United States
Environmental Protection
Agency

FINAL DRAFT
ECAO-CIN-G026
November, 1987

Research and Development

HEALTH AND ENVIRONMENTAL EFFECTS DOCUMENT FOR PROPYLENE GLYCOL

Prepared for

OFFICE OF SOLID WASTE AND
EMERGENCY RESPONSE

Prepared by

Environmental Criteria and Assessment Office
Office of Health and Environmental Assessment
U.S. Environmental Protection Agency
Cincinnati, OH 45268

DRAFT: DO NOT CITE OR QUOTE

NOTICE

DISCLAIMER

This report is an external draft for review purposes only and does not constitute Agency policy. Mention of trade names or commercial products does not constitute endorsement or recommendation for use.

PREFACE

Health and Environmental Effects Documents (HEEDs) are prepared for the Office of Solid Waste and Emergency Response (OSWER). This document series is intended to support listings under the Resource Conservation and Recovery Act (RCRA) as well as to provide health-related limits and goals for emergency and remedial actions under the Comprehensive Environmental Response, Compensation and Liability Act (CERCLA). Both published literature and information obtained from Agency Program Office files are evaluated as they pertain to potential human health, aquatic life and environmental effects of hazardous waste constituents. The literature searched for in this document and the dates searched are included in "Appendix: Literature Searched." Literature search material is current up to 8 months previous to the final draft date listed on the front cover. Final draft document dates (front cover) reflect the date the document is sent to the Program Officer (OSWER).

Several quantitative estimates are presented provided sufficient data are available. For systemic toxicants, these include Reference doses (RfDs) for chronic and subchronic exposures for both the inhalation and oral exposures. The subchronic or partial lifetime RfD, is an estimate of an exposure level that would not be expected to cause adverse effects when exposure occurs during a limited time interval, for example, one that does not constitute a significant portion of the lifespan. This type of exposure estimate has not been extensively used, or rigorously defined as previous risk assessment efforts have focused primarily on lifetime exposure scenarios. Animal data used for subchronic estimates generally reflect exposure durations of 30-90 days. The general methodology for estimating subchronic RfDs is the same as traditionally employed for chronic estimates, except that subchronic data are utilized when available.

In the case of suspected carcinogens, RfDs are not estimated. A carcinogenic potency factor, or q_1^* (U.S. EPA, 1980), is provided instead. These potency estimates are derived for both oral and inhalation exposures where possible. In addition, unit risk estimates for air and drinking water are presented based on inhalation and oral data, respectively.

Reportable quantities (RQs) based on both chronic toxicity and carcinogenicity are derived. The RQ is used to determine the quantity of a hazardous substance for which notification is required in the event of a release as specified under the CERCLA. These two RQs (chronic toxicity and carcinogenicity) represent two of six scores developed (the remaining four reflect ignitability, reactivity, aquatic toxicity, and acute mammalian toxicity). Chemical-specific RQs reflect the lowest of these six primary criteria. The methodology for chronic toxicity and cancer-based RQs are defined in U.S. EPA, 1983 and 1986a, respectively.

EXECUTIVE SUMMARY

Propylene glycol (CAS Registry number 57-55-6) is a colorless, viscous, hygroscopic liquid at room temperature (Brown et al., 1980). It is miscible in many organic solvents and in water. The compound is expected to undergo reactions typical of monohydric alcohols forming esters, acetals, ethers and similar products (Brown et al., 1980). Propylene glycol is produced commercially by the hydrolysis of propylene oxide (Brown et al., 1980). Current domestic manufacturers are as follows (CMR, 1987): Arco in Bayport, TX, Dow Chemical in Freeport and Plaquemine, TX, Olin in Brandenburg, KY, and Union Carbide in South Charleston, WV. In addition, Texaco has a plant on stand-by in Port Neches, TX (CMR, 1987). During 1985, 499.529 million pounds of propylene glycol were produced in the United States (USITC, 1986). The use pattern for this compound is as follows (CMR, 1987): unsaturated polyester resins, 46%; exports, 18%; pharmaceuticals and food, 8%; semi-moist pet food, 7%; humectant for tobacco, 5%; polymeric plasticizer, 5%; paint and coatings, 4%; functional fluids, 3%; cellophane, 2%; miscellaneous, 2%.

If released to air, propylene glycol is expected to exist almost entirely in the vapor phase. Reaction with photochemically generated hydroxyl radicals in the atmosphere is expected to be an important fate process. The half-life for this reaction has been estimated to be 20 hours (see Section 2.1.1.). The complete water solubility of propylene glycol (Riddick et al., 1986) suggests that significant amounts of this compound may also be removed from the atmosphere by wet deposition. Propylene glycol is not susceptible to reaction with ozone (U.S. EPA, 1987). If released to water, propylene glycol is expected to biodegrade readily under both aerobic

and anaerobic conditions. Results of several biodegradation screening studies suggest that the biodegradation half-life under aerobic conditions typically ranges between 1 and 4 days, and the biodegradation half-life under anaerobic conditions typically ranges between 3 and 5 days. Lactaldehyde, pyruvate and acetol have been identified as intermediates in the metabolism of propylene glycol under aerobic conditions (Kersters and DeLey, 1963; Miller, 1979; Willetts, 1979). Chemical hydrolysis, oxidation by reaction with hydroxyl radicals, bioaccumulation in aquatic organisms, adsorption to suspended solids and sediments and volatilization are not expected to be important fate processes. If released to soil, propylene glycol is predicted to biodegrade readily under both aerobic and anaerobic conditions. The biodegradation half-life in soil is expected to be comparable with or slightly lower than that in water. Rapid biodegradation is expected to limit the extent of leaching through soil. The relatively high vapor pressure of propylene glycol suggests that volatilization from dry soil surfaces may occur. Volatilization from moist soil is predicted to be insignificant.

Propylene glycol could potentially be released to the environment in the effluent and, to a lesser extent, emissions from manufacturing and use facilities, and as a result of spillage or improper disposal of consumer and industrial products that contain this compound. Propylene glycol may also form in the environment as a metabolite of propylene glycol dinitrate, a military propellant that may be found in the wastewater streams from munitions plants and loading operations (Kaplan et al., 1982). Considering the extensive use of propylene glycol in a wide variety of consumer products such as food, pharmaceuticals, cosmetics and functional fluids, the most probable routes of human exposure are likely to be ingestion and dermal

contact. The National Occupational Hazard Survey estimates that >2.5 million people may be exposed to propylene glycol in occupational settings (NIOSH, 1984). During August 1974, propylene glycol was qualitatively identified in the effluent from a chemical manufacturing plant in Memphis, TN (Shackelford and Keith, 1976). Propylene glycol has been detected in emissions from an industrial source (Graedel, 1978).

The few available data indicate that propylene glycol is relatively nontoxic to aquatic biota. The lowest concentration reported to have an effect was 3850 mg/ℓ, which slightly increased the ventilation rate of adult rainbow trout, Salmo gairdneri (Majewski et al., 1978). Reported lethal concentrations were all in the g/ℓ range.

Data on mice (Salter et al., 1935) and dogs (Lehman and Newman, 1937) suggest that small oral doses of propylene glycol are absorbed rapidly and virtually completely. Rapid and extensive gastrointestinal absorption is also suggested for humans (Yu et al., 1985), but the rate of absorption in dogs and humans appears to become rate-saturated at higher doses (Hanzlik et al., 1939). In humans, estimated apparent volume of distribution studies suggest that propylene glycol distributes throughout the body water compartment.

Propylene glycol appears to undergo biotransformation primarily by oxidative pathways to lactic acid and pyruvic acid, which can enter the tricarboxylic acid cycle, contributing to the body's energy sources and eventually become degraded to 1- or 2-carbon units that may become assimilated into the endogenous carbon pool. Excretion of unchanged compound appears to be primarily through the urine (Hanzlik et al., 1939). Plasma elimination half-time in humans is ~3.8-4.1 hours, with total body clearance estimated at 0.08-0.1 ℓ/hour/kg when normalized for body weight (Yu et al., 1985).

Gaunt et al. (1972) evaluated the carcinogenicity of propylene glycol in male and female Charles River CD rats fed 0, 6250, 12,500, 25,000 or 50,000 ppm of the compound in the diet for 2 years. In both treated and control groups, there was a high but similar incidence of mammary fibroadenomas, pituitary adenomas and subcutaneous fibrosarcomas. Mammary fibroadenomas have been shown to occur spontaneously in a high proportion of 2-year-old rats of the Charles River CD strain. No carcinogenic effects could be attributed to propylene glycol when administered in the diet of rats at doses $\leq$50,000 ppm for 2 years.

Subchronic and chronic studies suggest that propylene glycol has a very low order of toxicity. Gaunt et al. (1972) evaluated several parameters of toxicity in rats fed diets containing $\leq$50,000 ppm for 2 years. There were no statistically significant differences between treated and control rats in cumulative death rate, body weight gain, food consumption, hematology, urinary cell excretion or renal clearance. A wide range of histological abnormalities was reported in the kidney, liver and lung, but the incidence was similar in both test and control groups. These changes were also consistent with those expected in aging rats.

Weil et al. (1971) reported no effects on the parameters of toxicity evaluated in male and female beagle dogs receiving 2 g/kg bw/day propylene glycol in the diet for 2 years. Dogs receiving 5 g/kg/day for 2 years had lower total erythrocyte counts, lower hemoglobin and hematocrit values, increased total bilirubin, and increases in anisocytosis, poikilocytes and reticulocytes. These changes were indicative of some erythrocyte destruction with replacement from the bone marrow. There was no evidence of damage to bone marrow or spleen, and no histopathological or biochemical evidence of hepatic damage was observed at any dose.

Morris et al. (1942) reported slight hepatic damage in albino rats fed 2.45 or 4.9% propylene glycol for 2 years. No other details were provided. Okumura et al. (1986) reported some differences in hematological and serum biochemical effects in F-344 rats fed 2.5 or 5% propylene glycol in the diet for 2 years; however, the effects may not have differed significantly from the normal state.

Subchronic administration of propylene glycol at 1-10% in drinking water caused no gross or microscopic lesions in rats (Kesten et al., 1939; Seidenfeld and Hanzlik, 1932; Weatherby and Haag, 1938). Administration to rats for 20 weeks at $\geq$40% of the diet resulted in deaths, at $\geq$30% resulted in growth depression, and at $\geq$10% resulted in kidney lesions. There were no effects at $\leq$6% (Guerrant et al., 1947).

Continuous inhalation exposure of rats to 170-350 mg/m^3 for 3-18 months had no effects on appearance, growth, reproduction or histopathological appearance of tissues in rats (Robertson et al., 1947).

Acute toxicity data indicate that propylene glycol has a low order of toxicity, with oral LD_{50} values ranging from 21.8-45.9 g/kg in rats and 22.8-31.87 in mice (Laug et al., 1939; Weatherby and Haag, 1938; Smyth et al., 1941; Bornmann, 1955).

Propylene glycol was found to be nonmutagenic when tested in Salmonella typhimurium TA1535, TA1537 and TA1538 and Saccharomyces cerevisiae D4, with or without metabolic activation (Litton Bionetics Inc., 1976). Results of cytogenetic testing in vivo in the bone marrow of rats and in vitro with human embryonic lung culture cells WI-38 were negative. Propylene glycol was also nonmutagenic in the dominant lethal assay in rats (Litton Bionetics Inc., 1974). In a host-mediated assay using ICR mice, negative results were obtained with Salmonella TA1530, and questionably positive results were

obtained at the high dose only in Salmonella strain G 46. The results with the Saccharomyces D3 tester strain appeared weakly mutagenic in the host-mediated assay, but were difficult to interpret because propylene glycol may have been selectively toxic for mutants of this organism (Litton Bionetics Inc., 1974).

Food and Drug Research Labs. (1973) evaluated propylene glycol for teratogenicity in mice, rats, hamsters and rabbits. No adverse maternal or fetal effects were attributed to propylene glycol administration in any species. Male and female white rats exposed continuously to a super-saturated atmosphere of propylene glycol $\leq$18 months bred as regularly and produced litters as large as did the control animals (Robertson et al., 1947). No differences in appearance or weight gain between the offspring of treated and control groups were reported. However, maternal toxicity was not achieved in any of these experiments and there is concern about adequacy of dose-response range at upper limits.

Propylene glycol is classified in EPA Group D, not classifiable as to carcinogenicity to humans. An RfD of 2 mg/kg/day or 116 mg/day for a human with an inhalation rate of 20 m^3/day for subchronic or chronic inhalation exposure to propylene glycol was based on no effects in an 18-month study in which rats were exposed continuously to 170-350 mg/m^3 (mean: 260 mg/m^3) (Robertson et al., 1947). An RfD of 0.03 g/kg/day or 2 g/day for a 70 kg human for subchronic oral exposure to propylene glycol is based on a NOEL of 6% of the diet (3 g/kg/day) in a 20-week dietary study using rats (Guerrant et al., 1947). Kidney lesions were observed at 10% of the diet, the next higher concentration. The chronic oral RfD, 0.02 g/kg/day or 1 g/day for a 70 kg human was derived from the NOEL of 2.1 g/kg/day in female rats fed a

diet containing 50,000 ppm for 2 years(Gaunt et al., 1972). An RQ of 1000 was based on the observation of kidney lesions in rats fed a diet containing 10% (5 g/kg/day) for 20 weeks (Guerrant et al., 1947).

TABLE OF CONTENTS

TABLE OF CONTENTS (cont.)

LIST OF TABLES

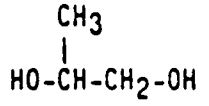
LIST OF ABBREVIATIONS

BCF	Bioconcentration factor
BODT	Biochemical oxygen demand, theoretical
bw	Body weight
CS	Composite score
DNA	Deoxyribonucleic acid
EC_{50}	Concentration effective to 50% of recipients (and all other subscripted concentration levels)
K_{oc}	Soil soprtion coefficient standardized with respect to soil organic water
K_{ow}	Octanol/water partition coefficient
LC_{50}	Concentration lethal to 50% of recipients (and all other subscripted dose levels)
LD_{50}	Dose lethal to 50% of recipients
MED	Minimum effective dose
NOEL	No-observed-effect level
ppm	Parts per million
RfD	Reference dose
RQ	Reportable quantity
RV_d	Dose-rating value
RV_e	Effect-rating value

1. INTRODUCTION

1.1. STRUCTURE AND CAS NUMBER

Propylene glycol is also known as 1,2-propanediol, 1,2-dihydroxypropane, methylethylene glycol and methyl glycol (SANSS, 1987). The structure, empirical formula, molecular weight and CAS Registry number are as follows:



Empirical formula: $C_3H_8O_2$

Molecular weight: 76.1

CAS Registry number: 57-55-6

1.2. PHYSICAL AND CHEMICAL PROPERTIES

Propylene glycol is a colorless, viscous, hygroscopic liquid at room temperature. It is practically odorless and has a slight characteristic taste (Brown et al., 1980). Propylene glycol is expected to undergo chemical reactions typical of monohydric alcohols forming esters, acetals, ethers and similar products (Brown et al., 1980). Glycol is miscible with alcohols, acetone, chloroform and many other organic solvents (Hawley, 1981; Windholz, 1983). Relevant physical properties are as follows:

Melting point, °C:	-60	Brown et al., 1980
Boiling point, °C:	187.3	Brown et al., 1980
Vapor pressure		
at 25°C:	0.22 mm Hg	Miller, 1979
at 20°C:	0.08 mm Hg	Weber et al., 1981
Water solubility:	complete	Riddick et al., 1986
Log K_{ow}:	-0.92	Hansch and Leo, 1985
Specific gravity:	1.038 (20/20°C)	Brown et al., 1980

Refractive index, n_D^{20}:	1.4326	Brown et al., 1980
Flashpoint: (Tag closed cup)	101°C	Brown et al., 1980
Conversion factors (25°C):	1 mg/m³ = 0.322 ppm 1 ppm = 3.11 mg/m³	Verschueren, 1983

1.3. PRODUCTION DATA

Propylene glycol is prepared by the hydrolysis of propylene oxide under pressure and at high temperature without a catalyst (Brown et al., 1980). The % yield of propylene glycol is controlled by the mol ratio of water to propylene oxide. Higher hydrolysis ratios increase the yield of propylene glycol but also result in increased purification costs (Brown et al. 1980). Current domestic manufacturers are listed in Table 1-1. Texaco has a 50 million pounds/year propylene glycol facility on stand-by in Porte Neches, TX. Also, Texaco markets material produced by Arco through a toll arrangement (CMR, 1987). During 1985, 499.5 million pounds of propylene glycol was produced in the United States (USITC, 1986).

1.4. USE DATA

The use pattern for propylene glycol is as follows (CMR, 1987): unsaturated polyester resins, 46%; exports, 18%; pharmaceuticals and food, 8%; semi-moist pet food, 7%; humectant for tobacco, 5%; polymeric plasticizer, 5%; paint and coatings, 4%; functional fluids, 3%; cellophane, 2%; miscellaneous, 2%. In the food industry propylene glycol is used as a solvent, humectant and preservative. It is also used in the manufacture of products that come into contact with food such as cork seals, bottle cap linings and plasticizers for food wraps, as a solvent for flavoring materials, extract preparations and food colors, and as a lubricant for food machinery (Brown et al., 1980; Miller, 1979). This compound is also used as a softening agent, spreader, emollient, intermediate, drug vehicle and preservative in

TABLE 1-1

Current Domestic Producers of Propylene Glycol[a]

Company	Location	Annual Capacity[b] (millions of pounds)
Arco Chemical	Bayport, TX	250
Dow Chemical	Freeport, TX	250
Dow Chemical	Plaquemine, LA	150
Olin Corp.	Brandenburg, KY	70
Union Carbide	South Charleston, WV	100

[a]Source: CMR, 1987

[b]Capacities at some locations can be supplemented by using hydration equipment normally used for ethylene glycol production (CMR, 1987; SRI, 1986).

the preparation of cosmetics and pharmaceuticals (Brown et al., 1980). As a functional fluid, it is used in brake and hydraulic fluids as a solvent, lubricant and coupling agent (Miller, 1979). Aqueous solutions of propylene glycol are used effectively as antifreeze mixtures and are preferred in refrigeration units found in breweries, dairies and packing houses (Brown et al., 1980).

1.5. SUMMARY

Propylene glycol (CAS Registry number 57-55-6) is a colorless, viscous, hygroscopic liquid at room temperature (Brown et al., 1980). It is miscible in many organic solvents and in water. The compound is expected to undergo reactions typical of monohydric alcohols forming esters, acetals, ethers and similar products (Brown et al., 1980). Propylene glycol is produced commercially by the hydrolysis of propylene oxide (Brown et al., 1980). Current domestic manufacturer are as follows (CMR, 1987): Arco in Bayport, TX, Dow Chemical in Freeport and Plaquemine, TX, Olin in Brandenburg, KY, and Union Carbide in South Charleston, WV. In addition, Texaco has a plant on stand-by in Port Neches, TX (CMR, 1987). During 1985, 499.529 million pounds of propylene glycol was produced in the United States (USITC, 1986). The use pattern for this compound is as follows (CMR, 1987): unsaturated polyester resins, 46%; exports, 18%; pharmaceuticals and food, 8%; semi-moist pet food, 7%; humectant for tobacco, 5%; polymeric plasticizer, 5%; paint and coatings, 4%; functional fluids, 3%; cellophane, 2%; miscellaneous, 2%.

2. ENVIRONMENTAL FATE AND TRANSPORT

2.1. AIR

Based on the vapor pressure of propylene glycol (see Section 1.2.), this compound is expected to exist almost entirely in the vapor phase in the atmosphere (Eisenreich et al., 1981).

2.1.1. Reaction with Hydroxyl Radicals. The rate constant for the reaction of propylene glycol with photochemically generated hydroxyl radicals in the atmosphere has been measured to be $(12\pm1)\times10^{-12}$ cm^3-molecule-sec at 22°C (Atkinson, 1985). Assuming a typical ambient hydroxyl radical concentration of 8.0×10^5 molecules/cm^3 (U.S. EPA, 1987), the hydroxyl reaction half-life has been estimated to be 20 hours. Thus, the reaction of propylene glycol with hydroxyl radicals in the atmosphere is expected to be an important fate process.

2.1.2. Reaction with Ozone. Propylene glycol is not susceptible to reaction with ozone in the atmosphere (U.S. EPA, 1987).

2.1.3. Photolysis. Because of the complete water solubility of propylene glycol (Riddick et al., 1986), significant amounts of this compound may be removed from the atmosphere by wet deposition.

2.2. WATER

2.2.1. Hydrolysis. Propylene glycol is expected to be resistant to chemical hydrolysis under environmental conditions (Lyman et al., 1982).

2.2.2. Oxidation. The half-life for propylene glycol reacting with photochemically generated hydroxyl has been determined to range from 1.3-2.3 years, based on measured reaction rate constants ranging between 0.94×10^9 and 1.68×10^9 ℓ/mol-sec (Anbar and Neta, 1967; Dorfman and Adams, 1973) and an ambient hydroxyl radical concentration of 10^{-17} mol/ℓ in natural waters (Mill et al., 1980). Pertinent data regarding the reaction of

propylene glycol with singlet oxygen or alkyl peroxy radicals could not be located in the available literature as cited in Appendix A.

2.2.3. Microbial Degradation. Propylene glycol was readily degradable in biodegradation screening studies using activated sludge, sewage seed and wastewater inoculum (Price et al., 1974; Bridie et al., 1979a; Kaplan et al., 1982; Lamb and Jenkins, 1952; Takemoto et al., 1981; Grunwald et al., 1984). According to Price et al. (1974), the typical biodegradation half-life for 3-10 mg/ℓ propylene glycol in unacclimated freshwater samples seeded with settled domestic wastewater is ~4 days. When incubated in mineralized dilution water seeded with settled domestic sewage, 2.5 ppm propylene glycol contained oxygen equivalent to 2.2, 56.7, 77.8 and 80% of BODT after 5, 10, 20 and 50 days, respectively (Lamb and Jenkins, 1952). When incubated in a nutrient broth seeded with activated sludge, 100 ppm propylene glycol underwent 50% loss in ~1 day (Kaplan et al., 1982). In synthetic seawater samples inoculated with settled domestic wastewater, propylene glycol consumed oxygen equivalent to 55, 72, 73 and 83% BODT after 5, 10, 15 and 20 days of incubation, respectively (Price et al., 1974). Under strongly aerobic conditions, metabolism of propylene glycol by a Flavobacterium sp. proceeded by catabolism to lactaldehyde followed by metabolizing to pyruvate and then oxidation to CO_2 (Willetts, 1979). Resting cells of both Gluconobacter oxydans (suboxydans) and the yeast, asenula miso IFO 0146, oxidized propylene glycol to acetol (hydroxy-2-propanone) (Kersters and DeLey, 1963; Miller, 1979). Propylene glycol is also amenable to biodegradation under anaerobic conditions (Speece, 1983; Chou et al., 1979). The half-life for 100 ppm propylene glycol incubated under anaerobic conditions in a nutrient broth containing digester sludge and a basal salt medium was ~3-5 days (Kaplan et al., 1982).

2.2.4. Bioaccumulation. Experimental data regarding bioaccumulation of propylene glycol in aquatic organisms could not be located in the available literature as cited in Appendix A.

A BCF of <1 was estimated for propylene glycol using a measured log K_{ow} of -0.92 (Hansch and Leo, 1985) and the following linear regression equation: log BCF = 0.76 log K_{ow} - 0.23 (Lyman et al., 1982). This BCF value and the complete water solubility of propylene glycol indicate that bioaccumulation in aquatic organisms should not be significant.

2.2.5. Adsorption. Experimental data regarding adsorption of propylene glycol to suspended solids and sediments in water could not be located in the available literature as cited in Appendix A. Considering the complete water solubility of this compound and its estimated K_{oc} value of 8 (Section 2.3.3.), physical adsorption to suspended solids and sediments is not expected to be significant.

2.2.6. Volatilization. Pertinent data regarding the volatilization of propylene glycol from water could not be located in the available literature as cited in Appendix A. Henry's Law constant for ethylene glycol has been measured to be 5.9×10^{-8} atm-m³/mol at 25°C (Hine and Mookerjee, 1975). Considering the structural similarity of ethylene and propylene glycol, Henry's Law constant for propylene glycol is expected to be on the same order of magnitude or slightly higher (Brown et al., 1980). Volatilization can be considered unimportant as an intermedia transfer mechanism for organic compounds with a Henry's Law constant $<3 \times 10^{-7}$ atm-m³/mol (Lyman et al., 1982). Therefore, volatilization of propylene glycol from water surfaces is not expected to be significant.

2.3. SOIL

2.3.1. Hydrolysis. Propylene glycol is not expected to undergo hydrolysis in the environment because it contains no hydrolyzable functional groups (Lyman et al., 1982).

2.3.2. Microbial Degradation. Limited data regarding the biodegradation of propylene glycol in soils were located in the available literature as cited in Appendix A. A variety of microorganisms capable of degrading propylene glycol under aerobic conditions has been isolated from soil, including Alcaligenes strains MC11 and TE8, Corynebacterium OEH8 and a bacterium strain, SA-1 (Harada and Nagashima, 1975; Tanaka et al., 1975; Fincher and Payne, 1962). Acetol, lactaldehyde, lactic acid and pyruvic acid have been produced as metabolites of propylene glycol by the bacterium strain, SA-1 (Tanaka et al., 1975). Based on results from biodegradation studies in aqueous media (see Section 2.2.3.), biodegradation of propylene glycol in soil under aerobic and anaerobic conditions is an important removal mechanism. The biodegradation half-life in soil is expected to be comparable with or slightly lower than that in water.

2.3.3. Adsorption. The complete water solubility and the relatively low log K_{ow} of propylene glycol suggest that it would leach readily through soil. The soil adsorption coefficient for this compound has been estimated using the following linear regression equation (Lyman et al., 1982): log $K_{oc} = 0.544 \log K_{ow} + 1.377$, where the log K_{ow} value is -0.92 (Hansch and Leo, 1985). A K_{oc} value of 8 also suggests that this compound would to be very highly mobile in soil (Swann et al., 1983); however, biodegradation should limit the extent of leaching into groundwater.

2.3.4. Volatilization. Pertinent data regarding volatilization of propylene glycol from soil could not be located in the available literature as cited in Appendix A. The vapor pressure of propylene glycol [0.22 mm Hg at 25°C (Miller, 1979)] suggests that volatilization from dry soil surfaces may occur. Evaporation from moist soil surfaces is expected to be insignificant because this compound should biodegrade fairly rapidly, may have a tendency to leach through soil and does not appear to evaporate significantly from water.

2.4. SUMMARY

If released to air, propylene glycol is expected to exist almost entirely in the vapor phase. Reaction with photochemically generated hydroxyl radicals in the atmosphere is expected to be an important fate process. The half-life for this reaction has been estimated to be 20 hours (see Section 2.1.1.). The complete water solubility of propylene glycol (Riddick et al., 1986) suggests that significant amounts of this compound may also be removed from the atmosphere by wet deposition. Propylene glycol is not susceptible to reaction with ozone (U.S. EPA, 1987). If released to water, propylene glycol is expected to biodegrade readily under both aerobic and anaerobic conditions. Results of several biodegradation screening studies suggest that the biodegradation half-life under aerobic conditions typically ranges between 1 and 4 days, and the biodegradation half-life under anaerobic conditions typically ranges between 3 and 5 days. Lactaldehyde, pyruvate and acetol have been identified as intermediates in the metabolism of propylene glycol under aerobic conditions (Kersters and DeLey, 1963; Miller, 1979; Willetts, 1979). Chemical hydrolysis, oxidation by reaction with hydroxyl radicals, bioaccumulation in aquatic organisms, adsorption to suspended solids and sediments and volatilization are not

expected to be important fate processes. If released to soil, propylene glycol is predicted to biodegrade readily under both aerobic and anaerobic conditions. The biodegradation half-life in soil is expected to be comparable with or slightly lower than that in water. Rapid biodegradation is expected to limit the extent of leaching through soil. The relatively high vapor pressure of propylene glycol suggests that volatilization from dry soil surfaces may occur. Volatilization from moist soil is predicted to be insignificant.

3. EXPOSURE

Propylene glycol could potentially be released to the environment in the effluent and, to a lesser extent, emissions from manufacturing and use facilities, and as a result of spillage or improper disposal of consumer and industrial products that contain this compound. Propylene glycol may also form in the environment as a metabolite of propylene glycol dinitrate, a military propellant that may be found in the wastewater streams from munitions plants and loading operations (Kaplan et al., 1982). Considering the extensive use of propylene glycol in a wide variety of consumer products such as food, pharmaceuticals, cosmetics and functional fluids, the most probable routes of human exposure are likely to be ingestion and dermal contact. The National Occupational Hazard Survey estimates that >2.5 million people may be exposed to propylene glycol in occupational settings (NIOSH, 1984). During August 1974, propylene glycol was qualitatively identified in the effluent from a chemical manufacturing plant in Memphis, TN (Shackelford and Keith, 1976). Propylene glycol has been detected in emissions from an industrial source (Graedel, 1978).

4. AQUATIC TOXICITY

4.1. ACUTE TOXICITY

The available information regarding the toxicity of propylene glycol to aquatic organisms is presented in Table 4-1. The few available data indicate that propylene glycol is relatively nontoxic to aquatic biota. The lowest concentration reported to have an effect was 3850 mg/ℓ, which slightly increased the ventilation rate of adult rainbow trout, Salmo gairdneri (Majewski et al., 1978). Reported lethal concentrations for propylene glycol were all in the g/ℓ range (see Table 4-1).

Majewski et al. (1978) compared propylene glycol with ethanol and acetone in terms of their toxicity and effect on cardiovascular/respiratory parameters. They concluded that propylene glycol was the least toxic of the three and recommended that it be used as a solvent for other compounds in aquatic toxicity studies.

4.2. CHRONIC EFFECTS

Pertinent data regarding the chronic toxicity of propylene glycol to aquatic organisms could not be located in the available literature as cited in Appendix A.

4.3. PLANT EFFECTS

Pertinent data regarding effects of propylene glycol on aquatic plants could not be located in the available literature as cited in Appendix A. Tarkpea et al. (1986) reported a 30-minute EC_{50} of 26,800 mg/ℓ for inhibition of luminescence in the Microtox assay with the bacteria, Photobacterium phosphoreum.

TABLE 4-1

Acute Toxicity of Propylene Glycol to Aquatic Organisms

Species	Concentration (mg/ℓ)	Exposure Conditions	Effect	Reference
FISH				
Rainbow trout *Salmo gairdneri*	50,000 3,850	static, aerated flowthrough, aerated	no mortality, fingerlings, 24 hours; slight (18%) increase in ventilation rate, adults, 9-24 hours	Majewski et al., 1978
	42,476	static	96-hour LC_{50}	Mayer and Ellersieck, 1986
Goldfish *Carassius auratus*	>5,000	static, aerated	24-hour LC_{50}	Bridie et al., 1979b
INVERTEBRATES				
Copepod *Nitocra spinipes*	>10,000	static, not aerated salinity = 0.7%	96-hour LC_{50}	Tarkpea et al., 1986

4.4. SUMMARY

The few available data indicate that propylene glycol is relatively nontoxic to aquatic biota. The lowest concentration reported to have an effect was 3850 mg/ℓ, which slightly increased the ventilation rate of adult rainbow trout, Salmo gairdneri (Majewski et al., 1978). Reported lethal concentrations were all in the g/ℓ range.

5. PHARMACOKINETICS

5.1. ABSORPTION

Absorption of propylene glycol from the gastrointestinal tract appears to be rapid and virtually complete. Salter et al. (1935) reported that intestinal absorption in mice was 77.8% complete in 30 minutes and 93.7% complete in 5 hours. Small dosages administered to dogs are rapidly and nearly completely absorbed. Lehman and Newman (1937) administered propylene glycol at 2 mℓ/kg bw by stomach tube or intravenously by injection and compared the concentration of propylene glycol in the blood at several time points from 0.5-9 or 10 hours after treatment. The concentration-time curves obtained from the two routes of administration were nearly identical; peak levels of propylene glycol in the blood were measured at 0.5 hours. Oral administration of larger doses (8-12 cc/kg bw) resulted in higher and later peaks in blood concentrations, which suggested that gastrointestinal absorption is a saturable process. Low blood levels were obtained after administration into the isolated stomach of the dog, which suggested that absorption from this organ is slight.

Hanzlik et al. (1939) administered propylene glycol at 1 mℓ/kg bw to humans and measured the concentration in blood at 0.5-10 hours after treatment. Blood concentrations of propylene glycol reached a maximum in 0.5 hour and remained at that level for ~4 hours before decreasing, which suggested that gastrointestinal absorption was delayed but able to keep pace with elimination. Within 10 hours of ingestion, 20-25% of the dose was excreted unchanged in the urine.

In two separate studies, Yu et al. (1985) examined the pharmacokinetics of propylene glycol in humans during multiple oral dosing regimens. In study I, 16 patients received 20 mℓ (20.7 g) propylene glycol every 8

hours as a solvent in a sodium phenytoin oral solution. In study II, six additional patients received 40 mℓ (41.4 g) of propylene glycol every 12 hours in the same oral formulation. Subjects were maintained on the formulation for a minimum of 3 days to allow establishment of steady-state, after which serial blood sampling was performed at 0, 1, 2, 3, 4, 6 and 8 hours postdosing in study I and II; an additional sample was drawn at 12 hours in study II. In both studies, propylene glycol was found to be absorbed rapidly, with plasma concentrations peaking within 1 hour after administration of the dose. Data to analyze the absorption rate of propylene glycol were insufficient, and the authors suggested that although it is likely that propylene glycol is absorbed completely into the systemic circulation, no direct evidence of this was available.

5.2. DISTRIBUTION

Yu et al. (1985) estimated apparent volumes of distribution from the pharmacokinetic study with humans discussed in Section 5.1. The average apparent volumes of distribution were 0.58 and 0.52 ℓ/kg in study I and II, respectively, and were not statistically different from one another. The value of 0.5 ℓ/kg approximates total body water and may indicate that propylene glycol distributes uniformly into total body water without preferential distribution to specific tissues. Considerable individual variation was noted, however, in the plasma concentrations of subjects in both studies. The investigators suggested that these differences resulted from individual differences in clearance rate and can result in an increased accumulation of propylene glycol in individuals with unusually low clearance rates.

5.3. METABOLISM

Ruddick (1972) reviewed the biochemistry of propylene glycol and its metabolism in the body. The metabolic pathways are depicted in Figure 5-1. Propylene glycol is oxidized to lactic acid or pyruvic acid by one of two pathways, depending on whether the substrate is the free glycol or phosphorylated glycol. Free propylene glycol is metabolized through lactaldehyde, methylglyoxal and lactic acid. The phosphorylated glycol is metabolized through acetol phosphate, lactaldehyde phosphate, lactyl phosphate and lactic acid. Once pyruvate or lactate is formed, energy can be provided by further oxidation through the tricarboxylic acid cycle or through the glycolytic pathway, the latter contributing to glycogen formation. Other information presented in the review by Ruddick (1972) suggests that the oxidation of propylene glycol is not just restricted to the formation of lactate or pyruvate, but the corresponding deoxyaldehyde, as well as propionaldehyde, lactaldehyde and 1- and 2-carbon units that may enter the endogenous carbon pool. In ruminants, the primary metabolite is propionate, which is formed in the rumen by the microbial population. In the chick, propylene glycol is metabolized by the bacteria in the cecum to propionaldehyde.

5.4. EXCRETION

Hanzlik et al. (1939) reported that 20-25% of an oral dose to humans of 1 mℓ/kg propylene glycol was excreted unchanged in the urine within 10 hours of ingestion. Browning (1965) stated that approximately one-third of a dose of propylene glycol is excreted through the kidneys as a conjugate with glucuronic acid, and the rest is metabolized or excreted unchanged in the urine.

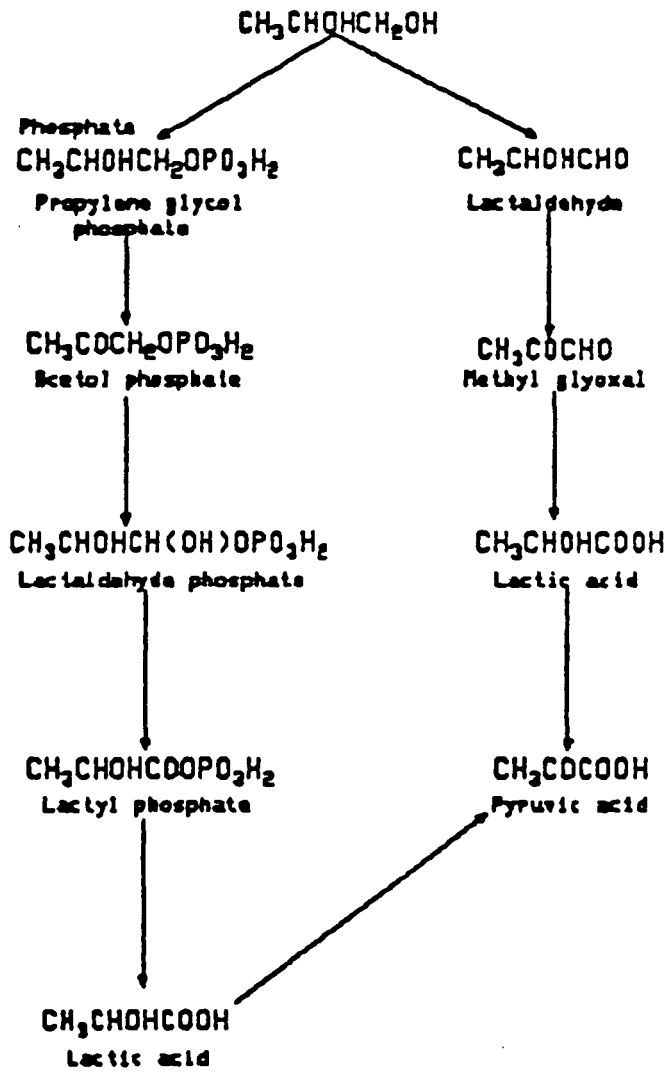


FIGURE 5-1

Metabolic Pathways of Propylene Glycol

Source: Rowe and Wolf, 1982

Yu et al. (1985) studied the elimination of propylene glycol in the plasma of humans given oral doses of 20 mℓ (20.7 g) every 8 hours (study I) or 40 mℓ (41.4 g) every 12 hours (study II) in a steady-state situation. Plasma concentrations peaked within 1 hour and declined in a monoexponential manner. Elimination half-times were ~3.8 hours for study I and 4.1 hours for study II. Total body clearance of propylene glycol varied considerably between individuals. When normalized for body weight, mean total body clearance rates of 0.106 and 0.109 ℓ/hour/kg bw were estimated for subjects in study I using steady-state assumptions and nonsteady-state assumptions, respectively. At the higher doses of study II, mean total body clearances, normalized for body weight, were ~0.079 and 0.086 ℓ/hour/kg using steady-state and non steady-state assumptions, respectively.

5.5. SUMMARY

Data on mice (Salter et al., 1935) and dogs (Lehman and Newman, 1937) suggest that small oral doses of propylene glycol are absorbed rapidly and virtually completely. Rapid and extensive gastrointestinal absorption is also suggested for humans (Yu et al., 1985), but the rate of absorption in dogs and humans appears to become rate-saturated at higher doses (Hanzlik et al., 1939). In humans, estimated apparent volume of distribution studies suggest that propylene glycol distributes throughout the body water compartment.

Propylene glycol appears to undergo biotransformation primarily by oxidative pathways to lactic acid and pyruvic acid, which can enter the tricarboxylic acid cycle, contributing to the body's energy sources and eventually become degraded to 1- or 2-carbon units that may become assimilated into the endogenous carbon pool. Excretion of unchanged compound appears to

be primarily through the urine (Hanzlik et al., 1939). Plasma elimination half-time in humans is ~3.8-4.1 hours, with total body clearance estimated at 0.08-0.1 ℓ/hour/kg when normalized for body weight (Yu et al., 1985).

6. EFFECTS

6.1. SYSTEMIC TOXICITY

6.1.1. Inhalation Exposures.

6.1.1.1. SUBCHRONIC -- Pertinent data regarding the systemic toxicity of propylene glycol as a result of subchronic inhalation exposures could not be located in the available literature as cited in Appendix A.

6.1.1.2. CHRONIC -- A group of twenty, 7-week-old male and female white rats were exposed continuously to a supersaturated atmosphere calculated to contain 170-350 mg/m³ propylene glycol vapor for 3-18 months (Robertson et al., 1947). A control group of 10 rats was maintained. Weight gain was substantially higher in the treated males than in the controls. Female weight data were not plotted; they varied because of the birth of young. No difference was noted in the general condition between the treated or control rats, and the treated rats bred as regularly and produced litters as large as did the controls. No differences were noted in general appearance and weight gain between pups of treated and control groups. Sacrifices were scheduled at intervals from 3-18 months, and urinalysis and gross and histo- logical examinations of the kidneys, liver, spleen and lung were conducted. Pathological effects related to exposure were not observed in any of the tissues examined. Some changes occurred in the cells of the lungs, commonly a perivascular and peribronchial accumulation of round cells. This change began to appear at the end of 5 months of exposure in the treated groups, but occurred with equal frequency in both control and test animals.

Robertson et al. (1947) also exposed 29 rhesus monkeys continuously to propylene glycol for ≤13 months. One exposure chamber held 15 monkeys and the other, 14. Concentrations of propylene glycol were ~100-220 mg/m³ in one chamber and 230-350 mg/m³ in the other. A control group of 16

unexposed monkeys was maintained. The results in exposed monkeys were reported without specifying to which concentration they had been exposed. Mortality and moribund sacrificed claimed 13 exposed and 10 control monkeys, primarily associated with parasitism or infection. Weight gains in control and treated monkeys appeared to be normal except in treated monkeys on months 5-8 when insufficient food was given. Comparisons between treated and control monkeys were not possible beyond 5 months because of the small number of surviving controls. Urine concentrating ability, a measure of kidney function, microscopic appearance of the urine, blood cell counts and hemoglobin determinations were similar in treated and control animals. Discoloration of the facial skin was observed in treated monkeys, which was attributed to the drying effect of the glycol and disappeared upon removal from the vapor chambers. Gross appearance on necropsy and histopathologic appearance of lung, liver, kidney, spleen, mesenteric lymph glands, adrenals and sometimes stomach, intestines and testes were not different between exposed and control monkeys. The investigators concluded that there were no adverse effects from exposure to propylene glycol.

6.1.2. Oral Exposures.

6.1.2.1. SUBCHRONIC -- Gaunt et al. (1972) conducted a short-term study, concurrent with a long-term study, on groups of 15 male and 15 female Charles River CD rats. In the short-term study, the rats were fed diets containing 0 or 50,000 ppm propylene glycol for 15 weeks. No compound-related effects were reported on hematological indices, serum and urine analysis or organ weights. No histopathology was performed.

Guerrant et al. (1947) reported a 20-week study in which groups of five male and five female young growing rats were fed diets containing propylene glycol at 0, 1, 3, 6, 10, 15, 20, 30, 40, 50 or 60%. At $\geq$40% of the diet,

mortality occurred within a few days. At ≥30%, there was a depression in growth rate. Hemoglobin determination revealed no adverse effects on hemoglobin formation. At ≥10%, the incidence and severity of pathological lesions increased. Lesions of the kidney consisting of degeneration, interstitial hemorrhage and edema, glomerular nephritis and calcification of the cortex predominated. No adverse effects were observed at ≤6% (60,000 ppm).

Hanzlik et al. (1939) provided diets in which propylene glycol was substituted for 25, 50, 75 or 100% of the carbohydrate (12.1, 24.2, 36.4 or 48.5% of the diet) for up to 24 months to groups of five rats. Retarded growth was observed at all dietary levels; the first death at 36.4% occurred at ~20 weeks and all rats at 48.5% died in ~1 month. In another part of this study, increased body weight gain compared with controls was observed in a group of six rats fed a diet containing 25% less carbohydrate than controls and intubated with propylene glycol equivalent to 12.8% of the diet consumed the previous day. The controls consisted of six littermates, and treatment continued for 5 months. Van Winkle and Newman (1941) performed a pair-feeding experiment using two groups of 10 young rats. One group received a control diet and the other received the same diet but with 25% of the carbohydrate replaced with an equicaloric amount of propylene glycol. After 163 days of feeding, body weights of propylene glycol-treated rats exceeded those of controls. Liver glycogen levels in treated rats were 2-7 times the levels in controls.

Oral administration of 1-10% solutions of propylene glycol in the drinking water of rats for periods of 100-234 days produced no gross or microscopic evidence of pathologic effects from propylene glycol treatment (Kesten et al., 1939; Seidenfeld and Hanzlik, 1932; Weatherby and Haag, 1938; Auerbach Associates, 1977).

Braun and Cartland (1936) performed a 50-day gavage study in which groups of one to three rabbits received dosages of 1050, 2100, 3150, 4200 or 8400 mg/kg/day for 50 days. There were no effects on gross appearance at necropsy. Anorexia and retarded growth occurred at ≥4200 mg/kg/day.

Van Winkle and Newman (1941) provided drinking water containing 5 or 10% propylene glycol to groups of four dogs for 5-9 months. Propylene glycol intakes were ~5.1 and 4.5 mℓ/kg/day (5.3 and 4.7 g/kg/day) (Informatics Inc., 1973). Clinical pathology tests and histopathologic examination of the kidney and liver indicated no lesions or functional impairment of these organs.

6.1.2.2. CHRONIC -- In the long-term portion of the study reported by Gaunt et al. (1972), 30 male and 30 female Charles River CD rats were fed diets containing 0, 6250, 12,500, 25,000 or 50,000 ppm propylene glycol for 2 years. The mean daily intakes of propylene glycol were reported to be 0, 0.2, 0.4, 0.9 and 1.7 g/kg in males and 0, 0.3, 0.5, 1.0 and 2.1 g/kg in females. No statistically significant differences were reported between treated and control rats in cumulative death rate, body weight gain, food consumption, hematology, urinary cell excretion or urine concentration tests. A wide range of nonneoplastic histological abnormalities was observed in the kidneys, liver and lungs; however, the incidence was similar in both test and control animals and the changes were consistent with those expected in aging rats. Therefore, no toxic symptoms were reported in rats fed diets containing ≤50,000 ppm propylene glycol for 2 years.

Morris et al. (1942) fed groups of six male and four female albino rats diets containing 0, 2.45 or 4.9% propylene glycol for 24 months. There were no effects on food consumption, body weight gain or survival. Slight hepatic damage was reported in a table, but it was not clear at which dose

this was found, how many animals were involved or what the nature of the damage was. The discussion in the text only stated that the group of animals receiving propylene glycol differed very slightly from the controls.

Weil et al. (1971) fed groups of five male and five female beagle dogs diets that provided dosages of 2.0 and 5.0 g/kg bw/day propylene glycol for 2 years. The concentration of proplyene glycol in the diet at the low dose was ~8% and at the high dose, ~20%. Controls received diets containing comparable caloric amounts of dextrose or no treatment. The concentrations of propylene glycol and dextrose in the diets were adjusted weekly for each group to approximate the predetermined dosage levels by using the mean body weights and mean diet consumptions for the group. The dogs were evaluated for mortality, organ and body weights, hematology, blood chemistry and urinalysis. Gross and histopathological evaluations were performed on a comprehensive set of organs and tissues. No effects were observed in any of the parameters evaluated in dogs receiving 2 g/kg/day for 2 years. Dogs receiving the high dose of propylene glycol had lower hemoglobin and hematocrit values, and the total erythrocyte counts were lower than the controls, while increases were seen in anisocytosis, poikilocytes and reticulocytes. These changes were indicative of some erythrocyte destruction with replacement from the bone marrow; the changes did not appear to be irreversible, and there was no evidence of damage to bone marrow or spleen. An increase in total bilirubin values was also reported in the dogs receiving the high dose of propylene glycol. No histopathological or biochemical evidence of hepatic damage was observed at any dose level.

Okumura et al. (1986) reported on the effects of the administration of 0, 2.5 or 5% propylene glycol in the diets of groups of 50 male and 50 female F-344 rats for 2 years. No significant differences were noted in

food intake, growth, appearance or behavior between treated and control animals. In male rats, the average erythrocyte and leukocyte counts and the mean corpuscular hemoglobin concentration values of both treated groups were significantly elevated compared with controls. In both groups of treated females, the mean corpuscular volume was significantly elevated. Although some differences existed in the hematology of treated and control groups, some of the values may not have differed from the normal state and may not represent compound-related adverse effects. In males, some serum biochemical data differed from the controls, suggesting slight liver damage, but may not have differed significantly from the normal state. Apparently, histopathologic examination was not performed.

6.1.3. Other Relevant Information. Acute toxicity data for propylene glycol are summarized in Table 6-1; the compound has a low order of toxicity. Several investigators reported that administration of lethal and sublethal doses of propylene glycol to rats, mice, rabbits, guinea pigs and dogs resulted in central nervous system depression (Bornmann, 1955; Hickman, 1965; Laug et al., 1939; Seidenfeld and Hanzlik, 1932; Zaroslinski et al., 1971; Braun and Cartland, 1936). Propylene glycol produced lack of muscular coordination (Hickman, 1965), loss of equilibrium (Latven and Molitor, 1939; Laug et al, 1939; Seidenfeld and Hanzlik, 1932), analgesia (Laug et al., 1939; Braun and Cartland, 1936; Seidenfeld and Hanzlik, 1932), muscle tremors (Weatherby and Haag, 1938; Braun and Cartland, 1936; Seidenfeld and Hanzlik, 1932) and occasionally convulsions (Hickman, 1965; Weatherby and Haag, 1938). Other effects of acute poisioning with propylene glycol were an increase in the respiratory rate (Braun and Cartland, 1936), depression of the respiratory rate and heartbeat, hypotension, irritation of the digestive tract, hemolysis and diuresis (Al-Khudhairi and Whitwam, 1986; Bornmann, 1955; Smyth et al., 1941; Seidenfeld and Hanzlik, 1932).

TABLE 6-1

Acute Effects of Propylene Glycol

Route	Species	LD_{50} (g/kg)	Reference
Oral	rats	33.5	Weatherby and Haag, 1938
	rats	21.8	Laug et al., 1939
	rats	29	Thomas et al., 1949
	rats	26.35	Smyth et al., 1941
	rats	45.9	Smyth et al., 1969
	rats	44.4	Smyth et al., 1970
	rats	25.9	Bartsch et al., 1976
	rats	35.8	Union Carbide Corporation, 1978
	mice	24.8	Laug et al., 1939
	mice	22.8	Latven and Molitor, 1939
	mice	31.87	Bornmann, 1955
	guinea pigs	19.6	Laug et al., 1939
	guinea pigs	18.35	Smyth et al., 1941
Intraperitoneal	rats	14.7	Hickman, 1965
	rats	13.5	Thomas et al., 1949
	rats	13.5	Bartsch et al., 1976
	mice	13.5	Holman et al., 1979
	mice	12.8	Holman et al., 1979
	mice	9.73	Karel et al., 1947
	mice	17.2	Zaroslinski et al., 1971
	mice	11.2	Budden et al., 1978

Pathological changes after acute oral administration of propylene glycol to rats, mice and guinea pigs were minimal, producing slight hydropic degeneration of the kidney, with debris and casts in a few cortical tubules, slight congestion of the liver and hemorrhagic areas in the small intestine (Laug et al., 1939).

6.2. CARCINOGENICITY

6.2.1. Inhalation. Pertinent data regarding the carcinogenicity of inhaled propylene glycol could not be located in the available literature as cited in Appendix A.

6.2.2. Oral. Gaunt et al. (1972) studied the potential carcinogenicity of propylene glycol in 30 male and 30 female Charles River CD rats fed 0, 6250, 12,500, 25,000 or 50,000 ppm of the compound in the diet for 2 years. The authors reported the mean daily intakes of propylene glycol to be 0, 0.2, 0.4, 0.9 and 1.7 gm/kg/day in male rats and 0, 0.3, 0.5, 1.0 and 2.1 g/kg/day in females. There were no statistically significant differences between treated and control rats in cumulative death rate, body weight gain, food consumption, hematology, urinary cell excretion or renal concentration tests. A wide range of histological abnormalities were reported, particularly in the kidneys, liver and lung; however, the incidence was similar in both test and control groups. The histopathological changes were consistent with those expected in aging rats. Among both treated and control rats, there was a high incidence of mammary fibroadenomas, pituitary adenomas and subcutaneous fibrosarcomas. The authors reported that mammary fibroadenomas have been shown to occur spontaneously in a high proportion of 2-year-old rats of Charles River CD strain. The results of this study indicate that no carcinogenic effects could be attributed to propylene glycol when administered in the diets of rats at doses $\leq$50,000 ppm for 2 years.

6.2.3. Other Relevant Information. Several carcinogenicity studies in which propylene glycol was administered to rats and mice as a vehicle control were reviewed by Miller (1979). In these reports, the compound was injected subcutaneously or applied topically to the oral mucosa repeatedly for ≥8 months. No increase in tumor incidence was observed.

Stenbach and Shubick (1974) tested the effect on tumor incidence of twice weekly applications of 0.02 mℓ solutions of 10, 50 and 100% propylene glycol to the shaved skin of groups of 50 female Swiss mice. Treatment was conducted for the lifespan of the animals and no statistically significant differences in incidence of skin or other tumors were reported.

Farsund (1978, 1981) reported that subcutaneous injection of 0.2 mℓ propylene glycol to 12 hairless mice, 3 times/week for 3 months, slightly increased the proportion of diploid cells, slightly reduced the proportion of tetraploid cells and virtually eliminated the octaploid class of cells in the bladder mucosa. DNA synthesis in the tetraploid cells ceased. The author stated that the changes observed in bladder mucosa cells that were due to propylene glycol treatment were qualitatively similar to but less severe than those observed after administration of the bladder carcinogen, dibutylnitrosamine, and the alkylating agent, cyclophosphamide.

6.3. MUTAGENICITY

Litton Bionetics, Inc. (1974, 1976) tested propylene glycol for mutagenic response in a variety of assays. The results are summarized in Table 6-2.

Negative results were obtained when propylene glycol was tested for genetic activity in a series of *in vitro* microbial assays with and without metabolic activation. The indicator organisms used were *Salmonella typhimurium* strains TA1535, TA1537 and TA1538 and *Saccharomyces cerevisiae* D4 (Litton Bionetics Inc., 1976).

TABLE 6-2

Mutagenicity Testing of Propylene Glycol

Assay	Indicator Organism	Application	Concentration or Dose	Activating System	Response	Comments	Reference
Reverse mutation	Salmonella typhimurium TA1535, TA1537, TA1538	plate incorporation	1.25-5%	±S-9	-	NC	Litton Bionetics Inc., 1976
Mitotic	Saccharomyces recombination	suspension cerevisiae D4	1.25-5%	±S-9	-	NC	Litton Bionetics Inc., 1976
Reverse mutation	S. typhimurium G46, TA1530	host-mediated in ICR mice: single dose or 5 daily doses (gavage)	30, 2500 or 5000 mg/kg	NA	-, ±	weak or questionable positive result with Salmonella G46 at high acute dose only	Litton Bionetics Inc., 1974
Mitotic recombination	S. cerevisiae D3	host-mediated in ICR mice: single dose or 5 daily doses (gavage)	30, 2500 or 5000 mg/kg	NA	+	results difficult to interpret due to low recoveries of organisms	Litton Bionetics Inc., 1974
Cytogenetic chromosome damage	bone marrow cells	in vivo male albino rats	30, 2500 and 5000 mg/kg	NA	-	NC	Litton Bionetics Inc., 1974
Chromosome aberration	human embryonic lung cells WI-38	culture	0.1 to >0.001 µg/ml	NA	-	NC	Litton Bionetics Inc., 1974
Dominant lethal	random-bred rats	in vivo random-bred rats	30, 2500 and 5000 mg/kg	NA	-	NC	Litton Bionetics Inc., 1974

NA = Not applicable; NC = no comment

Propylene glycol was tested for mutagenic response in a host-mediated assay using male ICR mice as hosts and Salmonella typhimurium G46 and TA1530 and Saccharomyces cerevisiae D3 as the indicator organisms (Litton Bionetics Inc., 1974). In both an acute and subacute study, the mice received one or five daily oral doses, respectively, of 30, 2500 or 5000 mg/kg propylene glycol and then were inoculated with the indicator organism. The mice were sacrificed 3 hours after treatment with the test organism. The results were negative with Salmonella TA1530, weak or questionably positive at the high acute dose only with Salmonella G 46 and difficult to interpret with Saccharomyces D3. The yeast showed increased recombinant frequencies at all dose levels except the acute high dose, which resulted in low recombinant frequency, which was possibly due to selective killing of the mutants.

Propylene glycol was tested in an in vivo cytogenetic assay to assess chromosomal damage in somatic cells (Litton Bionetics Inc., 1974). Groups of 15 random-bred male albino rats, 10-12 weeks old, received acute doses of propylene glycol at 30, 2500 or 5000 mg/kg. The animals were sacrificed after 6, 24 or 48 hours, and bone marrow metaphase chromosomes were examined. No significant aberrations of the bone marrow metaphase chromosomes were reported in propylene glycol treated animals. No significant aberrations in anaphase chromosomes were reported in human embryonic lung culture cells WI-38 exposed to doses of 0.1, 0.01 or 0.001 µg/mℓ (Litton Bionetics Inc., 1974).

In a dominant lethal assay, groups of ten, 10- to 12-week-old random-bred male rats were administered either one dose or one dose each day for 5 days of 30, 2500 or 5000 mg/kg propylene glycol (Litton Bionetics Inc., 1974). The males were subsequently mated to two females/week for 7-8

weeks. Fourteen days after exposure, the females were sacrificed and examined for early deaths, late fetal deaths and total implantations. No significant effects were reported, and propylene glycol was considered nonmutagenic in the dominant lethal assay at the dosages tested. However, the test was not carried out long enough (10 weeks postexposure) to fully evaluate impact on spermatogonia.

6.4. TERATOGENICITY

Food and Drug Research Labs. (1973) evaluated propylene glycol for teratogenicity in mice, rats, hamsters and rabbits. No adverse maternal or fetal effects were attributed to propylene glycol administration in any species. The results are summarized below.

Groups of 25-28 female albino CD-1 outbred mice and groups of 25-28 female Wistar rats were administered oral doses of 0, 16.0, 74.3, 345 and 1600 mg/kg propylene glycol on days 6-15 of gestation. The mice were sacrificed on day 17, the rats on day 20; no compound-related effects were observed in either species on the number of implantation sites, resorption sites, live and dead fetuses, pup body weight and presence of abnormalities in fetal soft or skeletal tissues.

Groups of 24-27 adult female Golden hamsters were administered oral doses of 15.5, 72.0, 334.5 and 1550 mg/kg propylene glycol on days 6-10 of gestation. The animals were sacrificed on day 14, and no compound-related effects were reported on the numbers of implantation sites, resorption sites, live and dead fetuses, pup body weight or anatomical abnormalities.

Groups of 15-20 Dutch-belted rabbits were administered oral doses of 12.3, 57.1, 267 or 1230 mg/kg propylene glycol on days 6-18 of gestation.

The animals were sacrificed on day 29, and no effects were reported on the numbers of corpora lutea, implantation sites, resorption sites, live and dead fetuses, fetal weight or visceral or skeletal abronmalities of the fetuses.

Since maternal toxicity was not achieved in any of the studies, there is concern about adequacy of dose-response range at upper limits.

6.5. OTHER REPRODUCTIVE EFFECTS

A group of twenty, 7-week-old male and female white rats were exposed continuously to an atmosphere of 170-350 mg/m^3 propylene glycol vapor for 3-18 months (Robertson et al., 1947). Weight gain was higher in the treated males than in the controls. Female weight data were not plotted; they varied because of the birth of young. No difference was noted in the general condition between the treated or control rats, and the treated rats bred as regularly and produced litters as large as did the controls. No differences were noted in general appearance and weight gain between pups of treated and control groups.

6.6. SUMMARY

Gaunt et al. (1972) evaluated the carcinogenicity of propylene glycol in male and female Charles River CD rats fed 0, 6250, 12,500, 25,000 or 50,000 ppm of the compound in the diet for 2 years. In both treated and control groups, there was a high but similar incidence of mammary fibroadenomas, pituitary adenomas and subcutaneous fibrosarcomas. Mammary fibroadenomas have been shown to occur spontaneously in a high proportion of 2-year-old rats of the Charles River CD strain. No carcinogenic effects could be attributed to propylene glycol when administered in the diet of rats at doses $\leq$50,000 ppm for 2 years.

Subchronic and chronic studies suggest that propylene glycol has a very low order of toxicity. Gaunt et al. (1972) evaluated several parameters of toxicity in rats fed diets containing ≤50,000 ppm for 2 years. There were no statistically significant differences between treated and control rats in cumulative death rate, body weight gain, food consumption, hematology, urinary cell excretion or renal clearance. A wide range of histological abnormalities was reported in the kidney, liver and lung, but the incidence was similar in both test and control groups. These changes were also consistent with those expected in aging rats.

Weil et al. (1971) reported no effects on the parameters of toxicity evaluated in male and female beagle dogs receiving 2 g/kg bw/day propylene glycol in the diet for 2 years. Dogs receiving 5 g/kg/day for 2 years had lower total erythrocyte counts, lower hemoglobin and hematocrit values, increased total bilirubin, and increases in anisocytosis, poikilocytes and reticulocytes. These changes were indicative of some erythrocyte destruction with replacement from the bone marrow. There was no evidence of damage to bone marrow or spleen, and no histopathological or biochemical evidence of hepatic damage was observed at any dose.

Morris et al. (1942) reported slight hepatic damage in albino rats fed 2.45 or 4.9% propylene glycol for 2 years. No other details were provided. Okumura et al. (1986) reported some differences in hematological and serum biochemical effects in F-344 rats fed 2.5 or 5% propylene glycol in the diet for 2 years; however, the effects may not have differed significantly from the normal state.

Subchronic administration of propylene glycol at 1-10% in drinking water caused no gross or microscopic lesions in rats (Kesten et al., 1939; Seidenfeld and Hanzlik, 1932; Weatherby and Haag, 1938). Administration to

rats for 20 weeks at ≥40% of the diet resulted in death, at ≥30% resulted in growth depression, and at ≥10% resulted in kidney lesions. There were no effects at ≤6% (Guerrant et al., 1947).

Continuous inhalation exposure of rats to 170-350 mg/m³ for 3-18 months had no effects on appearance, growth, reproduction or histopathological appearance of tissues in rats (Robertson et al., 1947).

Acute toxicity data indicate that propylene glycol has a low order of toxicity, with oral LD_{50} values ranging from 21.8-45.9 g/kg in rats and 22.8-31.87 in mice (Laug et al., 1939; Weatherby and Haag, 1938; Smyth et al., 1941; Bornmann, 1955).

Propylene glycol was found to be nonmutagenic when tested in Salmonella typhimurium TA1535, TA1537 and TA1538 and Saccharomyces cerevisiae D4, with or without metabolic activation (Litton Bionetics Inc., 1976). Results of cytogenetic testing in vivo in the bone marrow of rats and in vitro with human embryonic lung culture cells WI-38 were negative. Propylene glycol was also nonmutagenic in the dominant lethal assay in rats (Litton Bionetics Inc., 1974). In a host-mediated assay using ICR mice, negative results were obtained with Salmonella TA1530, and questionably positive results were obtained at the high dose only in Salmonella strain G 46. The results with the Saccharomyces D3 tester strain appeared weakly mutagenic in the host-mediated assay, but were difficult to interpret because propylene glycol may have been selectively toxic for mutants of this organism (Litton Bionetics Inc., 1974).

Food and Drug Research Labs. (1973) evaluated propylene glycol for teratogenicity in mice, rats, hamsters and rabbits. No adverse maternal or fetal effects were attributed to propylene glycol administration in any species. Male and female white rats exposed continuously to a super-saturated atmosphere of propylene glycol for ≤18 months bred as regularly

and produced litters as large as did the control animals (Robertson et al., 1947). No differences in appearance or weight gain between the offspring of treated and control groups were reported.

7. EXISTING GUIDELINES AND STANDARDS

7.1. HUMAN

Propylene glycol is a substance with GRAS status (Food Drug Cosmetic Law Reports, 1980) for which permissible levels in food have been established. Maximum levels permitted are 5% for alcoholic beverages, 24% for confections and frostings, 2.5% for frozen dairy products, 97% for seasonings and flavorings, 5% for nuts and nut products, and 2.0% for all other food categories.

7.2. AQUATIC

Guidelines and standards for the protection of aquatic organisms from the effects of propylene glycol could not be located in the available literature as cited in Appendix A.

8. RISK ASSESSMENT

8.1. CARCINOGENICITY

8.1.1. Inhalation. Pertinent data regarding the carcinogenicity of inhaled propylene glycol could not be located in the available literature as cited in Appendix A.

8.1.2. Oral. As reported in Section 6.2.2., Gaunt et al. (1972) studied the potential carcinogenicity of propylene glycol in 30 male and 30 female Charles River CD rats fed 0, 6250, 12,500, 25,000 or 50,000 ppm of the compound in the diet for 2 years. The mean daily intakes of propylene glycol were reported to be 0, 0.2, 0.4, 0.9 and 1.7 g/kg/day in male rats and 0, 0.3, 0.5, 1.0 and 2.1 g/kg/day in female rats. Among both treated and control rats, there was a high incidence of mammary fibroadenomas, pituitary adenomas and subcutaneous fibrosarcomas. According to the authors, mammary fibroadenomas have been shown to occur spontaneously in a high proportion of 2-year-old rats of Charles River CD strain. In this study, no carcinogenic effects could be attributed to propylene glycol when administered in the diet of rats at doses $\leq$50,000 ppm for 2 years.

8.1.3. Other Routes. No increase in tumor incidence was observed in carcinogenicity studies when propylene glycol was administered to rats and mice as a vehicle control (Miller, 1979). In these reports, the compound was injected subcutaneously or applied topically to the oral mucosa repeatedly for $\geq$8 months. When twice weekly applications of 0.02 mℓ of 10, 50 and 100% propylene gltcol was applied to the shaved skin of groups of 50 female Swiss mice for the lifespan of the animals, no statistically significant differences in incidence of skin or other tumors were reported (Stenbach and Shubick, 1974). Farsund (1978, 1981) observed changes in the

bladder mucosa cells, which were due to propylene glycol treatment, that were qualitatively similar to but less severe than those observed after administration of the bladder carcinogen, dibutylnitrosamine, and the alkylating agent, cyclophosphamide.

8.1.4. Weight of Evidence. No evidence of carcinogenicity was found with exposures of propylene glycol at levels of 50,000 ppm in the diet of rats for a period of 2 years (Gaunt et al., 1972). This study used several doses of the compound by a relevant route of exposure over the lifetime of the animal; in addition, a comprehensive set of tissues was examined histopathologically. No other human or animal data are available concerning the carcinogenicity of the compound. According to the Guidelines for Carcinogen Risk Assessment (U.S. EPA, 1986b), the animal and human data regarding carcinogenicity are inadequate; therefore, propylene glycol would be classified as an EPA Group D chemical, not classifiable as to human carcinogenicity.

8.1.5. Quantitative Risk Estimates. Insufficient data are available for quantitative assessment of the carcinogenicity of propylene glycol by either the oral or inhalation exposure routes.

8.2. SYSTEMIC TOXICITY

8.2.1. Inhalation Exposure.

8.2.1.1. LESS THAN LIFETIME EXPOSURES (SUBCHRONIC) -- One study (Robertson et al., 1947) was available for consideration for the subchronic inhalation RfD. In this study, 29 rhesus monkeys were exposed continuously to an atmosphere of 100-220 or 230-350 mg/m^3 propylene glycol vapors for 13 months. No compound-related pathological or hematological effects were reported; however, most of the control and treated animals were suffering from infections, and mortality in treated and control monkeys was high.

This study is inadequate for derivation of an RfD for subchronic inhalation exposure to propylene glycol. Therefore, the chronic inhalation RfD (Section 8.2.1.2.) of 2 mg/kg/day or 116 mg/day for a 70 kg human is adopted as the subchronic inhalation RfD for propylene glycol. Discussion, derivation and confidence in the RfD are presented in the following section.

8.2.1.2. CHRONIC EXPOSURES -- In an inhalation study reported by Robertson et al. (1947), groups of 20 male and female white rats were exposed continuously to an atmosphere of 170-350 mg/m³ propylene glycol vapor for 18 months. Weight gain was higher in treated males than in controls, but female weight data were not plotted because of the variation resulting from giving birth to young. An average weight of 0.35 kg for exposed male rats was estimated from graphic data provided by the investigators. No differences were noted in the general condition between treated and control rats, and the treated rats bred as regularly and produced litters as large as did the controls. No pathological effects related to exposure were observed in any of the tissues examined. No other parameters of exposure were measured. A chronic NOEL of 260 mg/m³, the mean of 170 and 350 mg/m³, is identified from the rat data reported by Robertson et al. (1947). An equivalent dosage of 166 mg/kg/day is estimated by multiplying the exposure concentration of 260 mg/m³ by 0.223 m³/day, the reference inhalation rate for rats, and dividing by 0.35 kg, the estimated body weight of the exposed rats in this study. Applying an uncertainty factor of 100 to the rat NOEL of 116 mg/kg/day results in a chronic inhalation RfD of 2 mg/kg/day or 116 mg/day for a 70 kg human. The uncertainty factor of 100 was selected based on a factor of 10 to account for interspecies extrapolation and another factor of 10 to protect the sensitive individuals of the population. The confidence in the RfD could be considered medium. Although the sample size was small, several endpoints of toxicity were evaluated.

Data from the monkey study, although inadequate for use in risk assessment, do provide support for the RfD from the rat data, since a NOEL of 350 mg/m^3 could also be identified from the monkey data. In addition, data from the literature indicate no evidence of carcinogenicity, developmental or reproductive toxicity resulting from the administration of propylene glycol.

8.2.2. Oral Exposure.

8.2.2.1. LESS THAN LIFETIME EXPOSURES (SUBCHRONIC) -- Data regarding the subchronic oral toxicity of propylene glycol, although limited, suggest that levels of 1-10% in the drinking water of rats are not associated with adverse effects (Kesten et al., 1939; Seidenfeld and Hanzlik, 1932; Weatherby and Haag, 1938). The most comprehensive dietary study was that by Guerrant et al. (1947) in which groups of five male and five female young growing rats were fed diets containing 0, 1, 3, 6, 10, 15, 20, 30, 40, 50 or 60% propylene glycol for 20 weeks. At $\geq$40% of the diet, mortality occurred within a few days. Growth rate was depressed at $\geq$30% and the incidence and severity of histopathological lesions, particularly of the kidney, were increased at $\geq$10%. No effects were reported at 6% (60,000 ppm), which may be considered a NOEL in this study. Assuming a food factor for rats of 0.05, a transformed dosage of 3 g/kg/day can be estimated. Applying an uncertainty factor of 100, 10 for species-to-species extrapolation and 10 to protect sensitive individuals, results in an RfD for subchronic oral exposure to propylene glycol of 0.03 g/kg/day or 2 g/day for a 70 kg human. Confidence in this RfD is considered medium because the other limited subchronic oral data support the NOEL in rats. The carcinogenicity of propylene glycol, however, has been adequately tested in only one species and the developmental toxicity, although tested in four species, has not been tested at levels as high as the subchronic toxicity NOEL in rats.

8.2.2.2. CHRONIC EXPOSURES -- Several chronic oral exposure studies (see Section 6.1.2.1.) are available for consideration for derivation of the RfD. Gaunt et al. (1972) reported no statistically significant differences in a dietary study between control Charles River CD rats and high-dose male rats receiving dosages of propylene glycol of $\leq$1.7 g/kg/day or female rats receiving dosages of $\leq$2.1 g/kg/day in cumulative death rate, body weight gain, food consumption, hematology, urinary cell excretion or renal concentration. A comprehensive histopathological examination was conducted. The incidence of tumors was similar in both test and control animals, and the changes observed were consistent with those expected in aging rats. Therefore, a NOEL of 2.1 g/kg/day can be identified from the female rat data in this study.

Morris et al. (1942) reported no renal pathology in albino rats fed propylene glycol at 2.45 or 4.9% of the diet for 2 years. Slight hepatic damage was reported, but it was not clear at which dosage level this was found, how many animals were involved and what the nature of the damage was. Therefore, since other well-documented studies are available, the study reported by Morris et al. (1942) will not be used for derivation of the RfD.

Weil et al. (1971) fed groups of beagle dogs diets that provided dosages of 2.0 and 5.0 g/kg bw/day propylene glycol for 2 years. In addition to a comprehensive histopathological evaluation, the dogs were evaluated for mortality, organ and body weights, hematology, blood chemistry and urinalysis. No effects were observed in any of the parameters evaluated in dogs receiving 2 g/kg/day. High-dose dogs had lower erythrocyte counts, hemoglobin and hematocrit values, and an increase in total bilirubin. These changes were considered indicative of some erythrocyte destruction with replacement from the bone marrow, although there was no evidence of damage to the bone marrow or spleen and the changes appeared to be reversible.

Therefore, a NOEL of 2 g/kg/day can be identified from the dog data reported by Weil et al. (1971).

Okumura et al. (1986) reported elevation in erythrocyte and leukocyte counts in male F-344 rats and mean corpuscular volume in female rats fed propylene glycol in the diet at 2.5 and 5% for 2 years. Some serum biochemical data in the males differed from controls, but may not have differed from the normal state. The presence of an infection in the colony was not disregarded. Because no hematological effects were observed in two other well-conducted chronic oral exposure studies where comparable doses were administered to rats (Gaunt et al., 1972) or dogs (Weil et al., 1971) for 2 years, the interpretation of data from this study is unclear. Histopathological examination was apparently not performed.

The most adequate study for derivation of an RfD for chronic oral exposure is the 2-year rat study by Gaunt et al. (1972). The highest NOEL of 2.1 g/kg/day comes from the female rat data reported by Gaunt et al. (1972). Applying an uncertainty factor of 100 to the rat NOEL of 2.1 g/kg/day results in a chronic oral RfD of 0.02 g/kg/day or 1 g/day for a 70 kg man. An uncertainty factor of 100 was selected, based on a factor of 10 to account for interspecies extrapolation and another factor of 10 to protect the most sensitive individuals of the population. The confidence in the RfD is medium since the study provided adequate toxicity endpoints in a well-designed oral study. The available data from the literature do not indicate evidence of carcinogenicity or developmental or reproductive toxicity of propylene glycol, but the carcinogenicity has not been tested in more than one species and the developmental toxicity has not been tested at doses equivalent to the NOEL in rats. A NOEL of 2 g/kg/day from the 2-year dog study reported by Weil et al. (1971) also supports the RfD.

9. REPORTABLE QUANTITIES

9.1. BASED ON SYSTEMIC TOXICITY

The toxic effects of subchronic and chronic inhalation and oral exposure to propylene glycol were discussed in Chapter 6. The dose-response data from these studies considered suitable for the derivation of the RQ are summarized in Table 9-1.

The only effects associated with exposure to propylene glycol were reduced body weight gain and kidney lesions in rats (Guerrant et al., 1947), and changes indicative of some erythrocyte destruction with replacement from the bone marrow reported in dogs by Weil et al. (1971). The effects in dogs occurred at a dose of 5 g/kg/day in dogs fed the compound for 2 years. The changes did not appear to be irreversible and there was no evidence of damage to the bone marrow or spleen. CSs are calculated and presented in Table 9-2. A CS is not calculated for reduced body weight gain in rats because a more severe effect, histopathologic lesions in the kidney, occurred at a lower survival dosage. A CS of 6 associated with kidney lesions in rats in a subchronic study corresponds to an RQ of 1000 and is chosen to represent the chronic toxicity of propylene glycol (Tables 9-2 and 9-3).

9.2. BASED ON CARCINOGENICITY

No evidence of carcinogenicity of propylene glycol was found in rats receiving multiple doses of the compound in the diet for a period of 2 years (Gaunt et al., 1972). Propylene glycol is assigned to EPA Group D, not classifiable as to carcinogenicity. Therefore, insufficient data preclude the derivation of carcinogenic potency factors and hazard ranking based on carcinogenicity.

TABLE 9-1

Oral Toxicity Summary for Propylene Glycol

Species/ Strain	Sex	No. at Start	Average Weight (kg)	Vehicle/ Physical State	Purity	Exposure	Transformed Animal Dose (g/kg/day)	Transformed Human Dose[a] (g/kg/day)	Response	Reference
Dog/beagle	M,F	5/sex	14[b]	diet	USP	5 g/kg/day for 2 years	5	2.9	Lower hemoglobin and hematocrit values, lower total erythrocyte counts, increase in total bilirubin (increase in anisocytosis, poikilocytes and reticulocytes)	Weil et al., 1971
Rat/NR	M,F	5/sex	0.35[b]	diet	NR	≥30% of diet (30,000 ppm) for 20 weeks	15[c]	0.26[d]	Reduced growth rate	Guerrant et al., 1947
Rat/NR	M,F	5/sex	0.35[b]	diet	NR	≥10% of diet (10,000 ppm) for 20 weeks	5[c]	0.09[d]	Histopathologic lesions of kidney	Guerrant et al., 1947

[a]Calculated by multiplying the transformed animal dose by the cube root of the ratio of the average animal body weight to the human body weight (14 kg/70 kg)$^{1/3}$.

[b]Reference body weight (U.S. EPA, 1985)

[c]Calculated by using a reference food factor for rats of 0.05 (U.S. EPA, 1985).

[d]A factor of 10 was applied to expand from subchronic to chronic exposure, although data from the chronic dietary study (Gaunt et al., 1972) suggest this manipulation may be unnecessarily conservative, since kidney lesions were not observed in the chronic study at 1.7 or 2.1 g/kg/day.

NR = Not reported

TABLE 9-2

Oral Composite Scores for Propylene Glycol

Species	Animal Dose[a] (g/kg/day)	Chronic Human MED[b] (g/day)	RV_d	Effect	RV_e	CS[c]	RQ	Reference
Dog	5	203	1.0	Lower hemoglobin and hematocrit values, lower total erythrocyte counts, increase in total bilirubin	3	3	5000	Weil et al., 1971
Rat	5	6.3	1.0	Histopathologic lesions of kidney	5	5	5000	Guerrant et al., 1947

[a]Calculated by multiplying the transformed anim l dose by the cube root of the ratio of the average animal body weight to the human body weight.

[b]Calculated by multiplying the equivalent human dose expressed in g/kg/day (see Table 9-1) by 70 kg.

[c]$CS = RV_d \times RV_e$

TABLE 9-3

Propylene Glycol

Minimum Effective Dose (MED) and Reportable Quantity (RQ)

Route:	oral/diet
Dose*:	6.3 g/day
Effect:	degenerative and inflammatory lesions and calcification in the kidney
Reference:	Guerrant et al., 1947
RV_d:	1.0
RV_e:	5
Composite Score:	5
RQ:	5000

*Equivalent human dose

10. REFERENCES

Al-Khudhairi, D. and J.G. Whitwam. 1986. Autonomic reflexes and the cardiovascular effects of propylene glycol. Br. J. Anaesth. 58(8): 897-902.

Anbar, M. and P. Neta. 1967. A compilation of specific bimolecular rate constant for the reactions of hydrated electrons, hydrogen atoms and hydroxyl radical with inorganic and organic compounds in aqueous solution. Int. J. Appl. Radiat. Isotopes. 18: 493-523.

Atkinson, R. 1985. Kinetics and mechanisms of the gas-phase reactions of hydroxyl radical with organic compounds under atmospheric conditions. Chem. Rev. 85: 69-201.

Auerbach Associates. 1977. Propylene Glycol. Auerback Assoc. Inc., Philadelphia, PA. 90 p. NTIS PB-280477.

Barstch, W., G. Sponer, K. Deitman and G. Fuchs. 1976. Acute toxicity of various solvents in the mouse and rat. Arzneim-Forsch. 26: 1581-1583.

Bornmann, G. 1955. Physiological properties of glycols and their toxicity. Arzneim-Forsch. 4: 643-646, 710-715 (1954); 5: 38-42. (CA 49:7131a)

Braun, H.A. and G.F. Cartland. 1936. The toxicity of propylene glycol. J. Am. Pharmacol. Assoc. 25: 746-749.

Bridie, A.L., C.J.M. Wolff and M. Winter. 1979a. BOD and COD of some petrochemicals. Water Res. 13: 627-630.

Bridie, A.L., C.J.M. Wolff and M. Winter. 1979b. The acute toxicity of some petrochemicals to goldfish. Water Res. 13(7): 623-626.

Brown, E.S., C.F. Hauser, B.C. Ream and R.V. Berthold. 1980. Glycols (ethylene and propylene). In: Kirk-Othmer Encyclopedia of Chemical Technology, Vol. 11, 3rd ed., M. Grayson and D. Eckroth, Ed. John Wiley and Sons, New York. p. 933-935, 951-956.

Browning, E. 1965. Toxicity and Metabolism of Industrial Solvents. American Elsevier, New York. p. 594-600, 624-628.

Budden, Von R., U.G. Kuhl and G. Buschmann. 1978. Studies on the pharmacokinetic activity of several drug solvents. Arzneim-Forsch. 28: 1586-1593. (Ger.) (Cited in SRC, 1982)

Chou, W.L., R.E. Speece and R.H. Siddiqi. 1979. Acclimation and degradation of petrochemical wastewater components by methane fermentation. Biotechnol. Bioeng. Symp. 8: 319-414.

CMR (Chemical Marketing Reporter). 1987. Chemical profile: Propylene glycol. February 9.

Dorfman, L.M. and G.E. Adams. 1973. Reactivity of the hydroxyl radical in aqueous solution. National Bureau of Standards. 51 p. NSRD-NBS-46. NTIS COM-73-50623.

Eisenreich, S.J., B.B. Looney and J.D. Thornton. 1981. Airborne organic contaminants of the Great Lakes ecosystem. Environ. Sci. Technol. 15(1): 30-38.

Farsund, T. 1978. Cell kinetics of mouse urinary bladder epithelium. 6. Changes in the proportions of cells with various nuclear DNA content after repeated doses of propylene glycol (1,2-propanediol). Virchows Arch. B. 27: 1-6.

Farsund, T. 1981. Disturbances of growth and polyploidy in mouse bladder epithelium by systemic injection of toxic and carcinogenic substances. Acta Pathol. Microbiol. Scand. Suppl. 274: 304-306.

Fincher, E.L. and W.J. Payne. 1962. Bacterial utilization of ether glycols. Appl. Microbiol. 10: 542-547.

Food Drug Cosmetic Law Reports. 1980. Food Additives, GRAS Substances. 21 CFR 184.1643.

Food and Drug Research Labs. 1973. Teratologic Evaluation of FDA 71-56 (Propylene Glycol). Report No. FDABF-GRAS-141. Food and Drug Research Labs, Inc., Maspeth, NY. NTIS PB-22822/8.

Gaunt, I.F., F.M.B. Carpanini, P. Grasso and A.B.G. Lansdown. 1972. Long-term toxicity of propylene glycol in rats. Food Cosmet. Toxicol. 10: 151-162.

Graedel, T.E. 1978. Chemical Compounds in the Atmosphere. Academic Press, New York. p. 244.

Grunwald, A., J. Koller, H. Hofmanova and J. Hezina. 1984. Biodegradability of Firdex and Friterm. Vodni. Hospod. 34: 247-251. (CA 102:66794t)

Guerrant, N.B., G.P. Whitlock, M.L. Wolff and R.A. Dutcher. 1947. Response of rats to diets containing varying amounts of glycerol and propylene glycol. Bull. Natl. Formulary Comm. 15: 205-229. (Cited in Informatics, Inc., 1973)

Hansch, C. and A.J. Leo. 1985. Medchem Project. Issue No. 26. Pomona College, Claremont, CA.

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

Harada, T. and Y. Nagashima. 1975. Utilization of alkylether compounds by soil bacteria. J. Ferment. Technol. 53: 218-222.

Hawley, G.G. 1981. The Condensed Chemical Dictionary, 10th ed. Van Nostrand Reinhold Co., New York. p. 864-865.

Hickman, J.R. 1965. Acute toxicity of radiation-sterilized propylene glycol. J. Pharm. Pharmacol. 17: 255-256.

Hine, J. and P.K. Mookerjee. 1975. The intrinsic hydrophilic character of organic compounds. Correlations in terms of structural contributions. J. Org. Chem. 40(3): 292-298.

Holman, N.W., Jr., R.L. Mundy and R.S. Teague. 1979. Alkyldiol antidotes to ethylene glycol toxicity in mice. Toxicol. Appl. Pharmacol. 49: 382-392. (Cited in SRC, 1982)

Informatics, Inc. 1973. GRAS (Generally Recognized As Safe) food ingredients-propylene glycol and derivatives. January, 1983. PB-221233.

Kaplan, D.L., J.T. Walsh and A.M. Kaplan. 1982. Gas chromatographic analysis of glycols to determine biodegradability. Environ. Sci. Technol. 16: 723-725.

Karel, L., B.H. Landing and T.S. Harvey. 1947. The intraperitoneal toxicity of some glycols, glycol ethers, glycol esters and pthalates in urine. J. Pharmacol. Exp. Therap. 90: 338-347.

Kersters, K. and J. DeLey. 1963. The oxidation of glycols by acetic acid bacteria. Biochim. Biophys. Acta. 71: 311-331.

Kesten, H.D. M.G. Mulinos and L. Pomerantz. 1939. Pathologic effects of certain glycols and related compounds. Arch. Pathol. 27: 447-465.

Lamb, C.B. and G.F. Jenkins. 1952. BOD of synthetic organic chemical. In: Proc. 8th Ind. Waste Conf., Purdue Univ. p. 326-329.

Latven, A.T. and H. Molitor. 1939. Comparison of the toxic, hypnotic and irritating properties of eight organic solvents. J. Pharmacol. Exp. Ther. 65: 89-94.

Laug, E.P., H.O. Calvery, H.J. Morris and G. Woodard. 1939. The toxicology of some glycols and derivatives. J. Ind. Hyg. Toxicol. 21: 173-200.

Lehman, A.J. and H.W. Newman. 1937. Propylene glycol: Rate of metabolism, absorption and excretion with a method for estimation in body fluids. J. Pharm. Exp. Therap. 60: 312-322.

Litton Bionetics, Inc. 1974. Mutagenic Evaluation of Compound FDA 71-56, Propylene Glycol. Report No. LBI-2446-294, FDABF-GRAS-294. Bionetics, Inc., Kensington, MD. 94 p. NTIS PB-245450/2.

Litton Bionetics, Inc. 1976. Mutagenic Evaluation of Compound FDA 71-56. 00057-55-6, Propylene Glycol. Food and Drug Administration, Washington, DC. NTIS PB-257868.

Lyman, W.J., W.F. Reehl and D.H. Rosenblatt. 1982. Handbook of Chemical Property Estimation Methods. McGraw Hill Book Co., New York. p. 4-9, 5-5, 7-4, 15-27.

Majewski, H.S., J.F. Klaverkamp and D.P. Scott. 1978. Acute lethality and sub-lethal effects of acetone, ethanol and propylene glycol on the cardio-vascular and respiratory systems of rainbow trout (Salmo ...). Water Res. 12(4): 217-221.

Mayer, F.L. and M.R. Ellersieck. 1986. Manual of Acute Toxicity: Interpretation and Data Base for 410 Chemicals and 66 Species of Freshwater Animals. U.S. Dept. Interior, Fish and Wildlife Service, Washington, DC. Resource Publ. 160. p. 408.

Mill, T., D.G. Hendry and H. Richardson. 1980. Free-radical oxidants in natural waters. Science. 207: 886-887.

Miller, L.M. 1979. Investigation of Selected Potential Environmental Contaminants: Ethylene Glycol, Propylene Glycols and Butylene Glycols. Franklin Research Center, Philadelphia, PA. 270 p. EPA-560/11-79-006. NITS PB 80-109119.

Morris, J.H., A.A. Nelson and H.O. Calvery. 1942. Observations on the chronic toxicities of propylene glycol, ethylene glycol, diethylene glycol, ethylene glycol mono-ethyl-ether, diethylene glycol mono-ethyl-ether. J. Pharmacol. Exp. Ther. 74: 266-273.

NIOSH (National Institute for Occupational Safety and Health). 1984. Current Awareness File. Registry of Toxic Effects of Chemical Substances (RTECS). NIOSH, Cincinnati, OH.

Okumura, M., S. Yamada, K. Hayakawa and M. Ito. 1986. Hematological effect in F344 rats after long term administration of propylene glycol. Aichi-ken Eisei Kenkyusho Ho. 36: 87-93.

Price, K.S., G.T. Waggy and R.A. Conway. 1974. Brine shrimp bioassay and seawater BOD of petrochemicals. J. Water Pollut. Control Fed. 46: 63-77.

Riddick, J.A., W.B. Bunger and T.K. Sakano. 1986. Organic Solvents: Physical Properties and Methods of Purification. Techniques of Chemistry, Vol. 2, 4th ed. Wiley-Interscience, New York. p. 1325.

Robertson, O.H., C.G. Loosli, T.T. Puck, H. Wise, H.M. Lemon and W. Lester. 1947. Tests for chronic toxicity of propylene glycol and oral administration. J. Pharmacol. Exp. Ther. 91: 52-75.

Rowe, V.K. and M.A. Wolf. 1982. Patty's Industrial Hygiene and Toxicology, Vol., IIC, 3rd ed. John Wiley and Sons, Inc., New York. p. 3852-3861.

Ruddick, J.A. 1972. Toxicology, metabolism and biochemistry of 1,2-propanediol. Toxicol. Appl. Pharmacol. 21(1): 102-111.

Salter, W.T., P.D. Robb and F.H. Scharles. 1935. Liver glycogen from derivatives of glucose. J. Nutr. 9(1): 11-23. (Cited in Informatics, Inc., 1973)

SANSS. 1987. Structure and Nomenclature Search System. Chemical Information System (CIS) computer data base.

Seidenfeld, M.A. and P.J. Hanzlik. 1932. The general properties, action and toxicity of propylene glycol. J. Pharmacol. Exp. Ther. 44: 109-121.

Shackelford, W.M. and J.L. Keith. 1976. Frequency of Organic Compounds Identified in Water. U.S. EPA, Athens, GA. EPA-600/4-76-062.

Smyth, H.F., J. Seaton and L. Fischer. 1941. The single dose toxicity of some glycols and derivatives. J. Ind. Hyg. Toxicol. 23: 259-268.

Smyth, H.F., C.S. Weil, J.S West and C.P. Carpenter. 1969. An explanation of joint toxic action: 27 industrial chemicals intubated in rats in all possible pairs. Toxicol. Appl. Pharmacol. 14: 340-347.

Smyth, H.F., C.S. Weil, J.S. West and C.P. Carpenter. 1970. An explanation of joint toxic action. II. Equitoxic vs. equivolume mixtures. Toxicol. Appl. Pharmacol. 17: 498-503.

Speece, R.E. 1983. Anaerobic biotechnology for industrial wastewater treatment. Environ. Sci. Technol. 17: 416A-427A.

SRC (Syracuse Research Corporation). 1982. Information Profile on Potential Occupational Hazards: Glycols.. NIOSH, Washington, DC.

Stenback, F. and P. Shubik. 1974. Lack of toxicity and carcinogenicity of some commonly used cutaneous agents. Toxicol. Appl. Pharmacol. 30: 7-13.

Swann, R.L., D.A. Laskowski, P.J. McCall, K. Vander Kuy and H.J. Dishburger. 1983. A rapid method for the estimation of the environmental parameters octanol/water partition coefficient, soil sorption constant, water to air ratio and water solubility. Res. Rev. 85: 17-28.

Takemoto, S., Y. Kuge and M. Nakamoto. 1981. The measurement of BOD in seawater. Suishitsu Odaku Kenkyu. 4: 80-90.

Tanaka, Y., K. Fujii, A. Tanaka and S. Fukii. 1975. Utilization of petrochemicals by microorganisms. III. Metabolism of 1,2-propanediol in a soil bacterium. Hakko Kogaku Zasshi. 53: 354-362.

Tarkpea, M., M. Hansson and B. Samuelsson. 1986. Comparison of the Microtox test with the 96-hr LC_{50} test for the herpacticoid Nitocra spinipes. Ecotoxicol. Environ. Saf. 11(2): 127-143.

Thomas, J.F., R. Kesel and H.C. Hodge. 1949. Range-finding toxicity tests on propylene glycol in the rat. J. Ind. Hyg. Toxicol. 31: 256-257.

Union Carbide Corporation. 1978. Glycols. Publ. F-41515B. Union Carbide Corp., New York. p. 6-9, 12-13, 52, 69.

U.S. EPA. 1980. Guidelines and Methodology Used in the Preparation of Health Effect Assessment Chapters of the Consent Decree Water Criteria Documents. Federal Register. 45(231): 49347-49357.

U.S. EPA. 1984. Methodology and Guidelines for Reportable Quantity Determinations Based on Chronic Toxicity Data. Prepared by the Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH for the Office of Solid Waste and Emergency Response, Washington, DC.

U.S. EPA. 1985. Reference values for risk assessment. Prepared by the Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office Cincinnati, OH for the Office of Solid Waste, Washington, DC.

U.S. EPA. 1986a. Methodology for Evaluating Potential Carcinogenicity in Support of Reportable Quantity Adjustments Pursuant to CERCLA Section 102. Prepared by the Office of Health and Environmental Assessment, Carcinogen Assessment Group, for the Office of Solid Waste and Emergency Response, Washington, DC.

U.S. EPA. 1986b. Guidelines for Carcinogen Risk Assessment. Federal Register. 51(185): 33992-34003.

U.S. EPA. 1987. Graphical Exposure Modeling System (GEMS). Fate of Atmospheric Pollutants (FAP). Office of Toxic Substances, U.S. EPA, Washington, DC.

USITC (U.S. International Trade Commission). 1986. Synthetic Organic Chemicals. United States Production and Sales, 1985. USITC Publ. 1745, Washington, DC.

Van Winkle, W., Jr. and H.W. Newman. 1941. Further results of continued administration of propylene glycol. Food Res. 6: 509-516. (Cited in Informatics, Inc., 1973)

Verschueren, K. 1983. Handbook of Environmental Data on Organic Chemicals, 2nd ed. Van Nostrand Reinhold Co., New York. p. 1029.

Weatherby, H.J. and H.B. Haag. 1938. Toxicity of propylene glycol. J. Am. Pharm. Assoc. 27: 466-471.

Weber, R.C., P.A. Parker and M. Bowser. 1981. Vapor Pressure Distribution of Selected Organic Chemicals. U.S. EPA, Cincinnati, OH. EPA-600/2-81-021.

Weil, C.S., M.D. Woodside, H.F. Smyth, Jr. and C.P. Carpenter. 1971. Results of feeding propylene glycol in the diet to dogs for two years. Food Cosmet. Toxicol. 9: 479-490.

Willetts, A. 1979. Bacterial metabolism of propane-1,2-diol. Biochim. Biophys. Acta. 588: 302-309.

Windholz, M., Ed. 1983. The Merck Index, 10th ed. Merck and Co., Inc., Rahway, NJ. p. 1130-1131.

Yu, D.K., W.F. Elmquist and R.J. Sawchuk. 1985. Pharmacokinetics of propylene glycol in humans during multiple dosing regimens. J. Pharmacol. Sci. 74(8): 876-879.

Zaroslinski, J.F., R.K. Browne and L.H. Possley. 1971. Propylene glycol as a drug solvent in pharmacologic studies. Toxicol. Appl. Pharmacol. 19: 573-378.

APPENDIX A

LITERATURE SEARCHED

This HEED is based on data identified by computerized literature searches of the following:

TSCATS
CASR online (U.S. EPA Chemical Activities Status Report)
TOXLINE
TOXBACK 76
TOXBACK 65
RTECS
OHM TADS
STORET
SRC Environmental Fate Data Bases
SANSS
AQUIRE
TSCAPP
NTIS
Federal Register

These searches were conducted in February, 1987. In addition, hand searches were made of Chemical Abstracts (Collective Indices 5-9), and the following secondary sources should be reviewed:

ACGIH (American Conference of Governmental Industrial Hygienists). 1986. Documentation of the Threshold Limit Values and Biological Exposure Indices, 5th ed. Cincinnati, OH.

ACGIH (American Conference of Governmental Industrial Hygienists). 1986-1987. TLVs: Threshold Limit Values for Chemical Substances in the Work Environment adopted by ACGIH with Intended Changes for 1986-1987. Cincinnati, OH. 111 p.

Clayton, G.D. and F.E. Clayton, Ed. 1981. Patty's Industrial Hygiene and Toxicology, 3rd rev. ed., Vol. 2A. John Wiley and Sons, NY. 2878 p.

Clayton, G.D. and F.E. Clayton, Ed. 1981. Patty's Industrial Hygiene and Toxicology, 3rd rev. ed., Vol. 2B. John Wiley and Sons, NY. p. 2879-3816.

Clayton, G.D. and F.E. Clayton, Ed. 1982. Patty's Industrial Hygiene and Toxicology, 3rd rev. ed., Vol. 2C. John Wiley and Sons, NY. p. 3817-5112.

Grayson, M. and D. Eckroth, Ed. 1978-1984. Kirk-Othmer Encyclopedia of Chemical Technology, 3rd ed. John Wiley and Sons, NY. 23 Volumes.

Hamilton, A. and H.L. Hardy. 1974. Industrial Toxicology, 3rd ed. Publishing Sciences Group, Inc., Littleton, MA. 575 p.

IARC (International Agency for Research on Cancer). IARC Monographs on the Evaluation of Carcinogenic Risk of Chemicals to Humans. WHO, IARC, Lyons, France.

Jaber, H.M., W.R. Mabey, A.T. Lieu, T.W. Chou and H.L. Johnson. 1984. Data acquisition for environmental transport and fate screening for compounds of interest to the Office of Solid Waste. SRI International, Menlo Park, CA. EPA 600/6-84-010. NTIS P884-243906.

NTP (National Toxicology Program). 1986. Toxicology Research and Testing Program. Chemicals on Standard Protocol. Management Status.

Ouellette, R.P. and J.A. King. 1977. Chemical Week Pesticide Register. McGraw-Hill Book Co., NY.

Sax, I.N. 1984. Dangerous Properties of Industrial Materials, 6th ed. Van Nostrand Reinhold Co., NY.

SRI (Stanford Research Institute). 1986. Directory of Chemical Producers. Menlo Park, CA.

U.S. EPA. 1986. Report on Status Report in the Special Review Program, Registration Standards Program and the Data Call in Programs. Registration Standards and the Data Call in Programs. Office of Pesticide Programs, Washington, DC.

U.S. EPA. 1985. CSB Existing Chemical Assessment Tracking System. Name and CAS Number Ordered Indexes. Office of Toxic Substances, Washington, DC.

USITC (U.S. International Trade Commission). 1985. Synthetic Organic Chemicals. U.S. Production and Sales, 1984, USITC Publ. 1422, Washington, DC.

Verschueren, K. 1983. Handbook of Environmental Data on Organic Chemicals, 2nd ed. Van Nostrand Reinhold Co., NY.

Windholz, M., Ed. 1983. The Merck Index, 10th ed. Merck and Co., Inc., Rahway, NJ.

Worthing, C.R. and S.B. Walker, Ed. 1983. The Pesticide Manual. British Crop Protection Council. 695 p.

In addition, approximately 30 compendia of aquatic toxicity data were reviewed, including the following:

Battelle's Columbus Laboratories. 1971. Water Quality Criteria Data Book. Volume 3. Effects of Chemicals on Aquatic Life. Selected Data from the Literature through 1968. Prepared for the U.S. EPA under Contract No. 68-01-0007. Washington, DC.

Johnson, W.W. and M.T. Finley. 1980. Handbook of Acute Toxicity of Chemicals to Fish and Aquatic Invertebrates. Summaries of Toxicity Tests Conducted at Columbia National Fisheries Research Laboratory. 1965-1978. U.S. Dept. Interior, Fish and Wildlife Serv. Res. Publ. 137, Washington, DC.

McKee, J.E. and H.W. Wolf. 1963. Water Quality Criteria, 2nd ed. Prepared for the Resources Agency of California, State Water Quality Control Board. Publ. No. 3-A.

Pimental, D. 1971. Ecological Effects of Pesticides on Non-Target Species. Prepared for the U.S. EPA, Washington, DC. PB-269605.

Schneider, B.A. 1979. Toxicology Handbook. Mammalian and Aquatic Data. Book 1: Toxicology Data. Office of Pesticide Programs, U.S. EPA, Washington, DC. EPA 540/9-79-003. NTIS PB 80-196876.

APPENDIX B

Summary Table for Propylene Glycol

	Species	Exposure	Effect	RfD or q_1^*	Reference
Inhalation Exposure					
Subchronic	rat	170-350 mg/m³ (mean: 260 mg/m³) continuously for ≤18 months	NOEL	2 mg/kg/day or 116 mg/day	Robertson et al., 1947
Chronic	rat	170-350 mg/m³ (mean: 260 mg/m³) continuously for ≤18 months	NOEL	2 mg/kg/day or 116 mg/day	Robertson et al., 1947
Carcinogenicity	NA	NA	NA	NA	NA
Oral Exposure					
Subchronic	rat	6% of diet (3 g/kg/day) for 20 weeks	NOEL	0.03 g/kg/day or 2 g/day for a 70 kg man	Guerrant et al., 1947
Chronic	rat	50,000 ppm in diet (2.1 g/kg/day) for 2 years	NOEL	0.02 g/kg/day or 1 g/day for a 70 kg man	Gaunt et al., 1972
Carcinogenicity	NA	NA	NA	NA	NA
REPORTABLE QUANTITIES					
Based on chronic toxicity:		5000			Guerrant et al., 1947
Based on carcinogenicity:		NA			NA

NA = Not applicable