of the test substance was observed during the study.
Source	:	Lyondell Chemical Co. Houston, Texas
Conclusion	:	>70% degradation after 28 days
Reliability	:	(2) valid with restrictions Details on the test procedure and study results are not provided. Details on the results of analytical measurement of test substance concentrations in the test solutions and sample purity is not provided.
Flag	:	Critical study for SIDS endpoint

23.05.2001 (2)

Type	:	aerobic
Inoculum	:	activated sludge
Deg. Product	:	
Method	:	OECD Guide-line 301 C "Ready Biodegradability: Modified MITI Test (I)"
Year	:	1992
GLP	:	no data
Test substance	:	no data
Method	:	Concentration: 30 mg/l substance and 100 mg/l sludge. Initial inoculation of 30 mg/l test substance to each flask. Respirometer used to evaluate test substance degradation. No agitation of exposure solutions during the study period. Carbon dioxide production measured continuously during the test. No additional study details given.
Remark	:	Original reference not available for review, so methods and results were described based on a reputable secondary source.
Result	:	no measurable degradation during the study period
Source	:	Lyondell Chemical Co. Houston, Texas
Conclusion	:	no degradation
Reliability	:	(2) valid with restrictions Details on the test procedure and study results are not provided. Details on the results of analytical measurement of test substance concentrations in the test solutions and sample purity is not provided.
Flag	:	Critical study for SIDS endpoint

23.05.2001 (28)

3.6 BOD5, COD OR BOD5/COD RATIO

BOD5		
Method	:	other: APHA Standard Methods, Number 219
Year	:	1979
GLP	:	no
Concentration	:	related to
BOD5	:	= 92 mgO2/l
COD		
Method	:	
Year	:	
GLP	:	

COD	:	= 1840 mg/g substance
RATIO BOD5 / COD		
BOD5/COD	:	= .49
Method	:	Test conducted in special BOD bottles containing test substance and nutrient media. Oxygen depletion measured at initiation and after 5 days of incubation. Degradation of test substance calculated from oxygen depletion. No additional study details given. Remarks: Because this study was conducted before any standardized guidelines were established, the question of guideline methodology and GLP conduct is not applicable.
Result	:	BOD5 = 92 mg/l; COD = 1840 mg/g; BOD5/COD = 0.49
Source	:	Lyondell Chemical Co. Houston, Texas
Test substance	:	no data
Conclusion	:	Low oxygen demand from test substance
Reliability	:	(2) valid with restrictions Details on the test procedure and study results are not provided. Details on the results of analytical measurement of test substance concentrations in the test solutions and sample purity is not provided.
Flag	:	Critical study for SIDS endpoint

29.05.2001 (7)

3.7 BIOACCUMULATION

Species	:	Cyprinus carpio (Fish, fresh water)
Exposure period	:	42 day at 25 degree C
Concentration	:	3mg/l
BCF	:	= .3 - 1.4
Elimination	:	no data
Method	:	OECD Guide-line 305 C "Bioaccumulation: Test for the Degree of Bioconcentration in Fish"
Year	:	1992
GLP	:	no data
Test substance	:	no data
Method	:	Fish exposed to test substance at concentration of 3 mg/l for exposure period of 42 days. Temperature of test solutions was maintained at 25 ºC. No additional details given on the extent of the depuration period or other test conditions.
Remark	:	Original reference not available for review, so methods and results were described based on a reputable secondary source.
Source	:	Lyondell Chemical Co. Houston, Texas
Conclusion	:	The BCF for carp after 42 days of exposure was 0.3 to 1.4.
Reliability	:	(2) valid with restrictions Details on the test procedure and study results are not provided. Details on the results of analytical measurement of test substance concentrations in the test solutions and sample purity is not provided.
Flag	:	Critical study for SIDS endpoint

23.05.2001 (28)

Species	:	Cyprinus carpio (Fish, fresh water)
Exposure period	:	42 day at 25 degree C
Concentration	:	3mg/l
BCF	:	< 2.2 - 4.6
Elimination	:	no data
Method	:	OECD Guide-line 305 C "Bioaccumulation: Test for the Degree of Bioconcentration in Fish"
Year	:	1992
GLP	:	no data
Test substance	:	no data

Method	:	Fish exposed to test substance at concentration of 3 mg/l for exposure period of 42 days. Temperature of test solutions was maintained at 25 ºC. No additional details given on the extent of the depuration period or other test conditions.
Remark	:	Original reference not available for review, so methods and results were described based on a reputable secondary source.
Source	:	Lyondell Chemical Co. Houston, Texas
Conclusion	:	The BCF for carp after 42 days of exposure was < 2.2 to 4.6.
Reliability	:	(2) valid with restrictions Details on the test procedure and study results are not provided. Details on the results of analytical measurement of test substance concentrations in the test solutions and sample purity is not provided.
Flag	:	Critical study for SIDS endpoint

23.05.2001 (28)

3.8 ADDITIONAL REMARKS

4.1 ACUTE/PROLONGED TOXICITY TO FISH

Type	:	other: static acute LC50 (TLm)
Species	:	Carassius auratus (Fish, fresh water)
Exposure period	:	24 hour(s)
Unit	:	mg/l
Analytical monitoring	:	yes
LC50	:	> 5000
Method	:	
Year	:	1978
GLP	:	no
Test substance	:	no data
Method	:	APHA (American Public Health Association) 1971 Fish exposed to serial dilutions of TS with local tap water as the dilution water source. Study conducted in 25 L all-glass tanks measuring 42 x 28 x 28 cm at 20 ± 1 ºC. Fish in the study had an average length of 6.2 ± 0.7 cm and an average weight of 3.3 ± 1.0 g. Calculation of LC50 (TLm) Interpolation from graph of logarithm of concentration vs. percentage mortality Remarks: Because this study was conducted before any standardized guidelines were established, the question of guideline methodology and GLP conduct is not applicable.
Remark	:	Original reference not available for review, so methods and results were described based on a reputable secondary source.
Result	:	Since the 24-hour LC50 (TLm) was >5,000 mg/L, the study was terminated at this point.
Source	:	Lyondell Chemical Co. Houston, Texas
Conclusion	:	The 24-hour LC50 (TLm) for goldfish was determined to be >5,000 mg/L.
Reliability	:	(2) valid with restrictions Details on the test procedure and study results are not provided. Details on the results of analytical measurement of test substance concentrations in the test solutions and sample purity is not provided.
Flag	:	Critical study for SIDS endpoint

23.05.2001 (8)

4.2 ACUTE TOXICITY TO AQUATIC INVERTEBRATES

4.3 TOXICITY TO AQUATIC PLANTS E.G. ALGAE

4.4 TOXICITY TO MICROORGANISMS E.G. BACTERIA

Type	:	other: static acute EC10
Species	:	Pseudomonas putida (Bacteria)
Exposure period	:	18 hour(s)
Unit	:	mg/l
Analytical monitoring	:	yes
EC10	:	= 1000

Method	:	
Year	:	1992
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	German Water Hazard Classification (Umweltbundesamt, Sept. 1979, LTwS-Nr.10) There were 3 flasks per exposure concentration and 10 flasks for control. Bacteria exposed to serial dilutions of TS for 18 ± 2 hours with concentrations of 1.95, 3.91, 7.81, 15.63, 31.25, 62.5, 125, 250, 500 and 1000 mg/L. Solutions evaluated with infrared spectroscopy (IR). Extinction of cultures measured at 436 mm.
Result	:	Based on measurements made in all exposure concentrations, the EC10 was 1,000 mg/L.
Source	:	Lyondell Chemical Co. Houston, Texas
Test substance	:	sample >99.9% purity
Conclusion	:	The 18-hour EC10 for Pseudomonas putida was determined to be 1,000 mg/L.
Reliability	:	(1) valid without restriction
Flag	:	Critical study for SIDS endpoint

22.05.2001 (13)

4.5.1 CHRONIC TOXICITY TO FISH

4.5.2 CHRONIC TOXICITY TO AQUATIC INVERTEBRATES

4.6.1 TOXICITY TO SOIL DWELLING ORGANISMS

4.6.2 TOXICITY TO TERRESTRIAL PLANTS

4.6.3 TOXICITY TO OTHER NON-MAMM. TERRESTRIAL SPECIES

4.7 BIOLOGICAL EFFECTS MONITORING

4.8 BIOTRANSFORMATION AND KINETICS

4.9 ADDITIONAL REMARKS

Memo	:	Toxicity to clawed toad (Xenopus laevis)
Method	:	Type: static acute LC50 Species: clawed toad (Xenopus laevis) Number of animals: 10 per exposure concentration Value: = 3,181 mg/L Year: 1987 GLP: No

Test substance: no compositional details given

Exposure Period: 48 hrs

Method: No methodology given.

Clawed toads exposed to serial dilutions of test substance with Dutch standard water as the dilution water source.

Study conducted in 1 L all-glass covered aquaria with 3-4 week old larvae at a study temperature of 20 ± 1 ºC.

Calculation of LC50
Calculated as projection from least square linear regression on log transformed nominal concentration data and probit transformed percent effect data.

Analytical monitoring: None

Result : Mortality measured after 48 hours of exposure resulted in determination of an LC50 of 3,181 mg/L.

Source : Lyondell Chemical Co. Houston, Texas

Conclusion : The 48-hour LC50 (TLm) for the clawed toad was determined to be 3,181 mg/L.

Reliability : (2) valid with restrictions
Details on the test procedure and study results are not provided. No analytical measurement of test substance concentrations in the test solutions or sample purity were conducted.

Flag : Critical study for SIDS endpoint
23.05.2001 (14)

5.1.1 ACUTE ORAL TOXICITY

Type	:	LD50
Species	:	rat
Strain	:	Wistar
Sex	:	male/female
Number of animals	:	50
Vehicle	:	other: none
Value	:	= 16000 mg/kg bw
Method	:	
Year	:	1980
GLP	:	no
Test substance	:	no data
Method	:	Guideline not specified. Animals and treatments Rats were selected with a body weight range of 182 to 283 g for males and 110 to 150 g for females. Dipropylene glycol was administered by stomach tube following an overnight fast to 5 males and 5 females per dose at doses of 8.6, 10.4, 12.4, 14.0 or 17.9 ml per kg of body weight. The animals were observed for signs of intoxication for 14 days following dosing. Postmortem examination All animals were necropsied after death or 14 days after dosing. There was no indication of histopathologic examination of any tissues. Calculation of LD50 Based on method of Weil et al, Biometrics (195X)=missing year; 3: 247-263. General signs of toxicity were not reported. Examination of the internal organs revealed no gross alterations. The LD50 in the rat was determined to be 15.8 ml/kg, with standard errors of 19.2 - 23.0 ml/kg (equivalent to 16000 mg/kg, standard error 15000-17500 mg/kg).(Reviewer) Remarks: Because this study was conducted before any standardized guidelines were established, the question of guideline methodology and GLP conduct is not applicable.
Source	:	Lyondell Chemical Co. Houston, Texas
Conclusion	:	Based on the results of this study, an LD50 of 16000 mg/kg was determined for dipropylene glycol in the rat.
Reliability	:	(2) valid with restrictions Test material characterization not documented; GLP compliance not indicated.
Flag	:	Critical study for SIDS endpoint

29.05.2001 (33)

Type	:	LD50
Species	:	mouse
Strain	:	CD-1
Sex	:	male
Number of animals	:	24
Vehicle	:	water
Value	:	> 2000 mg/kg bw
Method	:	
Year	:	1999

GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	Animals and treatments Six mice per group were treated by gavage on two consecutive days with 0, 500, 1000, or 2000 mg/kg dipropylene glycol in water at a volume of 10 ml/kg. Survivors were killed by carbon dioxide inhalation 24 hours after the second dose. Bone marrow was collected for assessment of micronuclei. Postmortem examination None.
Result	:	No mice died. General signs of toxicity or necropsy observations were not reported.
Source	:	Lyondell Chemical Co. Houston, Texas
Conclusion	:	Based on the results of this study, an LD50 of >2000 mg/kg was determined for dipropylene glycol in the mouse.
Reliability	:	(2) valid with restrictions limited necropsy performed; animals not observed full 14 days after dosing.
Flag	:	Critical study for SIDS endpoint

22.05.2001 (17)

5.1.2 ACUTE INHALATION TOXICITY

Type	:	LC50
Species	:	other: Rat & Guinea Pig
Strain	:	other: not specified
Sex	:	no data
Number of animals	:	
Vehicle	:	
Exposure time	:	
Method	:	
Year	:	1961
GLP	:	no
Test substance	:	
Method	:	Dose Level-Vapor concentrations not reported, aerosol nominal concentrations were 6000-8000 mg/m3. Dipropylene glycol was heated to 170°C for 8 hours, 6 rats individually exposed to vapors in small chambers. Dipropylene glycol was heated to 120°C for 4 hours, 6 rats individually exposed to vapors in small chambers. Dipropylene glycol was heated to 170°C for 5 hours with the vapors being drawn off, allowed to cool; then reheated to 120°C for 5 hours, 6 rats individually exposed to vapors in small chambers. Dipropylene glycol was heated to 170°C for 5 hours with the vapors being drawn off, allowed to cool; 6 rats were individually exposed in small chambers to an aerosol generated at room temperature. An aerosol of dipropylene glycol was generated at room temperature, 6 rats and 6 guinea pigs were individually exposed in small chambers. (duration not reported) Remarks: Because this study was conducted before any standardized guidelines were established, the question of guideline methodology and GLP conduct is not applicable.

Result	:	Five of 6 rats exposed to vapors generated at 170°C died ; there were no pathologic abnormalities. Vapors generated at 120°C were not lethal. When rats were exposed to vapors generated at 120°C after removal of vapors generated by heating dipropylene glycol to 170°C for 5 hours, there were no deaths. There was no lethality to rats or guinea pigs fromaerosol of dipropylene glycol generated at room temperature.
Source	:	Lyondell Chemical Co. Houston, Texas
Conclusion	:	Heating Dipropylene Glycol to 170°C resulted in toxic degradation products that did not occur from heating to 120°C and were not present in aerosols generated at room temperature or at 120°C.(Reviewer)
Reliability	:	(4) not assignable PreGLP/Guidline study with brief description of methods and results.
Flag	:	Critical study for SIDS endpoint

29.05.2001 (31)

5.1.3 ACUTE DERMAL TOXICITY

Type	:	LD50
Species	:	rabbit
Strain	:	
Sex	:	no data
Number of animals	:	
Vehicle	:	other: none
Value	:	> 5000 mg/kg bw
Remark	:	Original reference not available for review, so methods and results were described based on a reputable secondary source.
Result	:	No deaths; LD50 >5000 mg/kg
Source	:	Lyondell Chemical Co. Houston, Texas
Reliability	:	(4) not assignable details not provided in secondary source
Flag	:	Critical study for SIDS endpoint

29.05.2001 (6) (29)

5.1.4 ACUTE TOXICITY, OTHER ROUTES

5.2.1 SKIN IRRITATION

Species	:	rabbit
Concentration	:	other: undiluted
Exposure	:	
Exposure time	:	24 hour(s)
Number of animals	:	6
PDII	:	
Result	:	slightly irritating
EC classification	:	
Method	:	other: Not stated
Year	:	1974
GLP	:	no
Test substance	:	no data
Method	:	Limited experimental details are available for this study.

500 mg undiluted dipropylene glycol was applied to intact and abraded skin of rabbits and left occluded for 24 hours. Reactions were recorded at 24, 48, and 72 hr after application, using the scoring system of Draize et al (1944, J Pharmac. Exp Ther, 82, 377 - 390).

Remarks: Because this study was conducted before any standardized guidelines were established, the question of guideline methodology and GLP conduct is not applicable.

Remark : Original reference not available for review, so methods and results were described based on a reputable secondary source.
Result : Detailed results not available; listed as mildly irritating.
Source : Lyondell Chemical Co. Houston, Texas
Conclusion : The results from this study demonstrate that undiluted dipropylene glycol causes mild irritation of the rabbit skin. The response is insufficient to trigger classification of dipropylene glycol as an skin irritant. (Reviewer)
Reliability : (4) not assignable
PreGLP/Guidline study with brief description of methods and results; from secondary source.
Flag : Critical study for SIDS endpoint
29.05.2001 (6) (29)

Species : human
Concentration : 25 %
Exposure :
Exposure time : 24 hour(s)
Number of animals : 33
PDII :
Result :
EC classification :
Method :
Year : 1995
GLP : no data
Test substance : no data
Method : Limited experimental details are available for this study.
0.2 ml of a 25% solution of dipropylene glycol in distilled water for 24 hours via semi-occluded patches. Reactions were recorded at 4 and 24 hr after application.
Result : 2 subjects demonstrated no effects at 30 min. but mild erythema at 24 hrs. 2 subjects demonstrated mild to moderate erythema at 30 min. and mild erythema at 24 hrs. 7 subjects demonstrated mild to moderate erythema at 30 min. but no effects at 24 hrs.
22 subjects no reaction at 30 min or 24 hr.
Source : Lyondell Chemical Co. Houston, Texas
Conclusion : The results from this study demonstrated that 25% dipropylene glycol causes none to mild irritation of human skin.
Reliability : (2) valid with restrictions
Study details limited.
Flag : Critical study for SIDS endpoint
29.05.2001 (1)

5.2.2 EYE IRRITATION

Species : rabbit
Concentration : undiluted
Dose : .1 ml
Exposure Time : 4 hour(s)
Comment : other: Tested as 100% and formulation containing 7.2% dipropylene glycol

Number of animals	:	
Result	:	slightly irritating
EC classification	:	
Method	:	Draize Test
Year	:	1969
GLP	:	no
Test substance	:	no data
Method	:	Animals and treatments Limited experimental details are available for this study, which followed Draize method. 0.1 ml undiluted dipropylene glycol was applied to the lower conjunctival sac of rabbits. Reactions were recorded at 4, 24, 48, 72 and 96 hr post-instillation, using the scoring system of Draize et al (1944, J Pharmac. Exp Ther, 82, 377 - 390). Remarks: Because this study was conducted before any standardized guidelines were established, the question of guideline methodology and GLP conduct is not applicable.
Remark	:	Original reference not available for review, so methods and results were described based on a reputable secondary source.
Result	:	Detailed results were not presented. Neat mildly irritating; formulation transient irritation
Source	:	Lyondell Chemical Co. Houston, Texas
Conclusion	:	The results from this study demonstrate that undiluted dipropylene glycol causes mild, fully reversible irritation of the rabbit eye. The response is insufficient to trigger classification of dipropylene glycol as an eye irritant. (Reviewer)
Reliability	:	(4) not assignable PreGLP/Guidline study with brief description of methods and results.
Flag	:	Critical study for SIDS endpoint

29.05.2001 (6) (12) (15)

5.3 SENSITIZATION

Type	:	Patch-Test
Species	:	human
Number of animals	:	503
Vehicle	:	water
Result	:	
Classification	:	not sensitizing
Method	:	other: repeated insult patch test
Year	:	1995
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	Subjects 503 consecutive patients (212 men, 291 women) who entered the dermatology clinic with eczema were challenged with both cosmetic and synthesis grade dipropylene glycol. Challenge phase Patients received a challenge patch of 1, 2, 5, or 10% dipropylene glycol in water using a Finn chamber and Scanpor tape. The patch was left on the skin for 2 days. Reaction was graded after 2, 3, and 5-7 days. Scoring system A four point scale was used to record skin responses during induction and

challenge : -, TR, ?+, +
(Definition of -, TR, ?+, and + were not given in the report)

Statistics
No statistical methods were applied to the data.

Result : One patient was sensitized to dipropylene glycol

Score Number of responses
- cosmetic DPG = 488 patients; synthesis DPG = 480 patients
TR cosmetic DPG = 2 patients; synthesis DPG = 5 patients
?+ cosmetic DPG = 13 patients, synthesis DPG = 17 patients
+ cosmetic DPG = 0 patients; synthesis DPG = 1 patient

Source : Lyondell Chemical Co. Houston, Texas
Test substance : >97% pure from E.Merck (synthesis grade) and cosmetic grade (>96%)
Conclusion : The authors concluded that sensitization to dipropylene glycol was rare.
Reliability : (2) valid with restrictions
not standard guideline test
Flag : Critical study for SIDS endpoint
22.05.2001 (23)

5.4 REPEATED DOSE TOXICITY

Species : rat
Sex : no data
Strain : no data
Route of admin. : drinking water
Exposure period : 9 to 77 days
Frequency of treatment : continuous
Post obs. period : none
Doses : 1 to 10% dipropylene glycol in drinking water
Control group : no
NOAEL : = 5 %
LOAEL : = 10 %
Method :
Year : 1939
GLP : no
Test substance : no data
Method : Animals
32 rats; age, weight, sex and strain not specified.

Exposure
Dipropylene glycol was mixed in the drinking water of 7 rats at concentrations from 1 to 5% for 33 to 77 days. Dipropylene glycol was mixed in the drinking water of 25 rats at a concentration of 10% for 9 to 68 days. Further details of exact doses, number of animals at each dose level, or duration for individual animals not provided.

Terminal observations
Kidneys were examined microscopically for pathology. Report indicated that the liver and kidney were examined. No indication that other tissues were examined.

Statistical methods
None

Remarks: Because this study was conducted before any standardized guidelines were established, the question of guideline methodology and

GLP conduct is not applicable.

Result : Seven of 25 rats exposed to 10% dipropylene glycol in the drinking water died between days 10 and 30. Five had kidney lesions. Four of the 18 survivors had kidney lesions. The kidney lesions were described as hydropic degeneration of the tubular epithelium. No effects on mortality or the kidney and liver were seen in rats exposed to 5% dipropylene glycol in their drinking water.
Source : Lyondell Chemical Co. Houston, Texas
Reliability : (2) valid with restrictions
Not guideline, pre-GLP, methods and results only briefly described but generally acceptable.
Flag : Critical study for SIDS endpoint
29.05.2001 (24)

Species : dog
Sex : no data
Strain : no data
Route of admin. : gavage
Exposure period : not specified
Frequency of treatment : Not specified, the doses for another compound were administered 3 times daily.
Post obs. period : None
Doses : 9 cc/kg as 1.5 cc/kg administered for 6 doses, 12 cc/kg as 2.0 cc/kg administered for 6 doses, or 20 cc/kg as 5.0 cc/kg administered for 4 doses
Control group : no
NOAEL : = 20 ml/kg bw
Method :
Year : 1939
GLP : no
Test substance : no data
Method : Animals
4 dogs; age, weight, sex and strain not specified

General
Divided gavage doses given as follows: 9 cc/kg as 1.5 cc/kg administered for 6 doses, 12 cc/kg as 2.0 cc/kg administered for 6 doses, or 20 cc/kg as 5.0 cc/kg administered for 4 doses.

Details on evaluations conducted were not provided in the report.

Remarks: Because this study was conducted before any standardized guidelines were established, the question of guideline methodology and GLP conduct is not applicable.
Result : 1 dog dosed at 9 cc/kg - no evidence of toxicity
1 dog dosed at 12 cc/kg - no evidence of toxicity
1 dog dosed at 12 cc/kg - emesis; recovery
1 dog dosed at 20 cc/kg - no evidence of toxicity
Source : Lyondell Chemical Co. Houston, Texas
Conclusion : No evidence of systemic toxicity was detected under the conditions of this study.
Reliability : (2) valid with restrictions
Not guideline, pre-GLP, methods and results only briefly described but generally acceptable.
Flag : Critical study for SIDS endpoint
29.05.2001 (22)

Species : rat
Sex : no data
Strain : no data
Route of admin. : oral feed

Exposure period	:	15 weeks
Frequency of treatment	:	daily
Post obs. period	:	none
Doses	:	0, 12% of diet
Control group	:	yes, concurrent vehicle
NOAEL	:	= 12 %
Method	:	other: investigative study
Year	:	1940
GLP	:	no
Test substance	:	no data
Method	:	Limited study details ava ilable Dipropylene glycol mixed in diet at 12% and fed ad libitum. Observations The rats were observed for running activity after 15 weeks. Details on assessment of running activity not provided. Remarks: Because this study was conducted before any standardized guidelines were established, the question of guideline methodology and GLP conduct is not applicable.
Result	:	Running activity was decreased in rats fed 12% dipropylene glycol compared to control rats. The magnitude of the changes in running activity were not given in the report.
Source	:	Lyondell Chemical Co. Houston, Texas
Reliability	:	(2) valid with restrictions Not guideline, pre-GLP, methods and results only briefly described but generally acceptable.
Flag	:	Critical study for SIDS endpoint

29.05.2001 (10) (36)

5.5 GENETIC TOXICITY 'IN VITRO'

Type	:	Ames test
System of testing	:	Salmonella typhimurium TA98, TA100, TA1535, TA1537
Concentration	:	up to 10 mg/plate (lower concentrations not specified)
Cycotoxic conc.	:	>10 mg/plate
Metabolic activation	:	with and without
Result	:	negative
Method	:	other: Ame's standard plate assay
Year	:	1984
GLP	:	no data
Test substance	:	no data
Method	:	Study details not available.
Result	:	No increase in revertants was recorded for any of the strains exposed to dipropylene glycol with or without metabolic activation.
Source	:	Lyondell Chemical Co. Houston, Texas
Conclusion	:	Dipropylene glycol was not mutagenic in Salmonella typhimurium TA98, TA100, TA1535 and TA 1537, in the presence or absence of an S-9 fraction, under the conditions of this test.
Reliability	:	(2) valid with restrictions summary data only available from NCI program.
Flag	:	Critical study for SIDS endpoint

29.05.2001 (11)

Type	:	Mouse lymphoma assay
System of testing	:	L5178Y (TK+/TK-)

Concentration	:	29-60 ul/ml without activation; 30 - 50 ul/ ml with activation
Cycotoxic conc.	:	not reported
Metabolic activation	:	with and without
Result	:	negative
Method	:	other: Suspension/plate
Year	:	1987
GLP	:	no data
Test substance	:	no data
Method	:	Limited details reported.
Result	:	No increase in revertants was recorded for dipropylene glycol with or without activation.
Source	:	Lyondell Chemical Co. Houston, Texas
Reliability	:	(2) valid with restrictions summary data only available from NCI program.
Flag	:	Critical study for SIDS endpoint

29.05.2001 (11)

5.6 GENETIC TOXICITY 'IN VIVO'

Type	:	Micronucleus assay
Species	:	mouse
Sex	:	male
Strain	:	other: CD-1(ICR)BR
Route of admin.	:	gavage
Exposure period	:	2 days
Doses	:	500, 1000 and 2000 mg/kg
Result	:	negative
Method	:	other: US EPA OPPTS 870.5395 and OECD 474
Year	:	1999
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	Animals and treatments Eight week old male CD-1 mice from Charles River Labs were used in these investigations. Six mice were used per treatment group (control, positive control, 3 levels of dipropylene glycol). The dose levels were based on a preliminary study. Dipropylene glycol was administered for two consecutive days by gavage at 500, 1000 or 2000 mg/kg/day in water at a dose volume of 10 ml/kg. 120 mg/kg/day cyclophophamide was administered on two consecutive days by gavage at a dose volume of 10 ml/kg. Preparation and examination of bone marrow smears Mice were killed by carbon dioxide inhalation 24 hr after second gavage dose of dipropylene glycol. Femoral marrow cells were isolated, smeared onto clean glass slides, fixed with methanol and stained with Wright-Giemsa. The preparations were coded and analyzed without identification of animal number or treatment. Two thousand polychromatic erythrocytes (PCEs) per mouse were examined using light microscopy (x100), and the number of micronucleated polychromatic erythrocytes (MNPCEs) was recorded. The proportion of PCEs among the total erythrocytes was also evaluated by observation of 200 erythrocytes on the same slide. Positive control substance 120 mg/kg/day cyclophosphamide administered two consecutive days by gavage. Statistical analysis The frequency of MNPCEs in each treatment was analyzed by one-way

analysis of variance, A result was considered positive if the increase in MNPCEs differed from the spontaneous data at P<0.01. Any dose-response relationship was tested using the Cochran-Armitage trend test, with P<0.01 indicating a positive result.

Result : No mice died during the course of the study. There was no statistically significant increase or trend in MNPCE numbers following gavage administration of dipropylene glycol atdoses up to and including 2000 mg/kg. The percentage of PCEs in the dipropylene glycol-treated groups were not significantly different from controls. A significant, dose-related increase in MNPCEs was obtained with the positive control, cyclophosphamide, indicating that the test system was capable of detecting a positive response.

Dose	MN-PCE/2000 PCE	%PCE
0	2.8±2.5	60.7±4.7
500	2.8±1.9	57.6±8.7
1000	1.3±0.5	58.7±4.5
2000	1.5±1.4	52.0±8.2
cyclophosphamide	40.0±16.9	50.2±6.7

Source : Lyondell Chemical Co. Houston, Texas
Conclusion : Dipropylene glycol produced no detectable increase in micronucleated polychromatic erythrocytes when administered by gavage to mice at doses up to 2000 mg/kg.
Reliability : (1) valid without restriction
meets all criteria: follows guidelines, GLP.
Flag : Critical study for SIDS endpoint
22.05.2001 (17)

5.7 CARCINOGENITY

5.8 TOXICITY TO REPRODUCTION

5.9 DEVELOPMENTAL TOXICITY/TERATOGENICITY

Species : rat
Sex : female
Strain : other: Crl: CD BR VAF/Plus
Route of admin. : gavage
Exposure period : GD 6 - 15
Frequency of treatment : daily
Duration of test : 20 days
Doses : 800, 2000, and 5000 mg/kg / day in water at dose volume of 5 ml/kg
Control group : other: Yes; treated with water
NOAEL Maternalt. : = 800 mg/kg bw
NOAEL Teratogen : = 5000 mg/kg bw
Method : other: NTP
Year : 1992
GLP : yes
Test substance : as prescribed by 1.1 - 1.4
Method : Animals and treatment
Mated and presumed pregnant female rats were allocated to a sham control group (n = 27) or one of three treatment groups (800, 2000, and 5000 mg / kg /day, n = 27, 26, and 26 respectively) at the start of the study. Treatment commenced on GD6 and continued to GD15.

Maternal observations
All animals were observed daily for appearance and behavior. Body weights were recorded on GD0, 3, 6 - 15, 18 and 20. Food and water consumption data were collected during the periods of gestation days 0-3, 3-6, 6-9, 9-12, 12-15, 15-18, and 18-20.

Fetal examination
On GD20 all dams were subjected to Caesarian section under anesthesia, and the numbers of implantation sites, resorption sites and live and dead fetuses recorded. The body weights of the live pups were also recorded. All fetuses were examined for visceral (Staples technique) and skeletal abnormalities (Alcian Blue/Alizarin Red S stain).

Statistical analysis
Standard ANOVA for parametric data and Fisher's exact for nominal scale data.

Result : Maternal parameters
One of 25 pregnant dams treated at 2000 mg/kg and 2 of 24 at 5000 mg/kg died on GD14. All other dams survived. Signs of toxicity at 2000 and 5000 mg/kg/day included ataxia, unstable gait, and piloerection. Significantly reduced body weight gain, reduced food consumption and increased water consumption were seen at 5000 mg/kg/day.

At necropsy on GD 20, dams treated at 2000 and 5000 mg/kg/day had increased relative liver weights compared to controls.

Pregnancy parameters
Treatment with dipropylene glycol was without effect on the number of live litters, the total or average number of implant sites, total and partial resorptions, the total and average number of live fetuses and their sex ratio, the number of dead fetuses or fetal weight.

Fetal parameters
No increase in visceral or skeletal abnormalities or variations occurred with exposure to dipropylene glycol.

Source : Lyondell Chemical Co. Houston, Texas
Test substance : Identity and purity verified by chemical analysis: >96% pure
Conclusion : Under the conditions of the study, there was no adverse effect on pregnancy parameters or malformations at exposures of dipropylene glycol up to 5000 mg/kg/day. Dipropylene glycol induced maternal toxicity occurred at 2000 and 5000 mg/kg as evidenced by deaths, signs of CNS depression, reduced feed consumption and body weight gain, and increased relative liver weights.
Reliability : (1) valid without restriction
meets guideline and GLP.
Flag : Critical study for SIDS endpoint
22.05.2001 (4)

Species : rabbit
Sex : female
Strain : New Zealand white
Route of admin. : gavage
Exposure period : GD 6 - 19
Frequency of treatment : daily
Duration of test : 30 days
Doses : 200, 400, 800, 1200 mg / kg / day in water at dosing volume of 2 ml/kg.
Control group : other: Yes, treated with water
NOAEL Maternalt. : = 1200 mg/kg bw
NOAEL Teratogen : = 1200 mg/kg bw

Method : other: NTP
Year : 1992
GLP : yes
Test substance : as prescribed by 1.1 - 1.4
Method : Animals and treatment
Rabbits were artificially inseminated with sperm from proven male breeders. Inseminated female rabbits (n = 24/group) were allocated to a sham control group and four treatment groups (200, 400, 800 and 1200 mg / kg /day) at the start of the study. Treatment commenced on GD6 and continued to GD19.

Maternal observations
All animals were observed daily for appearance and behavior. Body weights were recorded on GD0, 6- 19, 25, and 30. Food weights were recorded on gestations days 0, 6, 9, 12, 15, 18, 19, 22, 25, 28, and 30. Maternal livers and kidneys were weighed at necropsy.

Fetal examination
On GD30 all dams were subjected to Caesarian section under anesthesia, and the numbers of implantation sites, resorption sites and live and dead fetuses recorded. The body weights of the live pups were also recorded. All fetuses were examined for external abnormalities. All fetuses were examined for visceral (Staples technique) and skeletal abnormalities (Alcian Blue/Alizarin Red S stain).

Statistical analysis
Standard ANOVA for parametric data and Fisher's exact for nominal scale data.
Result : Maternal parameters
There was no evidence of maternal toxicity in this study based on signs of toxicity, body weight, food consumption, organ weights or gross necropsy. The high dose (1200 mg/kg/day) was in the lethal range for dipropylene glycol in pregnant NZW rabbits; in a preliminary study 22 and 38% maternal mortality was found from gavage exposures GD6-19 at 800 and 1500 mg/kg/day, respectively.

Pregnancy parameters
Treatment with dipropylene glycol was without effect on the number of live litters, the total or average number of implant sites, total and partial resorptions, the total and average number of live fetuses and their sex ratio, the number of dead fetuses or fetal weight.

Fetal parameters
There was no increase in visceral or skeletal defects attributed to treatment with dipropylene glycol.
Source : Lyondell Chemical Co. Houston, Texas
Test substance : Analytical data verified identity: 97 to 99% pure.
Conclusion : Under the conditions of the study, there was no adverse effect on pregnancy parameters or maternal or fetal survival after exposure to up to 1200 mg/kg/day dipropylene glycol.
Reliability : (1) valid without restriction
meets guideline and GLP.
Flag : Critical study for SIDS endpoint
22.05.2001 (3)

5.10 OTHER RELEVANT INFORMATION

Type : Metabolism

Method : Species: rat
Sex: male
Strain: F344
Number of a nimals: 10
Route of admin.: gavage
Exposure period: one dose
Frequency of treatment: once
Duration of test: 24 hrs
Doses: 40 mg/kg/day TPG in water at dosing volume of 4 ml/kg.
Control group: No

Year: 1995
GLP: yes

Animals and treatment
Male F344 rats weighing between 187 and 197 g were obtained from Charles River and allowed 2 days for acclimation in metabolism cages before dosing. After dosing, the animals were held in the metabolism cages for 24 hours.

Sample collections
Air drawn through the metabolism chambers was passed through a trap for collection of radioactive CO2. All voided urine was collected and frozen for analysis. Feces were collected in dry-ice chilled containers for analysis. After 24 hours the animals were sacrificed for collection of blood, liver, kidney, fat, brain, muscle, and the remaining carcass.

Sample analysis
Radioactivity in all collected samples was determined using a liquid scintillation counter. Urine samples were analyzed by gas chromatography for tripropylene glycol, dipropylene glycol and propylene glycol following derivatization to pentafluorobenzoyl esters.

Source : Lyondell Chemical Co. Houston, Texas

Test substance : Analytical data verified identity: 99.8% tripropylene glycol., 0.08% dipropylene glycol pure. 14C-labelled test material TM = 14C-labelled TPG.

Conclusion : Result: 91.4±2.1% of the administered dose was recovered from CO2, urine, feces, tissues and carcass. 20.7±0.6% was recovered as CO2; 52.3±3.5% was recovered in urine. Approximately 10% of the administered radioactivity remained in the carcass after 24 hours.

Urine analysis
13% of the administered dose of tripropylene glycol was recovered in the urine as free or conjugated tripropylene glycol, 8.4% as free or conjugated dipropylene glycol, and 3.9% as free or conjugated propylene glycol. Administration of propylene glycol resulted in 12% recovered as propylene glycol in the urine.

Conclusion: Tripropylene glycol is rapidly and extensively metabolized to dipropylene glycol which is further metabolized to propylene glycol and subsequently to lactic or pyruvic acids followed by oxidation through the citric acid cycle (21% to CO2) or production of glycogen. Much of the radioactivity remaining in the carcass probably represented metabolically incorporated carbons atoms derived from propylene glycol. (author conclusion)

Reliability : (1) valid without restriction
meets guidelines and GLP.

Flag : Critical study for SIDS endpoint
29.05.2001 (18)

Type : other: Carcinogenicity
Method : Species: rat
Sex: male/female
Strain: Charles River, CD strain
Route of admin.: oral feed
Exposure period: 104 wk
Frequency of treatment: daily
Post. obs. period: none
Doses: 6250, 12500, 25000 or 50000 ppm
Result: negative
Control group: yes, concurrent vehicle
Year: 1972
GLP: No
Method: Animals
30 male (bw 120 - 150g) and 30 female (bw 120 - 140g) rats

General
Individual body weights were recorded at 2-wk intervals, with food intake measured over the preceding 24 hr.

Hematology
Blood was collected (tail vein) from 8 male and 8 female rats fed diets containing 0, 25000 or 50000 ppm propylene glycol at wk 13, 21, 52 and 80. Additional samples were collected from 6250 and 12500 ppm groups at wk 54. Samples were analysed for Hb content, PCV and counts of erythrocytes, and
total and differential leucocytes. Reticulocyte counts were determined at wk 52, 54 and 80. Terminal observations (wk 104) were limited to Hb concentration and microscopic examination of a stained smear.

Renal function
A urinary concentration test was conducted on 6 - 10 rats from the control, 25000 and 50000 ppm groups. Measurements included specific gravity, urine volume under different water loading conditions and a urinary cell count.

Terminal observations
Surviving animals were killed at wk 104 (exsanguination under barbiturate anesthesia) and subject to a full necropsy, including macroscopic observations and key organ weights. Samples of the following tissues were preserved for subsequent histopathological assessment : brain, heart, liver, spleen, kidneys, adrenals, gonads, stomach, small intestine, cecum, salivary gland, trachea, aorta, thymus, lymph nodes, pituitary, urinary bladder, colon, rectum, pancreas, uterus, muscle and any additional tissue that
appeared abnormal.

Statistical methods
Applied, but details not given.

Remarks: Because this study was conducted before any standardized guidelines were established, the question of guideline methodology and GLP conduct is not applicable.
Remark : Current guidelines indicate that the concentration of test substance should not exceed 5% of the diet to avoid any concerns about nutritional imbalances.
Source : Lyondell Chemical Co. Houston, Texas
Test substance : structurally related propylene glycol
Conclusion : Result: There was a high incidence of mammary fibroadenomas and pituitary adenomas, affecting mostly female rats, but this did not differ

statistically between the treated and control animals and no dose-response relationship was present. There was no evidence of any treatment-related increase in tumors.

Conclusion: No carcinogenic potential was detected under the conditions of this study following dietary administration up to 50000 ppm (approx 1700 - 2100 mg/kg bw/day).

Reliability : (1) valid without restriction
Flag : Critical study for SIDS endpoint
29.05.2001 (21)

Type : other: Continuous Breeding
Method : Species: mouse
Sex: male/female
Strain: CD-1
Route of admin.: drinking water
Exposure period: continuous (see methods)
Frequency of treatment: daily
Premating exposure period
Male: 7 days prior to first mating, then continuous exposure
Female: 7 days prior to first mating, then continuous exposure
Doses: 1%, 2.5%, 5% in drinking water
Control group: yes, concurrent vehicle
NOAEL Parental: = 5%
NOAEL F1 Offspr.: = 5%
NOAEL F2 Offspr.: = 5%
Method: NTP Reproductive Assessment by Continuous Breeding
Year: 1989
GLP: no data
Method: Animals
There were 40 controls per sex, along with 20 males and 20 females per treatment group in the F0 generation. The F1 mating groups comprised 20 animals per sex from the control and high dose groups only. Animals were housed in single sex groups during a one week pre-mating period, then in breeding pairs or individually. Deionised filtered water and ground rodent chow were available ad libitum.

Treatment
The mice were exposed during a 7-day premating period, after which they were randomly assigned to mating pairs and cohabited and treated continuously for 98 days. At the end of the cohabitation period, the pairs were separated but treatment continued. Any litters born during this time (F1) were delivered, and kept until weaning on PND21 : treatment of the mothers continued throughout this period. Treatment of high dose animals from the F1 generation continued until mating at around 74 days of age

Parental observations
Body weight and water consumption data were collected at unspecified times during the study.

Pup observations
Data (body weight, proportion of males, number of litters per pair, number of live and dead pups) were collected on all new born animals within 12 hr of birth. Litters were then discarded, with the exception of the final F1 generation which was used for breeding purposes. The F2 litters were examined for litter size, sex and pup weight.

Necropsy observations
No necropsy data were collected on the F0 generation, however the F1 adults were subjected to a detailed examination after delivery of the F2

pups.

Statistical analysis
Methods used included Cochran-Armitage test, Fisher's exact test, Kruskall-Wallis test, Wilcoxon-Mann-Whitney test and two-sided t-test

Remark : Remark: The treatment levels used in this study were extremely high : dams from the high dose group received the equivalent of 10000 mg/kg bw/day.

Source : Lyondell Chemical Co. Houston, Texas

Test substance : related substance

Conclusion : Result: Results are reported briefly, either as a text summary or in tabulated form in the reference, and no quantitative data were available for evaluation.

Based on data collected during a preliminary dose range finding study, treated animals received the equivalent of 1800, 4800 and 10100 mg/kg bw/day.

Water consumption was consistently higher (6 - 15%) for all groups in the F0 generation, but this was not statistically significant. Body weight in the F0 generation was unaffected by treatment.

There was no treatment-related effect on pup weight adjusted for litter size in either the F1 or F2 generations. The viability and growth of the F1 litter was unaffected by propylene glycol treatment. There were no treatment-related effects on mating, fertility or on the number, weight or viability of the F2 pups.

Necropsy of the F1 adults revealed no effect on body weight or organ weight in males and females, no change in sperm endpoints and no alteration in estrous cycle parameters.

Conclusion: Under the conditions of the study, propylene glycol had no effect on fertility or reproduction in F0 or F1 mice, up to a maximum dose of 10000 mg/kg bw/day. Based on metabolism of dipropylene glycol to propylene glycol, these data on propylene glycol are relevant to dipropylene glycol toxicity characterization. (Reviewer)

Reliability : (1) valid without restriction

Flag : Critical study for SIDS endpoint

29.05.2001 (26) (30)

Type : other: OECD 422 Combined repeat dose and reproductive/developmental toxicity screening test

Method : Species: rat
Sex: male/female
Strain: Crj: CD(SD)
Route of admin.: gavage
Exposure period: Premating through day 3 lactation: see methods
Frequency of treatment: daily
Premating exposure period
Male: 28 day
Female: 14 days
Duration of test: Through day 3 of lactation
Doses: 8, 40, 200, and 1000 mg/kg/day
Control group: yes, concurrent vehicle
Method: OECD 422 Combined repeat dose and reproductive/developmental toxicity screening test :
GLP: Yes
Method: Animals
There were 12 males and 12 females per treatment group.

Treatment
The rats were exposed during a 14-day premating period, after which they were randomly assigned to mati ng pairs and cohabited until evidence of mating.

Parental observations
Clinicial signs, body weight, food consumption, hematology, and clinical chemistry were assessed during the study. At termination, the rats were necropsied, organs were weighed and examined histopathologically.

Pup observations
Litter size, sex and viability on day 0 and 4 of lactation. Visual external examination on day 4.

Statistical analysis
not described

OECD Combined repeat dose and reproductive/developmental toxicity screening test

Source : Lyondell Chemical Co. Houston, Texas
Test substance : Tripropylene glycol CAS #24800-44-0
Conclusion : Result: The report is in Japanese; summary results and tables are available in English.

Parental animals
There was no effect on parental body weight, food consumption, hematology, clinical chemistry, necropsy or histopathology. Increased salivation was noted in males treated at 1000 mg/kg/day. Males and females at 1000 mg/kg/day had increasd liver weights and males also had increased kidney weights. There was no effect on estrus cycle, mating, pregnancy index, length of gestation, or gestation index.

Pups
There was no difference in mean litter size, mean live pups born/litter, survival to day 4, sex ratio, or frequency of external abnormalities.

NOAEL
Parental: 200 mg/kg/day
Reproductive: 1000 mg/kg/day
Developmental: 1000 mg/kg/day

Conclusion: Under the conditions of the study, tripropylene glycol had no effect on fertility or reproduction. Based on metabolism of tripropylene to dipropylene glycol to propylene glycol, these data on tripropylene glycol are relevant to dipropylene glycol toxicity characterization.

Reliability : (2) valid with restrictions
Not guideline, pre-GLP, methods and results only briefly described but generally acceptable.
Flag : Critical study for SIDS endpoint
29.05.2001 (35)

5.11 EXPERIENCE WITH HUMAN EXPOSURE

(1) Acklin, A., and Plaza, M.E. (1995). Evaluation of Primary Irritation Potential in Humans. Hill Top Research, Inc. 94-1373-70. Submitted to Dow Chemical Company.

(2) BASF (1989). Dipropylene Glycol. DIN-Sicherheitsdatenblatt vom Juli 1989, BASF Aktiengesellschaft, Ludwigshafen, 2 S.

(3) Bates, K.H. et al (1992). Final Report on the Developmental Toxicity of Dipropylene Glycol (CAS -No. 25265-71-8) in New Zealand White Rabbits. National Toxicology Program, National Institute of Environmental Health Sciences, PO Box 12233, Research Triangle Park, NC 27709; NTIS # PB92-238294.

(4) Bates, K.H. et al (1992). Final Report on the Developmental Toxicity of Dipropylene Glycol (CAS -No. 25265-71-8) in Sprague-Dawley (CD) Rats. National Toxicology Program, National Institute of Environmental Health Sciences, PO Box 12233, Research Triangle Park, NC 27709; NTIS # PB92-196179.

(5) Battersby, R.V. (1993c). Berechnung eines Verteilungs - koeffizienten fuer Dipropylenglykol. Schriftliche Mitteilung vom 18.10.1993, IBR Forschungs GmbH, Hannover, 9S.

(6) BIBRA Toxicology International (1991). Dipropylene glycol - Toxicity profile. BIBRA Toxicology International - British Industrial Biological Research Association, 1-4.

(7) Bridie, A.L.; Wolff, C.J.M.; Winter M. (1979). BOD and COD of some petrochemicals. Water Res. 13, 627-630.

(8) Bridie, A.L.; Wolff, C.J.M.; Winter, M. (1979a). The acute toxicity of some petrochemicals to goldfish. Water Res. 13, 623-626.

(9) Brown, E.S.; Hauser, C.F.; Ream, B.C.; Berthold, R.V. (1980). Glycols. Kirk-Othmer Encyclopedia of Chemical Technology, Band 11, 3. AFL., John Wiley & Sons, New York, ISBN 0-471-02063-8; 933-956.

(10) Browning, E. (1965). Dipropylene Glycol. Toxicity and Metabolism of Industrial Solvents, Elsevier Verlag, Amsterdam, 653-655.

(11) CCRIS (Chemical Carcinogenesis Research Information System from National Cancer Institute): Dipropylene glycol; available online through ToxNet (http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?CCRIS).

(12) CIR, Cosmetic Ingredient Review (1985). Final report on the safety assessment of butylene glycol, hexylene glycol, ethoxydiglycol and dipropylene glycol. J. Am. Coll. Toxicol. 4: 223-248.

(13) Claussen, T. (1993). Dipropylene Glycol: Determination of the Acute Toxicity to Pseudomonas putida. Research and Development Report, Health & Environmental Sciences, Dow Europe S.A.

(14) De Zwart, D.; Slooff, W. (1987). Toxicity of Mixtures of Heavy metals and Petrochemicals to Xenopus laevis. Bull. Environ. Contam. Toxicol. 38, 345-351.

(15) Deichmann, W.B.; Gerarde, H.W. (1969). Acute toxicity of glycols. Toxicology of Drugs and Chemicals, 4. AFL., Academic Press, New York, 731.

(16) DOW (1991). Dipropylene Glycol. DIN -Sicherheitsdatenblatt vom Juni 1991, DOW Deutschland Inc., Frankfurt, 5 S.

(17) Dow Chemical Company (1999). Evaluation of dipropylene glycol in the mouse bone marrow micronucleus test. Unpublished report from: Health and Environmental Research Laboratory, The Dow Chemcial Company,Midland MI, pp. 1-21.

(18) Dow Chemical Company. (1995). Metabolism of tripropylene glycol in rats. Unpublished Report from The Toxicology Research Laboratory, The Dow Chemical Company, Midland, Michigan, pp. 1-36.

(19) EPIWIN (Estimation Program Interface for Windows).

(20) Gallant, R.W. (1967): Physical properties of hydrocarbons XIV. Glycols and glycerin, Hyd. Proc. 46: 201.

(21) Gaunt, IF, Carpanini, FMB, Grasso, P and Lansdown, ABG (1972). Long-term toxicity of propylene glycol in rats. Fd Cosmet Toxicol, 10, 151 - 162.

(22) Hanzlik, P.J. Newman, H.W., Van Winkle, W., Jr., Lehman, A.J., and Kennedy, N.K.. (1939). Toxicity, fats and excretion of propylene glycol and other glycols. J. Pharmacol. Exp. Therap. 67: 101-113.

(23) Johansen, J.D., G.B.E. Jemec, and S.C. Rastogi. (1995). Contact sensitization to dipropylene glycol in an eczema population. Contact Dermatitis. 33:211-212.

(24) Kesten, H.D. (1939) et al. Pathologic effects of certain glycols and related compounds. Arch. Pathol. 27: 447-465.

(25) Kirk-Othmer Encyclopedia, 3rd edition, 1978.

(26) Lamb, JC, Gulati, DK, Barnes, LH and Welch, M (1997). Propylene glycol. Envir Hlth Perspect, 105 (suppl 1), 231 - 23.

(27) Material Safety Data Sheet, Arco Chemical Company, 1993.

(28) MITI (1992). Dipropylene glycol. Chemicals inspection & testing institute Japan: Data of existing chemicals based on the CSCL Japan. Japan Chemical Industry Ecology-Toxicology & Information Center, 2-56.

(29) Moreno, O (1974). Report to RIFM, dated 26 August 1974, as cited in BIBRA Toxicology International (1991). Dipropylene glycol - Toxicity profile. BIBRA Toxicology International - British Industrial Biological Research Association, 1-4.

(30) Morrissey, RE, Lamb, JC, Morris, RW, Chapin, RE, Gulati, DK and Heindel, JJ (1989). Results and evaluations of 48 continuous breeding reproduction studies conducted in mice. Fund Appl Toxicol, 13, 747 - 777.

(31) Oettel, H; Hofmann H T (1961). Report of Acute Inhalation of Dipropylene Glycol n Rats and Guinea Pigs. BASF internal report.

(32) Sexton, A.R.; Britton, E.C. (1953). Synthesis and identification of dipropylene glycol isomers. J. Am. Chem. Soc. 75: 4357-4358.

(33) Spanjers, MT; Til, HP. (1980). Determination of the acute oral toxicity of dipropylene glycol in rats. Report from CIVO -TNO to Dow Chemical Europe, Horgen, Switzerland.

(34) Stull, D.R., (1957): Ind. Eng. Chem. 39: 517.

(35) Tanaka, N; Yamakage, K.; Kusakabe, H., Hashimoto, K.; Shibuya, T.; Hara, T.; Kato, M.; Ishihara, N. (no date). Toxicity studies with tripropylene glycol. Research Report; Hatano Research institute, Food and Drug Safety Center, Hadano, Kanagawa, Japan, pp. 253-276.

(36) Van Winkle, W. Jr; Kennedy, N.K. (1940). Voluntary activity of rats fed propylene glycol and other glycols. J.Pharmac. exp. Ther. 69: 140.

7.1 END POINT SUMMARY

7.2.1 HAZARD SUMMARY

7.3 RISK ASSESSMENT