INFORMATION PROFILES ON POTENTIAL OCCUPATIONAL HAZARDS

VOLUME II. CHEMICAL CLASSES

Center for Chemical Hazard Assessment
Syracuse Research Corporation
Merrill Lane
Syracuse, New York 13210

Final Report
Contract No. 210-78-0019

December 1979

Prepared for:

National Institute for Occupational Safety and Health
5600 Fishers Lane
Rockville, Maryland 20857

PB81 148041

PAGE NA NA

4. Title and Subtitle
Potential Occupational Hazards, Volume II, Chemical Classes
Polypropylene Glycols

5. Report Date
December 1979

6. NA

7. Author(s)
Anonymous

8. Performing Organization Rept. No.
NA

9. Performing Organization Name and Address
Center for Chemical Hazard Assessment
- Syracuse Research Corporation
Syracuse, New York

10. Project/Task/Work Unit No.
NA

11. Contract(C) or Grant(G) No.
(C) 210-78-0019
(G)

12. Sponsoring Organization Name and Address
National Institute for Occupational Safety and Health
Rockville, Maryland

13. Type of Report & Period Covered
Contract Final Report

14. NA

15. Supplementary Notes
NA

16. Abstract (Limit: 200 words)

ABSTRACT: This information profile on polypropylene glycols is part of a group of 46 such profiles that provide information about chemicals or industrial processes considered to be potential occupational hazards. Each profile contains summary data on known and suspected health effects, the extent of worker exposure and the industrial importance of either a single chemical, class of chemicals, or a particular industrial process. The report was developed for use by occupational safety and health professionals in industry, and labor and other areas, to provide them with a synopsis of information on each subject and to identify potential hazards in their workplaces.

17. Document Analysis a. Descriptors

Toxicology
Physiological-efficts
Chemical-properties
Occupations
Industrial-processes
Work-environment
Safety-research

b. Identifiers/Open-Ended Terms

c. COSATI Field/Group

18. Availability Statement
Available to the public

19. Security Class (This Report) NA
20. Security Class (This Page)
21. No. of Pages 10
22. Price

Disclaimer

The contents of this report are reproduced as received from the contractor, and have not been edited nor evaluated by the National Institute for Occupational Safety and Health (NIOSH). The opinions, findings, and conclusions expressed are not necessarily those of NIOSH, nor does mention of company names or products constitute endorsement by NIOSH.

INTRODUCTION

An information profile is a working paper used by the National Institute for Occupational Safety and Health (NIOSH) to assist in establishing Institute priorities. It is an initial step in determining the need to develop comprehensive documents or to initiate research. Each profile summarizes data on known and suspected health effects, the extent of worker exposure, physical and chemical properties, and the industrial importance of individual chemicals and classes of chemicals. The profile may also be used by industry, labor, and the occupational health community as a synopsis of information on each subject and to identify possible health hazards associated with their workplaces.

Although detailed literature searches are conducted using computerized and manual searching techniques to identify pertinent and recent information, not all the literature obtained is incorporated in the report due to the summary nature of the profiles. Further, literature published after 1978 may not be included in these profiles because it was generally unavailable at the time the search was completed.

POLYPROPYLENE GLYCOLS

SUMMARY

The polypropylene glycols are a class of nonvolatile, highly water-soluble liquid organic polymers with molecular weights ranging from 200 to 2000. Annual commercial production of these compounds is probably about 359 million pounds, with a growth rate in excess of 10 percent per year. The polypropylene glycols find diverse applications in the production of urethan foams and elastomers, emulsifiers, alkyd resins, and lubricants.

In marked contrast to the structurally-related but relatively non-toxic polyethylene glycols, certain polypropylene glycols exhibit considerable pharmacologic activity following their acute administration to animals. Lethal doses can be as low as 15-20 mg/kg of body weight. Actions on the central nervous system (convulsions, tremors), histopathologic damage of various organs, and cardiovascular (pressor) effects have been noted following acute exposures.

Although the polypropylene glycols appear to be highly toxic, our state of knowledge concerning these compounds is derived from only a few experimental studies conducted nearly 30 years ago. Furthermore, virtually nothing is known regarding the potential effects of chronic exposure or the toxicity of these compounds to humans. There have been no standards developed for occupational exposure to polypropylene glycols. It is unlikely that sufficient data are presently available for health risk assessment. These compounds appear to be logical candidates for high priority toxicologic research in the future.

1. Synonyms

2. Chemical Abstracts Service (CAS) Number

3. Registry of Toxic Effects of Chemical Substances (RTECS) Number

4. Molecular Formula

5. Chemical Structure

6. Physical and Chemical Properties

The above information for the polypropylene glycols discussed in this profile is presented in Table 1.

Table 1. Polypropylene Glycols

	Polypropylene Glycols (PPG)	
Synonyms	Poly(propylene oxide) Polyglycol Poly[oxy(methyl-1,2-ethanediyl)], α-hydro-Ω-hydroxy-	
CAS Number	25322-69-4	
RTECS Number	PPG 150 - TR5300000 PPG 400 - TR5425000 PPG 425 - TR5600000 PPG 750 - TR5775000	PPG 1025 - TR5950000 PPG 1200 - TR6125000 PPG 2025 - TR6200000
Molecular Formula	$(C_3H_6O)_nH_2O$	
Chemical Structure	$HO(C_3H_6O)_nH$	
Physical and Chemical Properties		
Molecular Weight	(76.11 monomer)400-2025	
Physical State	Liquid	
Boiling Boint °C	189°C (monomer)	
Melting Point°C	Does not crystallize	
Vapor Pressure	Nonvolatile	
Evaporation Rate		
Solubility	Infinite in H_2O	
Specific Gravity	1.002 - 1.007	
Stability		

7. Producer and User Data

Production and Trends

Polypropylene glycols with varying molecular weight averages ranging from 200-2000 are commercially produced in a manner very similar to the polyethylene glycols discussed in a previous Information Profile.

The 1977 production of polypropylene glycol has been reported by the U.S. Tariff Commission as 30.4 million pounds (USITC, 1977); however, because of the nature of reporting procedures and the lack of total reporting, the Tariff Commission figure is considered to be much too low (Blackford, 1974). A more accurate annual production figure for polypropylene glycol is 359 million pounds (Dorigan et al., 1976). Based upon consumption patterns, growth for polypropylene glycol may be in excess of 10 percent per year.

Uses

The polypropylene glycols find extensive use in the field of urethan foams and elastomers. They are useful as intermediates in the preparation of emulsifiers, alkyd resins, and lubricants. The monoesters of polypropylene glycol are nonionic surface-active agents useful in a number of applications. The glycols themselves are used as lubricants, hydraulic fluids, and as components of automotive brake fluids. They are also used in certain cosmetic applications (Wagner, 1966).

Producers and Distributors

Polypropylene glycols are manufactured and distributed by the following companies (SRI, 1978):

BASF Wyandotte
Dow Chem.
Hodag Chem.
Pelron Corp.
Texaco (Jefferson Chem.)
Union Carbide
Witco Chem.

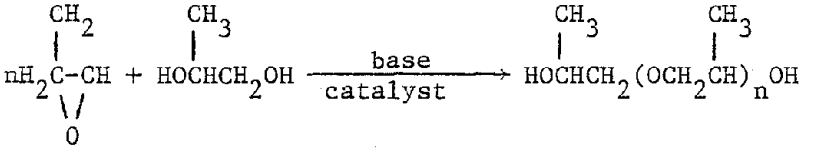
Additional distributors include (Chem. Week, 1978; OPD, 1978):

Ashland Chem.	Reichhold Chem.
FBC Chem. Corp.	Union Chem.
Helm Chem.	VanWaters & Roger
Mazar Chem.	A.I.D. Chem
McKesson Chem.	Coyne Chem.
Nippon Soda Ltd.	C.P. Hall Co.
Olin Corp.	Suburban Chem.

3

Manufacturing Process

Propylene glycols are manufactured by the addition of propylene oxide to water, propylene glycol, or dipropylene glycol, using a caustic catalyst, in much the same manner as in the production of polyethylene glycols (Wagner, 1966). The general reaction of propylene oxide with propylene glycol may be represented as follows (Blackford, 1974):



8. Biological Effects of Exposure

a) Acute Effects

The polypropylene glycols (PPG), unlike the polyethylene glycols, exhibit a marked degree of pharmacologic activity. Oral, intraperitoneal, or intravenous administration of these compounds stimulates the central nervous system, produces tremors, prostration, convulsions, increased cerebral cortical activity, and may result in death (Shaffer et al., 1951; Shideman and Procita, 1951). They do not, however, cause irritation of the eyes or skin of laboratory animals (Shaffer et al., 1951).

The acute toxicity data for PPG are summarized in Table 2. Sluggishness, prostration, tremors, convulsions, and rapid death were symptoms experienced by rats given large oral doses of PPG 425, 1025, and 2025 (Shaffer et al., 1951). Autopsies revealed pathological abnormalities including minor hemorrhage of the lungs, congestion of the liver and spleen, ischemia of the kidneys, and injection of the blood vessels of the kidney. Lethal intraperitoneal and intravenous doses caused tremors, prostration, frothing at the mouth, and audible rales.

The reaction of mice to intraperitoneal injections of polypropylene glycols begins within a few seconds to minutes (Shideman and Procita, 1951). Symptoms of central nervous system stimulation include increased activity and tonic spasm. If a lethal dose has not been administered, a severe depression will precede recovery. The number of seizures increased with increasing molecular weight of the PPG. Diphenylhydantoin sodium, when administered orally to mice, afforded protection against the convulsant and lethal action of PPG 750; when injected intraperitoneally, it afforded no protection.

PPG 1025 and 2025 probably do not readily penetrate the skin of rabbits, as demonstrated when all animals survived a 24-hour contact period with 20 ml/kg (Shaffer et al., 1951). Two of five rabbits, however, died when exposed to 20 ml/kg of PPG 425 and one of five died when exposed to 10 ml/kg. Repeated application of PPG to rabbit bellies produced no irritation. When instilled into the eyes of rabbits, only trace injuries were noted.

Table 2. Acute Toxicity for Polypropylene Glycols

Species	Route	Dose	Result	References
Polypropylene glycol				
rat	oral	419 mg/kg	LD_{50}	EPA, 1976
Polypropylene glycol 150				
rat	oral	15 mg/kg	LD_{50}	NIOSH, 1977
Polypropylene glycol 400				
mouse	ipr	700 mg/kg	LD_{50}	Shideman and Procita, 1951
Polypropylene glycol 425				
rat	oral	2910 mg/kg	LD_{50}	Shaffer et al., 1951
rat	ipr	460 mg/kg	LD_{50}	Shaffer et al., 1951
rat	ivn	200 mg/kg	LD_{50}	Shaffer et al., 1951
Polypropylene glycol 750				
mouse	ipr	195 mg/kg	LD_{50}	Shideman and Procita, 1951
dog	ivn	20 mg/kg	LD_{50}	Shideman and Procita, 1951
Polypropylene glycol 1025				
rat	oral	2150 mg/kg	LD_{50}	Shaffer et al., 1951
rat	ipr	230 mg/kg	LD_{50}	Shaffer et al., 1951
rat	ivn	120 mg/kg	LD_{50}	Shaffer et al., 1951
Polypropylene glycol 1200				
mouse	ipr	113 mg/kg	LD_{50}	Shideman and Procita, 1951
dog	ivn	20 mg/kg	LD_{50}	Shideman and Procita, 1951
Polypropylene glycol 2025				
rat	oral	9760 mg/kg	LD_{50}	Shaffer et al., 1951
rat	ipr	4470 mg/kg	LD_{50}	Shaffer et al., 1951
rat	ivn	710 mg/kg	LD_{50}	Shaffer et al., 1951

5

Inhalation of PPG 425 mist was lethal to all members of a group of six rats exposed for two hours, and to one of six rats exposed for one hour (Shaffer et al., 1951). PPG 1025 and 2025 caused the death of all of six rats in an eight hour exposure; no deaths occurred among six rabbits exposed for four hours.

The toxicity of the polypropylene glycols to intact dogs was greater than that observed in mice (Shideman and Procita, 1951). Table 3 summarizes the toxicity data for dogs. Intravenous administration of a convulsant dose causes an immediate stimulation of the central nervous system manifested as muscle tremors, and fasiculations appearing first in the facial muscles and spreading caudally. A tonic spasm followed by clonic convulsions developed, lasting one to thirty minutes depending on the molecular weight of the PPG. There was a latent period of ten minutes after oral or intramuscular administration before symptoms occurred. Cerebral cortical activity as measured by an electroencephalograph was increased in unanesthesized, curarized dogs following the intravenous administration of 20 mg/kg of PPG 400. PPG 750 and 1200 produced the same effect at half of the dosage. These heavier compounds produced a more rapid spread of the electric activity, which lasted for a longer period of time and caused additional spontaneous bouts of renewed activity.

Anesthesized, uncurarized dogs who received 5 mg/kg of PPG 400, PPG 750, or PPG 1200 experienced an increase in respiration rate and amplitude. Muscle tremors and movements, and enhanced stretch reflexes were all indicators of central nervous system stimulation. Experiments on decerebrated dogs indicated the site of action of the polypropylene glycols as the midbrain and possibly spinal cord level.

The cardiovascular effects of the polypropylene glycols differ with molecular weight (Shideman and Procita, 1951). PPG 400 and 750 produce both pressor and positive chronotropic responses, whereas PPG 1200 and 2000 do not. Administration of adrenergic blocking agents abolished the epinephrine-like pressor effects but not the chronotropic effect. Both responses were absent after adrenal ligation. To determine whether the release of epinephrine was the result of action on the higher nervous system or directly on the adrenal medulla, the ganglionic blocking agent tetraethylammonium chloride (TEA Cl) was used. The pressor response was found to continue even after the administration of TEA Cl.

The cardiopulmonary effects of the polypropylene glycols on anesthesized dogs are summarized in Table 4 (Shaffer et al., 1951).

Rat brain homogenate was used to determine the effects of the polypropylene glycols on certain enzymatic reactions (Shaffer et al., 1951). A concentration of 5×10^{-3}M of each compound was used. PPG 425 did not affect the rate of anaerobic glycolysis or cholinesterase activity nor the amount of urease. When the concentration of PPG 425 was elevated to 1.2×10^{-2}M, the effects were identical. PPG 1025 and 2025 caused an inhibition of the succinoxidase system, but PPG 425 did not. PPG 2025 was found to inhibit the activity

Table 3. Acute Toxicity of Polypropylene Glycols for the Dog

Compound	Route	Dose mg/kg	Effect
PPG 400	i.v.	10-20	Tremors and convulsions
PPG 750	i.v.	5-7	Tremors; no convulsions
	i.v.	8-15	Convulsions; survival
	i.v.	20	Convulsions; death
PPG 1200	i.v.	5-7	Tremors; no convlusions
	i.v.	15	Convulsions; survival
	i.v.	20	Convulsions; death
	i.m.	45	Subconvulsant
	i.m.	50-50	Mild convulsion
	p.o.	50	Subconvulsant
PPG 2000	i.v.	100	No visible effects

7

Table 4. Cardiopulmonary Effects of Polypropylene Glycols

	Route	Dose	Result
Polypropylene glycol 425	iv	10 mg/kg	Acceleration of cardiac and respiratory rates. EKG - barely perceptible changes and occasional ventricular extrasystoles.
	iv	50 mg/kg	Acceleration of cardiac and respiratory rates. Violent clonic convulsions, doubled heart rate and shallow spasmodic respiration were noted. EKG - multiple ventricular ectopic beats.
	oral	50 mg/kg	No Effects
	oral	0.1 gm/kg	Increase in heart rate. Slight changes in EKG within 3 minutes. After 10 minutes, premature ventricular beats were recorded.
	oral	0.5 gm/kg	Convulsions within 3 minutes of dosage. Heart rate almost doubled within 4 minutes. Frequent ventricular extrasystoles were recorded.
Polypropylene glycol 1025	oral	1-5 gm/kg	No effects.
Polypropylene glycol 2025	oral	1-5 gm/kg	No effects.

of the cytochrome oxidase system by 25 percent. Although the polypropylene glycols had no direct inhibitory effect on the anerobic phase of glycolysis, all three compounds exerted an inhibitory effect on the oxidative phase. A progressive increase with time of incubation in inhibition of aerobic glycolysis was caused by all compounds.

The absorption and excretion of the polypropylene glycols from the gastrointestinal tract were monitored by the collection of urine and feces after a single oral dose to rabbits (Shaffer et al., 1951). The results are summarized in Table 5. Although the experimental techniques were not highly accurate, they do indicate some biotransformation of the lower polymers.

Table 5. Urinary Excretion of Polypropylene Glycols Following a Single Oral Dose to Rabbits

	Dose	% Recovery in urine	% Recovery in feces
PPG 425	0.5 - 1.0 gm/kg	17-39	<10
PPG 1025	0.5 - 1.0 gm/kg	40	<10
PPG 2025	2 gm/k	∿0	40-70

b) Subchronic Effects

No data were encountered.

c) Chronic Effects

i. Carcinogenicity

No data were encountered.

ii. Mutagenicity

No data were encountered.

iii. Teratogenicity

No data were encountered.

iv. Other Effects

No data were encountered.

d. Human Effects

An isolated report has recently been published which may have relevance to the potential toxicity of polypropylene glycols. Stevens (1976) described the case of a 31-year old female worker who developed a severe asthmatic reaction upon inhalation of fumes from a soldering flux. The flux was composed of 95 percent of an alkyl aryl polyether alcohol and 5 percent polypropylene glycol. Subsequent inhalation challenge with fumes from the flux confirmed that it was responsible for the production of severe bronchospasms. Since the components of the flux were not tested individually, it is impossible to determine whether polyproplyene glycol was the etiologic agent.

9. Threshold Limit Values, OSHA Standards, NIOSH Recommended Standards

No tolerance levels have been established for the polypropylene glycols.

10. Other Standards

No other standards were encountered.

11. Occupational Exposures

No data were available.

REFERENCES

Blackford, J. (1974), Polyether Polyols, Chemical Economics Handbook, Stanford Research Institute, Menlo Park, Cal.

Chem. Week (1978), 1979 Buyers Guide Issue, Chemical Week, Part 2, Oct. 25, 1978.

Dorigan, J., Fuller, B., and Duffy, R. (1976), Preliminary Scoring of Selected Organic Air Pollutants Appendix IV - Chemistry, Production and Toxicity of Chemicals O Through Z, Environmental Protection Agency, NTIS #PB264 446.

EPA (1976), Preliminary Scoring of Selected Organic Air Pollutants, (Appendix I) Chemistry, Production, and Toxicity of Chemicals A-C. p. AI-6-7, U.S. EPA-405/3-77-008e, NTIS PB-264 446, Oct. 1976.

NIOSH (1977), Registry of Toxic Effects of Chemical Substances, National Institute for Occupational Safety and Health, Rockville, Maryland.

OPD (1978), 1978-79 OPD Chemical Buyers Directory, 66th annual edition, Schnell Publ. Co., New York.

Shaffer, C.B., Carpenter, C.P., Critchfield, F.H., Nair, J.H., and Franke, F.R. (1951), A Toxicology Study of Some Polypropylene (Polyoxypropylene) Glycols, Arch. Ind. Hyg. and Occup. Med., 3: 448.

Shideman, F.E. and Procita, L. (1951), Some Pharmacological Actions of Polypropylene Glycols of Average Molecular Weight 400, 750, 1200 and 2000, J. Pharmacol. and Expital. Therapeutics, 103: 293.

SRI (1978), Directory of Chemical Producers: United States, Stanford Research Institute, Menlo Park, Cal.

Stevens, J.J. (1976), Asthma Due to Soldering Flux: A Polyether Alcohol - Polypropylene Glycol Mixture, Annals of Allergy, 36: 419-422.

USITC (1977), Synthetic Organic Chemicals U.S. Production and Sales, U.S. International Trade Commission, Washington, D.C.

Wagner, F. (1966), Glycols, Kirk-Othmer Encycl. Chem. Tech., 2nd ed., 10: 654-659.