NATIONAL TOXICOLOGY PROGRAM

EXECUTIVE SUMMARY OF SAFETY AND TOXICITY INFORMATION

PROPYLENE GLYCOL t-BUTYL ETHER

CAS Number 57018-52-7

November 30, 1990

Submitted to:

NATIONAL TOXICOLOGY PROGRAM

Submitted by:

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OVERVIEW[1]

Nomination History: *Propylene glycol t-butyl ether was nominated for reproductive and chronic toxicity testing by the U. S. Consumer Product Safety Commission in 1988. The nomination of propylene glycol t-butyl ether was based on its widespread use, the potential for exposure at high concentrations, and the lack of toxicological information.*

Chemical and Physical Properties: *Propylene glycol t-butyl ether is a colorless liquid with a boiling point of 151°C (304°F). Propylene glycol t-butyl ether has a vapor pressure of 3.7 mm Hg@ 25° C and is soluble in water.*

Production/Uses/Exposure: *Propylene glycol t-butyl ether was recently formulated for use as a substitute solvent for ethylene glycol monobutyl ether because of toxicity concerns regarding ethylene glycol mono alkyl ether-based solvents, which have been found to cause testicular atrophy, fetotoxicity, teratogenicity, depression of bone marrow and hemolysis in animals. Propylene glycol t-butyl ether is used in a wide variety of commercial applications, including all-purpose cleaners, coatings, inks, nail polish lacquers and latex paints. No information was found concerning total U.S. annual production of propylene glycol t-butyl ether. This compound is not listed in the National Occupational Exposure Survey. OSHA has not established a permissible exposure limit for propylene glycol t-butyl ether. ACGIH has not recommended a threshold limit value; NIOSH has not recommended an exposure limit for this compound.*

Toxicological Effects: *Toxicology information on propylene glycol t-butyl ether was submitted to the National Toxicology Program by ARCO Chemical Company, a major producer of this compound. No toxicology data was found in the literature that was specific to propylene glycol t-butyl ether.*

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[1] The information contained in this Executive Summary of Safety and Toxicity Information (ESSTI) is based on data from current published literature. The summary represents information provided in selected sources and is not claimed to be exhaustive.

Human: *Low molecular weight glycol ethers are capable of penetrating the skin. Therefore, systemic exposure to propylene glycol t-butyl ether may result from dermal contact. No other data were found on the acute, prechronic, chronic, carcinogenic, reproductive or teratogenic effects of propylene glycol t-butyl ether in humans.*

Animal: *Propylene glycol t-butyl ether has been found to be severely irritating to the eyes of rabbits, and slightly to moderately irritating following application to abraded rabbit skin. However, propylene glycol t-butyl ether was not found to cause delayed contact sensitivity in guinea pigs. Propylene glycol t-butyl ether is moderately toxic by the oral route of administration to rats (LD_{50} =3771 mg/kg). The acute toxicity of propylene glycol t-butyl ether was observed to be minimal following a single 4-hour inhalation exposure to a test atmosphere containing 2,680 ± 107 mg/m^3, as no mortalities reportedly occurred prior to the termination of the study. The dermal LD_{50} of propylene glycol t-butyl ether in rabbits has been determined to be greater than 2.0 g/kg . Prechronic inhalation exposure to propylene glycol t-butyl ether for 13 weeks has been found to cause a statistically significant increase in liver, kidney and spleen weight in rats. However, no gross or histopathological treatment-related findings were observed in these organs. There are no data available on the chronic or carcinogenic effects of propylene glycol t-butyl ether in animals. Propylene glycol t-butyl ether was not found to cause maternal toxicity or teratogenic effects following inhalation exposure in inseminated rabbits during days 7-19 of gestation. In addition, inhalation exposure to proylene glycol t-butyl ether during days 6 through 15 of gestation was not found to cause developmental toxicity in rats. However, signs of maternal toxicity including paleness and an increase in liver weight were observed.*

Genetic Toxicology: *In the one study reported concerning the genotoxicity of propylene glycol t-butyl ether in prokaryotic systems, this substance was found to be non-mutagenic to Salmonella typhimurium in the presence and absence of metabolic activation. Propylene glycol t-butyl ether has been found to cause a "borderline" statistically significant increase in chromosome damage in Chinese*

hamster ovary cells in the absence of metabolic activation. However, in the presence of metabolic activation, propylene glycol t-butyl ether was non-mutagenic in this test system.

Structure Activity Relationships: *Ethylene glycol mono alkyl ethers have been found to cause testicular atrophy, fetotoxicity, teratogenicity, pancytopenia and hemolysis in animals. However, propylene and dipropylene monoethers have not been found to induce these effects. Propylene glycol methyl ether has reportedly caused central nervous system depression and liver weight increases in mice and rabbits.*

I. NOMINATION HISTORY AND REVIEW

A. Nomination History

1. Source: U.S. Consumer Product Safety Commission [USCPSC, 1988]

2. Date: June, 1988

3. Recommendations:
   - Reproductive testing
   - Chronic toxicity testing

4. Priority: Not provided

5. Rationale/Remarks:
   - Frequently used solvent that may be used to a greater extent in the future as a potential substitute for other ethylene glycol-based ethers that have been shown to be teratogenic.
   - Exposure may be widespread and occur at high levels, depending on the conditions of use.
   - Toxicological data base for this compound is inadequate.

B. Chemical Evaluation Committee Review

1. Date of Review: September 12, 1990

2. Recommendations:
   - Carcinogenicity
   - Reproductive and teratogenicity studies
   - Dermal and oral chemical disposition studies

3. Priority:
   - Moderate for carcinogenicity and chemical disposition studies
   - High for reproductive and teratogenicity studies

4. NTP Chemical Selection Principles: 2, 3, 8

5. Rationale/Remarks:
   - Widely used solvent
   - Replacement for ethylene glycol monoalkyl ethers, which cause reproductive and teratogenic effects in animals
   - Potential for both worker and consumer exposure
   - Lack of toxicological data
   - Dermal route of exposure is more important than inhalational route

C. Board of Scientific Counselors Review

1. Date of Review: October 15, 1990

2. Recommendations:
   - Carcinogenicity
   - Chemical disposition by dermal and oral routes
   - Reproductive studies

3. Priority:
   - High for carcinogenicity and chemical disposition studies
   - High for reproductive studies if no information is found on testicular effects in previous subchronic rat studies; moderate if such data are available

4. Rationale/Remarks:
   - Widely used solvent
   - Replacement for ethylene glycol monoalkyl ethers, which cause reproductive and teratogenic effects in animals
   - Potential for human exposure
   - Lack of carcinogenicity data
   - Good model for analysis of structure-activity relationships of glycol chemical class
   - Review available prechronic rat studies to ascertain whether histopathology indicated testicular effects
   - Adequate teratogenicity data are available
   - Perform chemical disposition studies prior to other toxicological studies

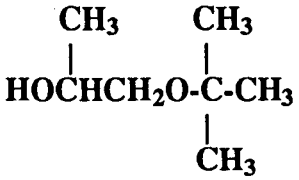
D. Executive Committee Review

1. Date of Review:

2. Decision:

II. CHEMICAL AND PHYSICAL DATA

A. Chemical Identifiers



PROPYLENE GLYCOL t-BUTYL ETHER

Molecular formula: $C_7H_{16}O_2$ Molecular weight: **132.2**

CAS No. 57018-52-7
RTECS No. N/A

B. Synonyms and Trade Names

Synonyms: 2-propanol, 1-(1,1-dimethylethoxy); 1-(1,1-dimethylethoxy)-2-propanol; 1-tert-butoxy-propan-2-ol

Trade names: Arcosolv PTB

C. Chemical and Physical Properties

Description: Colorless liquid

Melting Point: <-85°C (-121°F) [Hunt and Morris, 1989]

Boiling Point: 151°C (304°F) [Greany and Gillman, 1989]

Specific Gravity: 0.872 @25°C [Greany and Gillman, 1989]

Solubility in Water: Soluble in water:
184.61 g/L ± 5.21 @10°C
187.65 g/L ± 14.70 @20°C
175.79 g/L ± 5.30 @30°C [ARCO (e), 1988]

Solubility in Other Solvents: Soluble in coconut oil @ 37°C [ARCO (e), 1988]

Log Octanol/Water Partition Coefficient: 0.73 [ARCO (e), 1988]

Flammability Hazards:	• Combustible • Vapor Pressure: 3.7 mm Hg @25°C [Greany and Gillman, 1989] • Autoignition Temperature: No data available • Flash Point: 45°C (113°F) [Greany and Gillman, 1989]

III. PRODUCTION/USE

A. Production

1. Manufacturing Process

- Propylene glycol t-butyl ether is prepared by the reaction of isobutylene with an excess quantity of propylene glycol in the presence of a solid resin etherification catalyst. This reaction produces a crude product comprised of the desired propylene glycol t-butyl ether, by-product (2-t-butoxy-1-propanol), unreacted isobutylene and propylene glycol as well as minor amounts of tertiary butyl alcohol and water. The hydroxyl groups of the glycol ether products further react with isobutylene to form an additional by-product, di-ether, 1,2-di(t-butoxy) propane. The crude reaction product is distilled, to give a 1-t-butoxy-2-propanol-containing distillate. This distillate is then distilled to separate 1-t-butoxy-2-propanol from the higher boiling materials 1,2-di (t-butoxy)propane and 2-t-butoxy-1-propanol [Gupta, 1987].

2. Producers and Importers

U.S. Producers:

- Arco Chemical Company (propylene glycol t-butyl ether)
  Philadelphia, Pennsylvania [SRI, 1989]

- Haltermann Ltd, Co. (propylene glycol t-butyl ether)
  Houston, Texas [USITC, 1989]

Importers:

No information was found on importers of propylene glycol t-butyl ether from the public file of the EPA Toxic Substances Control Act (TSCA) Inventory.

3. Volume

There are no production data available on propylene glycol t-butyl ether from the public file of the EPA TSCA Inventory.

Propylene glycol t-butyl ether is not included in the United States International Trade Commission's publication Synthetic Organic Chemicals for the years 1986-1989. However, the United States International Trade Commission reports production data for ethylene

glycol mono-n-butyl ether, for which propylene glycol t-butyl ether is being manufactured to replace. In 1988 approximately 400 million pounds (dry basis) of the mono-n-butyl ether compound were produced [USITC, 1989].

4. Technical Product Composition

Commercial grade propylene glycol t-butyl ether (ARCOSOLV PTB®) available from ARCO, is approximately 99% pure, with the primary alpha isomer comprising approximately 99%, and the beta isomer comprising less than 0.5% [ARCO (f), 1985].

B. Use

Glycol ether solvents were first introduced as commercial products in the 1920's [Smith, 1984]. Propylene glycol t-butyl ether was recently formulated for use as a substitute solvent for ethylene glycol monobutyl ether because of the concern about toxicity of certain ethylene oxide-based solvents which have been found to cause reproductive and teratogenic effects in animals [Begley, 1986].

Propylene glycol t-butyl ether is employed in a variety of commercial applications including all-purpose cleaners [Nudy and Johnston, 1990] and electronic chemicals [Gupta, 1987], inks [American Ink Maker, 1985], odorless nail polish lacquers and adhesives [Kessler, 1989]. Propylene glycol t-butyl ether is also used as a coalescent in latex paints [Guthrie, 1987] and other water reducible coatings [Heckman, 1986].

IV. EXPOSURE/REGULATORY STATUS

A. Consumer Exposure

There are no quantitative data available on consumer exposure to propylene glycol t-butyl ether. However, because this compound is used in a variety of consumer products, the potential exists for frequent consumer exposure. Systemic exposure to propylene glycol t-butyl ether may occur from dermal contact with products containing this solvent [Gibson, 1989].

B. Occupational Exposure

Propylene glycol t-butyl ether is not listed in the National Occupational Exposure Survey (NOES).

C. Environmental Exposure

No information was found on environmental exposure to propylene glycol t-butyl ether. It has been speculated that the half-life of glycol ethers in the atmosphere may be less than one day. Because of their high water solubilities, glycol ethers are most likely significantly removed from air through wet deposition. In addition, it believed that this family of compounds may biodegrade in aquatic media and that biodegradation and leaching may

play significant roles in determining the fate of glycol ethers in soils. Their mobility in soils is expected to be highest in sandy soils with low organic carbon content due to the low soil sorption property of this type of soil [USEPA, 1984].

D. Regulatory Status

- OSHA has not established a permissible exposure limit (PEL) for propylene glycol t-butyl ether.

E. Exposure Recommendations

- ACGIH has not recommended a threshold limit value (TLV) for propylene glycol t-butyl ether.
- NIOSH has not recommended an exposure limit (REL) for propylene glycol t-butyl ether.

V. TOXICOLOGICAL EFFECTS

A. Chemical Disposition

1. Human Data

No information was found on the chemical disposition of propylene glycol t-butyl ether in humans.

2. Animal Data

No information was found on the metabolism of propylene glycol t-butyl ether. However, it is hypothesized that this chemical should be metabolized to propylene glycol by O-dealkylation through a hepatic microsomal enzyme system [ARCO (a), 1986]. The resulting propylene glycol is known to be extensively metabolized to lactic acid and pyruvic acid, which subsequently enter the tricarboxylic acid cycle [Miller, 1987].

B. Acute

1. Human Data

Low molecular weight glycol ethers are capable of penetrating the skin. Therefore, systemic exposure to propylene glycol t-butyl ether may result from dermal contact [Gibson, et al., 1989]. No other data were found on the acute effects of propylene glycol t-butyl ether in humans.

2. Animal Data

- The acute oral toxicity of propylene glycol t-butyl ether has been tested (coded) using Sprague-Dawley rats. Propylene glycol t-butyl ether was administered by oral gavage in a single dose at concentrations of 2,239,

2,818, 3,548 and 4,467 mg/kg. Sixty-four rats were used (8 males and 8 females per dose level). The oral LD_{50} was determined to be 3,771 mg/kg for all male and female animals. Surviving rats from all test groups were observed to gain weight from day 1 of dosing to the day of sacrifice (day 14). However, all animals found dead during the study reportedly lost weight.

Toxic effects observed prior to the death of the rats included lethargy, ataxia, prostration, irregular breathing, lacrimation, crusty eyes and muzzle, red or yellow/brown stained fur, salivation, squinting and emaciation. Study animals that survived the 14-day duration of the study generally exhibited the same abnormal toxicological effects as early as 0 to 1 hour after dosing, and as late as day 4. However, surviving animals were not observed to exhibit salivation or emaciation, or have a crusty muzzle or red stained fur.

Gross necropsy examinations of animals found dead during the study revealed the following: red depressions on the lungs, red or dark discolorations of the lungs, black depressions on glandular portions of stomachs, red or black discoloration of glandular portions of stomachs, smooth mucosal surfaces of stomachs, red discolorations of the small intestine, pale discolorations of the liver, tan or red exudate on the skin around the muzzle or nose and opacity of one eye.

Necropsy of surviving rats revealed red depressions or discolorations of the lung and mild dilation of the kidney. No other abnormalities were observed. Based on the above findings the authors report that propylene glycol t-butyl ether is moderately toxic by the oral route of administration [ARCO (m), 1982].

- The acute inhalation toxicity of propylene glycol t-butyl ether has been tested (coded) in Sprague-Dawley rats. Male (5) and female rats (5) were given a single, 4-hour inhalation exposure to propylene glycol t-butyl ether at a concentration of 2,680 $\pm$ 107 mg/m^3. Control rats (5 males, 5 females) were exposed to HEPA filtered air only. After exposure, all rats were observed daily for 14 days for signs of toxicity. Body weights were recorded before exposure and again on days 7 and 14. On day 14, all rats were sacrificed and necropsied.

  No mortalities reportedly occurred prior to study termination. The mean body weights of the exposed rats were not found to differ significantly from those of the control group. In addition, no clinical signs of toxicity were observed in any of the animals, and all rats appeared normal at necropsy.

  Mild extramedullary hematopoiesis was observed microscopically in the livers of two of the five exposed males, and two of the five exposed females, but not in the control rats (P values not reported). This lesion consisted of small foci of hematopoietic cells in some portal triads in affected livers and was considered to be related to exposure to propylene glycol t-butyl ether. According to the authors, this finding suggests that

the bone marrow might have been stressed in some of the rats exposed to propylene glycol t-butyl ether. However, this could not be confirmed as no hematopoietic organs were examined and no hematological measurements were made.

Based on the results of this study the authors concluded that the acute toxicity of propylene glycol t-butyl ether is minimal at most following a single, 4-hour exposure to a test atmosphere containing 2,680 ± 107 mg/m^3 [ARCO (l), 1988].

- The acute dermal toxicity of propylene glycol t-butyl ether has been tested (coded) in 5 male and 5 female New Zealand White albino rabbits at a dose level of 2 g/kg applied undiluted to abraded skin for a 24-hour exposure period. All animals survived the fourteen day study and no abnormal clinical signs were observed during the study period.

  Very slight to well defined erythema was observed for 4 males and all 5 females from day 1 up to day 6. One female rabbit was found to have very slight edema on days 4 to 6. Three males and 3 females were observed to have slight to moderate atonia on days 4 through 11. Slight to moderate desquamation was observed for all rats on days 4-14. Fissures (slight to moderate) were observed for all 5 males and 3 females during days 4-12. In addition, a black, scab-like depression was observed for one female on days 5 to 10 which peeled off on day 11.

  Gross necropsy examination of 4 males and 2 females revealed brown, red, or tan discolorations of the treated skin. Necropsy examinations of one other male and one other female revealed solitary, raised, thickened areas of the treated skin. No other abnormalities were observed upon necropsy of the remaining females [ARCO (n), 1982].

- The primary eye irritation potential of propylene glycol t-butyl ether has been evaluated (coded) in New Zealand White albino rats. Neat compound (0.1 ml/eye) was used for dosing. Group 1(unwashed eyes) consisted of 6 females, and group 2 (washed eyes- 1 min, 30 sec. with water after treatment with propylene glycol t-butyl ether) consisted of 3 females.

  The right eye of each animal was visually examined for ocular irritation and lesions at 24, 48, and 72 hours after installation of the test article and again on days 4,7,10 and 13. The left eye remained untreated and served as the control. The authors reported that propylene glycol t-butyl ether is a severe eye irritant based on the examination of the above animals [ARCO (o), 1982].

- The acute toxicity of propylene glycol t-butyl ether has been studied in rainbow trout (*Salmo gairdneri*) at concentrations of 100, 180, 320, 560 and 1000 mg/l. Ten fish were used for both the exposure and control groups. The 24-hour, 48-hour and 96-hour LC_{50} values were determined to be >1000 mg/liter.

In addition, a 96-hour, no observed effect concentration was estimated to be 320 mg/l based on the lack of mortality and abnormal effects observed at this concentration. During the 96-hour exposure period at the 560 and 1000 mg/l dose levels, abnormal effects including mortality, surfacing, loss of equilibrium, dark discoloration and/or fish on the bottom of the chamber were observed [ARCO (c), 1986].

- The acute toxicity of propylene glycol t-butyl ether at concentrations of 100, 180, 320, 560 and 1000 mg/l to bluegill sunfish *(Lepomis macrochirus)* has been investigated in a 4-day static fish toxicity study. Ten fish were used for each exposure and control group. The 24-hour, 48-hour and 96-hour LC_{50} values were determined to be >1000 mg/liter.

  A 96-hour, no-observed effect concentration was estimated to be 1000 mg/l, based on the lack of mortality and abnormal effects at this concentration. In addition, no effects were observed at the other concentrations tested [ARCO (b), 1986].

C. Prechronic

1. Human Data

   No information was found on the prechronic effects of propylene glycol t-butyl ether in humans.

2. Animal Data

- The toxicity of propylene glycol t-butyl ether (95% alpha isomer, 4-5% beta isomer) has been studied using 5 groups (50 males and 50 females each) of Fischer-344 CDF rats. Groups 1, 2, 3, 4 and 5 were exposed by inhalation at concentrations of 0, 25, 80, 250, and 750 ppm , respectively, for 6 hours per day, 5 days per week, for a minimum of 13 weeks. This treatment was followed by a three week regression period. The control group was exposed only to room air. Sub-groups were removed from the study after 4 and 13 weeks of treatment for clinical pathology and gross histopathological examination.

  No deaths or signs of clinical toxicity or opthamological abnormalities were observed during the study that were related to propylene glycol t-butyl ether. In addition, body weight gain was not observed to be affected by propylene glycol t-butyl ether, although a statistically significant increase, not considered to be treatment-related, in the body weight of group 2 males (25 ppm) during weeks 11 ($p<0.05$), 12 ($p<0.001$) and 13 ($p<0.05$) was reported.

  The authors concluded that food consumption was unaffected by treatment. A trend toward marginally higher food consumption in treated animals was observed from week 6 onward. The magnitude of the increase was approximately 2% to 5%, and there was no evidence of a dose-related response.

Hemograms were reportedly unaffected by treatment with propylene glycol t-butyl ether. Statistically significant differences between the treated and control groups were observed that were reportedly "small in magnitude, within the range of normal variation" and were observed in one sex and at one assessment only and were therefore considered to be unrelated to treatment. Statistically significant differences between the treated and control groups were noted for the following hematologic parameters: mean corpuscular hemoglobin in group 5 males ($p<0.05$), hemoglobin in group 5 females ($p<0.05$) after 4 weeks of treatment, mean corpuscular volume in group 5 males ($p<0.05$) after 13 weeks of treatment and white blood cell count in females after 13 weeks of treatment ($p<0.05$).

Propylene glycol t-butyl ether was not found to have an effect on blood chemistry. The statistically significant differences that were observed (serum chlorine in group 5 males at week 4 ($p<0.05$) and total protein in group 5 males at week 13 ($p<0.05$) were reportedly "small, within normal ranges, occurred in one sex at one occasion only and were unrelated to treatment."

Urinalysis performed during the fourth and thirteenth weeks of treatment, and during the regression period after 14 weeks of treatment and after 2 weeks of regression reportedly yielded "a range of values for the various parameters that was similar in treated and control groups." However, a higher frequency of trace quantities of occult blood in the urine of treated males particularly at the end of the treatment and at the end of the regression (p values not reported) was observed. The authors state that "this apparent effect may be related to treatment, however, there was no histopathological change observed in the kidney, liver, spleen or bone marrow, or change in the peripheral blood profile of animals treated for 4 or 13 weeks which was suggestive of hemolysis and which could be correlated with this marginal finding."

Significant absolute weight increases were observed in the liver and kidney of males and females and in the spleen of males treated with propylene glycol t-butyl ether (see Tables 1, 2 and 3). Absolute liver weight increases were observed in males after 4 weeks of treatment at the highest dose level ($p<0.05$), and after 13 weeks of treatment at all dose levels ($p<0.05$), and in females after thirteen weeks of treatment at 250 ppm and 750 ppm (<0.05 at both dose levels). In addition, absolute liver weight increases were observed in male rats exposed to 750 ppm after three weeks regression ($p<0.05$).

Relative liver weight increases were observed in males after four weeks of treatment at 250 ppm and 750 ppm ($p<0.05$), after 13 weeks of treatment at 80 ppm ($p<0.05$), 250 ppm ($p<0.001$), and 750 ppm ($p<0.001$) and after three weeks regression at 250 ppm ($p<0.05$) and 750 ppm($P<0.05$). The above liver weight increases ranged from 4 to 16%, with the largest increases observed in the high-dose animals after 13 weeks of treatment.

A significant increase in absolute spleen weight was observed in male rats exposed to propylene glycol t-butyl ether at levels of 25 ppm ($p<0.05$), 250 ppm ($p<0.05$) and 750 ppm ($p<0.05$), and in female rats at 25 ppm ($p<0.05$) and 80 ppm ($p<0.05$) after 13 weeks of treatment. A significant increase in relative spleen weight was observed in male rats exposed to 750 ppm after 13 weeks of treatment ($p<0.01$).

Absolute kidney weight was significantly increased in male rats at 80 ppm ($p<0.05$) and 750 ppm ($p<0.05$), and in female rats at 750 ppm ($p<0.05$) after 13 weeks of treatment. Relative kidney weights increased for male rats exposed to 80 ppm ($p<0.05$), 250 ppm ($p<0.05$) and 750 ppm ($p<0.001$) and in female rats exposed to 750 ppm ($p<0.001$) after 13 weeks of treatment.

Statistically significant increases in adrenal weight (absolute-$p<0.05$ and relative-$p<0.05$) of males exposed to 750 ppm thirteen weeks after treatment were observed.

No gross or histopathological findings, including extramedullary hematopoiesis, were found in any of the tissues which could be related to treatment with propylene glycol t-butyl ether. In addition, a qualitative assessment of bone marrow smears in groups 1 and 5 revealed that this compound had no effect on hematopoiesis. The authors concluded that although the weight increases observed in several organs were reportedly related to treatment with propylene glycol t-butyl ether, this increase may represent an adaptive response to treatment since no histopathological findings were observed which could be correlated with the weight increase [ARCO (f), 1985].

TABLE 1
Group Mean Absolute Liver Weights (grams)

Group # (propylene glycol t-butyl ether dose)

	1 (0 ppm)	2 (25 ppm)	3 (80 ppm)	4 (250 ppm)	5 (750 ppm)
Male Rats, 4 Weeks	6.251	6.543	6.323	6.614	7.005*
Male Rats, 13 Weeks	7.249	7.799*	7.737*	7.813*	8.313*
Female Rats, 4 Weeks	4.308	4.277	4.101	4.243	4.503
Female Rats, 13 Weeks	4.198	4.377	4.349	4.462*	4.466*

TABLE 2
Group Mean Absolute Kidney Weights (grams)

Group # (propylene glycol t-butyl ether dose)

	1 (0 ppm)	2 (25 ppm)	3 (80 ppm)	4 (250 ppm)	5 (750 ppm)
Male Rats, 4 Weeks	1.478	1.525	1.549	1.554	1.559
Male Rats, 13 Weeks	1.817	1.901	1.932*	1.883	1.953*
Female Rats, 4 Weeks	1.135	1.136	1.116	1.182	1.167
Female Rats, 13 Weeks	1.211	1.211	1.210	1.236	1.302*

TABLE 3
Group Mean Absolute Spleen Weights (grams)

Group # (propylene glycol t-butyl ether dose)

	1 (0 ppm)	2 (25 ppm)	3 (80 ppm)	4 (250 ppm)	5 (750 ppm)
Male Rats, 4 Weeks	0.482	0.528	0.516	0.502	0.500
Male Rats, 13 Weeks	0.577	0.625*	0.624*	0.610	0.623*
Female Rats, 4 Weeks	0.379	0.400	0.379	0.386	0.411
Female Rats, 13 Weeks	0.450	0.486	0.489	0.455	0.457

* $p<0.05$

- The skin sensitization potential of propylene glycol t-butyl ether has been studied in Hartley/Dunkin Albino guinea-pigs using the guinea-pig maximization test. Twenty test and ten control guinea pigs were used.

  For the induction portion of the study, the animals were administered the following preparations by intradermal injections: 1.) Freund's complete adjuvant diluted with an equal volume of water for irrigation; 2.) ARCOSOLV PTB (propylene glycol t-butyl ether), 5% v/v in water for irrigation; 3.) propylene glycol t-butyl ether, 5% in a 50:50 mixture of Freund's complete adjuvant and water for irrigation. The control animals were treated with the above preparations excluding propylene glycol t-butyl ether. One week after the induction, a topical application of neat propylene glycol t-butyl ether was applied for 48 hours.

  The test and control animals were challenged topically two weeks after the induction period with propylene glycol t-butyl ether, 30% v/v (anterior side of left flank) and 20% v/v (posterior side of flank) in distilled water.

  The challenge sites were evaluated 24, 48 and 72 hours after removal of the patches for erythema and eschar edema formation using numerical

scoring. Propylene glycol t-butyl ether was not found to induce delayed contact hypersensitivity in any of the guinea-pigs tested [ARCO (g), 1988].

D. Chronic/Carcinogenicity

1. Human Data

No information was found on the chronic/carcinogenic effects of propylene glycol t-butyl ether in humans.

2. Animal Data

No information was found on the chronic/carcinogenic effects of propylene glycol t-butyl ether in animals.

E. Reproductive Effects and Teratogenicity

1. Human Data

No information was found on the reproductive effects of propylene glycol t-butyl ether in humans.

2. Animal Data

- The developmental toxicity of propylene glycol t-butyl ether has been studied (coded) in inseminated New Zealand SPF rabbits. One control group and three treatment groups (16 animals each) were used. Mean actual exposure concentrations of 229, 750 and 1100 ppm were administered by whole body inhalation exposure for 6 hours per day on days 7 through 19 of gestation. The control group was exposed to filtered air using a comparable regimen. Propylene glycol t-butyl ether was not found to cause maternal toxicity or reproductive/ teratogenic effects (Because 1100 ppm was near the maximum attainable vapor concentration in the chamber, a maximum tolerated dose {MTD} was not established.) [ARCO (k), 1988].

- The developmental toxicity of propylene glycol t-butyl ether has been studied (coded) in mated, Charles River CDF female rats. One control and three treatment groups (25 rats each) were used. Mean actual concentrations of 230, 726 and 990 ppm were administered by whole body inhalation exposure for six hours per day on days 6 through 15 of gestation. The control group was exposed to filtered air on a comparable regimen.

  The pregnant rats were observed twice daily for mortality and changes in appearance and behavior. Clinical toxicity was evaluated on days 6 through 15 of gestation and maternal body weight, food consumption and water consumption were recorded throughout gestation. All pregnant rats were sacrificed on day 20 of gestation, and the number and location of viable and non-viable fetuses, early and late resorptions, and the number

of total implantations and corpora lutea were recorded. In addition, the abdominal and thoracic cavity and organs were examined for morphological changes and the adrenal glands, thymus, liver, kidneys and spleen were weighed.

No maternal mortality was observed during gestation. Eleven of 25 females from the 990 ppm exposure group were observed to be pale from gestation days 7 through 15. This effect was believed to be related to exposure to propylene glycol t-butyl ether. Clinical findings reportedly occurred in low incidence (one to four animals per group) and were not considered to be related to exposure to this compound. In addition, body weights of the exposed animals were comparable to those of the control group. The maternal food consumption calculated as g/kg/day was not affected by propylene glycol t-butyl ether at the three dose levels. However, maternal food consumption measured as g/animal/day was significantly less ($p<0.05$) for animals exposed at the highest dose level than the control animals during gestation days 6-9. The food intake values (g/animal/day) for the low- and mid-exposure groups were significantly greater ($p<0.05$) than the control value for the overall exposure period (gestation days 6 through 16). However, the authors report that "these increases were not thought to be relevant." In addition, maternal water consumption values (g/animal/day and g/kg of body weight/day) for all exposed groups were significantly greater ($p<0.05$ or $p<0.01$) than those for the control group. However, it was reported that "as no trends were apparent with respect to exposure levels, the increases were not considered to be induced by propylene glycol t-butyl ether."

The absolute and relative liver weight values of the rats exposed to 726 ppm and 990 ppm were significantly greater than the corresponding control values ($p<0.01$ for relative and absolute liver weights at the highest dose level {990 ppm} and the relative liver weight at the mid dose level and $p<0.05$ for the absolute liver weight at the mid dose level {726 ppm}). These increases in liver weight became greater with increasing exposure levels and were reported by the authors to be "considered to be related to propylene glycol t-butyl ether." The absolute and relative weights of the remaining organs did not differ from the control values.

Fetuses removed from the mothers by Cesarean section on day 20 were weighed and examined for external malformations and developmental variations. None of the cesarean section parameter values of the groups exposed to propylene glycol t-butyl ether were reportedly affected including mean corpora lutea, implantations, post implantation loss, viable fetuses values, mean uterine and fetal weights and fetal sex distribution. Two fetuses from the high exposure group reportedly had malformations (folded retina, anophthalmia). However, the number of malformations observed was not statistically significant and the authors reported that propylene glycol t-butyl ether was not found to elicit developmental toxicity [ARCO (j), 1988].

F. Genetic Toxicology

1. Human Data

No information was found on the genotoxic effects of propylene glycol t-butyl ether in humans.

2. Prokaryotic Data

- Propylene glycol t-butyl ether was found to be non-mutagenic to *Salmonella typhimurium* strains TA 1535, TA 1537, TA 1538, TA 98 and TA 100 in the presence and absence of metabolic activation. The standard Ames protocol was carried out at concentrations of 50 µg, 150 µg, 500 µg, 1500 µg and 5000 µg of propylene glycol t-butyl ether per plate. Results from negative solvent control (ethanol) and the various positive controls used (2-aminoanthracene, 2-nitrofluroene, 9-aminoacridine, n-ethyl-n'-nitro-N-nitrosoguanidine) were reportedly within normal limits [ARCO (h), 1987].

3. Eukaryotic Data

- Propylene glycol t-butyl ether has been tested *in vitro* for its ability to induce chromosomal aberrations in Chinese hamster ovary cells (strain K_1-BH4). Cells were incubated with propylene glycol t-butyl ether at concentrations of 0.1% to 1% v/v in the presence and absence of rat S-9 metabolic activation.

  In the absence of metabolic activation, propylene glycol t-butyl ether was found to cause a slight but just statistically significant increase in the incidence of chromosome damage compared to the control (distilled water) at concentrations of 0.5% v/v ($p<0.05$, excluding gaps) and 1 % v/v ($p<0.05$, including gap damage only). However, the authors report that the levels of damage were on the borderline for statistical significance and were "well within the historical control range for this laboratory."

  In the presence of metabolic activation, propylene glycol t-butyl ether was not found to cause a statistically significant increase in aberrant cells at any dose level.

  Both control compounds used, cyclophosphamide and mitomycin C exhibited large, statistically significant increases in the incidence of chromosomal damage ($p<0.001$) [ARCO (i), 1987].

4. Other Data

No information was found on the genotoxic effects of propylene glycol t-butyl ether.

G. Other Toxicological Effects

1. Immunotoxicity

No information was found on the immunotoxic effects of propylene glycol t-butyl ether in animals or humans.

2. Neurotoxicity

No information was found on the neurotoxic effects of propylene glycol t-butyl ether in animals or humans.

3. Biochemical Toxicology

No information was found on the biochemical toxicology of propylene glycol t-butyl ether in animals or humans.

VI. STRUCTURE ACTIVITY RELATIONSHIPS

Short-chain ethylene glycol mono alkyl ethers (and their acetates) have been found to cause testicular atrophy, fetotoxicity, teratogenicity, depression of bone marrow (pancytopenia) and hemolysis. However, longer chain ethylene glycol ethers (e.g., propylethers) have not been found to induce such effects [ECETOC, 1985].

The propylene and dipropylene monoether series has not been found to cause any of the major effects seen with the ethylene glycol monoethers. Propylene glycol methyl ether has not been found to induce testicular atrophy, fetotoxicity or teratogenicity [ECETOC, 1985], although propylene glycol methyl ether has been found to cause central nervous system depression and liver weight increases in mice and rabbits [Verschuuren, 1984].

The differences in reproductive/developmental toxicity between "E" and "P" series ethers may be explained by differences in metabolism. "E" series ethers such as ethylene glycol monomethyl ether are metabolized to alkoxyacetic acids by alcohol dehydrogenase. Alkoxyacetic acids produce the same spectrum of reproductive/developmental toxicity, possibly by altering the availability of one-carbon units for incorporation into purine and pyrimidine bases during development. In contrast, "P" series ethers such as PM and PTB are metabolized to propylene glycol and further to carbon dioxide and water [Miller et al., 1982, 1983; Moss et al, 1985; Sleet et al., 1988; Mebus and Welsch, 1989; Mebus et al., 1989].

VII. REFERENCES

American Ink Maker, "PTB Solvent From ARCO." American Ink Maker (December, 1985), p.153.

American Paint and Coatings Journal, "PTB Solvent." American Paint and Coatings Journal, Vol 70, No. 2 (November 11, 1985), p. 61.

ARCO Chemical Company (a), Glycol Ethers/Acetates, Toxicology Update, 1986.

ARCO Chemical Company (b), Acute Toxicity of Arcosolv®PTB to Bluegill Sunfish (*Lepomis macrochirus*) (Static Acute Toxicity Report # 3425), Submitted by Analytical Bio-Chemistry Laboratories, Inc., Columbia, Missouri to ARCO Chemical Company, Newton Square Pennsylvania, October 14, 1986.

ARCO Chemical Company (c), Acute Toxicity of ARCOSOLV®PTB to Rainbow Trout (*Salmo gairdneri*) (Static Toxicity Report #34255). Submitted by Analytical Bio-Chemistry Laboratories, Inc., Columbia, Missouri to ARCO Chemical Company, Newton Square Pennsylvania, January, 1986.

ARCO Chemical Company (d), Ready Biodegradability: Modified Sturm Test of PTB (ABC Preliminary Rep #34076). Submitted by Analytical Bio-Chemistry Laboratories, Inc., Columbia, Missouri to ARCO Chemical Company, Newton Square, Pennsylvania, October 6, 1986.

ARCO Chemical Company (e), Determination of Water and Lipid Solubility and Octanol-Water Partition Coefficient of Propylene Glycol Mono-Tertiary Butyl Ether (PTBE), Submitted by Battelle Columbus Division, Columbus, Ohio to ARCO Chemical Company, Newton Square Pennsylvania, April, 1988.

ARCO Chemical Company (f), A 4- and 13-Week Inhalation Toxicity Study (With 3-Week Regression) of ARCOSOLV® PTB in the Albino Rat (project # 81910). Submitted by Bio-Research Laboratories Ltd., Quebec, Canada to ARCO Chemical Company, Newton Square, Pennsylvania, July, 1985.

ARCO Chemical Company (g), Delayed Contact Hypersensitivity in the Guinea-Pig With Arcosolv PTB, Submitted by Huntingdon Research Centre Ltd., Huntingdon, Cambridgeshire, England to ARCO Chemical Company, Newton Square Pennsylvania, June 1988.

ARCO Chemical Company (h), Ames Metabolic Activation Test to Assess the Potential Mutagenic Effect of ARCOSOLV PTB, Submitted by Huntington Research Centre Ltd., Huntingdon, Cambridgeshire, England to ARCO Chemical Company, Newton Square Pennsylvania, October 1987.

ARCO Chemical Company (i), Analysis of Metaphase Chromosomes Obtained From CHO Cells Cultured *In Vitro* and Treated with 1-(1,1-Dimethylethoxy)-2-Propanol, Submitted by Huntingdon Research Centre Ltd., Huntingdon, Cambridgeshire, England to ARCO Chemical Company, Newton Square, Pennsylvania, November 1987.

ARCO Chemical Company (j), Inhalation Developmental Toxicity Study in Rats, Submitted by International Research and Development Corporation, Mattawan, Michigan to ARCO Chemical Company, Newton Square, Pennsylvania, June 3, 1988.

ARCO Chemical Company (k), Inhalation Developmental Toxicity in Rabbits, Submitted by International Research and Development Corporation, Mattawan, Michigan to ARCO Chemical Company, Newton Square, Pennsylvania, June 3, 1988.

ARCO Chemical Company (l), Acute Inhalation Toxicity Test in Sprague-Dawley Rats Using A209429 (project # 7450-B), Submitted by Midwest Research Institute (MRI), Kansas City, Missouri to ARCO Chemical Company, Newton Square Pennsylvania, November 12, 1982.

ARCO Chemical Company (m), Acute Oral LD_{50} Study in Rats of A 209429 (Study 410-0935), Submitted by Toxigenics, Inc., Decatur, Illinois to ARCO Chemical Company, Newton Square, Pennsylvania, June 4, 1982.

ARCO Chemical Company (n), Acute Dermal Toxicity Study in Rabbits of A 209429 at a Dose Level of 2 Grams Per Kilogram of Body Weight (Study 410-0936). Submitted by Toxigenics, Inc., Decatur, Illinois to ARCO Chemical Company, Newton Square Pennsylvania, May 27, 1982.

ARCO Chemical Company (o), Primary Eye Irritation Study In Rabbits of A 209429 (Study 410-0937). Submitted by Toxigenics, Inc., Decatur, Illinois to ARCO Chemical Company, Newton Square Pennsylvania, May 26, 1982.

Begley, R., "Solvent Makers Eye Compliance Deadline." Chemical Marketing Reporter (November 3, 1986), pp.34,40.

Browning, E., Toxicity and Metabolism of Industrial Solvents, New York: Elsevier, 1965, pp. 651-652.

Carpenter, C.P., Weil, C.S. and Smyth, H.F., "Range-Finding Toxicity Data: List VIII." Toxicology and Applied Pharmacology, Vol. 28 (1974), pp. 313-319.

Chem Bus Newsbase database, File 319 Dialog Information Services, May 11, 1990.

Clayton, G.D. and Clayton, F.E., eds., Patty's Industrial Hygiene and Toxicology, Vol. 2C, Third Revised Edition. New York: Wiley-Interscience, 1982, pp. 3909-3911, 3974, 3984-3986.

"Dow's Answer to VOCs." Chemical Week, Vol. 144, No. 18 (May 3, 1989), p.32.

"Dow Commercializes New Glycol Ethers." Chemical and Engineering News, Vol. 67, No. 13 (March, 27, 1989), p.16.

European Chemical Industry Ecology and Toxicology Centre (ECETOC), The Toxicology of Glycol Ethers and its Relevance to Man: an Up-Dating of ECETOC Technical Report No. 4. Technical Report No. 17, Brussels, April, 1985.

Fassett, D., and Irish, D., Industrial Hygiene and Toxicology, Vol. II, Second Revised Edition. New York: Interscience, 1963, pp. 1572-1573.

Gibson, W.B., Nolen, G.A., and Christian, M.S., "Determination of the Developmental Toxicity Potential of Butoxypropanol in Rabbits after Topical Administration." Fundamental and Applied Toxicology, Vol. 13 (1989), pp.359-365.

Goodman, L.S. and Gilman, A., The Pharmacological Basis of Therapeutics, Seventh Edition. New York: Macmillan, 1985, p. 1637.

Gosselin, R.E., Smith, R.P., Hodge, H.C., Braddock, J.E., Clinical Toxicology of Commercial Products: Acute Poisoning, Fifth Edition. Baltimore: Williams & Wilkins, 1984, pp. II-39, II-182, III-172, III-179.

Grant, W.M., Toxicology of the Eye, Third Edition. Springfield, Illinois: C.C. Thomas, 1986, pp. 769-770.

Greany, J.P., and Gillman, H.D., "PTB: The Safe and Economical Alternative to EB." Soap, Cosmetics, Chemical Specialties (July, 1989), pp.28-32.

Gupta, V.P., Recovery of Propylene Glycol Mono T-Butoxy Ether. United States Patent, Number 4,675,082, June, 23, 1987.

Guthrie, D.H., "Coalescent Interaction Determines Proper Latex Film Formation." Modern Paint and Coatings (November, 1987), pp.60-62.

Guthrie, D.H., Olson, C.M., and Vance, R.G., "PnB and DPnB Glycol Ethers-Practical Alternatives to EtO-Based Glycol Ethers in Water-Borne and Water-Reducible Coatings." American Paint and Coatings Journal (June 26, 1989), pp.37-43.

Hardin, B.D., and Lyon, J.P., "Summary and Overview: NIOSH Symposium on Toxic Effects of Glycol Ethers." Environmental Health Perspectives, Vol. 57 (1984), pp. 273-275.

Heckman, R.A., "Using P-Series Glycol Ethers In Water-Reducible Coatings." Modern Paint and Coatings, Vol.76, No. 6 (1986), pp.36-42.

Hunt, D.G. and Morris, N.H., "PNB and DPnB Glycol Ethers." Household and Personal Products Industry (April, 1989), pp.78-82.

Innis, J.D., and Nixon, G.A., "No Evidence of Toxicity Associated With Subchronic Dermal Exposure of Rabbits to Butoxypropanol." Toxicologist, Vol. 8 (1988), p.213.

Johnson, E.M., Gabel, B.E.G., and Larson, J., "Developmental Toxicity and Structure/Activity Correlates of Glycols and Glycol Ethers." Environmental Health Perspectives, Vol. 57 (1984), pp.135-139.

Kessler, D.G., "Regulations Bring New Products and Services." CPI Purchasing, (October, 1989), pp. 46-53.

Kirk-Othmer, Encyclopedia of Chemical Technology, Third Edition, Vol. 2. New York: Wiley-Interscience, 1980, pp. 933-962.

Klaassen, C.D., Amdur, M.O., and Doull, J.B., Casarett and Doull's Toxicology: The Basic Science of Poisons, Third Edition. New York: Macmillan, 1986, pp. 656-658.

Mann. A.H., "Toxicology of Glycol Ethers-A Review of the Present Position." Plastics and Rubber Industry, London, 1984, pp.17.1-17.7.

McGregor, D.B., "Genotoxicity of Glycol Ethers." Environmental Health Perspectives, Vol. 57 (1984), pp. 97-103.

Mebus, C.A. and Welsch, F., "The Possible Role of One-Carbon, Moietles in 2-Methoxy Ethanol and 2-Methyoxy Acetic Acid-Induced Development Toxicity." Toxicology and Applied Pharmacology, Volume 99, (1989), pp. 98-109.

Miller, R.R., Hermann, E.A., Langvardt, P.W, McKenna, M.J., and Schwetz, B.A., "Comparative Metabolism and Disposition of Ethylene Glycol Monomethyl Ether and Propylene Glycol Monomethyl Ether in Male Rats." Toxicology and Applied Pharmacology, Vol. 67 (1983), pp. 229-237.

Miller, R.R., Langvardt, P.W, Calhoun, L.L., and Yahrmardt, M.A., "Metabolism and Disposition of Propylene Glycol Monomethyl Ether (PGME) Beta Isomer in Male Rats." Toxicology and Applied Pharmacology, Vol. 83 (1986), pp. 170-177.

Miller, R.R., "Metabolism and Disposition of Glycol Ethers." Drug Metabolism Reviews, Vol. 18, No. 1 (1987), pp. 1-22.

Moss, E.J., Thomas, L.V., Cook, M.W., Walters, D.G., Foster, P.M.D., Creasy, D.M. and Gray, T.J.B. "The Role of Metabolism in 2-Methoxy-Ethanol-Induced Testicular Toxicity, Toxicology and Applied Pharmacology, Vol. 79 (1985), pp. 480-489.

National Institute for Occupational Safety and Health (NIOSH), National Occupational Exposure Survey (NOES), Data Communicated by Joseph A. Seta, Acting Section Chief, Hazard Section, Surveillance Branch, Division of Surveillance, Hazard Evaluations and Field Studies, May 2, 1990.

National Toxicology Program, Review of Current DHHS, DOE, and EPA Research Related to Toxicology. NTP 89-168, U.S. Department of Health and Human Services, November, 1989.

Nudy, L.R., and Johnston, W.A., "PTB: A Safe, Effective Solvent For Hard Surface Cleaners." Household and Personal Products Industry, (April, 1990), pp.90-92.

"PO-Based Glycol Ethers Seen Replacing EG Line." Chemical Marketing Reporter, Vol. 235, No. 13 (March 27, 1989), p.5.

"PO-TBA Facility Starts up in France." Chemical Marketing Reporter, Vol. 233, No. 23 (June 6, 1988), p. 4.

Roytech Publications, Suspect Chemicals Sourcebook. California: Roytech Publications, 1989, pp. 3-113, 4-1.

Sax, N.I. and Lewis, R.J., Sr., Dangerous Properties of Industrial Materials, Volume II. Seventh Edition. New York: Van Nostrand Reinhold, 1989, pp. 606-607, 1582.

Sleet, R.B., Greene, J.A. and Welsch, F., "The Relationship of Embryotoxicity to Disposition of 2-Methoxyethanol in Mice, Toxicology and Applied Pharmacology, Vol. 93 (1988, pp. 195-207.

Smith, R.L., "Review of Glycol Ether and Glycol Ether Ester Solvents Used in the Coating Industry." Environmental Health Perspectives, Vol. 57 (1984). pp. 1-4.

Smyth, H.F., Carpenter, C.P., Weil, C.S., Pozzani, U.C., Striegel, J.A., and Nycum, J.S., "Range-Finding Toxicity Data: List VII." American Industrial Hygiene Association Journal, Vol. 30 (1969), pp. 470-476.

Soap, Cosmetics, Chemical Specialties, "PTB Solvent." Soap, Cosmetics, Chemical Specialties, Vol. 61, No. 12 (December, 1985), p.115.

SRI International, 1989 Directory of Chemical Producers, United States of America, 1989, Menlo Park, California, pp.496,390,391.

SRI International, 1989 Directory of Chemical Producers, Western Europe, 1989, Menlo Park, California, pp. 1031, 325.

U.S. Consumer Product Safety Commission, Letter from Andrew G. Ulsamer, AED Health Sciences, to Dorothy Canter, NTP, June 13, 1988.

United States Environmental Protection Agency, Health Effects Assessment For Glycol Ethers, (PB86-134632). U.S. Environmental Protection Agency, Office of Research and Development, Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office: U.S. Environmental Protection Agency, Office of Emergency and Remedial Response, Office of Solid Waste and Emergency Response, September, 1984.

United States Environmental Protection Agency, 1990. Personal communication from Mr. Jeff Davidson, OTS, U.S. Environmental Protection Agency to Dr. Victor Fung, NTP. April, 1990.

United States International Trade Commission, Synthetic Organic Chemicals, United States Production and Sales, 1985-1988. U. S. Government Printing Office, Publication No.'s 1892, 2009, 2118, 2219, Washington, D.C.: 1985-1989.

Verschuuren, H. C.,"And What About the Propylene Glycol Ethers?" Hommage Professeur Rene Truhaut Fac. Pharm. University Paris (1984), pp. 1136-1140.

Weast, R.C., ed., CRC Handbook of Chemistry and Physics, Sixty-ninth Edition. Boca Raton, Florida: CRC Press, Inc., 1988-1989, p. c-447.

APPENDIX I. ON-LINE DATABASES SEARCHED

	DATE OF SEARCH	TIME PERIOD
BRS:		
HZDB	May, 1990	
DIALOG:		
Agricola	May, 1990	1970-1990
Agris International	May, 1990	1974-1990
Aquatic Science Abstracts	May, 1990	1978-1990
Biosis Previews	May, 1990	1969-1990
Biotechnology Abstracts	May, 1990	1982-1990
CAB Abstracts	May, 1990	1972-1990
Cancerlit	May, 1990	1963-1990
Chemical Engineering Abstracts	May, 1990	1971-1990
Chem Bus Newsbase	May, 1990	1984-1990
Chemical Exposure	May,1990	1974-1987
Compendex Plus	May, 1990	1970-1990
CRIS USDA	May, 1990	
Embase	May, 1990	1974-1990
Enviroline	May, 1990	1970-1990
Environmental Bibliography	May, 1990	1974-1990
Federal Register	May, 1990	1977-1990
Foods Adlibra	May, 1990	1974-1990
FSTA	May, 1990	1969-1990
Life Sciences Collection	May, 1990	1978-1990
Medline	May, 1990	1966-1990
NTIS	May, 1990	1964-1990
Occupational Safety and Health	May, 1990	1973-1990
Pascal	May, 1990	1984-1990
PTS Newsletter	May, 1990	1987-1990
PTS Prompt	May, 1990	1972-1990
Pollution Abstracts	May, 1990	1970-1990
Scisearch	May, 1990	1974-1990
Trade and Industry ASAP	May, 1990	1983-1990
Trade and Industry Index	May, 1990	1981-1990
World Translations Index	May, 1990	1984-1990
MEAD:		
Nexis/Lexis-BNA ENV	May, 1990	
NLM:		
Chemid	May, 1990	
Chemline	May, 1990	
HSDB	May, 1990	
RTECS	May, 1990	
Toxline 65	May,1990	1965-1980
Toxline	May, 1990	1981-1990
Toxlit	May, 1990	1981-1990
Toxlit 65	May, 1990	1965-1980
STN:		
Beilstein	May, 1990	
CA	May, 1990	1967-1990
Chemlist	May, 1990	
Registry	May, 1990	

APPENDIX II. SAFETY INFORMATION

- **HANDLING AND STORAGE**

  Propylene glycol t-butyl ether is stable under normal laboratory conditions.

- **EMERGENCY FIRST AID PROCEDURES**

  Eye: First check the victim for contact lenses and remove if present. Flush victim's eyes with water or normal saline solution for 20 to 30 minutes while simultaneously calling a hospital or poison control center. Do not put any ointments, oils, or medication in the victim's eyes without specific instructions from a physician. Immediately transport the victim, after flushing eyes, to a hospital, even if no symptoms (such as redness or irritation) develop.

  Skin: IMMEDIATELY flood affected skin with water while removing and isolating all contaminated clothing. Gently wash affected skin areas thoroughly with soap and water. If symptoms such as inflammation or irritation develop, IMMEDIATELY call a physician or go to a hospital for treatment.

Inhalation: IMMEDIATELY leave the contaminated area and take deep breaths of fresh air. If symptoms (such as wheezing, coughing, shortness of breath, or burning in the mouth, throat, or chest) develop, call a physician and be prepared to transport the victim to a hospital.

Provide proper respiratory protection to rescuers entering an unknown atmosphere. Whenever possible, Self-Contained Breathing Apparatus (SCBA) should be used.

Ingestion: If the victim is conscious and not convulsing, give 1 or 2 glasses of water to dilute the chemical and IMMEDIATELY call a hospital or poison control center. Be prepared to transport the victim to a hospital if advised by a physician.

If the victim is convulsing or unconscious, do not give anything by mouth, ensure that the victim's airway is open and lay the victim on his/her side with the head lower than the body. DO NOT INDUCE VOMITING. IMMEDIATELY TRANSPORT THE VICTIM TO A HOSPITAL.

- **PROTECTIVE EQUIPMENT**

  Eye: Splash-proof safety goggles.

  Gloves: Two pairs of dissimilar protective gloves shall be worn when handling the neat chemical, otherwise one pair. When contact with this chemical has been known to occur, change gloves immediately.

Clothing: Minimally, a disposable laboratory suit (e.g. Tyvek®) shall be worn, as specified in the most current NTP Statement of Work or NTP Health and Safety Minimum Requirements).

Respiratory Protection: A NIOSH-approved chemical cartridge respirator with an organic vapor cartridge.

- **EXTINGUISHANT**

Dry chemical, carbon dioxide or halon extinguisher

- **MONITORING PROCEDURES**

There is no NIOSH analytical method reported in the NIOSH Manual of Analytical Methods for propylene glycol t-butyl ether.

- **SPILLS AND LEAKAGE**

Persons not wearing the appropriate protective equipment and clothing shall be restricted from areas of spills until cleanup has been completed. When exposure to unknown concentrations may occur, air-purifying respirators may not be used. Chemical cartridge respirators with organic vapor cartridges may not be used when airborne concentrations exceed 1000 ppm.

If propylene glycol t-butyl ether is spilled the following steps shall be taken:

1. Remove all sources of ignition.

2. If a liquid solution is spilled, use vermiculite, sodium bicarbonate, sand, or paper towels to contain and absorb the spill.

3. Clean the spill area with dilute alcohol (approximately 60-70%) followed by a strong soap and warm water washing.

- **DECONTAMINATION OF LABORATORY EQUIPMENT**

TDMS Terminal: Whenever feasible, a protective covering (e.g.,plastic wrap) shall be placed over the keyboard when in use.

General Equipment: Before removing general laboratory equipment (i.e.lab carts, portable hoods and balances) from animal dosing rooms and/or chemical preparation areas, a decontamination process shall be conducted in addition to routine housekeeping procedures.

- **WASTE MANAGEMENT AND DISPOSAL PROCEDURES**

Waste Management: If an inhalation study is to be conducted, all exhaust air from the inhalation chamber must be cleaned with appropriate air cleaning devices unless the laboratory

has informed local and state air pollution regulatory agencies of both the laboratory's operating practices and the potential hazards of the chemical's in use. Compliance with all federal, state and local air pollution laws and regulations is required. A specific air cleaning system design must consider the specific conditions of the laboratory (eg., air flow rates and volumes, mixing of exhaust streams, size of inhalation chamber, etc,) and the dosing regimen selected. Air cleaning systems designs must be described by the laboratory and approved by the NTP Office of Laboratory Health and Safety.

Waste Disposal: Securely package and label, in double bags, all waste material. All potentially contaminated material (i.e.,carcasses, bedding, disposable cages, labware) shall be disposed of by incineration in a manner consistent with federal (EPA), state, and local regulations or disposed of in a licensed hazardous waste landfill.